POLITECNICO DI TORINO

Master Degree Course in Biomedical Engineering

Master Degree Thesis

Quantitative assessment of posture instability in Parkinson's disease patients using smartphone sensors.

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Abstract

Parkinson's disease (PD) is a neurodegenerative disorder that mainly affects movement and compromises the quality of life. Motor fluctuations (alternation of ON and OFF states) usually appear after several years of levodopa use. In particular, during the OFF state, one of the main problems are falls and their possible consequences.

The aim of the study was to find a quantitative method for the patient's motor assessment. In fact, the most used clinical scale, the MDS-UPDRS, does not exhibit a great objectivity and reproducibility. Moreover, the neurologist sees the patients only once or twice per year; this means that the doctor cannot observe short-term variations of the pharmacological or surgical treatments typical in PD patients.

A routine patient monitoring could enable the neurologist to track the evolution of the disease and adapt the drug posology. Difficulty in arising from chair is an important sign associated with PD. 24 PD patients participated in this thesis work. During the normal medical examination a 3-D inertial sensor on their lower back was worn by the subjects.

This thesis work can be divided in two parts. In the first one, some classifiers have been employed in order to detect postural transitions (PT), such as sit-to-stand (Si2S) and stand-to-sit (St2S). The aim of the second part was to classify patients based on the UPDRS task "arise from chair". From the combination of three sub-optimal results, the classification between sit-to-stand and stand-to-sit reaches an accuracy of 96.3%. Then, a set of features were extracted and a feature reduction was applied by means of PCA in order to perform a multiclass classification.

Aknowledgements

I would like to thank firstly my supervisor Prof. Gabriella Olmo for the opportunity to carry out this formative Master thesis under her supervision.

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In addition, I want to thank my flatmates, friends and colleagues for all the great moments shared together and being there for me in times of need.

Last, but not least, I must express my very profound gratitude to my parents for providing me with unfailing support to face and overcome any difficulty throughout my years of study.

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List of Acronyms

DAT Dopamine Transporter

DBS Deep Brain Stimulation

GP Globus Thalamus

IPG Implantable Pulse Generator

MEMS Micro Electro-Mechanical Systems

ML Machine Learning

PD Parkinson's Disease

PT Postural Transition

RBD REM Behavior Disorder

SN Subthalamic Nucleus

Si2S Sit to Stand

St2S Stand to Sit

UPDRS Unified Parkinson's Disease Rating Scale

Introduction

Parkinson's disease is a complex neurodegenerative disorder that presents different motor manifestations such as postural instability, tremor, bradykinesia and freezing of gait. Those symptoms change with the course of the disease, therefore the main goal of neurologists is to adapt medications according to the needs of the patients. It is not an easy task because of some issues. First of all, the clinical rating scales utilized in order to make a PD evaluation rests, besides medical history, on observing and listening the patients. This means that the evaluation is based on a very short time frame if we consider that a patient is visited only once or twice per year. Furthermore, physicians may rates differently similar manifestations depending on their training and experience. It follows that the needs for objective evaluation of patient symptoms is really important, especially beyond the short meeting the physician and the patient. Recently, the quantification of symptoms has been performed successfully by several research groups by utilizing accelerometers and gyroscopes [1, 2, 3, 4].

This thesis is a component of a bigger project for developing an easier and more objective tools for Parkinson's disease symptoms evaluation and monitoring. The main goal of this thesis work is to find an appropriate model for the identification and quantification of postural transition, in particular stand-to-sit and sit-to-stand, in Parkinson's patients. Starting with very simple signals acquired form smartphone, after the data processing, the features extracted were used to evaluate different classification algorithms comparing their results to the task of arise from chair present in the Unified Parkinson's Disease Rating Scale (UPDRS).

Thesis Organization

The structure of this thesis is outlined below:

Chapter 1 describes about Parkinson's disease, from its pathophysiology to its medications and therapy.

Chapter 2 presents the working principles of the smartphone sensors used in this work.

Chapter 3 summarizes the available data from Parkinson's disease, the methods that were used during the acquisition sessions and the data analysis.

Chapter 4 illustrates the results obtained from the analysis and the classification processes.

Chapter 5 and 6 are devoted to discussion of the results, conclusions and future works.

Chapter 1

Parkinson's Disease

1.1 History and Epidemiology

Parkinson's disease is a progressive disorder of the nervous system that affects both motor and non-motor systems. It is the second most common neurodegenerative disease in people aged over 60 years, second only to Alzheimer's disease [5].

In 2015, the Global Burden of Disease Study estimated the PD affects approximately 6.3 million people worldwide. In industrialized countries, the prevalence of PD is about 0.3% , increasing to 1% over the age of 65 and 4% over 80. As the incidence of Parkinson's rises significantly with age, and people are living longer, the prevalence of Parkinson's is bound to increase significantly in the future. It is estimated that there may be nearly 13 million people with Parkinson's by 2040 [6].

Parkinson's disease was described for the first time as a neurological syndrome by James Parkinson, an English doctor, in his famous treatise "*An Essay on the Shaking Palsy*", published in 1817, as:

> *Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured* [7].

About 50 years later Jean-Martin Charcot illustrated more accurately the PD clinical picture and named it Parkinson disease. Despite the illness was widely described, until the middle of 1900's the pathophysiology and the pharmacological therapy were almost unknown. In the late 1950s, the discovery of the dopamine presence in the human brain, specifically in the corpus

striatum, lead to numerous studies for experimentation of drugs containing levodopa, the precursor of dopamine [8].

1.2 Pathophysiology and Risk Factors

Dopamine plays a key role because, when its neuronal production starts to decrease, the PD symptoms appears. Dopamine acts as a neurotransmitter, a molecule released by neurons to send signals to other nerve cells.

Dopamine is secreted into the synapse, a cellular junction that allows the communication among nerve cells. The synapse is made up of a presynaptic membrane, containing the dopamine in the vesicles, a synaptic cleft, a gap between the pre- and postsynaptic cells, and a postsynaptic membrane. The presynaptic membrane releases the dopamine in the synaptic cleft; this latter crosses the synapse and binds to the postsynaptic membrane, where it activates the dopamine receptors and the consequent triggering of postsynaptic cell depolarization. A certain amount of dopamine may not be utilized and it is absorbed back into the presynaptic cell for the next utilization.

The reduced level of dopamine is due to neuron degeneration in a specific area called *Substantia Nigra*. The neurons in this region are responsible for the coordination of the movements of human body. The death of those cells causes a reduction of dopamine production jeopardizing the cells interaction; as a consequence patients loss movement control, with slowed movement and other abnormal movements [9].

Alpha-Synuclein is a protein that is linked genetically and neuropathologically to PD. It may contribute to PD pathogenesis in different ways, but the factors that lead the aggregation of this protein and the death of dopaminergic neurons in PD are not fully discovered [10].

Two unavoidable factors risk for PD are age and sex. Symptoms generally become noticeable at the age of 60 years, in only 10% of cases they appear earlier. Men seems to have a 50% higher probability of developing PD than women. However, when we talk about PD factors risk, we need to consider a more complex situation in which genetic features and lifestyle exposure can influence the outbreak of the disease. When a young person (below 40 years old) that shows PD symptoms, most likely it is a familiar disease, caused by genetic factors.

1.3 Symptoms

There are some main manifestations (motor signs) that characterize PD: bradykinesia, tremor, rigidity, postural instability to whom secondary non-motor symptoms are associated such as neuropsychology, perceptive and sleep disorder. The four principal motor symptoms are:

- **Bradykynesia and akinesia**: it is a condition where a person exhibits general slowed movements or cannot move their muscles as they wish. This represents one of the most annoying symptoms for the patients. They often report associated muscular weakness, difficult to make daily activities and inability to initiate the movement.

- **Rest tremor**: it is a movement disorder that consists in involuntary and rhythmic oscillation, at a frequency of approximately 4-6 Hz, of one or more parts of the body (hands, arms, legs, face and jaw). It is one of the most evident symptoms, but actually, it is not the most meaningful: about the 30% of the patients do not have it. It is important to make a distinction between typical tremor of PD and essential tremor, a common form of tremor that may be confused with Parkinson's tremor. On the one hand, the essential tremor is triggered by the beginning of a movement, on the other hand, the Parkinson's tremor is more evident during the rest and improves with intentional movement [11].

- **Rigidity**: it is an involuntary increase of the muscular tone in a limb, neck or torso. A reduced arm swing during walking is signal of rigidity; other symptoms are difficult turning during walking or in bed, stand up from a chair and a reduced facial expression. At the beginning, rigidity is often asymmetrical in just one side of the body.

- **Postural instability**: maintaining a balance might be difficult because of alterations of postural reflex and balance, therefore the patient is no more able to spontaneously correct possible imbalance. The postural instability is evident especially while walking, change of direction or when the patient is walking and he/she wants to do another task as looking a shop window or grabbing something from a shelf. Probably, it is the most perilous symptom because of the increased risk of falls.

Rest tremor, bradykynesia and rigidity are generally the first signs of the disease. On the other hand, postural instability is a late sign and it emerges typically after several years into the disease [12]. Moreover, the PD posture is combined with lateral bending of the trunk with a tendency to lean to one side, called "Pisa's syndrome" [13]. PD walking is characterized by slow,

short steps in both length and height. In individuals with several years of disease, festination episodes might occur, a gait in which the patient drags the feet and speed up the step. Another phenomenon is the so-called "freezing", a sudden motor block of the gait.

In the last decade, a greater priority has been given to non-motor signs because of they are not only detectable in the disease progression, but also sometimes they precede the motor symptoms:

- **Olfactory impairment**: most of the patients(above 90%) report olfactory impairment that may appear several years before the first motor manifestations[14]. Although this may be due to a damage of the peripheral olfactory system, actually, it is associated to a central harm [15];
- **Orthostatic hypotension**: after a postural change, Orthostatic hypotension is due to incorrect attempts of the autonomic nervous system to regulate blood pressure. Prevalence can reach the 60%, but only 30% is symptomatic, with dizziness limiting daily activity and lead to falls [16];
- **Dysphagia**: more than 80% of PD patients develop dysphagia during the course of the disease. Swallowing difficulty reduces quality of life, complicates medication intake and leads to malnutrition and aspiration pneumonia, which is a major cause of death in PD[17];
- **Sleep disorder**: it is one of the most common non-motor sign of PD, about 90% and increase in advanced stages of the disease. Some sleep disorders like REM sleep behavior disorder (RBD) may lead several injurious movements that can hurt people around the patients like caregivers [18].

Depression, constipation, sexual dysfunction, hypersalivation, speech problems, sweating, fatigue and hallucinations are other significant non-motors manifestation [19].

1.4 Diagnosis

No specific test exists to diagnose Parkinson's disease with absolute certainty. The diagnosis is based on a neurological visit, where the neurologist evaluates the medical history of the patient and performs a neurological test. Because

of the difficulty to diagnose the disease, especially in the early stage, a functional neuroimaging technique is typically performed such as SPECT (Single Photon Emission Computed Tomography) or PET (Positron Emission Tomography). DaTscan is the brand name of a type of SPECT imaging using ^{123}I-Ioflupane, a tracer able to bind to the DAT(dopamine transporter); consequently this bonds can be observed through the SPECT imaging. If there is a loss of this type of cell, it can be visualized in the images through this technique.

It has been proven that the DaTscan is the most sensitive technique for PD diagnosis and allows differentiation of Parkinsonism with nigrostriatal degeneration from Parkinsonism without loss of dopaminergic terminals[20]. DAT normally helps to reabsorb dopamine from the synaptic cleft in the presynaptic membrane, but in patients with PD they are reduced 50%-70%[21].

1.5 Pharmacological therapy

Although no available therapies can modify the neurodegenerative process, symptomatic therapies can improve the patients quality of life for many years[22]. Controlling manifestations and symptoms while minimizing side effects is the aim of medical treatment of PD.

Levodopa is the mainly medication for Parkinson's disease. It is the precursor of the neurotransmitter dopamine and it is able to cross the blood-brain barrier and then it is quickly metabolized in dopamine in the brain, restoring its correct level. Dopamine itself is not effective as a medication because it cannot cross the blood-brain barrier. Since the dopamine at peripheral level has not therapeutic effects, but on the contrary it has several side effects, the Levodopa bloodstream conversion is inhibited through the contemporary administration of carbidopa in order that a greater amount of the drug can reach the brain. Consequently, a smaller dose of levodopa can be administered.

The most known combination of levodopa/carbidopa is called Sinemet®, but there are several preparations of this mix on the market: Rytary®, a set of beads that release the mix at different speeds as they are dissolved in the stomach; Parcopa®, a formulation that dissolves in the mouth without water; Stalevo®, a mixture with also the COMT inhibitor *entacapone*; the latest drug is Ongentys®, a special mixed with the enzyme inhibitor *opicapone*.

A different way to deliver levodopa is Duopa^{TM}, a mixture of carbidopa and levodopa in a suspension, delivered through a pump directly into the small intestine bypassing the stomach. It is recommended for patients with an advanced Parkinson's who still respond effectively to carbidopa-levodopa, but have many fluctuations. It allows a continuous infusion over 16 hours, so reducing motor fluctuations. Duopa^{TM}can be also a good option for PD patients with dysphagia. The main drawbacks are due to the tube placement that can cause infection at the insertion point, bleeding in the small intestine, dislocation or some obstruction[23].

1.6 Surgical treatment

The pharmacological treatment in the first phase of the disease is very effective, but because of the progressively worsening of the illness and the complications due to the prolonged use such as motor fluctuation and involuntary movement (dyskinesia), levodopa progressively loses his effectiveness[24]. Motor fluctuations are alterations between periods of being "on," during which the patient experiences a positive response to medication, and being "off," during which the patient have again the Parkinson symptoms suppressed during the "on" state[24].

Deep brain stimulation (DBS) is a neurosurgical procedure that consists in the implantation of two leads into the brain in a specific area for reducing motor symptoms of PD. The brain spot where to put the definitive wire is localized through neurophysiological and clinical tests. Moreover, the Implantable Pulse Generator (IPG) is implanted under the skin in the abdominal region or just below the collarbone. Its aim is to improve the operation of the motor pathways and hence improving the PD clinical situation by directing a burst of electrical energy into the electrodes placed in the brain. Each lead contains four electrodes and the DBS can work in monopolar stimulation if only one electrode is turned on, or in bipolar stimulation if more than one electrodes are working.

Only 10% of PD population is suitable for this kind of implantation. In fact, this treatment is recommended only for a small group of PD patients with certain characteristics. For example, there must be no surgical contraindications, the pharmacological therapy must be no actually able to control the symptoms, few comorbidities must be present, the patient must be motivated and not exhibiting of psychiatric disorders[25]. Generally, great results and clear improvements can be noticed just in a few days from the implantation.

1.7 The Unified Parkinson's Disease Rating Scale (UPDRS)

The UPDRS (Unified Parkinson's Disease Rating Scale), presented in 1987, is a system for the evaluation of PD symptoms. In 2003 the Movement Disorder Society (MDS) produced new version, MDS-sponsored UPDRS revision (MDS-UPDRS). It maintains the overall format but it solves some ambiguities and weakness such as the lack of important clinical impairments related to PD.

The MDS-UPDRS is made up of four section: Section I (Non-motor experiences of daily living), Section II (Motor experiences of daily living), Section III (Motor examination), Section IV (Motor complications).

Section I is subdivided in two parts: in section IA, the investigator evaluates some behavioral aspect from an interview with the patient or the caregiver; the patients fill in section IB, like section II, with or without the caregiver's help, but independently of the investigator. However, these two last sections can be reviewed by the investigator to make sure that they are completed and easy to understand. The investigator also can explain any possible ambiguities.

Section III contains instructions of specific task in order to complete the PD assessment that the investigator provides to the patients.This section is completed by the examiner.

In conclusion, for Section IV the investigator is required to conduct the interview. There are 42 questions, with a score form 0 to 4:

- **0 - Normal**: no problem for that specific task;
- **1 - Slight**: symptomatology with low frequency or intensity that does not cause any impact in daily living;
- **2 - Mild**: symptomatology with sufficient frequency or intensity to cause a modest impact in daily living;
- **3 - Moderate**: symptomatology with sufficient frequency or intensity to cause an important impact in daily living, but does not prevent the function;
- **4 - Severe**: symptomatology prevent the function.

The UPDRS allows to obtain a numerical evaluation enabling a comparison of the same patients during the years and tracking the illness developing.

A score equal to zero means that the patients can perform all the daily tasks without difficulty, otherwise the larger the score, more severe is the disease advancement.

1.8 Sit to stand evaluation: Arising From Chair

Arising from a chair is a task in Section III to perform motor evaluation, in particular evaluate the strength of lower limb. It is similar to the general task Sit to Stand (Si2S), utilized not only for PD, but also for general medical evaluation of legs. The patients sit down comfortably in a chair, with both the feet in the ground, the spine leans to the back of the chair. Ask the patient to cross his arms and then to stand up. According to the guidelines of the Movement Disorder Society this task must be evaluated observing the following parameters: speed of execution, attempts, moving forward in the chair, pushing the arms of the chair.

Chapter 2

Smartphone inertial sensors

Introduction

Nowadays, the technology improvements, in particular the miniaturization, have allowed to make wearable many devices. In this way, technology can reach the personal life of the people.

Smartphones are the wearable devices most utilized because practically every person owns at least one. Among the uses, the most important are certainly motion tracking and movement recognition applications. Motion tracking can be performed at different scales: from low precision tracking in closed buildings or navigation, to high precision tracking of fine measurements of human body movement[26]. Smartphones are undoubtedly part of our daily life. They are equipped with several sensors that allow to retrieve information about the world around them. The first sensors installed and the most important are accelerometers and gyroscopes which measure accelerations and angular velocity, respectively.

There are several examples in literature about smartphone utilization for monitoring people. First of all, GPS data are passively collected with smartphone, and this introduces new opportunities to monitor Schizophrenic Patients and Alzheimer disease patients[27]. Another example can be smartphone use for gait monitoring and balance rehabilitation training in clinical and home environments[28]. A major health hazard for both the elderly and people with neurodegenerative diseases is surely falls. In order to contain the serious consequences of falling, a great deal of research has been conducted, and some of them are based on smartphone sensors[29]. Other solutions available through smartphone are the FOG detection system in PD patients[30].

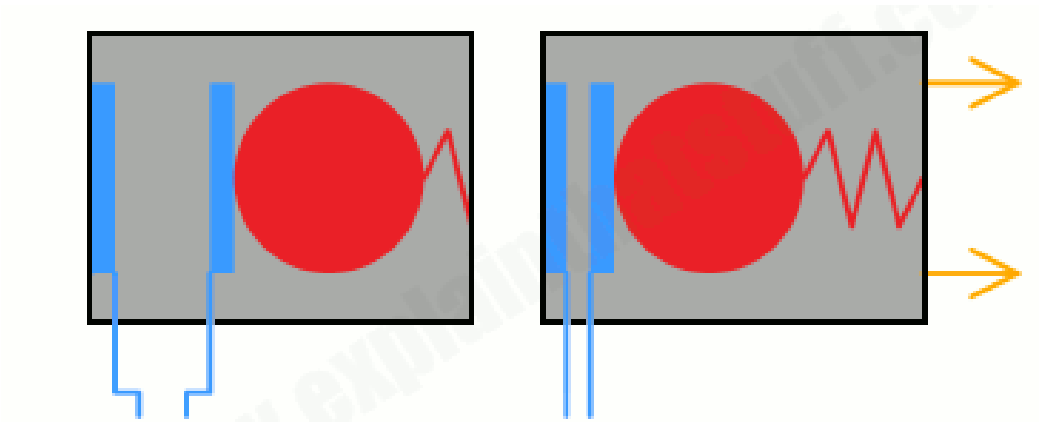


Figure 2.1: MEMS accelerometer.

Microelectromechanical systems (MEMS) is the technology of microscopic devices (range from 20 micrometres to one millimetres), particularly those with moving parts. Only at the end of '60s MEMS became practical once microfabrication techniques such as molding, plating and etching, developed. MEMS are making significant progress towards high performance and low power consumption. They are able to detect and consequently respond to many variables such as pressure, flow, position, motion and strain[31]. In the bioengineering field, MEMS applications can be from Lab-On-Chip to MicroTotalAnalysis (biosensor, chemosensor), or embedded in medical devices. Wearability is facilitated by the small size of the MEMS, and combined to a wireless communication, it allows the realization of a telemedicine platform[32].

An overview of MEMS accelerometers and gyroscopes technology and their operating principle are provided in this chapter.

2.1 MEMS Accelerometer

An accelerometer is a device that measures proper acceleration. It is not the same as coordinate acceleration, being the acceleration in a fixed coordinate system, but it is the acceleration of a body in its own instantaneous rest frame. For example, an accelerometer at rest on the surface of the Earth will measure an acceleration due to Earth's gravity, straight upwards of g = 9.81 m/s2. By contrast, accelerometers in free fall (falling toward the center of the Earth at a rate of about 9.81 m/s2) will measure zero.

Modern accelerometers are MEMS. The basic principle is simple: dis-

placement measurement of a damped mass on a spring during acceleration. When an acceleration is applied to the accelerometer, the mass is displaced to the point that the spring is able to accelerate the mass at the same rate as the outer shell. The displacement is then measured to yield the acceleration. There are usually a set of fixed beams and a set beams attached to the proof mass that measure the capacitance between them.

2.2 MEMS Gyroscope

MEMS gyroscopes measures angular rate through the Coriolis force. It is a fictitious force that appears when a mass (m) is moving in direction v and angular rotation velocity (omega) is applied. As shown in Figure 2.2, the mass will experience a force in the direction of the arrow as a result of the Coriolis force. Viewed from the frame of the moving plane, the mass seems to move in a curved path; on the contrary, if the mass is observed from the inertial reference frame, it moves in rectilinear motion. For this reason this kind of force is called a fictitious or inertial force.

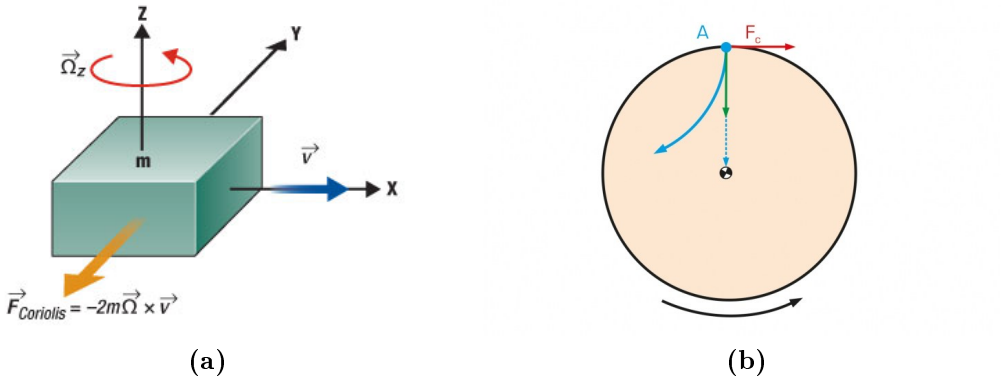


Figure 2.2: Coriolis force (a) and deflection due to Coriolis effect (b).

2.3 Sensor Log App

There are a lot of applications for retrieval data in order to perform post process analysis.**Sensor Log** (Google Commerce, Ltd.) is the application that we used to collect accelerometer and gyroscope data. This application is developed to ease the process of collecting and labeling sensory data from smartphones. This application is developed to ease the process of collecting and labeling sensory data from smartphones.

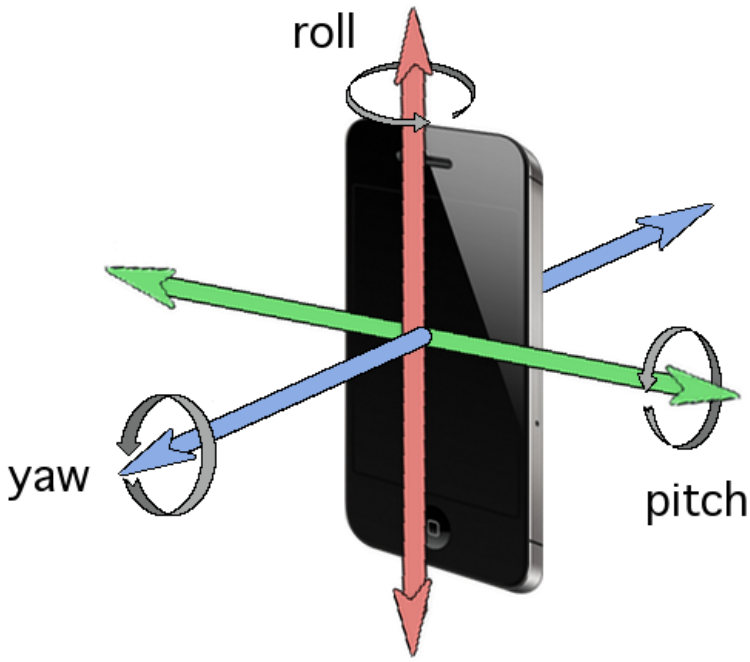


Figure 2.3: Smartphone rotation asses.

Chapter 3

Materials and methods

3.1 Data collection

This study utilizes the data of 24 patients collected between October and December 2018 in the Parkinson's disease and movement disorders Centre at Molinette Hospital, Turin (Italy). Clinical diagnosis of Parkinson's Disease with motor symptoms has been considered as inclusion criteria. Subjects with record of cerebrovascular problems or prosthesis at lower limbs were discarded because this can have an influence on the motor task. A general overview about PD population used in this thesis work is shown in Table 3.1

Table 3.1: Characteristics of PD patients.

Number of patients	**Mean age (years ± SD)**	**Years from PD diagnosis**
24 (54.2% male)	72.4 ± 9.2	6.1 ± 4

During the visit in the clinic, a smartphone (Samsung Galaxy S5 mini) was placed through a belt in the lower back so that the device was near to the person's center of gravity. This position should enable patients to wear the sensor in a comfortable way allowing to detect different motor symptoms. According to the literature, waist is considered the best position in terms of information to estimate human motion parameters based on a single sensor [33].

The physician conducted the visit as he/she usual perform it, adding only a couple of simple tasks such as taking a book from a shelf and washing

their hands. This was performed in order to simulate activity of daily living (ADL). Fig. 3.1 illustrate how the smartphone was worn by patients.

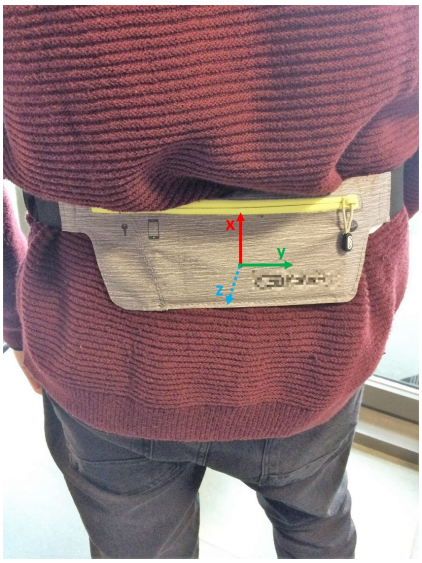


Figure 3.1: Smartphone position and axis orientation adopted during the examination.

The collected data were the three components of angular velocity and acceleration acquired through the app Sensor Log. This exhibits a very user-friendly interface, and you can add an "activity" button with all the sensors are expected to be useful. The data were exported in csv format, then were processed offline in MATLAB version R2018b.

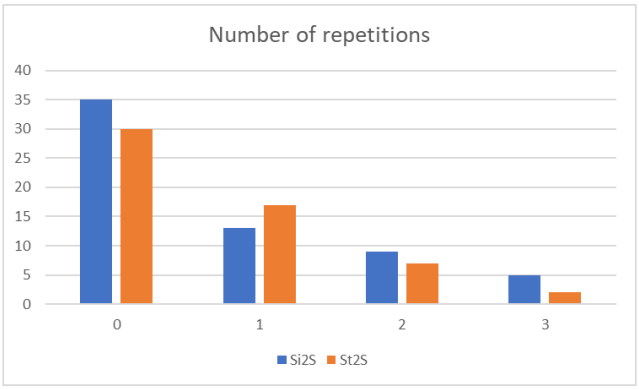


Figure 3.2: Number of repetitions for St2S and Si2S according the UPDRS task arise from chair.

As can be seen in Fig. 3.2, there are a low number of repetitions for UPDRS 3, especially for St2S. Consequently, class 3 will not be considered in this thesis project.

3.2 Pre-processing

3.2.1 Calibration

The smartphone is not always placed exactly in the same way during the acquisition of the signals in patients. There could be some differences in the inclination of the device due to the patient's posture that can increase the variability. At the basis of calibration, there is the idea that when a person is naturally standing still, the gravitational acceleration (g) is completely in the vertical axis. So, we look at 10 seconds of user standing, and perform the redistribution of the acceleration on only the vertical axis by applying a quaternion rotation transformation as described in [34].

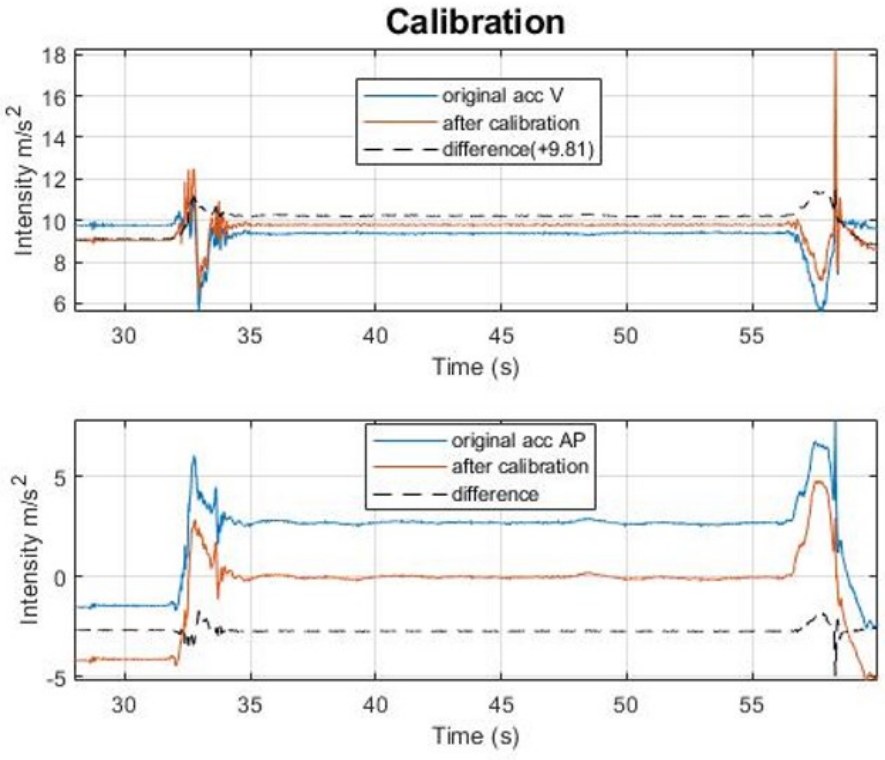


Figure 3.3: Differences between signals before and after calibration.

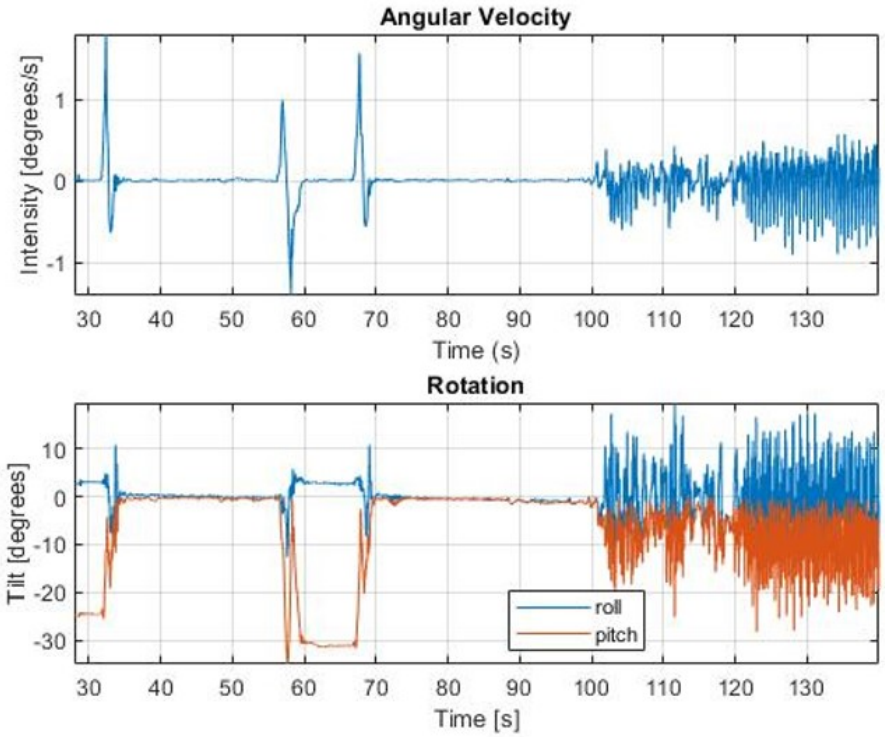


Figure 3.4: Example of angular velocity, pitch and roll.

3.2.2 Derived signals

Bias has been removed from angular velocity around traversal axis (AV_y), through `imufilter System object`® , a `Matlab` tool that fuses accelerometer and gyroscope sensor data to estimate angular velocity and device orientation. Roll (tilt angle waist towards left or right), and pitch (tilt angle waist forward or backward) were calculated following the formula presented in [35], obtaining angles in degrees:

$$\theta_{roll} = \tan^{-1}\left(\frac{-a_{ml}}{a_v}\right) \tag{3.1}$$

$$\theta_{pitch} = \tan^{-1}\left(\frac{-a_v}{\sqrt{a_{ap}^2 + a_{ml}^2}}\right) \tag{3.2}$$

where, a_{ml}, a_v and a_{ap} are the accelerations along the medio-lateral, vertical and antero-posterior axes of the accelerometer, respectively.

3.3 Wavelet transform

Before running the algorithm to detect Postural transition (PT), and the differentiation between sit-to-stand (Si2S) and stand-to-sit (St2S), some pre-processing was needed.

Hardly any biological or human signals is comparable to a stationary process because the parameters change during the time, and therefore also the spectrum. These changes are often the most interesting parts of the data in terms of the information they provide [36].

The Fourier transform is a powerful tool for data analysis, but it does not represent changes efficiently. In fact, in Fourier transform analysis data are represented as sum of sine waves, which are not localized in time or space. Those sine waves oscillate forever. Therefore, to accurately analyze signals that have abrupt changes, we need to use a new class of functions that are well localized in time and frequency: the Wavelet transform.

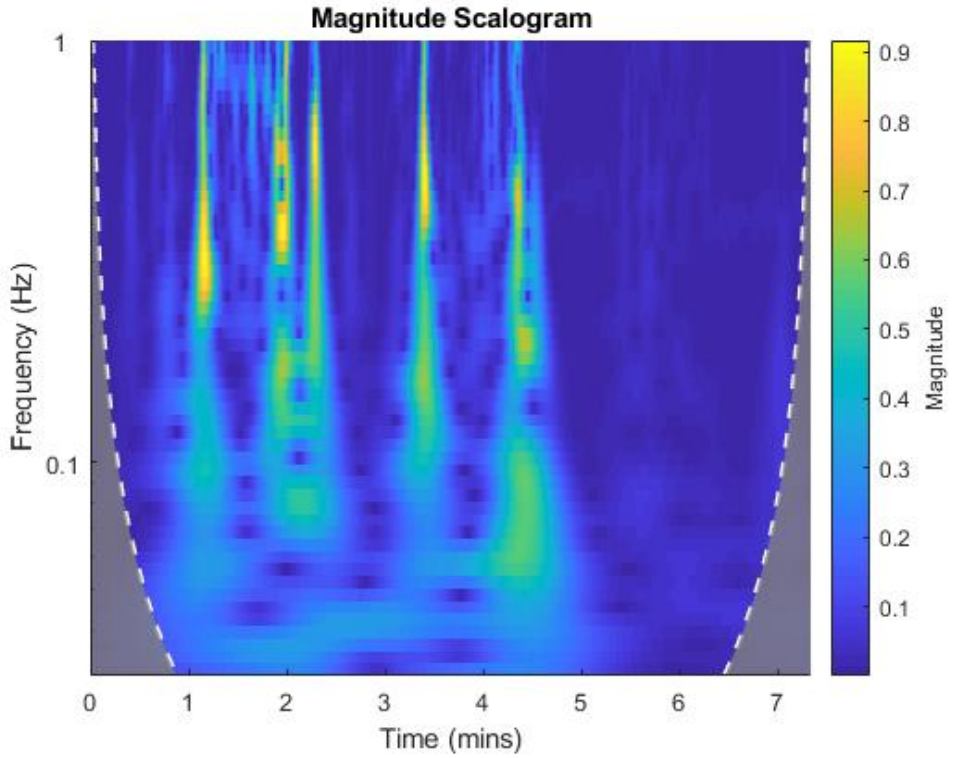


Figure 3.5: Example of scalogram where five PT events are highlighted.

The Wavelet transform was introduced by Morlet and Grossmann as a

method to obtain time frequency analysis of a signal [37]. It allows to analyze the signal in both the time and frequency domains, thus, in term of time-frequency localization, it permits to handle events that can be at opposite extremes. Thanks to time localization, a drift in a signal can be isolated while important high-frequency transients are preserved [38]. Fig. 3.5 shows an example of scalogram, which represents the absolute value of the continuous wavelet transform obtained with the MATLAB function cwt.

A wavelet is wave-like oscillation that has zero mean which is utilized for the representation of a signal. Unlike sinusoids, which extend to infinity, a wavelet exists for a finite duration. This makes this technique especially suitable for the analysis of non-stationary signals such as human motion signals [36].

Furthermore, Wavelet transform allows the use of a suitable basic function, which is more similar to the PT pattern. For this reason, a Morse wavelet has been chosen.

PT are in the frequency band 0.04-0.68 Hz [39], therefore a passband filter was applied by using the continuous wavelet transform with the analytic Morse wavelet; the range of passband is 0.03-1Hz;

3.4 Detection of Postural Transition

In this section the algorithm to detect PT is described, initially without distinguishing between Si2S from St2S. The steps are as follows:

- the filtered signal was normalized between -1 and 1 m/s^2;
- peaks above a certain threshold ($th = 0.395$) are localized in the A_{ap} signal;
- peaks are reported in the AV_y;
- the start and the end of each single event are looked for.

An higher value of Th increases the false positive (an event that is not a PT is marked as PT), on the other hand a lower value raises the false negative (an event that is a PT is not marked as PT). The $th = 0.395$ is chosen in order to minimize both false positive and false negative.

Si2S and St2S can be both divided in two phases: the preparation of the movement, and the real execution.

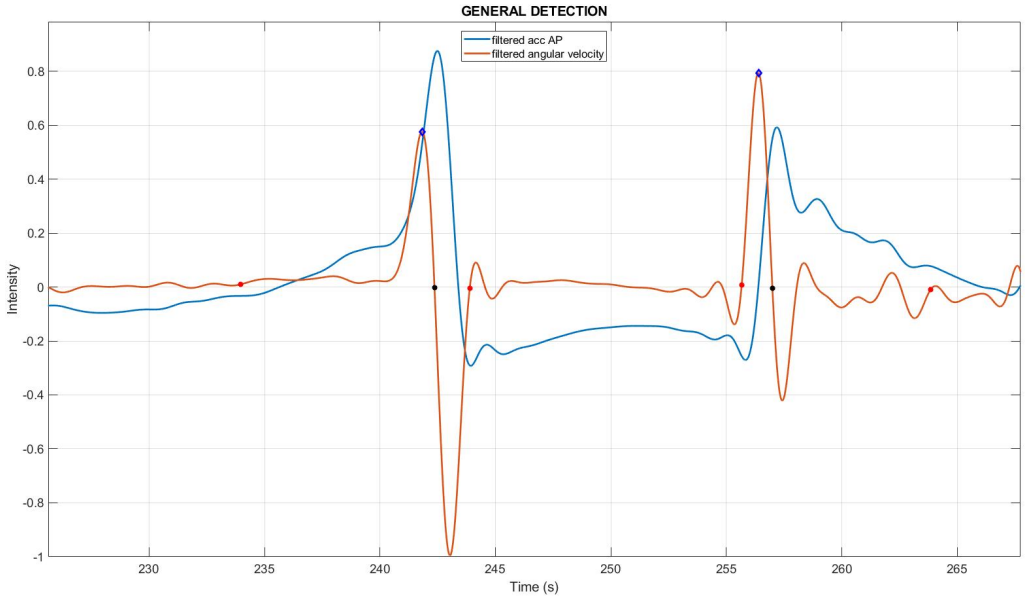


Figure 3.6: Example of Si2S and St2S detection. The red points are the start and the end of the S2S, the blue point is the maximum of the acceleration, and the black point is the MD point

The starting point is detected when there is a change in AV_y caused by leaning forward as the individual prepares to perform the movement. The first phase terminate just before the moment when the AV_y takes on an opposite direction, and the inversion of direction is the mid point (MD) that divide into two part the PT.

When the subject comes back to the upright position, the postural transition is characterized by a negative angular velocity. The AV_y reaches the minimum, and then increases back to zero. The time when it becomes positive is considered the end of the lift up phase and the end of the PT[40]. In figure 3.6 there is an example of a consecutive Si2S and St2S event and their related marked points.

3.5 Distinction between Si2S and St2S

Once the general detection has been performed, the postural transition must be analyzed. Three different classifiers have been utilized with a good, yet sub-optimal accuracy, whose combined output will give the final classification with a better accuracy.

3.5.1 Decision Tree classification

The first classifier implemented is a decision tree. The three accelerations are lowpass filtered with cut off frequency at 40 Hz because it is the frequency recommended to study human motion[41]. Then the derivative of the vertical acceleration is calculated (a'$_v$).

The features to be input to the classifier are a_{ap} and $M = \sqrt{a_{ap}^2 + a_{ml}^2 + a_v^2}$, which is the resultant magnitude of three acceleration axes. Not the whole signals are given as input, but a threshold sets the period that will be examined. The period to be analyzed includes t_r,...,t_s and is given by:

$$\forall t_i \in t_r, ..., t_s | a'_v | > DT \tag{3.3}$$

where DT is the threshold and it is set as [41]

$$DT = 0.3|a'_v| \tag{3.4}$$

M and a_{ap} are low-pass filtered with cut off frequency at 0.8 Hz by using `yulewalk` for design recursive IIR digital filters and then filtering through the function `filtfilt`.

3.5.2 Magnitude vector classification

By observing the magnitude signal, the following difference was noticed:

$$M(i_{max}) \geq M(i_{end}) \tag{3.5}$$

$$M(i_{max}) < M(i_{end}) \tag{3.6}$$

E1q. 3.5 refers to St2S, whereas the formula 3.6 is related to Si2S. Fig. 3.7 shows the relationship just described.

3.5.3 Post walk classification

Each PT event is compared with the nearest walk event and PT position. For example, if before a PT event there is a walk detection, and after there is another PT event, then that specific one will mark as St2S. Otherwise, if a PT episode is preceded by another one, and followed by a walk event, it will assigned a Si2S label.

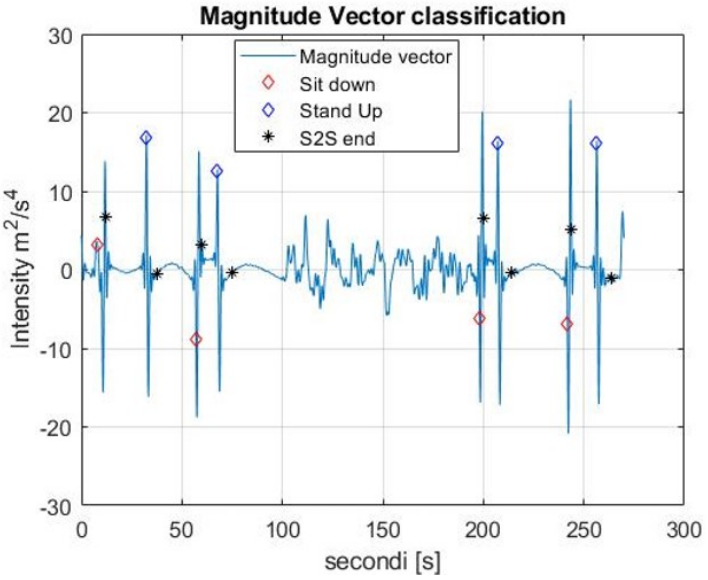


Figure 3.7: Signals marked as sit down (Si2S) or stand up (St2S) according to magnitude vector classification

3.5.4 Final classification

The output of the classifiers developed has been put together by hard voting, the simplest case of majority voting. In hard voting, the final class label will be the class label that has been predicted most frequently by the classification models. Assuming that we combine three classifiers that classify a training sample as follows:

- classifier 1 -> 1
- classifier 2 -> 2
- classifier 3 -> 1

Via majority vote, we would classify the sample as "class 1."

3.6 Defined features

In this section are described the features utilized for discriminate the patients according to their UPDRS score in the task "arise from chair". Both temporal and frequency features are analyzed. Three frequency ranges has been investigated: 0.04-0.68Hz, 0.68-4Hz, 4-12Hz, that are respectively the postural transition band, the voluntary movements band, and the tremor band [42]. Each parameter is obtained for the three acceleration components.

3.6.1 Duration

The duration is the time in seconds where a signal is actually present. It is simply the time between the start and the end of the single task. Obviously it is determined just once and for all:

$$\Delta t = a_{ap}(end) - a_{ap}(start) \tag{3.7}$$

3.6.2 Range

The amplitude range during the S2S time interval is given by:

$$r = max(x[n]) - min(x[n]) \tag{3.8}$$

where n = 1,2,...,N is the sample index and x is the acceleration.

3.6.3 Jerk

Jerk is the acceleration derivative; it has been considered because it should be a good descriptor for the amount of movement. Its expression is given by:

$$J = \sum_{n=1}^{N} \frac{a_{n+1} - a_n}{\Delta t} \tag{3.9}$$

Taking a cue from [4], jerk and range features were calculated also for the two phases of S2S described above. The features related to the first part are rangeA and jerkA, those related to the second one are rangeB and jerkB.

3.6.4 Number of hesitations

The number of hesitations, defined as peaks in the signal, can describe how many attempts or blocks can occur during the S2S. This might be an important parameter for evaluating the difficulty that a patient can have. The ready-made function `findpeaks` of `MATLAB` was utilized to find the peaks, then through the `length` function, the number of hesitations was calculated.

3.6.5 Power percentage

A frequency analysis is required to extract features from the frequency domain by estimating the power spectral density (PSD) of signals.

There are several ways to make an estimation of PSD, we have chosen the Welch's periodogram. A discrete window function is applied to divide the signal into segments in order to reduce spectral leakage. A rectangular window is chosen because, even if is not the best choice for spectral leakage, it leads a better resolution because of its narrower main lobe. In fact, working in frequency range of mHz, the main problem is resolution. Lastly, an overlap of 50% between segments is allowed. The `Matlab` function `pwelch` has been used.

The three frequency ranges are deeper investigated by dividing them in four or five sub-band. The aim is to determine what is the weight for each sub-band related to its reference band. Table 3.2 shows the number and the division of the the frequencies range analyzed.

Table 3.2: List of sub-band used for power percentage features.

Reference Band	**0.04-0.68**	**0.68-4**	**4-12**
sub-band n.1	0.04-0.2	0.68-1	4-5.5
sub-band n.2	0.2-0.35	1-2	5.5-7
sub-band n.3	0.35-0.5	2-3	7-8.5
sub-band n.4	0.5-0.68	3-4	8.5-10
sub-band n.5	/	/	10-12

3.6.6 Dominant Frequency

The dominant frequency and its derived parameters have been used in several studies like in Patel et al. [2] and Bonato et al. [1] for accelerometer measurements in PD application. The dominant frequency f_{dom} is the frequency for which the PSD $P(f)$ is the largest, and it was found through the Matlab function `max`. The features derived from the dominant frequency utilized in this thesis are:

- **Ratio of dominant frequency power to total**
- **Dominant Width** calculated with the function `findpeaks` of `MATLAB`

3.6.7 Spectrogram standard deviation

For a random variable vector as PSD made up of N scalar observations, the standard deviation is defined as

$$S = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}|PSD_i - \mu|^2}, \tag{3.10}$$

where μ is the mean value of PSD:

$$\mu = \frac{1}{N}\sum_{i=1}^{N} PSD_i \tag{3.11}$$

The standard deviation is helpful to quantify the amount of dispersion of the power spectrum. A low standard deviation denotes that the data points tend to be close to the mean, so a narrow spectrum, vice versa a high standard deviation indicates that the data points are spread out a wider range of values, then a wide spectrum.

3.6.8 Number of harmonics

The number of harmonics is a parameter that count the peaks in the spectrum. `Findpeaks` was used to detect the peaks by setting the parameters MinPeakHeight at 0.2 times the spectrum maximum, and MinPeakDistance at 0.8 times the width of the principal harmonic. They respectively allows to find harmonics with a certain intensity and well spaced out.

3.6.9 Total Area of Harmonics

The total Area of Harmonics is an approximate calculation of the area of all harmonics detected as described in the previous subsection. The formula is the following

$$\sum_{i=1}^{N} h_i * w_i, \tag{3.12}$$

where N is the number of harmonics detected, h and w are respectively the intensity and the width of the harmonic.

3.7 Machine learning algorithms

Machine learning (ML) is a field of artificial intelligence (AI) that gives to computer the ability to learn from experience and then produces a model able to make previsions. Learning is the process to extract knowledge from experience. In particular, pattern recognition is the capability to recognize patterns inside the data. A pattern is a regular sequence of data subset whose elements are somehow predictable. ML is the study of algorithms that improve their performance through experience with respect to a specific goal[43].

The main types of machine learning are unsupervised learning and supervised learning. The first one deals with unlabeled data or with unknown structure. The algorithm explores the data structure without the guidance of a labeled training in order to find patterns. Otherwise the supervised learning is based on labeled input necessary to build the classifier. In this thesis the latter one has been used.

Supervised learning is divided in two main phases:

- **training phase** needed to teach the algorithm how to understand the data for a specific goal;
- **test phase** to understand how much the model is accurate and robust.

There are different approaches used for evaluating the performance of a trained model. One of the most common is dividing the data set in a training set and a test set. A large data set is necessary to reach statistical significance, but often, in clinical world, there are not many data. The data set available in this project is quite limited, so another validation method has been chosen: the cross validation method.

The k-fold cross-validation divides the data set in k number of folds with the same size. The procedure consists in k iterations in which, at each iterations, k-1 folds are used as training sets, and the last one as the test set. At each iteration, the fold for the test set is different. The advantage of this model is a virtual enlargement of our training set because of the repeated random sub-sampling.

The machine learning techniques used in this thesis work are briefly described in the following paragraphs.

3.7.1 Decision Tree

The classification system has a tree structure. The root is the input classifier, internal nodes are tests and leaf nodes are the terminal pointss which represent class labels.

The prediction process begins from the root, where the value of the root feature is compared with the vector feature. Based on the outcome of the node, a branch follows in order to jump to the next node. A decision role is implemented in the nodes based on one or more attributes of the feature vector. The tests are performed until the process reaches the leaf node, and so the class value is predicted [44].

The `MATLAB` function `fitctree` was used to get a decision tree learner template and build the model.

3.7.2 Support Vector Machine (SVM)

Support Vector Machine is a supervised learning model that can be used both for classification and regression problem. Initially, it has been designed to solve binary classification, but its use has been extended also for multiclass problems.

SVM is based on the idea to find an hyperplane that divides the data set in two classes at the maximum distance [45]. The support vectors, the points nearest to the hyperplane, are the data most important dot because the position of the hyperplane depends only on this point. The aim of the algorithm is to leave from the hyperplane the support vector at maximum distance [46].

A multiclass problem is approached generally by combining several binary SVM classifiers, each of them solving a sub-problem of the original multi-class classification problem.

The functions `templateSVM` and `ficecoc` implement a SVM classifier in `MATLAB` software.

3.7.3 K-nearest neighbor classifier (KNN)

The K-nearest neighbor classifier is a non-parametric method used for both classification and regression predictive problems. The algorithm assumes that the data are placed in the so-called feature space, consequently the data

points have the concept of distance. Since it does not make any assumptions on the data distribution, it is a non parametric algorithm [47].

The distance is computed between the new data point and all the samples of the training set. The algorithm assigns the class of the nearest point, that represents the neighbourhood, to the new sample. It can be extended by considering more samples as neighbourhood and computing the majority voting among the nearest neighbors [47].

It is very easy to implement because it requires only the number of neighbors k, the distance metric and the training data set. Its limitations is the choice of k parameter because of the classifier is very sensitive to this parameter. As general rule, a large value of k extends the neighborhood to the domain of other categories, while a small value may introduce noise. The built-in function `fitcknn` has been used for training the classifier.

3.7.4 Linear Discriminant Analysis (LDA)

Linear discriminant analysis is a classification dimensionality reduction method useful in determining whether a data set is effective in predicting class label [48].

Since it works by searching for a linear combinations of features which best represent the data, it is strictly related to Principal Component Analysis.

The Matlab function `fitcdiscr` is used to make a classifier besed on LDA, setting the parameters DiscrimType as Linear.

3.8 Feature reduction

Often a classification problem is characterized by a huge number of features that can lead to a slower process and may introduce noise. The feature reduction speeds up the processing and reduces noise. There are two main approaches:

- **Feature selection**, consisting in a selection of a subset of the original features;
- **Dimensionality reduction**, based on mathematical recombination of the original features

3.8.1 Principal component analysis (PCA)

Principal component analysis (PCA) is the main linear technique for dimensionality reduction. It performs a data mapping to a lower-dimensional space in order to maximize the variance of the data. The algorithm considers the covariance matrix of the original variables and calculates its eigenvectors. The eigenvectors that correspond to the largest eigenvalues are used to reconstruct high percentage of the variance of the original data. Those eigenvectors are also called the principal components.

In order to perform the dimensionality reduction, the concept of variance explained is quite important. The total variance is the sum of variances of all individual principal components. The fraction of variance explained by a principal component is the ratio between the variance of that principal component and the total variance. For several principal components, add up their variances and divide by the total variance. So, when PCA keeps enough components to explain 95% variance, the total of the first component that reach the 95% of total variance are kept.

The `MATLAB` function `pca` is used. It calculates the principal component coefficients, also known as loadings, and the principal components scores.

3.9 Statistical and performance descriptors

3.9.1 Box plot

A box plot is a graphical representation utilized for describing the distribution of data set. In a box plot, the central mark indicates the median, and the bottom and top edges of the box indicate the 25th percentile (or 1st quartile) and 75th percentile (or 3rd quartile), respectively. It means that 50% of the population is in the box, also known as the interquartile range (IQR). The larger is the IQR, the spreader are the values of the population [49].

The T-bars out of the boxes are called whiskers; they are the most extreme data points not considered outliers (more than three times the height of the boxes). The outliers are plotted individually using symbols like the '+' or 'o' symbols.

3.9.2 Confusion matrix

A confusion matrix is a table for the representation of performance in a classification problem, typically supervised learning. It is a square matrix

where each column represents the predict class and the rows the real one.

In the specific case of binary classification, the confusion matrix is a simple square matrix with two rows and two columns that reports the true negatives, true positives, false positives, false negatives. If the data set is unbalanced, accuracy can get misleading results, so just accuracy is not a reliable metric for the real performance of a classifier. In addition to accuracy, other parameters are calculate for a binary classification:

		predicted class	
		0	1
true class	0	True Positive (TP)	False Negative (FN)
	1	False Positive (FP)	True Negative (TN)

Figure 3.8: A confusion matrix for a binary classifier and its terminology.

- **Accuracy** = $\frac{\mathbf{TP+TN}}{\mathbf{TP+TN+FP+FN}}$
- **Sensitivity** or **True Positive Rate** = $\frac{\mathbf{TP}}{\mathbf{TP+FN}}$
- **Specificity** or **True Negative Rate** = $\frac{\mathbf{TN}}{\mathbf{TN+FP}}$
- **Precision** or **Positive Predictive Value** = $\frac{\mathbf{TP}}{\mathbf{TP+FP}}$
- **Negative Predictive Value** = $\frac{\mathbf{TN}}{\mathbf{TN+FN}}$

3.10 Balance of number of events

One of the main issue of this thesis is that data has imbalanced classes. Excluding the class 3, the 50% of patients belong to class 0. Generally, greater the UPDRS score, the more severe is the disease and consequently the patient cannot perform the task as he/she desires, completing a minor number of repetitions. So, looking the percentage of repetitions, the issue get worse, the class 3 reaches 62% of repetitions.

Imbalanced data set occurs when there is an unequal representation of classes. Since the probability of instances belonging to the majority class is

significantly high in imbalanced data set, the new data are much more likely to be classified to the majority class.

In order to mitigate this issue, the data for class 1 and 2 has been duplicated, narrowing the gap among classes as shown in Fig. 3.9

Figure 3.9: Number of repetitions after balance.

3.11 Leave-one-out Validation

Since the data has been duplicated, the k-fold cross-validation is no more recommended because a sample that contribute to the validation, may be used also for the test; consequently this sample is surely identified, so the result becomes biased.

As validation for the last data set, the leave-one-out has been chosen. Suppose that the data set is composed of N elements. A sample is removed from the data set, the classifier is build with the N-1 elements and then the data set is performed with the removed sample. This one is reinserted in the data set and the following sample will be removed. This process is repeated until all the N elements are utilized as test set.

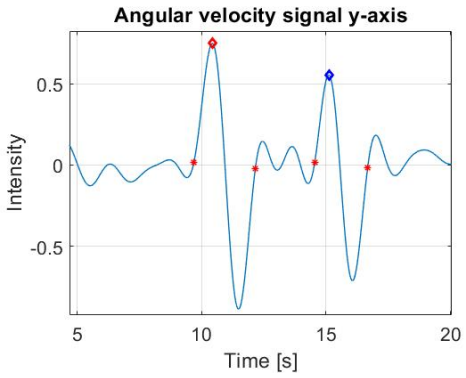
Chapter 4

Results

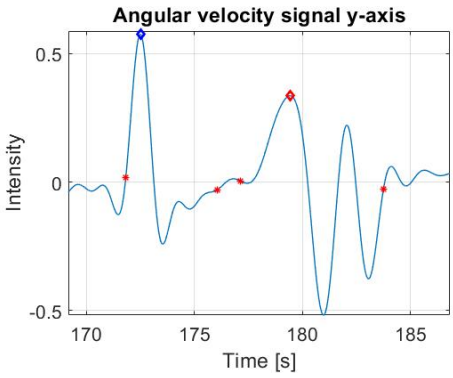
In this chapter, the results obtained in this thesis work are presented. In sections 4.1 and 4.2 the signals on which the subsequent classification is based, are presented: angular velocity and acceleration signals. In Sect. 4.3 the results of PT detection are presented, whereas in Sect. 4.4 and 4.5 namely: the results of the discrimination between Si2S and St2S are reported in terms of box plots and confusion matrices. Finally in Sect. 4.6 a classification by duplicating patients and events in order to reduce the imbalance among classes is performed.

4.1 Examples of angular velocity signals

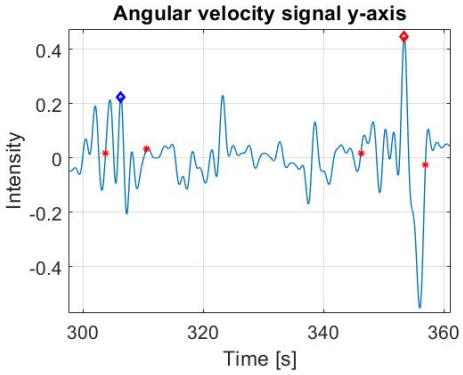
In Fig. 4.2 are plotted the angular velocity and the PT label. Angular velocity has been used mostly for the detection of PT.



(a) UPDRS 0



(b) UPDRS 1



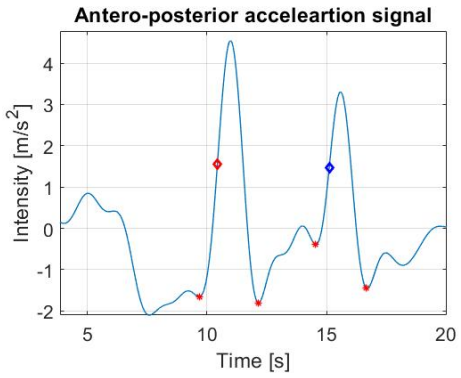
(c) UPDRS 2

Figure 4.1: Angular velocity of y-axis from UPDRS 0 to 2. The PT are marked with diamonds (blue for Si2S, red for St2S), whereas the starting and the end point are marked with stars.

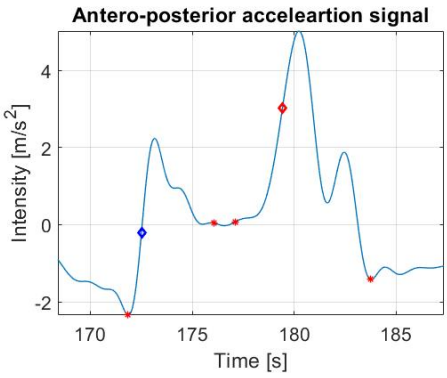
4.2 Examples of accelerometer signals

Accelerometer signals have been utilized to distinguish St2S from Si2S and to extract features in order to perform the classification among patients with different UPDRS score in the task "arise from chair".

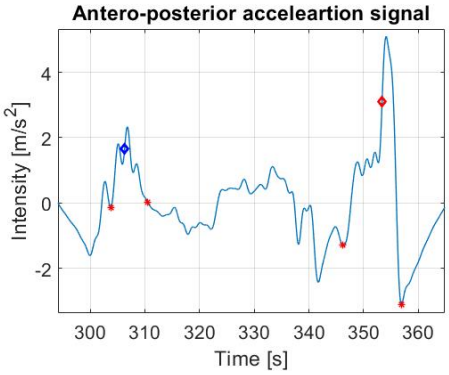
Some interesting features changes can be noticed by observing the signals. The irregularity of signals increases from UPDRS 0 to UPDRS 2. In the UPDRS 0 class, most of the time there is only one peak, whereas in UPDRS 1 and UPDRS 2 frequently more peaks can be detected because of attempts or hesitations in standing up or sitting down.



(a) UPDRS 0



(b) UPDRS 1



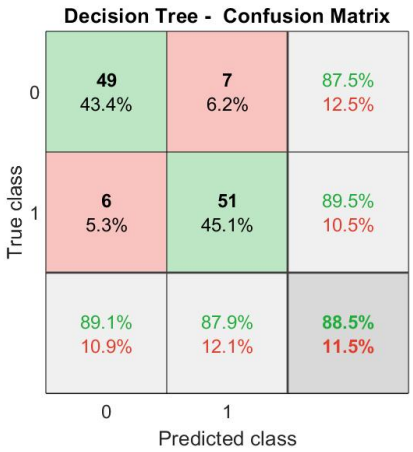
(c) UPDRS 2

Figure 4.2: Anterior-posterior acceleration from UPDRS 0 to 2. The PT are marked with diamonds (blue for Si2S, red for St2S), whereas the starting and the end points are marked with stars.

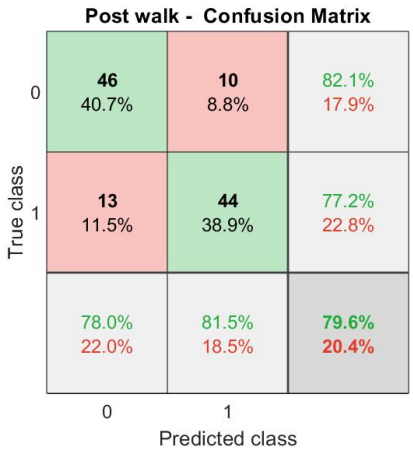
4.3 Postural transition detection: confusion matrices

In this subsection the confusion matrices are illustrated for the Postural Transition detection. Class 0 represents St2S, whereas class 1 is Si2S. The dark gray in the right bottom shows the overall correct classification percentage and incorrect classification percentage. The correctly classified cases are placed in diagonal (green), whereas the misclassifies are in the red cells.

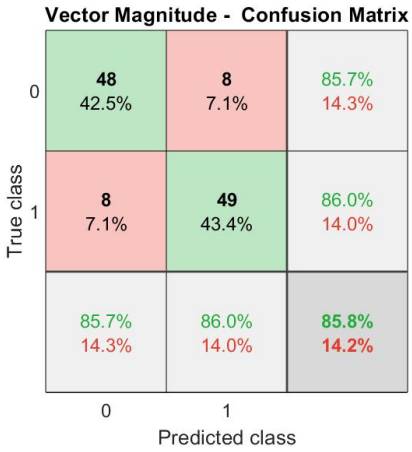
As can be seen from Fig.4.3, the results are good, yet sub-optimal performance. The most of the error in post walk classification are due to not a perfect classification of walk event. In fact, false positives and false negative in walk detection can confuse this kind of classification. Decision tree classi-



(a) Decision Tree classification



(b) Post walk classification



(c) Magnitude Vector classification

Figure 4.3: Confusion matrices of the three independent classifier which underlies the postural transition classification

fication and vector magnitude reaches the best results in term of accuracy: 88.5% and 85.8%, respectively. Both of them have sensitivity and specificity very similar, that means they do not classify a class better the other one, but the classification is balanced. For example, the difference between sensitivity and specificity in Vector Magnitude classification is only 0.3%.

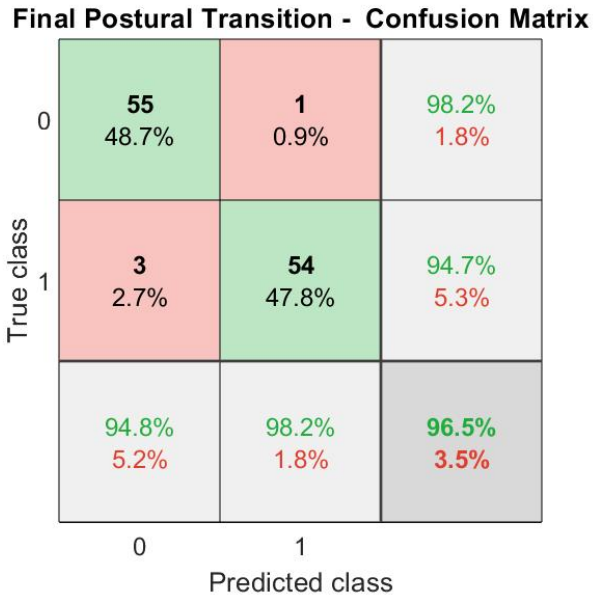


Figure 4.4: Confusion Matrix of the Final Postural Transition classification.

Then a final classification has been performed. The output of this three classifiers are put together by majority vote. The final classification becomes far better then the three taken separately, getting a 96.5% of accuracy. This classifier is very strong in predicting correctly St2S with a specificity of 98.2%. The classification of Si2S is slightly lower (94.7%). Another positive important point is when the classifier gives in output Si2S (1), 98.2% of the time the classification is correct, a very good percentage.

4.4 Box plots

In this subsection the most relevant features are illustrated through box plots. In Fig. 4.5 two acceleration-based features in the time domain are reported, namely: duration and jerk, calculated for the vertical acceleration. The box plot of the duration shows an increasing trend from the UPDRS 0 to UPDRS 2. It can be easily explained because, as the disease progresses, the patients make more effort to stand up spending more time.

On the contrary, the jerk plot is only slightly decreasing. Since it represents the amount of activity, along with the severity of the symptom, PD patients make less movements because of other PD manifestations such as rigidity or bradikynesia.

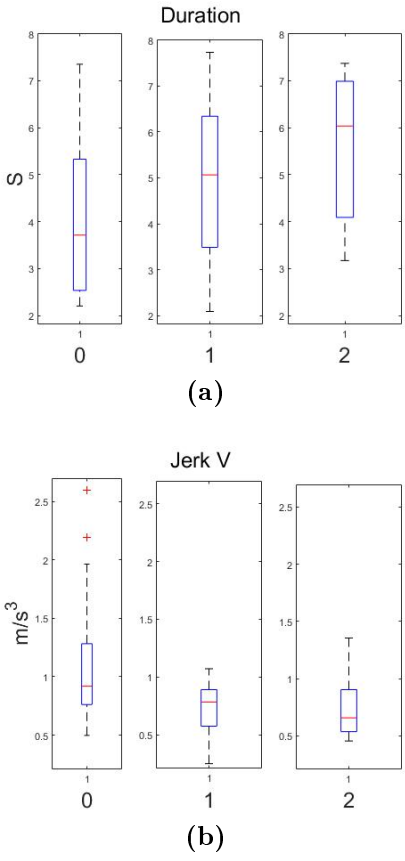


Figure 4.5: Box plots showing the trend for Si2S of both duration (a) and jerk for vertical acceleration signal (b) along with the severity of the symptom (increasing the UPDRS score "arise from chair").

4.5 Feature selection

In this section the results of classification after feature selection are reported.

A research of possible optimal results has been conducted by exploring the space solution. First of all, a classification with all features has been tried; then SVM, KNN, LDA and the decision tree algorithm have been investigated by using PCA as feature selection, changing the parameter of explained variance. Tab. 4.2 and Tab. 4.1 show the best results obtained for each explained variance level.

Table 4.1: Summary of best results for Si2S after feature selection.

Explained variance	Classifier	n components	accuracy
No PCA	SVM	all features	64.9%
99%	SVM	10	75.4%
98%	KNN	7	73.7%
97%	SVM	5	73.7%
96%	KNN	4	66.7%
95%	SVM	3	64.9%

Table 4.2: Summary of best results for St2S after feature selection.

Explained variance	Classifier	n components	accuracy
No PCA	LDA	all features	66.7%
99%	SVM	15	68.5%
98%	LDA	11	70.4%
97%	SVM	9	66.7%
96%	LDA	7	66.7%
95%	LDA	6	68.5%

By examining Tables 4.1 and 4.2, it can be noticed that a better accuracy is reached using PCA than using all the features (Explained variance = 100). It can happen that during the calculation of the principal components, the

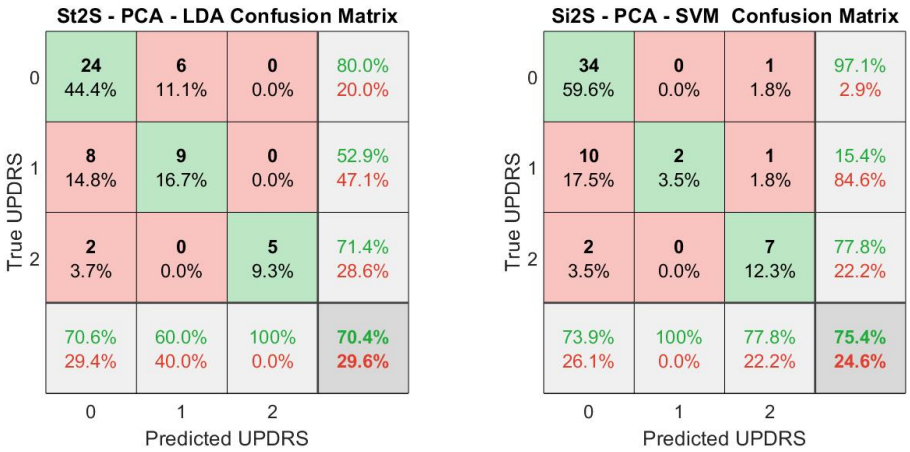


Figure 4.6: Confusion matrix showing the two best results after the use of PCA for St2S(a) and Si2S(b)

features that introduce noise or irrelevant information for the purpose of classification are excluded.

By examining Fig. 4.6 some important considerations can be made that apply to both Si2S and St2S. First, the classifiers mainly misclassify by one step one the UPDRS scale, especially "true UPDRS 1" was incorrectly predicted as "UPDRS 0". Second, although the events for patients in UPDRS 2 are fewer, a good classification (above 70%) is achieved. For St2S, when the classifier predicts UPDRS 2, no mis-classification is actually evidenced. In the Si2S classifier, the UPDRS 0 shows a very good correct classification of 97.1%.

4.6 Classification with duplicated events

Since the imbalanced classes is one of the main problem, observing the behavior of the classifiers after duplicate the classes "UPDRS 1" and "UPDRS 2" may be interesting. First, a classification of the events is reported, second, a classification of patients based on majority voting among the output of the classification of the events for the same patient is reported.

4.6.1 Classification of events

In this section the results with the duplicated events will be discussed.

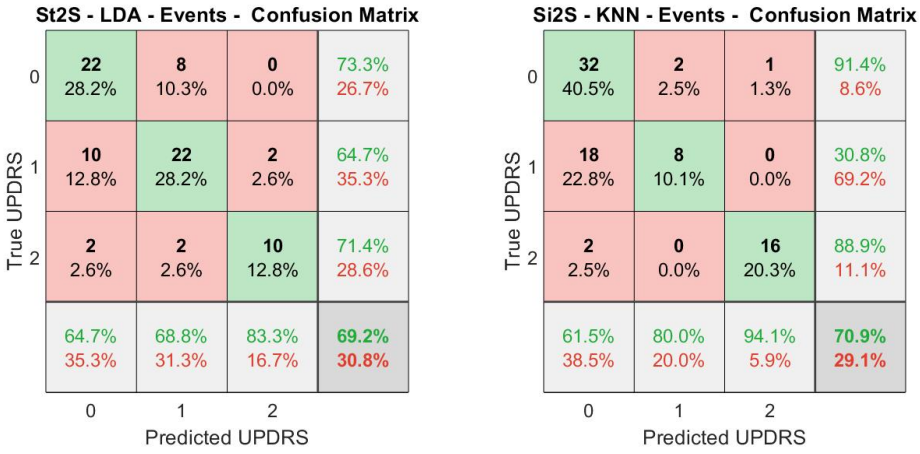


Figure 4.7: Confusion matrices showing the classification of events for St2S(a) and Si2S(b) after duplicating the class "UPDRS 1" and '"UPDRS 2"

It can be noticed in Fig. 4.7 that the accuracy for both Si2S and St2S remains quite stable; this means that the system is fairly robust. The most difficult class to classify is "UPDRS 1" that may be mostly confused with "UPDRS 0". Most of the time, the models classify incorrectly only by one step on the UPDRS scale.

4.6.2 Classification of PD patients

Finally, in Fig. 4.8 the results of classification of patients are reported

Similar considerations may apply to the classifications of patients: classs "UPDRS 0" and "UPDRS 2" are the best ones in terms of accuracy, whereas class "UPDRS 1" may be confused with class "UPDRS 0". However the overall accuracy is improved, in fact the accuracy reaches 77.3% for St2s and 81.8%

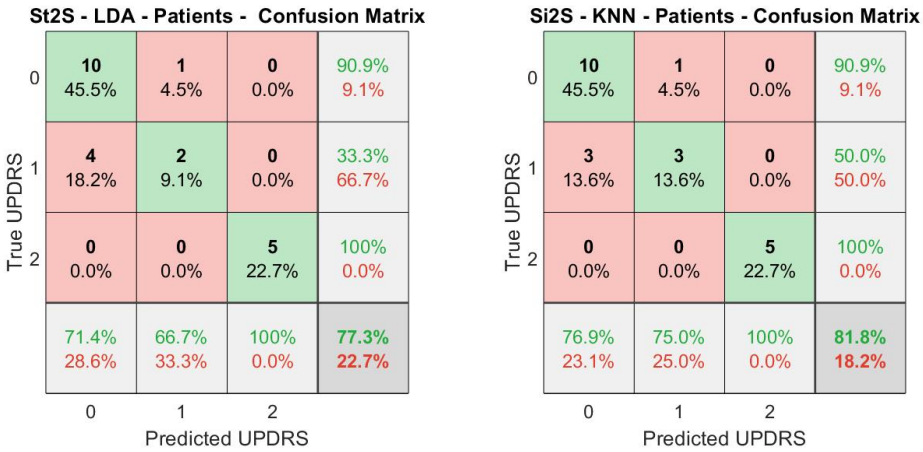


Figure 4.8: Confusion matrices showing the classification of patients for St2S(a) and Si2S(b)

for Si2S. Since there are few patients, just only mis-classification lead a 4.5% difference in the accuracy.

Chapter 5

Discussion

This work has been conducted in order to develop an algorithm able to monitoring PD patients, especially for fluctuations and fall prediction. In particular, this work has been focused on detection and estimation of postural transitions.

First of all, the PT has been detected and labeled as sit-to-stand or stand-to-sit. The development of three sub-optimal classifiers leads at a final optimal classification reaching accuracy of 96.5%. It should be emphasised that when an input is classified as Si2S, 98.2% of the time the classification is correct.

The acquired signals acquired have different trends depending on the UPDRS score. For example, looking at the signals belonging to UPDRS 1 and UPDRS 2, a higher number of peaks can be detected more frequently, representing the attempts or hesitations during the movement. From the box-plots presented in Chapter 4, other differences can be noticed, as the fact that the duration for Si2S is proportional to the severity of the motor symptoms.

In Chapter 4 the results of classification of PT are shown according the score UPDRS "arise from chair", using machine learning techniques such as SVM, KNN, LDA and decision tree. It is important to note that feature selection through PCA leads a better classification than considering all features, especially for Si2S. This means that PCA excludes some irrelevant features, essentially that bring noise. It could be interesting to investigate which features are excluded; the PCA does not allow to appreciate this selection because, performing dimensionality reduction, the algorithm computes new features that does not have a real physical meaning.

In order to face the problem of imbalanced classes, the results with duplicated events for class UPDRS 1 and UPDRS 2 are analyzed in the last part of Chapter 4. Changing the validation method, the accuracy of classification remains constant. Most of the time, the models classify incorrectly only by one step on the UPDRS scale, especially between UPDRS 0 and UPDRS 1.

The same considerations can be made for PD classification, except for the accuracy that reaches a value as high as 81.8% thanks to majority voting among the events for the same patient.

Chapter 6

Conclusion

The goal of this thesis is to contribute in developing algorithms for postural transition detection and UPDRS score "arise from chair" estimation of PD patients in their daily life.

In this thesis, a tri axial accelerometer was located at the lower back. The position is comfortable and suitable to measure the main motor symptoms of PD. In particular, the signals were acquired by a common smartphone during the visit conducted by the physician, adding a couple of tasks to simulate ADL. The system allows the patients and physician to not have much interaction with the technology.

Three different classifiers have been implemented in order to detect PT and distinguish between Si2S and St2S by using machine learning technique. Then, several parameters have been evaluated both in the time and frequency domain in order to investigate the connection between the UPDRS scores assigned to patients by physicians and the measured kinematic variables.

The first part of the work has yielded very good results in terms of accuracy in PT detection. The second phase has demonstrate a promising capability to diagnose symptoms in PD patients. These results are limited by the small number of patients, in particular from UPDRS 2 and UPDRS 3 classes.

This thesis is part of a bigger project for developing an objective tool to monitor PD symptoms. Other motor task are being investigated to obtain a more complete general overall picture. This a simple system that allows physicians to get a clearer view of symptom fluctuations during patient's daily life. It means a better quality of life for both patients and their caregivers.

Bibliography

[1] P. Bonato, D. M. Sherrill, D. G. Standaert, S. S. Salles, and M. Akay, "Data mining techniques to detect motor fluctuations in parkinson's disease," in *Engineering in Medicine and Biology Society, 2004. IEMBS'04. 26th Annual International Conference of the IEEE*, vol. 2, pp. 4766–4769, IEEE, 2004.

[2] S. Patel, K. Lorincz, R. Hughes, N. Huggins, J. Growdon, D. Standaert, M. Akay, J. Dy, M. Welsh, and P. Bonato, "Monitoring motor fluctuations in patients with parkinson's disease using wearable sensors," *IEEE transactions on information technology in biomedicine*, vol. 13, no. 6, pp. 864–873, 2009.

[3] F. Parisi, G. Ferrari, M. Giuberti, L. Contin, V. Cimolin, C. Azzaro, G. Albani, and A. Mauro, "Body-sensor-network-based kinematic characterization and comparative outlook of updrs scoring in leg agility, sit-to-stand, and gait tasks in parkinson's disease," *IEEE journal of biomedical and health informatics*, vol. 19, no. 6, pp. 1777–1793, 2015.

[4] A. Weiss and M. P. T. Herman, "Can an accelerometer enhance the utility of the timed up & go test when evaluating patients with parkinson's disease?," *Medical Engineering and Physics*, vol. 32, no. 2, pp. 119–125, 2010.

[5] J. Jankovic, "Parkinson's disease: clinical features and diagnosis," *Journal of neurology, neurosurgery & psychiatry*, vol. 79, no. 4, pp. 368–376, 2008.

[6] EPDA, "About parkinson's."

[7] J. Parkinson, "An essay on the shaking palsy," *The Journal of neuropsychiatry and clinical neurosciences*, vol. 14, no. 2, pp. 223–236, 2002.

[8] C. G. Goetze, "The history of parkinson's disease: Early clinical descriptions and neurological therapies.," *Cold Spring Harb Perspect Med*, vol. 1, no. 1, 2001.

[9] M. Trail, E. Protas E, and E. Lai, *Neurorehabilitation in Parkinson's disease: an evidence-based treatment model*. SLACK Incorporated, 2008.

[10] L. Stefanis, "alpha-synuclein in parkinson's disease," *Handbook of Neurotoxicity*, vol. 2, no. 2, pp. 223–236, 2012.

[11] A. A. Moustafa, S. Chakravarthy, J. R. Phillips, A. Gupta, S. Keri, B. Polner, M. J. Frank, and M. Jahanshahi, "Motor symptoms in parkinson's disease: A unified framework," *Neuroscience & Biobehavioral Reviews*, vol. 68, pp. 727–740, 2016.

[12] R. A. Hauser and T. A. Zesiewicz, *Parkinson's disease: Questions and Answers*. Merit, 2006.

[13] P. Barone, GabriellaSantangelo, MariannaAmboni, and M. TeresaPellecchia, "Pisa syndrome in parkinson's disease and parkinsonism: clinical features, pathophysiology, and treatment," *The Lancet Neurology*, vol. 15, pp. 1063–1074, 2016.

[14] E. Iannilli, L. Stephan, T. Hummel, H. Reichmann, and A. Haehner, "Olfactory impairment in parkinson's disease is a consequence of central nervous system decline," *Journal of neurology*, vol. 264, no. 6, pp. 1236–1246, 2017.

[15] M. E. Fullard, B. Tran, S. X. Xie, J. B. Toledo, C. Scordia, C. Linder, R. Purri, D. Weintraub, J. E. Duda, L. M. Chahine, *et al.*, "Olfactory impairment predicts cognitive decline in early parkinson's disease," *Parkinsonism & related disorders*, vol. 25, pp. 45–51, 2016.

[16] J. Isaacson, Skettini Stuart, "Neurogenic orthostatic hypotension in parkinson's disease: evaluation, management, and emerging role of droxidopa," *Vascular Health & Risk Management*, vol. 10, pp. 169–176, 2014.

[17] T. Suttrupi, Warnecke I, "Dysphagia in parkinson's disease.," *Clinical Cases in Dysphagia*, pp. 53–65, 2015.

[18] M. Menza, R. D. Dobkin, H. Marin, and K. Bienfait, "Sleep disturbances in parkinson's disease," *Movement Disorders*, vol. 25, no. S1, pp. S117–S122, 2010.

[19] J.-G. G. Hou and E. C. Lai, "Non-motor symptoms of parkinson's disease," *International Journal of Gerontology*, vol. 1, no. 2, pp. 53–64, 2007.

[20] T. A. Catafu and e. a. P. Laloux E., "Impact of dopamine transporter spect using 123i-ioflupane on diagnosis and management of patients with clinically uncertain parkinsonian syndromes," *Movement Disorders*, vol. 19, no. 10, pp. 1175–1182, 2004.

[21] K. D. Seifert and J. I. Wiener, "The impact of datscan on the diagnosis and management of movement disorders: A retrospective study," *American journal of neurodegenerative disease*, vol. 2, no. 1, p. 29, 2013.

[22] B. S. Connolly and A. E. Lang, "Pharmacological treatment of parkinson disease: a review," *Jama*, vol. 311, no. 16, pp. 1670–1683, 2014.

[23] S. L. Greig, "Carbidopa/levodopa enteral suspension in advanced parkinson's disease: a guide to its use," *Drugs & Therapy Perspectives*, vol. 32, 2016.

[24] J. Jankovic and MD, "Motor fluctuations and dyskinesias in parkinson's disease: Clinical manifestations," *Movement Disorder*, vol. 20, no. 11, pp. S11–S16, 2005.

[25] S. J. Groiss, L. Wojtecki, M. Sudmeyer, and A. Schnitzler, "Deep brain stimulation in parkinson's disease," *Therapeutic Advances in Neurological Disorders*, vol. 2, no. 6, pp. 379–391, 2009.

[26] A. Umek, Kos Anton, "Validation of smartphone gyroscopes for mobile biofeedback applications," *Personal and Ubiquitous Computingy*, vol. 20, no. 5, pp. 657–666, 2016.

[27] F. Difrancesco, v. d. V. Sonia, A. Paolo, A. Sabine N., B. Bader, P. John, and N. Riccardo, "Out-of-home activity recognition from gps data in schizophrenic patients," *29th International Symposium on Computer-Based Medical Systems (CBMS)*, 2016.

[28] B.-C. Lee, J. Kim, S. Chen, and K. H. Sienko, "Cell phone based balance trainer," *Journal of neuroengineering and rehabilitation*, vol. 9, no. 1, p. 10, 2012.

[29] M. A. Habib, M. S. Mohktar, S. B. Kamaruzzaman, K. S. Lim, T. M. Pin, and F. Ibrahim, "Smartphone-based solutions for fall detection and prevention: challenges and open issues," *Sensors*, vol. 14, no. 4, pp. 7181–7208, 2014.

[30] H. B. Kim, H. J. Lee, W. W. Lee, S. K. Kim, H. S. Jeon, H. Y. Park, C. W. Shin, W. J. Yi, B. Jeon, and K. S. Park, "Validation of freezing-of-gait monitoring using smartphone," *Telemedicine and e-Health*, 2018.

[31] G. Ciuti, L. Ricotti, A. Menciassi, and P. Dario, "Mems sensor technologies for human centred applications in healthcare, physical activities, safety and environmental sensing: a review on research activities in italy," *Sensors*, vol. 15, no. 3, pp. 6441–6468, 2015.

[32] M. Magno, C. Spagnol, L. Benini, and E. Popovici, "A low power wireless node for contact and contactless heart monitoring," *Microelectronics Journal*, vol. 45, no. 12, pp. 1656–1664, 2014.

[33] E. Martin, V. Shia, and R. Bajcsy, "Determination of a patient's speed and stride length minimizing hardware requirements," *Body Sensor Networks (BSN)*, vol. 14, pp. 144–149, 2011.

[34] M. Tundo, E. Lemairei, and N. Baddour, "Correcting smartphone orientation for accelerometer-based analysis," *2013 IEEE International Symposium on Medical Measurements and Applications*, pp. 58–62, 2013.

[35] B. Ando, S. Baglio, M. Marletta, and et al, "A multisensor architecture for the assessment of postural sway in elderly and people with neurological disease," *SAS 2017 - 2017 IEEE Sensors Applications Symposium, Proceedings*, pp. 1–5, 2017.

[36] M. P. Wachowiak, G. S. Rash, P. M. Quesada, and A. H. Desoky, "Wavelet-based noise removal for biomechanical signals: A comparative study," *Transactions on Biomedical Engineering*, vol. 47, pp. 360–368, 2000.

[37] A. Grossman and J. Morlet, "Decomposition of hardy functions into square integrable wavelets of constant shape," *Journal on Mathematical Analysis*, vol. 15, no. 4, pp. 723–736, 1984.

[38] B. Najafi, K. Aminian, F. Loew, Y. Blanc, and P. A. Robert, "Measurement of stand-sit and sit-stand transitions using a miniature gyroscope and its application in fall risk evaluation in the elderly," *IEEE Transactions on Biomedical Engineering*, vol. 49, no. 8, pp. 843–851, 2002.

[39] B. Najafi, K. Aminian, F. Loew, Y. Blanc, and P. A. Robert, "Measurement of stand-sit and sit-stand transitions using a miniature gyroscope and its application in fall risk evaluation in the elderly," *IEEE Transactions on Biomedical Engineering*, vol. 49, no. 8, pp. 843–851, 2002.

[40] M. Milosevic, E. Jovanov, and A. Milenkovic, "Quantifying timed-up-and-go test: A smartphone implementation," *Proc. IEEE Int. Conf. Body Sensors Netw.*, pp. 1–6, 01 2013.

[41] D. Rodriguez-Martin and et al.l, "Svm-based posture identification with a single waist-located triaxial accelerometer," *Expert Systems with Application*, vol. 40, pp. 7203–7211, 2013.

[42] T. Heida, E. Wentik, and E. Marani, "Power spectral density analysis of physiological, rest and action tremor in parkinson's disease patients treated with deep brain stimulation," *Journal of NeuroEngineering and Rehabilitation*, vol. 10, pp. 1–11, 2013.

[43] Y. Kodratoff, *Introduction to machine learning.* Elsevier, 2014.

[44] L. Rokach and O. Maimon, "Top-down induction of decision trees classifiers - a survey," *IEEE Transactions on Systems, Man and Cybernetics Part C: Applications and Reviews*, vol. 35, no. 4, pp. 476–487, 2005.

[45] T. Hastie, R. Tibshirani, and J. Friedman, *The elements of Statistical Learning.* Springer, 2008.

[46] C. Cortes and V. Vapnik, "Support-vector networks," *Machine learning*, vol. 20, no. 3, pp. 273–297, 1995.

[47] N. S. Altman, "An introduction to kernel and nearest-neighbor nonparametric regression," *The American Statistician*, vol. 46, no. 3, pp. 175–185, 1992.

[48] S. B. Green, N. J. Salkind, and T. M. Akey, *Using SPSS for Windows and Macintosh: Analyzing and understanding data.* New Jersey: Prentice Hall, 2008.

[49] N. M. Qarmalah, J. Einbeck, and F. P. Coolen, "k-boxplots for mixture data," *Statistical papers*, vol. 59, no. 2, pp. 513–528, 2018.