UNIVERSIDAD POLITÉCNICA DE MADRID

ESCUELA TÉCNICA SUPERIOR
DE INGENIEROS DE TELECOMUNICACIÓN

MASTER EN INGENIERÍA BIOMÉDICA

TRABAJO FIN DE MASTER

DESIGN AND IMPLEMENTATION OF A NEUROPROSTHESIS FOR THE TREATMENT OF FREEZING OF GAIT IN PATIENTS WITH PARKINSON'S DISEASE

JORGE QUIJORNA SANTOS

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2023

Resumen

Actualmente, es muy común utilizar la tecnología en el diagnóstico y tratamiento de distintas enfermedades. Debido a las facilidades que ofrece a los médicos y los buenos resultados obtenidos, posibilitando realizar tareas que hace unos años parecían imposibles, se espera que esta tendencia continúe.

Debido a esto, el presente Trabajo Fin de Master se centra en el diseño e implementación de una neuroprótesis de estimulación aferente para el tratamiento de la congelación de la marcha en pacientes con Parkinson. Hasta este momento, no existe una solución para esta patología que afecta a cerca del 60 % de pacientes con la enfermedad. De esta manera, representará un avance importante en el tratamiento de la enfermedad de Parkinson, que podrá ayuda a los pacientes a lidiar con la enfermedad, haciéndoles más independientes en su día a día.

El objetivo es alcanzar un sistema capaz de estimular los músculos de los pacientes de acuerdo al ciclo de la marcha y a cómo serían activados en pacientes sanos. Para conseguir esto, en primer lugar, se investigó acerca de la enfermedad y, concretamente, sobre este síntoma para tener un conocimiento más profundo que nos permitiera saber cuáles eran los requisitos que nuestro sistema debía cumplir. A continuación, se analizaron distintos componentes para decidir cuáles se ajustaban mejor para conseguir nuestro objetivo. En tercer lugar, se implementó el tratamiento de la señal y los métodos predictivos que permitieron trabajar al sistema en tiempo real. Y, finalmente, se realizaron distintos tests a sujetos sanos para obtener resultados clínicos y técnicos que permitieron validar que nuestro sistema, es capaz de estimular los músculos de manera síncrona con la marcha y puede ser utilizado por personas con la enfermedad.

Palabras clave: Enfermedad de Parkinson, congelación de la marcha, ciclo de la marcha, patrones de la marcha, estimulación muscular

Abstract

Nowadays, it is very common to use the technology for the diagnosis and treatment of different diseases. Due to the eases that it gives to doctors and the good results obtained, making possible to conduct tasks that some years ago seemed impossible, this tendency is expected to continue.

For this reason, the present Master's Thesis is focus on the design and implementation of a neuroprosthesis of afferent stimulation for the treatment of freezing of gait in patients with Parkinson's Disease. Until this moment, there is no solution for this pathology which affects near to 60 % of patients with this disease. In fact, it will represent an important advance in the treatment of Parkinson's Disease, that could help patients to cope with this symptom, making them more independent in their day-to-day.

The aim is to reach a system able to stimulate the muscles of the patients according to the gait cycle and how they would be stimulated in healthy subjects. To achieve this purpose, firstly, a research about the disease and, specifically, about this symptom was done to have a deep knowledge about what were the requirements for the system. Then, an analysis of different components was needed to know what were the ones which fitted better for getting our objective. Thirdly, the treatment of the signal and prediction methods were implemented in order to get that the system works in real time. And, finally, different tests were performed to healthy subjects in order to obtain clinical and technical results that allow to validate that our system, is able to stimulate the muscles synchronously with gait and can be used by people with the disease.

Keywords: Parkinson's Disease, freezing of gait, gait cycle, walking patterns, muscle stimulation

Acknowledgements

I would like to use these lines to thank, first of all, my family for all the support they have given me throughout my career. Without them it would not have been possible.

Secondly, I would like to thanks to my colleagues at CAR for creating an ideal environment in which to work and, above all, to share moments. And especially to Gabriel, for having supervised this Master's Thesis and for his advices and his infinite help; and to Tom, for being the second half of this project.

Thirdly, I am very grateful to Álvaro and Eduardo for the opportunity to work on this project, their confidence from the beginning, their patience and their willingness to meet when I needed them.

Finally, I would also like to say a few kind words to all the teachers that I have had throughout my life. They have been more or less demanding, but they have all contributed to my training over these years and to my becoming the person I am today.

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List of Acronyms

ETSIT: Escuela Técnica Superior de Ingenieros de Telecomunicación.

UPM: Universidad Politécnica de Madrid.

TFG: Trabajo Fin de Grado.

AI: Artificial Intelligence.

CT: Computed Tomography.

MRI: Magnetic Resonance Imaging.

PET: Positron Emission Tomography.

ROS: Robot Operating System.

IMU: Inertial Measurement Unit.

PCB: Printed Board Circuit.

GPi: Globe Pallidus internus.

MLR: Mesencephalic Locomotor Region.

SLR: Subthalamic Locomotor Region.

CLR: Cerebellar Locomotor Region.

fMRI: Functional Magnetic Resonance Imaging.

BOLD: Blood-Oxygen-Level-Dependent.

IMU: Inertial Measurement Unit.

SPI: Serial Peripheral Interface.

I2C: Inter-Integrated Circuit.

RTP: Real-Time Playback.

SDA: Serial Data Line.

SCL: Serial Clock Line.

BPF: Band Pass Filter.

AFO: Adaptative Frequency Oscillator.

Chapter 1

Introduction

Biomedical engineering was borned with the aim of applying a technical knowledge in the health sector to make better the monitoring and treatment of patients. To start with, it is irrefutable the increasing use of robots for surgeries. The first robotic surgery took place in Spain in 2005, when Da Vinci robot was used to treat a patient with a prostate tumor [1]. From this moment, the number of Da Vinci robots in Spain raised and a new surgical robot appeared, Hugo, which did its first operation in Spain last year and with as good results as Da Vinci [2].

In second place, the monitoring of patients has experimented very important advances in terms of reliability and the information that it could be obtained from a measure. Due to very comfortable wearable, it is possible to analyze circadian rhythm or neurohormonal factors in a short-term measure (within 24h) or to study vascular factors and determine choice of antihypertensive therapy in a medium-term or long-term measures (day-to-day and visit-to-visit, respectively) [3].

Thirdly, it is a well-known fact the excitement AI has generated in the medical imaging research and how it is opening a world of possibilities. Despite it has a lot of aspects to improve, at this moment, it is becoming a very important tool in oncology. Specially for the screening, prediction and treatment of different neoplasms. Additionally, it is important to have in mind that it is compatible with the typical medical imaging modalities like CT, MRI, PET or ultrasonography [4].

Furthermore, the world of protheses has a longer life that it could be expected. The first prothesis of the world was made around 3000 thousand years ago and even in that moment, they tried to create a prothesis as adjustable as possible [5]. Nowadays, there are different types of prothesis available, that they will be analyzed in the next section, which offer a huge range of functionalities and are easily portable and easy to use daily. The present Master's Thesis focuses on the design and implementation of a neuroprothesis to study if afferent stimulation has a positive effect in the treatment of freezing of gait in patients with Parkinson's Disease.

1.1. Clinical problem

Parkinson's disease (PD), which is estimated to afflict 7 to 10 million people all over the world, is defined as Non-Communicable Disease (NCD) without cure that subject to numerous comorbidities and with a huge economic burden to patients, their families, and to the healthcare system [6].

The main treatment is focus on keeping the patient functioning independently as long as possible while minimising disability. For this purpose, the most typical treatment is medication. However, there are some conditions in which it is not the best solution, like patients who do not feel any effect of the medication or patients that cannot take specific medication. Moreover, if we assume that the majority of patients with this disease are old people, surgical solutions are not advisable.

Freezing of gait is one of the most disabling symptoms of this disease. It is estimated that more than 63 % of patients suffer from this symptom being more prone men who started to feel the disease in the left side, with early gait abnormalities, higher daily dose of Levodopa and other symptoms like hallucinations, depression or anxiety [7]. Nevertheless, apart from some studies in which the effect of physiotherapy and medication was analyzed for the improvement of symptom [8] or some studies in which they used vibration stimulation [9] [10], there is no real solutions for this problem.

As a result, the main aim of this Master Thesis is to develop a system that could help to go deeper in the research of this symptom.

1.2. Motivation and objectives summary

The main motivation for developing this Master's Thesis is the big number of patients with Parkinson's Disease who suffer freezing of gait events without any actual solution. Furthermore, despite investigators have done some research about walking patterns and the influence of vibration in the gait cycle, there are neither clear conclusions nor a system for further study.

As a result, the aim of this Master's Thesis is to create an afferent stimulation system that is synchronized with the gait cycle and can be used to move forward in the research of freezing of gait. Moreover, it could be a new solution that can be used as a treatment in the near future.

To reach this objective, the system is composed by: inertial measurements units, which monitors the position of different parts of the body of the patient; a microprocessor, that receives the information from the inertial measurement units and it controls the behaviour of the actuators; and, motors, that are used to stimulate the muscles of the patient.

1.3. Expected organization and planification

In what follows, the steps followed to develop the research project are enumerated:

1. Familiarization with Python and ROS.
2. Familiarization with Raspberry Pi 4, IMUs and motors.
3. To analyse IMUs functioning, to see if we are able to get the relevant data for our system, publish it on ROS and detect the peaks that correspond to the different phases of the gait.
4. To design a circuit able to cover our aim that could be easily portable and allow us to stimulate the motors without problems of power supply.
5. To do a first integration of all the components.
6. To do some tests with people to analyze if the system is working properly.
7. To design a PCB to integrate all the components in a better way.
8. To do some tests with healthy people to analyze their speed, equilibrium and posture control.

1.4. Report structure

This document is divided into 6 chapters in which the steps followed for the development of this Master's Thesis and other relevant aspects are explained in detail:

In Chapter 1, a brief introduction to the clinical problem and their existing solutions are shown. Moreover, motivation and objectives have been set out. In Chapter 2, Parkinson's Disease, its symptoms, diagnosis and treatment are explained. Furthermore, freezing of gait symptom is presented. In Chapter 3, the hardware needed for the correct functionality of the system and the communication between the components have been described. In Chapter 4, the way the data is transmitted from one components to others, the treatment needed to apply to the signal and the creation of a graphical user interface is explained. In Chapter 5, the results of the different tests performed are presented. Finally, in Chapter 6, the conclusions drawn from this Master's Thesis are presented, as well as future lines of action.

Chapter 2

Parkinson's Disease and Freezing of Gait: Diagnosis and Treatment

2.1. Parkinson's Disease

Parkinson's Disease is considered the second most common age-related neurodegenerative disorder after Alzheimer's Disease [11]. It is an idiopathic disease that was first described as a "shalking palsy" by James Parkinson in 1817 [12]. Its prevalence is between 0,3 and 0,4 % in the general population, 2% in people older than 60 years and 4% in people older than 80 years [13].

To understand better the physiology of this disease, it is important to have in mind that the nervous system is composed by individual units known as nerve cells or neurons. They make possible the communication between the brain and other parts of the body through the use of neurotransmitters [11]. Additionally, we cannot talk about Parkinson's Disease without talking about the extrapyramidal system. It is a component of the motor system that goes from the brain to the spinal cord, as it is shown in Figure 2.1, and it causes involuntary reflexes, movement and modulation of the movement.

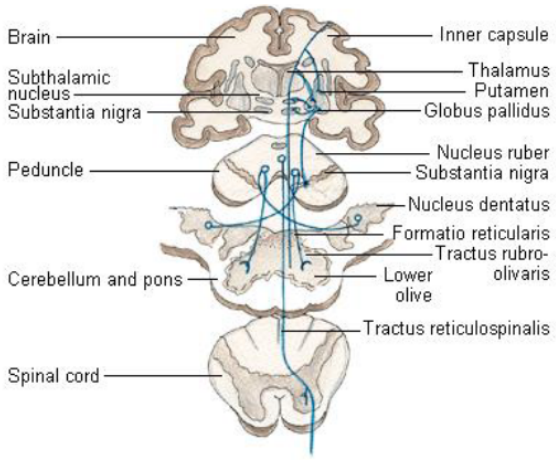


Figure 2.1: Extrapyramiral Motor System [14].

Its principal functions are [15]:

- Regulation of voluntary motor activity.
- Control of the muscle tone.
- Maintenance of emotional and associative movements.
- Inhibition of involuntary movements (hyperkinesias).

When the extrapyramidal system fails, it could cause a disturbance in the control of voluntary motor activity resulting in involuntary movements that could be rhythmic and regular (typical in parkisonism) or dysrhythmic and irregular (more common in chorea, athetosis and distonia); disturbance in the normal muscle tone resulting in hypertonia (rigidity); and, disturbance in the maintenance of emotional and associated movements resulting in bradykinesia (mask face, infrequent blinking and loss of swinging during walking). This disturbance can ocassionate two main types of extrapyramidal disorders: the akinetic-rigid syndromes in which poverty of movements predominates and the dyskinesias in which there are a variety of excessive involuntary movements [16].

Parkinson's Disease belongs to the first group of extrapyramidal disorders mentioned above. In general, the 95 % cases of this disease are caused by the degeneration of the nigrostriatal system. In a normal situation, neurons in the substantia nigra produces a neurotransmitter called dopamine, which has an important relevance in movement and it helps to transmit messages within the brain to make sure muscles produce controlled and purposeful movements. In a patient with this disease, the production of dopamine is significantly reduced and this is translated into abnormal nerve firing patterns that impair the movement [16].

Additionally, it is believed that alpha-synuclein has an important role in this disease. It is a protein that, in a normal functionality, is in charge of the storage and release of neurotransmitters. When there is a mutation, this protein is produced without control and it forms aggregates that result in tiny protein threads called fibrils, which make possible the formation of Lewy bodies, abnormal structures also sign of Parkinson's Disease and also present in others diseases like dementia [16].

Furthermore, it is important not to forget that the other 5% of patients with Parkinson's Disease is caused by genetic fators. Specifically, when there is a mutation in chromosome 4 or 6. If there is a mutation in chromosome 4, it is translated into a bad folding of alpha-synuclein in the presynaptic neurons. On the other hand, if there is a mutation in chromosome 6, it produces anomalies in Parkin proteine, which is in charge of protecting neurons by the elimination of bad folding proteins. If this proteins has anomalies, it is not able to eliminate the aggregate of bad folded proteins occasioning the dead of the neuron [16].

2.1.1. Symptoms

As it is mentioned above, Parkinson's Disease is a nervous system pathology, so the main symptoms are related to problems in the movement. The five more important are:

- Bradykinesia: it is the most important symptom in Parkinson's Disease. It means slowness of movement and it is presented in different ways: reduction of automatic movements, difficulty in initiating voluntary actions, general slowness in physical movements and an abnormal stillness or a decrease in facial expression [17].
- Akinesia: it is related to the previous symptom but, in this case, there is a loss of emotional and associative movements. It produces immobility in the face, infrequent blinking, monotonous speaking, bad coordination and the impossibility of produce the natural swinging of arms while they are walking [16].
- Stiffness in muscles: it is more common in proximal than in distal muscles and in flexor than extensor muscles. This makes more difficult to do movements and walk, which results in an slow walking with short steps [16].
- Static tremor: this is the most known symptom related to Parkinson's Disease. It is rhythmic and asymmetric and it could start in a hand and expand to the rest of the body[16]. It is increased with anxiety periods and reduced while the patient is sleeping or doing specific movements [18]. To know if a tremor belongs to Parkinson's Disease or to another medical problem like a trauma, there is a simple test which consists on asking the patient to do another activity. If it is a parkisonian tremor, it is going to remain the same frequency whereas in a tremor caused by another pathology, the frequency is going to change.
- Freezing of gait: it is a phenomenom which takes place in advanced Parkisonians syndromes. Freezing is a temporary involuntary inability to move and it is typical in patients with this disease in a mid-stage or advanced stage. Specifically, in freezing of gait, this inability to step occurs on initiation or turning while walking [7]. This symptom will be explained in more detail in Section 2.2.

2.1.2. Diagnosis

The main procedure that doctors have for the diagnosis of this disease is by different test in which they analyze patients' capabilities doing specific activities. The exam starts from the moment they enter to the room when doctors put their attention in their walking, how they communicate or how they develop easy tasks like open and close the door or to sit in the chair. Once they are in the room, neurologist perform different tests to evaluate if they have any of the symptoms mentioned in the

previous section. They tend to test bradykinesia, rigidity, tremor and walking. For bradykinesia, they use rapid alternative movements exercises such as finger and toe tapping, open and close the hands or pronation and supination of hands. To test the rigidity of the patients, they do a passive manipulation of the extremities. In the case of tremor, they do different exercises to test resting, kinetic or postural tremor. And finally, to analyze the symptoms related to gait and balance abnormalities they ask the patient to stand up from their chair, to do free walking or a pull test to analyze their balance, where neurologists tries to make patients fall backwards in order to see how they correct their position [19].

In general, the exam has a subjective result based on the neurologist's experience and the ability of the patients for each exercise. Nevertheless, there are some objective scales and the most known is the Unified Parkinson's Disease Rating Scale (UPDRS), which evaluates four parts: intellectual fuction, mood and behavior; activities of daily living; motor examination and motor complications [20]. All those parts are scaled with marks from zero (normal results without problems) to four (severe problems). Despite it seems to be a more complete exam, it is only used for research activities because it takes too much time to do it in consultations.

2.1.3. Treatment

At this moment there is no cure for Parkinson's Disease, so the treatment is focused on reducing the symptoms to get that patient could have a normal lifestyle. The main techniques to face it can be divided into three groups: pharmacology treatment, invasive solutions and other methods.

In terms of a pharmacology treatment, there are two main possibilities: to raise dopamine levels or to reduce acetylcholine levels. To increase dopamine levels, one option is to use L-Dopa, which is the metabolic precursor of dopamine. By increasing L-Dopa levels in the brain, more dopamine is secrete by neurons and the symptoms are significantly reduced. This is a temporal solution because, in a long-term, neurons die and it has not any effect [16]. Additionally, there are some secondary effects like dyskinesia or hallucinations. Another possibility is to take dopamine agonists, which helps to stimulate the production of dopamine in the brain. It could also helps to take some enzyme inhibitors like MAO-B inhibitors or COMT inhibitors, which increase the amount of dopamine by reducing the enzymes that break down dopamine in the brain. On the other hand, to reduce acetylcholine levels, they are used antihistaminics or anticholinergics that helps to reduce tremors and muscle rigidity [21].

Furthermore, there are four main invasive solutions: fetal tissue transplantation, neural stem cell transplantation in the black area, pallidotomy and deep brain stimulation. The aim of fetal tissue transplantation is to re-establish the secretion of DA in the neostriatum. For this purpose, tissue is obtained from the SN of aborted human fetuses and implanted into the caudate nucleus and putamen. Then, fetal

cells grow in their new host and secrete DA, reducing symptoms. The problem is that alpha synuclein protein also affect to this new cells and this could aggravate the symtoms causeing more severe dyskinesias, so it is no longer recommended. In second place, with neural stem cell transplantation it is pretended to introduce in the black area cells able to develop neurons that can produce dopamine. At this moment, it is in research phase but, they have discovered that the transplantation of a large numerous of cells has a positive effect in their survival and the first tests with monkeys has showed that their motor behavior has improved. Thirdly, in pallidotomy, GPi is located by MRI asking patients to move their hands and, when you touch the GPi, the movement stops and you have found it. Once its location is known, it is burned by a low intensity and high frequency stimulation. With this technique, metabolic activity in premotor and supplementary motor areas returns to normal levels. Finally, in deep brain stimulation, there is an implanted electrode into subthalamic nucleus, to control all symptoms of Parkinson's Disease, but it has some disadvantages like the need of periodic adjustements and battery changes, risk of infection and possible complications during the surgery [16].

Additionally, there are other techniques that help patients to manage better their symptoms. For example, there are physical, occupational, and speech therapies, that helps them with gait and voice disorders, tremors and rigidity. Another typical treatment is to do rehabilitation with physiotherapists in which they do massage therapy to reduce their tension and some exercises to strengthen muscles and improve balance, flexibility and coordination.

2.2. Freezing of gait

Firstly, to understand correctly what is the freezing of gait, it is essential to know what the gait cycle is. It could be defined as a period of time between any two nominally identical events in gait process [22]. Those events correspond to the moment in which one foot touch the floor with its tip and the moment in which the same foot touch the floor with its heel. In a normal gait cycle, two different phases can be differentiated: stance phase (around 60 % of gait cycle), in which the foot is in contact with the floor; and swing phase (around 40 % of gait cycle), in which the foot is in the air, without contact with the floor [22].

If a more exhaustive study about each phase of the gait cycle is done, five different sequential sub-phases in the stance phase could be found and three sub-phases in the swing phase. The stance phase is composed by: initial double support, when the tip of one foot and the heel of the other are in contact with the floor; an initial contact of one complete foot whereas the other starts to be in the air; a middle contact of the same foot when the center of mass changes due to the movement of the other foot; a terminal contact of the same foot when the center of mass changes again; and, finally, a second double support, in which the foot that was in contact with the floor starts to lose the contact and the other starts to have it. On the other hand, the swing phase is

composed by: an initial swing, in which the foot in the air goes backwards; a middle swing, when the foot in the air cross the vertical position; and, finally, a terminal swing, when the foot in the air is close to be in contact with the floor. Everything can be seen more clearly in the next picture [22].

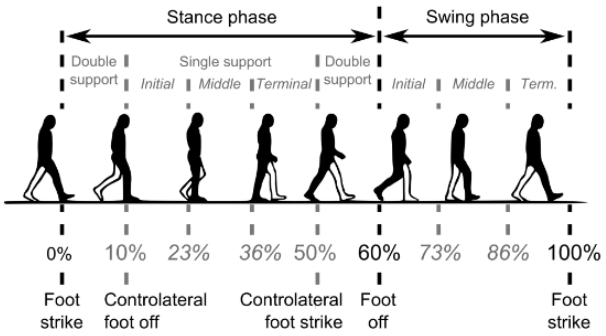


Figure 2.2: Temporal divisions of the gait cycle.

As it has been explained in Section 2.1.1, freezing of gait is a brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk [10]. It is estimated that more than 63 % of patients suffer from this symptom being more prone men who started to feel the disease in the left side, with early gait abnormalities, higher daily dose of Levodopa and other symptoms like hallucinations, depression or anxiety. It is more usual to take place when patients are initiating their gait, turning or passing through narrow spaces. Between the levels of freezing of gait, it can be observed trembling in place, shuffling forward or complete akinesia [7]. It is very important to face this problem because it has a very negative effect in patient's quality of life causing falls that could result in more dangerous pathologies like infections.

On the basis that there is not too much knowledge about the pathophysiology of freezing of gait and in which part of the brain it is originated, there are some hypotheses. But, to understand in a better way those theories, it is important to have in mind what are the main locomotor regions involve in the process of walking. They are: the MLR in the mesopontine tegmentum, the SLR in the lateral hypothalamic region and CLR in the mid-part of the cerebellum [7].

The first hypothesis is related to substantia negra, which is an important part in the basal ganglia in charge of producing dopamine that has a crucial role for the modulation of motor movement. It suggests that freezing of gait is caused by the uncontrolled raise of substantia nigra pars reticulata, which inhibits the MLR [7].

A second theory appeared due to the use of resting-state fMRI in a study with 17 patients [7]. This is a technique which measures spontaneous low-frequency fluctuations in the BOLD signal [23] to analyze the functional structure of the brain. The results of this research open the possibility that freezing of gait could be the

consequence of a frontal activation of an inusual stopping signal that goes to the STN.

The last hypothesis that it is going to be mentioned suggests that freezing of gait is the result of a reduced functional connectivity in sensorial areas related to the motor activity. As a consequence of this reduced functional connectivity between the MLR and the CLR with the SMA, there is a reduction in the automatic control of movement [7].

To treat this invasive symptom, a non invasive therapies have been applied. The difference between both of them is that the first one requires a surgical intervention whereas the second one can be used without surgery. The first group is composed by deep brain stimulation of the subthalamic nucleus, globus pallidus internus, pedunculopontine nucleus and spinal cord stimulation while transcranial magnetic stimulation, transcranial direct current stimulation and noninvasive vagus nerve stimulation are the main used techniques in the second group [7].

Deep brain stimulation consists on the activation of the different parts mentioned above by the implantation of electrodes. In the case of subthalamic nucleus, some improvements have been identified in aspects like tremor or dopaminergic medication control but it is not clear how efficient it would be for freezing of gait, with a little improvement long time after the surgery. Secondly, the stimulation of globus palllidus internus provide patients only a temporal improvement [24]. On the other hand, the best results have been obtained for a stimulation in the pedunculopontine nucleus. The symptom is significantly improved by the conditions that it has to pass three months after surgery in the drug-OFF state. One thing that it could come to our minds is if it is better to have a bilateral or an unilateral stimulation and some studies have revealed that with an unilateral stimulation the number of falls is significantly reduced at least one or two years after the surgery. Furthermore, spinal cord stimulation (inspired by the good results obtained in akinesia, abnormal gait, posture and bradykinesia with epidural stimulation of the spinal cord) has presented also important improvements in freezing of gait, being more representative in patients who has been treated before with deep brain stimulation or patients without pain [7].

Additionally, between the non invasive treatments, transcranial magnetic stimulation is a technique in which electromagnetic coil is placed against the scalp of the head. Then, a rapidly changing magnetic field is applied to the superficial layers of the cerebral cortex, that induces small electric currents [25]. It has presented very optimistic results with improvements in the gait in ten days after the therapy and with long term effects [26]. In second place, transcranial direct current stimulation is a procedure in which due to a portable system, a fixed current between one and two amperes is typically applied and, has also showed very promising results [27]. Finally, in vagus nerve stimulation the auricular branch of the vagus nerve and the cervical vagus nerve are activated by the use of a medical portable device [28]. It has been reported a reduction of freezing time after this treatment [29].

Furthermore, the use of motors in different muscles to produce an afferent stimulation is a non invasive alternative treatment that it has not been mentioned above and it is on research. There are studies [9] which agree that it would be beneficial for the gait cadence and speed in patients while other studies [10] suggest that it may not have a significant effect.

As result of the absence of consensus with the last treatment, this Master's Thesis focus on it. A neuroprosthesis of afferent stimulation is going to be designed and implemented to understand if the last treatment would be effective and in what way best results can be obtained.

Chapter 3

Description of hardware

Figure 3.1 shows a diagram of the hardware system to design. Firstly, a group of accelerometers receives information about the orientation, acceleration and gyro of predefined parts of the patients' body. They send all these data to a microprocessor. The microprocessor, depending on the information received, activates specific actuators. Finally, the actuators stimulate some muscles of the patient according to the moment in which they are involve in the gait. The system is shown as a close loop, because when the muscles are stimulated, they cause changes in the posture of the different parts of the patient's body and the process repeats. Hereafter, the different components of the system are described in detail.

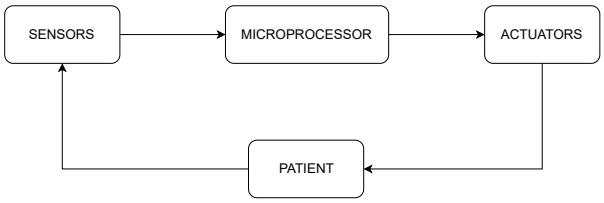


Figure 3.1: Block diagram that shows all the components of the system.

3.1. Sensor

The IMU BNO055 [30] will be used as inertial sensor (see Figure 3.2). As we can see, the main pins of this component are: Vin, that must be supply with 3,3V; GND, that must be connected to the GND pin of the microprocessor; and, SDA and SCL, which correspond to the data and clock lines of the I2C communication.

Figure 3.2: IMU [31].

Additionally, it is important to consider that this sensor has 9 DoF. In this context, a DoF refers to the different types of motion or orientation data that can be obtained. They are:

- **Absolute Orientation (Euler Vector)**: it is a three axis orientation data based on a 360° sphere. It can be transmitted at 100 Hz.
- **Absolute Orientation (Quaternion)**: it is a four point quaternion output which allows a more accurate data manipulation. It can be transmitted at 100 Hz.
- **Angular Velocity Vector**: the output is a three axis 'rotation speed' in rad/s. It can be transmitted at 100 Hz.
- **Acceleration Vector**: it is three axis of acceleration (gravity + linear motion) in m/s^2. It can be transmitted at 100 Hz.
- **Magnetic Field Strength Vector**: it is a three axis of magnetic field sensing in micro Tesla. It can be transmitted at 20 Hz.
- **Linear Acceleration Vector**: it is a three axis of linear acceleration data (acceleration minus gravity) in m/s^2. It can be transmitted at 100 Hz.
- **Gravity Vector**: it is a three axis of gravitational acceleration (subtracting any movement) in m/s^2. It can be transmitted at 100 Hz.
- **Temperature**: it is the ambient temperature in degrees celsius. It can be transmitted at 1 Hz.
- **Fused Absolute Orientation**: it is data calculated from the Linear Acceleration Vector, the Angular Velocity Vector and the Magnetic Field Strength Vector.

The parameters that we need for this study are: the angular velocity, whose data are used for the detection of the gait cycle; and the absolute orientation, which help us to know the inclination of patient's body.

3.2. Microprocessor

The microprocessor will be in charge of managing the communication between the sensors and the actuators. It will receive data from the IMUs and based on it, it will stimulate a specific number of actuators with a predefined vibration frequency. The microprocessor chosen for this system is the Raspberry Pi 4 [32] (see Figure 3.3).

Figure 3.3: Raspberry Pi 4 [33].

Between the main characteristics of this microprocessor, the most relevant for this project are the following:

- It uses a Quad core 64-bit ARM-Cortex A72, which requires less energy than other options and it is able to work at 1.5 GHz.
- It requires a good quality USB-C power supply capable of providing 5V at 3A.
- It has two pins able to provide a supply of 3.3V and two pins that can provide 5V to other components.
- There are four pins that can be used for Pulse Width Modulation (PWM), which is the conversion from digital signal to analog signal. In general this type of modulation is used to define the period of time in which a component is active.
- There are some options for the communication between the microprocessor and other components. Between them, there are five pins that can be used to establish a SPI communication, which allows the exchange of data between a master and a slave; two pins for the UART communication, which is a type of sending and receiving information where the message is transmitted sequentially bit by bit; and, four pins for the I2C communication, that it is the one that this system is going to use, how it is going to be explained in the Section 3.7.

The decision of using this microprocessor comes from the big amount of possibilities that it offers to the system, making possible to raise its functionality if it is needed in the future. It allows to work at 1.5GHz, which is enough for the speed that we need for the exchange of data. Additionally, it offers some protocols of communication between

the components and it can be programmed in Python, C++, Java and JavaScript, among others.

3.3. Actuators

In the beginning, the actuator considered for this system was the 5mm Vibration Motor Model 304-116 [34] (see Figure 3.5a). It has a Rated Vibration Speed of 16,700 rpm [± 3,700] with a Typical Normal Amplitude of 1G.

As shown in Figure 3.4, the input voltage variates from 0V to 3.6V and, depending on it, the vibration amplitude, current consumed and frequency of vibration change.

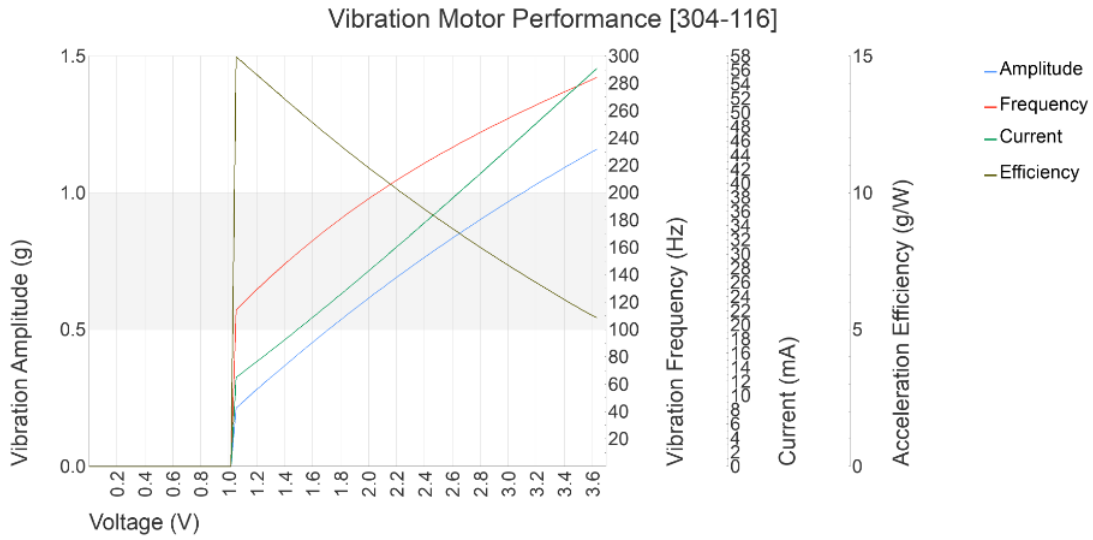


Figure 3.4: 5 mm Vibration Motor Model 304-116 performance [34].

However, with this motor it is not possible to select an accurate frequency of vibration lower than 120 Hz. This represent an issue because a vibration frequency of 80 Hz is needed. This value has been chosen because it has been demonstrated that stimulation at this frequency drives kinaesthetic illusions and, as a result, it modulates proprioceptive uncertainty [35].

To solve this problem, another motor has been selected. Specifically, the 9mm Vibration Motor Model 307-103.005 [36] (see Figure 3.5b). This motor has a Rated Vibration Speed of 13,800 rpm [± 2,700], a little bit smaller than the previous one, but with a Typical Normal Amplitude of 7G, much bigger than the other option.

(a) 5 mm Vibration Motor Model 304-116 [34].

(b) 9mm Vibration Motor Model 307-103.005 performance [36].

Figure 3.5: Comparison between the two models of motors used in our system.

As it is shown in Figure 3.6, this motor has a more lineal behaviour, which makes possible to select the desired frequency in a more accurate way.

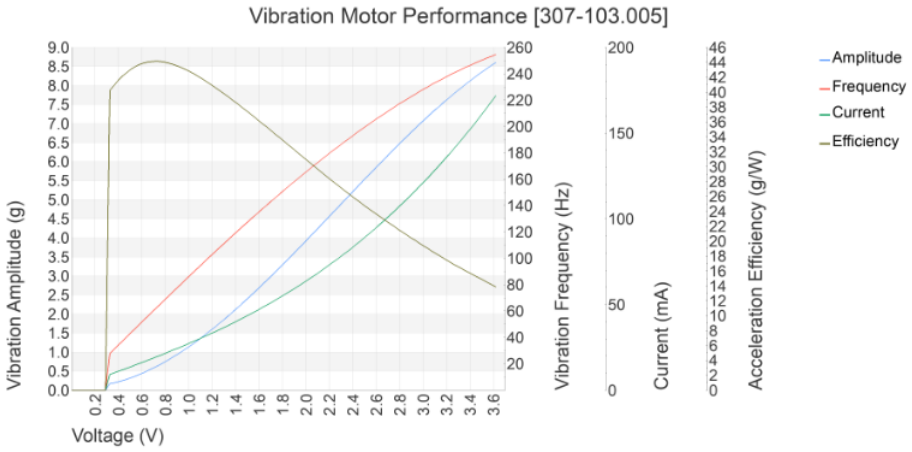


Figure 3.6: 9mm Vibration Motor Model 307-103.005 performance [36].

According to the graph, to get a frequency of vibration of 80 Hz, an input voltage of 0.9V is needed.

3.4. Driver

To control the motors, it is advisable to use the DRV2650L Haptic controller [37] (see Figure 3.7). This component is typically used because, as haptic controller, it allows to control the waveform of the output signal, what could be useful to adjust the vibration feeling.

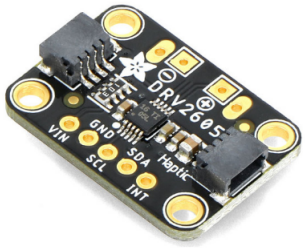


Figure 3.7: DRV2650L Haptic controller [38].

As it is shown in the picture, it has seven pins, five inputs and two outputs:

- Vin: it needs an input voltage between 2 and 5.2V.
- GND: ground.
- SCL: I2C clock.
- SDA: I2C data.
- IN: multimode input in which I2C could be selectable as PWM, analog or trigger.
- +: this output is connected to the positive wire of the motor.
- -: this output is connected to the negative wire of the motor and GND.

To use this Driver, three main options are available. The first option is to use one of the 123 predefined effects that the Driver has and that can be used to stimulate the motors [37]. In our system, a good option would be the effect 118, which is a long buzz that stimulate the motor during 10 seconds. To make the motor vibrate more than 10 seconds, this effect can be repeated as many times as needed without interruptions.

Another option could be to use the RTP Mode. This makes possible to stimulate a motor without the restriction of time. Once it is activated, it vibrates until the user stops it. To use this mode, it is needed to previously select the amplitude that it is desired, taking into account that the value 127 corresponds to the maximum amplitude and, in fact, to the maximum vibration frequency.

The third option could be to use a PWM signal that could enter to the Driver by the IN input. In this case, it could be easier to control the frequency of the motors

but it would be more difficult to stop them when needed.

Thus, taking into consideration all what it is mentioned above, the option chosen for the system is the second one. Using the RTP Mode is easier to stop the motors in the instant of time that it is needed. And, to select the desired vibration frequency (80Hz), it is important to have in mind the graph showed in Figure 3.6,. As we can see, it can be obtained by applying around 0.9V, so knowing that a value of 127 corresponds to 3.6V it is easy to adjust a value of 34 to stimulate with 0.9V. Furthermore, to check that this tension is being applied, a multimeter has meaused 0.9V in the point in which the motor is supplied.

3.5. Multiplexer

During the design process, the CD74HC4067 Multiplexer [39] has been used. As it is going to be explained in Section 3.9, its function is to make possible that motors can be stimulated independently from the others. To do this, it is important to introduce the correct inputs to S3, S2, S1 and S0, which are the ones that are going to select the stimulated output. It works with binary numbers, so to stimulate a specific output it is mandatory that the binary input corresponds to its number. For example, to stimulate the output 7, S3=0, S2= 1, S1=1 and S0=1.

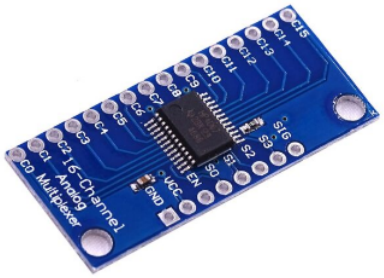


Figure 3.8: CD74HC4067 Multiplexer [40].

3.6. I2C Multiplexer

There is a limitation with the IMUs, they only have two different directions. As it is going to be explained in the Section 3.9, the system is composed by five IMUs, so there are not enough directions for them. Furthermore, eight drivers are going to be used for our system but only one direction is available for them.

To solve this issues, a TCA9548A [41] is used. It is an I2C multiplexer which works as the typical multiplexer but for this type of communication.

As shown in Figure 3.9, it has the four typical inputs used in I2C: Vin, GND, SDA

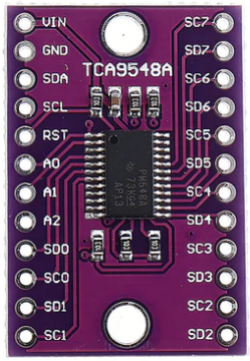


Figure 3.9: TCA9548A [42].

and SCL. This is because it also uses I2C to work. Additionally, it has three inputs (A0, A1 and A2) which makes possible to change its direction allowing eight different directions (2^3). As it is shown, due to the use of this component, it is possible to use the I2C with eight different components. They are going to share the same direction, which is the one that the I2C Multiplexer has but, they work independently from each other by selecting the correct output.

3.7. I2C Communication

As aforementioned, the protocol of communication chosen for this system is I2C. It has been chosen because, I2C is a multi-slave, half-duplex, single-ended 8-bit oriented serial bus specification, which uses only two wires to interconnect a given number of slave devices to a master [43]. As shown in Figure 3.10, the two wires needed for this protocol are SDA and SCL. SDA corresponds to the data sent whereas SCL corresponds to the clock that master and slave shares to have a synchronization in the exchange of data.

This protocol has some rules that are important to take into account before using it. Firstly, it is crucial to know that each device has a unique direction in the I2C bus, which is typically composed by 7 bits. Secondly, all transactions are always initiated and completed by the master. And, thirdly, all message exchanged in the I2C bus are divided into two frames: address frame, in which the master select the slave to communicate with; and data frame, which is 8 bits of information transmitted from the master to the slave or from the slave to the master. As it can be seen in the Figure 3.11, all transactions are initiated by a Start and finished by a Stop. The Start is defined by a transition from the high level to the low level while the Stop is defined by a transition from the low level to the high level, both in the SDA Line. Both conditions are established by the master and once the transmission starts, the bus is busy.

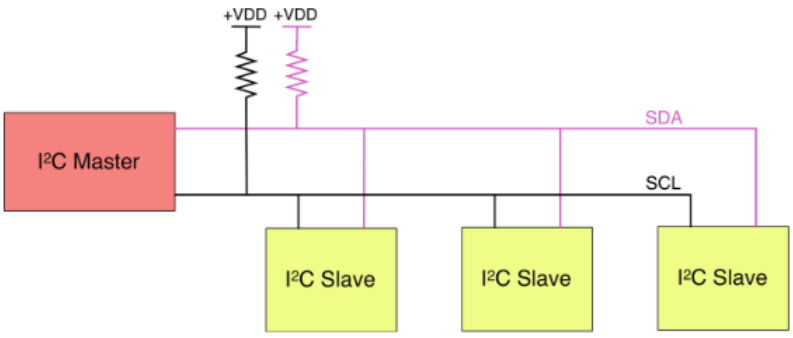


Figure 3.10: Graphical representation of the I2C bus [43].

Figure 3.11: Structure of a typical I2C message [43].

As shown in Figure 3.11, there are seven bits for Slave Address, 8 bits for the data transmitted, 1 bit to specify the action Read or Write, and 2 bits for ACK that are used to tell the transmiter that the message has been received. Furthermore, the most typical bus speed is 100 KHz and it must be defined in the protocol specification.

3.8. Power supply

As power supply the ANS Powerbank 15000 mAh Type-C 18W PD BK [44] is used (see Figure 3.12). To choose the most appropriate power supply for a system, it is crucial to know the current that each of the main components of our circuit needs to work in the worst conditions. Next, the current needed for each component and the total current consumed by our system are shown taking into account that all those components could be used:

- IMU: in the worst conditions it is going to consume 12.3 mA [30]. As explained in Section 3.9, in the final design of our system there are 5 IMUs, so the total current needed for this part is 61.5 mA.
- Microprocessor: 2.5A of supply are recommended.
- Motor: to make it vibrates at 80Hz it is necessary a current close to 60 mA. In our final design, there are 8 motors, so the current for this part is 480 mA.
- Driver: the maximum current required for this component is 3.5 mA. How 8 drivers are going to be used in the system, hence the total current for the drivers is 28 mA.

- Multiplexer: the maximum input current could be 25 mA. Taking into account that 2 multiplexers could be used, the total current for this part is 50mA.
- I2C Multiplexer: the maximum current supply required for this component is 100 mA. Two I2C Multiplexers are going to be used in the system, so the total current for them is 200 mA.
- **Total Current:** summing up all elements, a total current of 3.32 A is needed.

Figure 3.12: ANS Powerbank 15000 mAh Type-C 18W PD BK [44].

Taking into account that the powerbank chosen can provide 15,000 mAh and that we need 3.32A for all the circuit, the time that our system is able to work autonomously is close to 5 hours.

3.9. Designs

As a consequence of the limitations that the system has presented during its design, six different designs has been proposed and tested before reaching the one which it is better adjusted to our purpose. They and their limitations are explained hereafter.

3.9.1. Sensors block

3.9.1.1. Design 1

To start with, the location and number of IMUs were tested in order to know what was the best way to recollect data. In this first design, four IMUs were considered, two for each leg. One in the quadriceps and a second one in the shin, as shown in Figure 3.13.

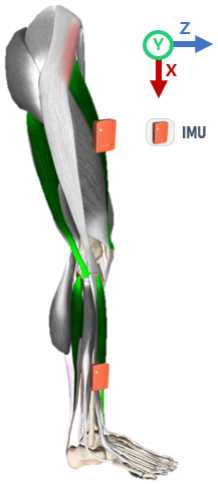


Figure 3.13: IMUs Design 1.

It is a good design because it allows to have data about all the movements of the legs but, patients with Parkinson's Disease, in some cases, walk dragging their feet. As a consequence, to put the IMUs with this location maybe is not valid in specific situations.

3.9.1.2. Design 2

In this case, five IMUs are used instead of four. The original IMUs remains in the same position, as they bring us important information but an additional IMU has been added to the chest (see Figure 3.14).

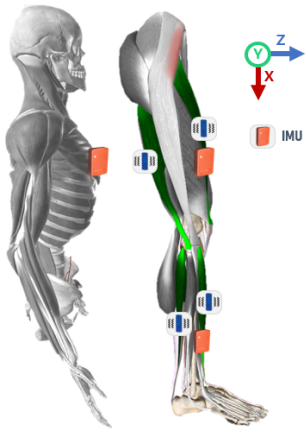


Figure 3.14: IMUs Design 2.

With an additional IMU, we can solve the previous problem. In this way, apart from the movements of the legs, the inclinations are measured, which makes possible

to do a better approximation about the gait phase.

3.9.2. Actuators block

In this part, the location of the vibration motors is going to be established from the beginning and the designs aim to get the best way of stimulating them. As shown in Figure 3.15, the muscles chosen for their stimulation are: quadriceps (Q), hamstring (HS), triceps surae (TS) and tibialis anterior (TA). It has been demonstrated that the stimulation of these muscles have a relevant influence in the inclination of the trunk and the speed of walking of the patients [45].

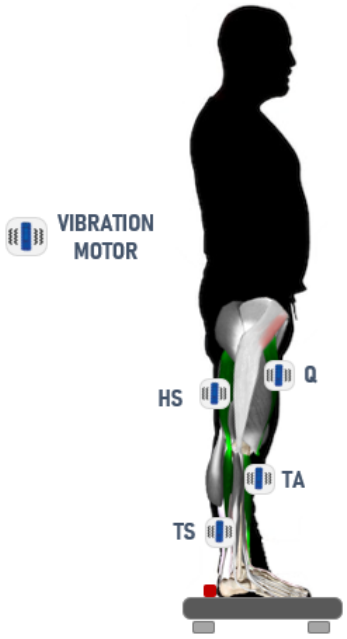


Figure 3.15: Localization of the vibration motors.

3.9.2.1. Design 3

This proposal stimulates all the motors of one leg with just one driver and multiplexer which was used to choose what output was stimulated. Figure 3.16 shows the circuit for one leg, the other would need the same circuit. One important thing to take into account is that in this design, the vibrations motors used were the Model 304-116 [34] that do not have enough amplitude to feel the vibration. As a result, two vibration motors of this model were used per muscle.

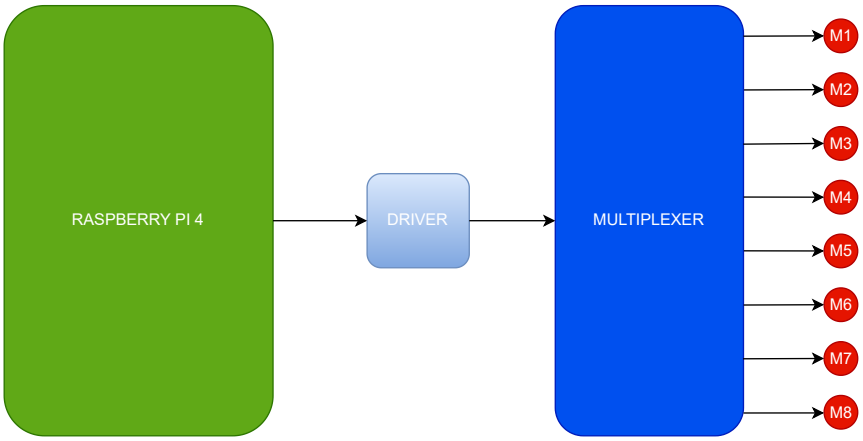


Figure 3.16: Design 3.

The problem with this design was that the current which went out from the multiplexer was not enough to stimulate the motors. To be stimulated, the vibration motors, in a regular situation, need a current of 44 mA whereas the maximum current that can go out from the multiplexer is 20 mA.

3.9.2.2. Design 4

To solve the previous problem, a power stage was used to raise the current that when out from the multiplexer and entered to the motors. To do this, a NPN transistor was used. Among all the functionalities that it could have, one of them is to use it like an amplifier with the help of a resistor. In a transistor, there are three important parts: the collector, that is the part that it is connected to the voltage in the design; the base, which is the branch connected to a resistor; and the emitter, that it is connected to the ground. To get an amplifier from this component, it is crucial to define the value of the resistor very well. To get this value, in the first place, it is needed to define the value of the current that pass through the collector, in our case a current of 100 mA because the motors need 44 mA and it is a good habit to leave a margin. Secondly, it is needed to have in mind the DC Current Gain needed for the current chosen. In this case, this value is 35 [46]. With these two values, the current for the base branch can be obtained applying the Equation $I_b = \frac{I_c}{h_F}$, where I_b is the current in the base, I_c is the current in the collector and h_F is the DC Current Gain. The value obtained is 3,33 mA that, applying the Ohm Law, the resistor needed to get the appropriate amplifier is 1,5 k Ω.

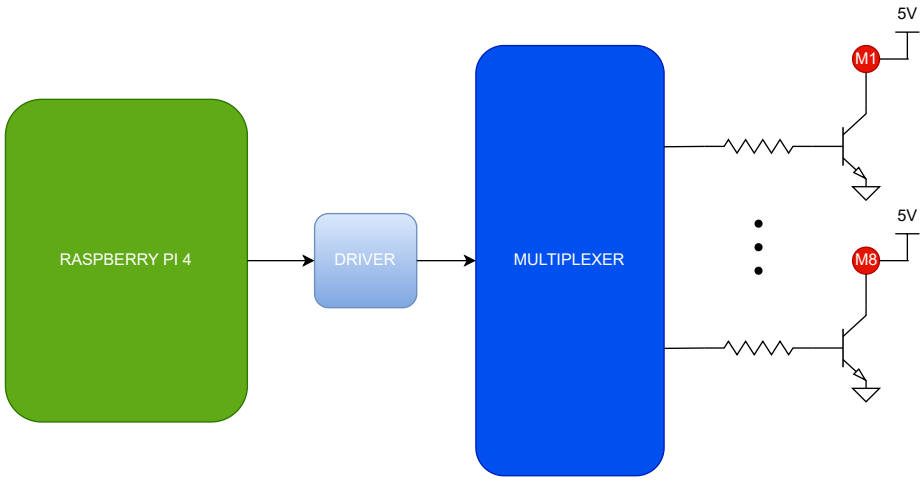


Figure 3.17: Design 4.

With this design, the problem of the supply has been solved because all the motors can be stimulated, but it is not possible to choose the 80 Hz of vibration frequency that it is needed for our system.

3.9.2.3. Design 5

To adjust the desired vibration frequency, a potenciometer has been used. As shown in Figure 3.18, it is a variable resistor that can be replaced by two resistors when its value is obtained.

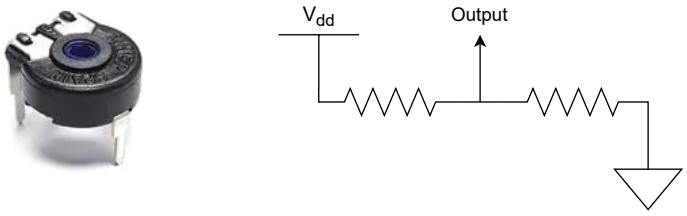


Figure 3.18: Potenciometer.

In Figure 3.19, the design for one leg with the resistors that replace the potenciometer is shown. The other leg would need the same circuit.

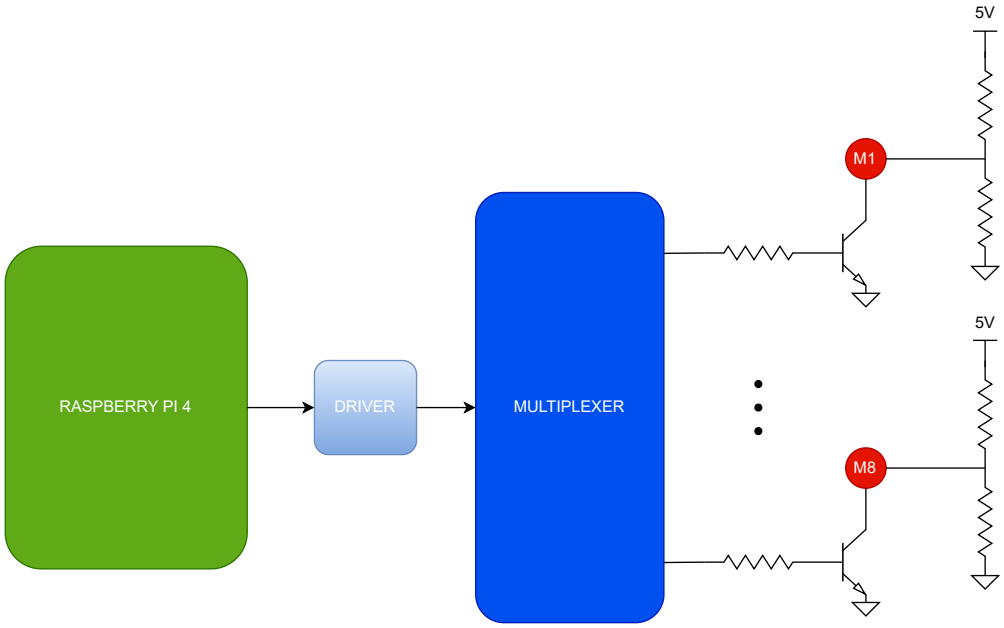


Figure 3.19: Design 5.

With this design, the vibration frequency of the motors was 80 Hz as we needed but just when all of them were activated at the same time. If one motor is stimulated and the others are off, the speed of vibration for this motor is much higher.

3.9.2.4. Design 6

The best option to solve the problem of the vibration frequency is to use one driver per motor. In this way, each motor can be stimulated independently at 80 Hz due to the use of a resistor which regulates the tension of the motor. Additionally, it is important to take into account that, for this design and the following, the motors used are the Model 307-103.005 [36], which are larger and have a bigger amplitude. As result, the vibration felt by the patient was stronger, so only one motor per muscle instead of two is used. In fact, the next picture shows the circuit needed for the actuators part of the two legs.

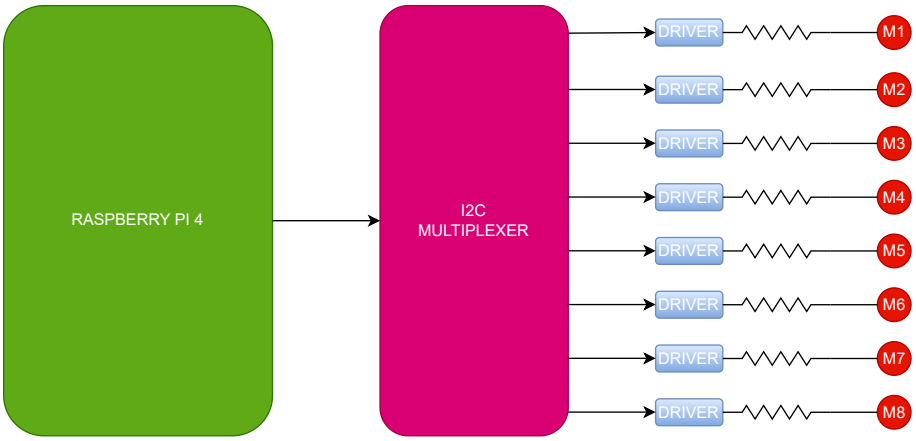


Figure 3.20: Design 6.

This design worked as it was expected, with all the motors vibrating at the desired frequency.

3.9.3. Final design

Finally, the last design could be optimize by removing the resistor by using the RTP Mode of the Driver, as explained in Section 3.4.

Thus, taking the sensor and the actuator design chosen into consideration, Figure 3.21 shows the final design of the system.

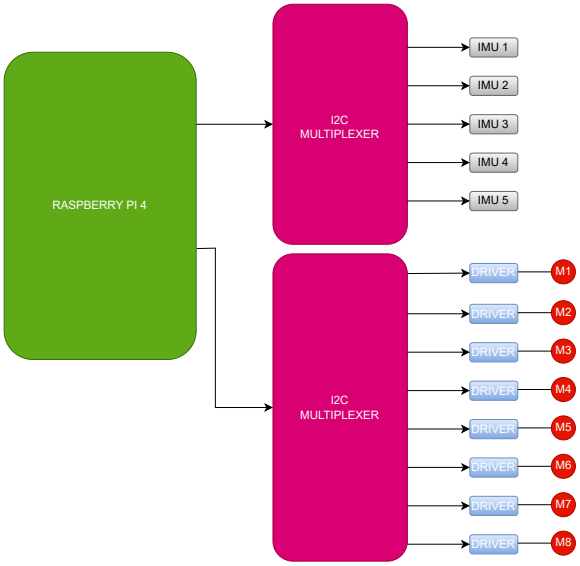


Figure 3.21: Final design.

3.10. PCB Design

The tool used for the PCB Design was *Altium Designer* [47], which is the most widely used software for the professional design of printed circuit boards.. The typical flow to make a board can be summarize in three steps: schematic, placement and routing. Additionally, if it is not possible to find a component in the libraries available, it could be needed to create the symbol and footprint of the component to use.

In the schematic stage, the aim is to define the connection of the components that form our system. For this task, it is advisable to create a main sheet with the general blocks, as it is shown below:

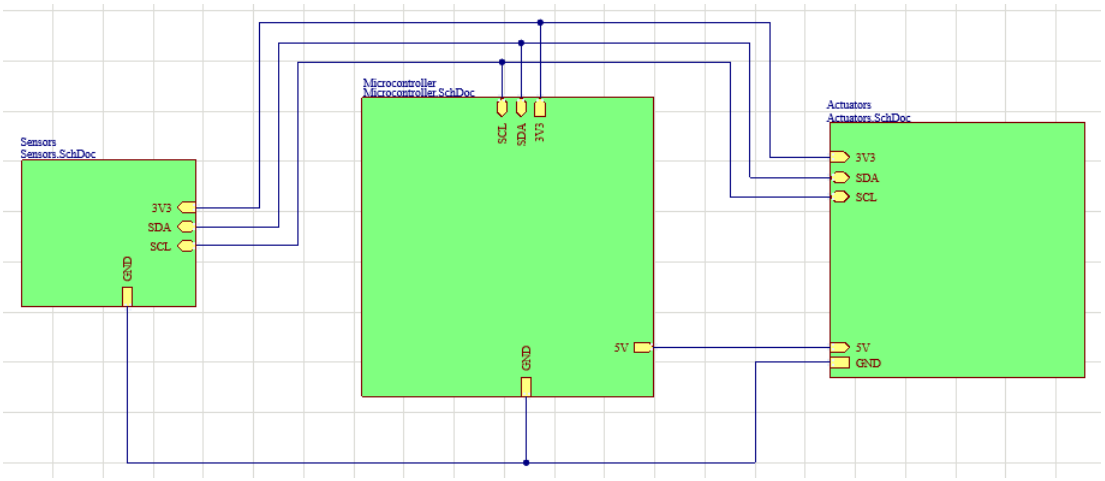


Figure 3.22: Main sheet of the schematic stage.

In this case, the same structure that has been mentioned above in this document is shown. The main blocks of this system are sensors, microprocessor and actuators. Moreover, there are the pins connection between the blocks what it is going to make us to have a cleaner view about the system and, with this, the next tasks are going to be easier.

In what follows, the all design blocks are described. The sensor circuit is shown in Figure 3.23.

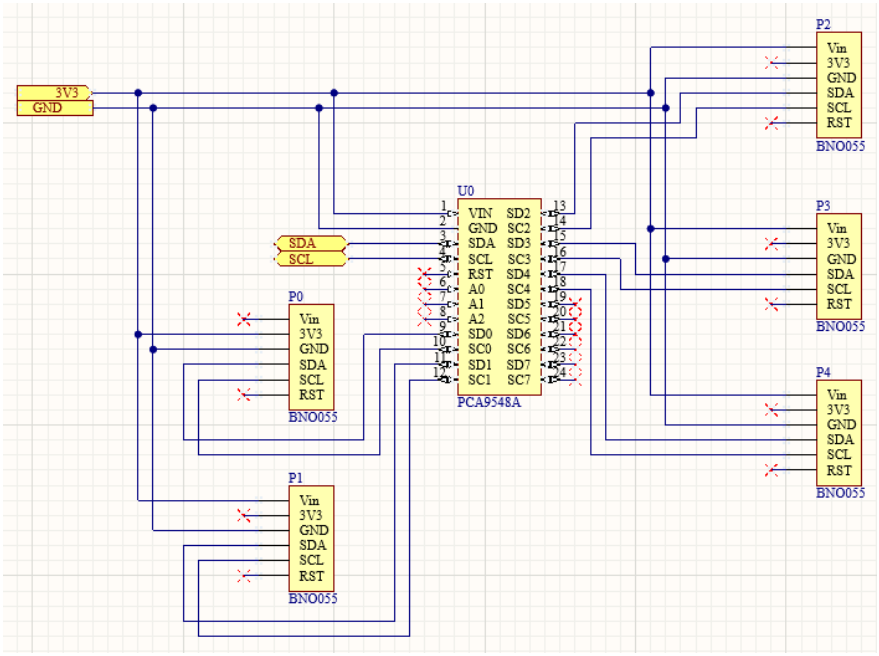


Figure 3.23: Sensor sheet of the schematic stage.

The five IMUs are directly connected to the I2C Multiplexer, that it is connected to the I2C Bus of the Raspberry Pi. It is possible that the reader could be curious about why the first IMU differ from the others in the tension pin and this is because this sensor did not have a functional input voltage inside it. But, using the 3V3 input, the functionality is exactly the same as the rest of the IMUs because they work with the same input voltage.

Secondly, the Raspberry Pi sheet is very simple as it is shown below. It was only needed to define the pins that they are going to be used.

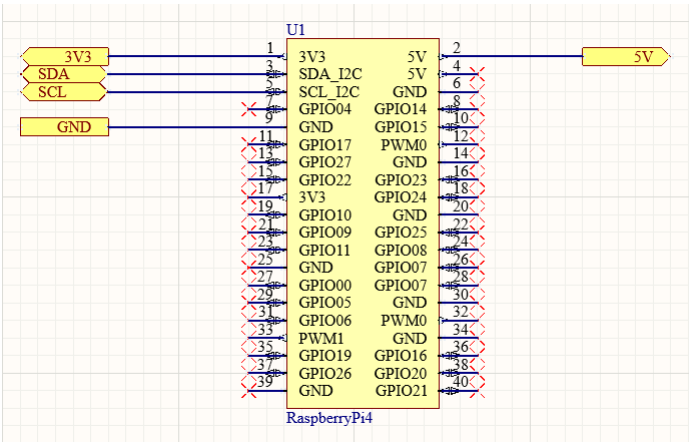


Figure 3.24: Raspberry Pi sheet of the schematic stage.

Finally, the actuators sheet is the biggest. As it can be seen, the actuators design

used for the PCB is the Design 6, which used a resistor after the Driver. Furthermore, sixteen motors connections were putted instead of eight just in case the user needs more motors. Moreover, a fuse (F1) was added between the 5V output of the Raspberry Pi and the voltage input of the Drivers to protect the microprocessor. If the circuit requires more current than the allowed, the circuit is not going to work but it is going to be avoided that the Raspberry Pi is burned due to the use of this fuse.

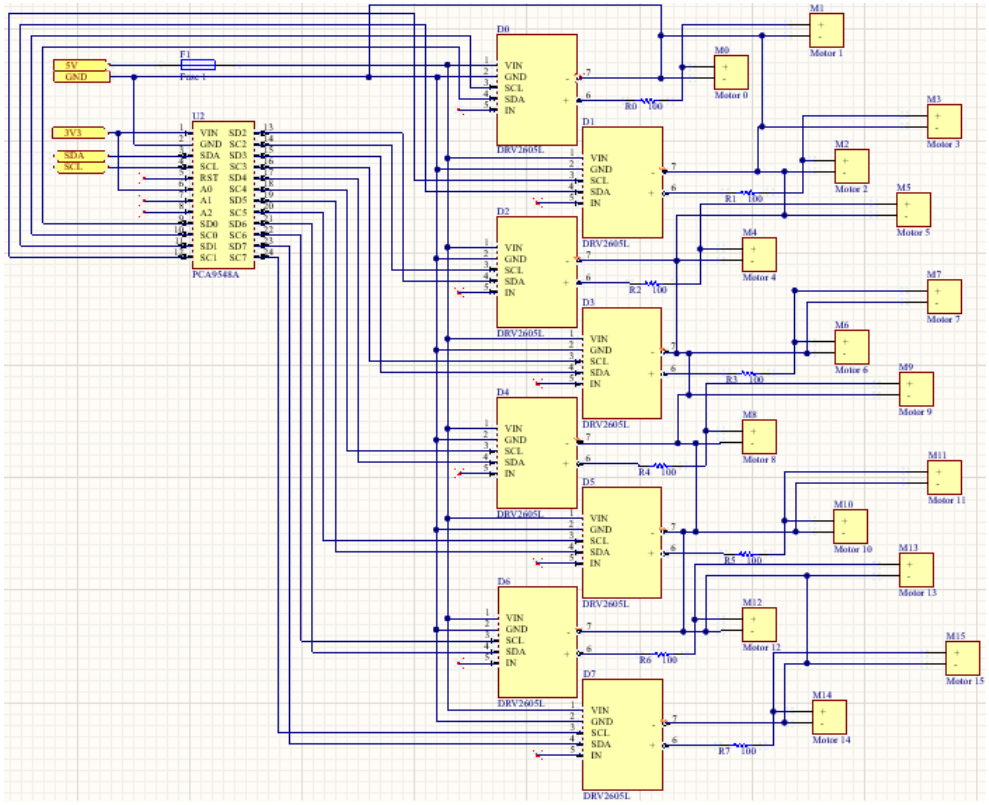
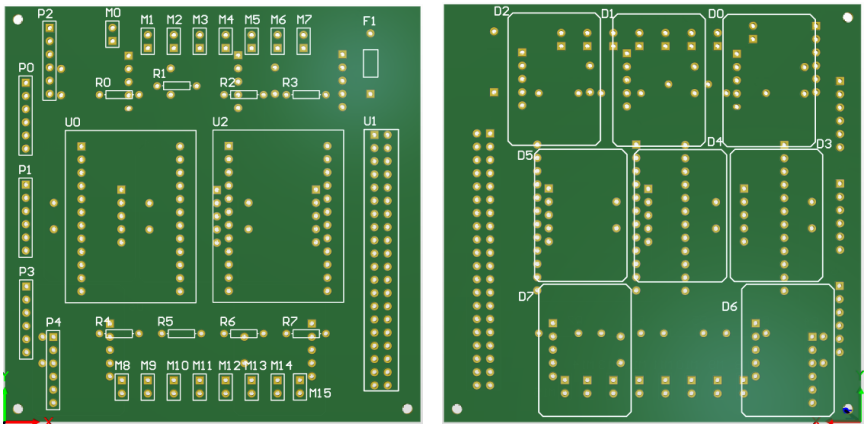


Figure 3.25: Actuators sheet of the schematic stage.

The second step in the creation of a Printed Circuit Board is the components placement. This stage requires to have some considerations before place the components. In this system, there are not an antenna or another component that could radiate the other components, so this problem has not to be considered. Nevertheless, we have some connectors that the user is going to manipulate, the ones for the IMUs and the motors. In fact, it is advisable that those connectors are in the more extrernal part of the board to avoid that he or she manipulates the rest of the components. Also, this board is expected to be connected with the Raspberry Pi, so the connector for it should be in the external part too and with the appropriate distance to the borders wich guarantees that the board is not going to collide with any component of the Raspberry Pi. To gain space in the top layer, it is advisable to put some components in the bottom layer. The components that have been chosen for it were the drivers because they are very big and it was demonstrated that their temperature are not increased with the functionality of the circuit. The last consideration is that the

components that are connected to each other must be placed as together as possible to make easier the routing.

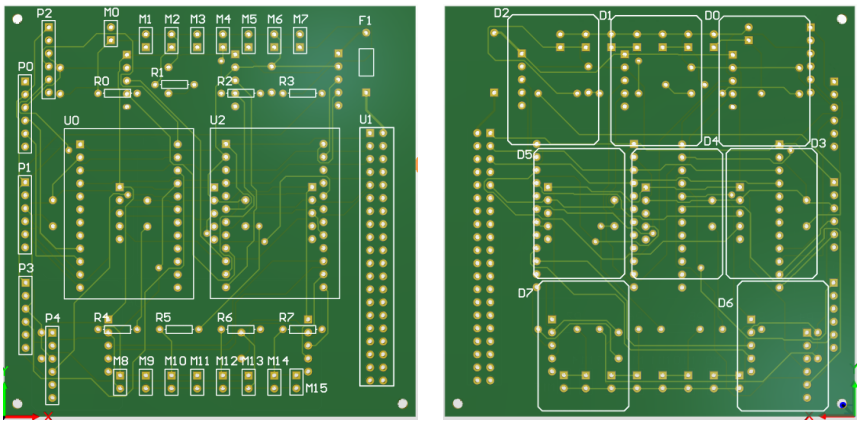
After having considerate everything mentioned above, the placements for the top and the bottom layer are shown in Figure 3.26.



(a) Top Placement of the PCB. (b) Bottom Placement of the PCB.

Figure 3.26: Top and Bottom Placement of the PCB.

The last step of design is the routing. In this stage, all the tracks are created to connect all the components as it has been defined in the schematics. To do this, it is important to take into account that any track can crash with another and that the maximum and minimum widths of those tracks are defined by the manufactures. Additionally, it is crucial the use of vias to connect the components of the top layer with the components of the bottom layer and to avoid the collision of two tracks. The result of this stage can be seen below:

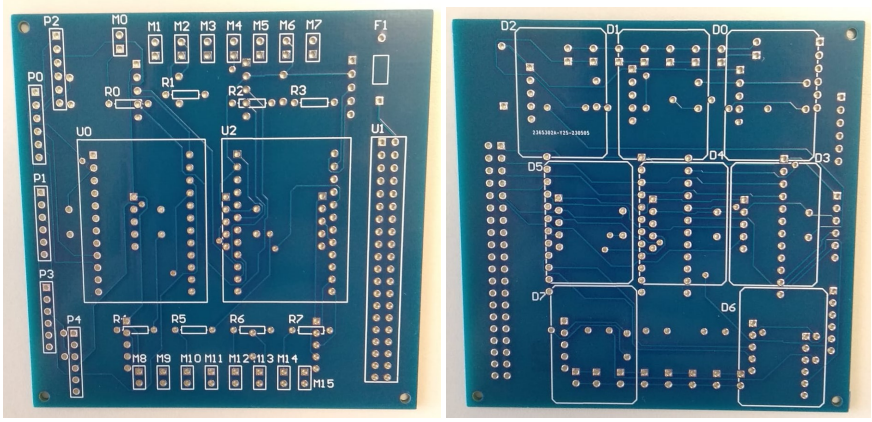


(a) Top Routing of the PCB. (b) Bottom Routing of the PCB.

Figure 3.27: Top and Bottom Routing of the PCB.

Finally, once the three steps has been done and there are no errors in the board, it has to be sent to a manufacturer to make it. The manufacturer chosen is JLCPCB, which is the main manufacturer for this boards due to its low prices, good quality and reduced delivery time.

The final result of the PCB Design is the following:



(a) Top of the PCB. (b) Bottom of the PCB.

Figure 3.28: Top and Bottom of the PCB.

Chapter 4

Description of software

4.1. ROS

Robot Operating System (ROS) is a free and open source software that defines the components, interfaces and tools for building advanced robots [48]. In this case, our system is not a robot, but it is composed by sensors, microprocessor and actuators, so it is the ideal way of sending messages between the components. Specifically, it is going to be used ROS 2, the last version of ROS, which has the novelty that it can be used in Windows 10, apart from Linux or MAC.

To understand how ROS is working, it is important to take into account that there are some main elements that should be defined in any communication that uses ROS. They are: node, topic, publisher, subscriber, service and client.

A node is an executable responsible for a single, modular task which is used to communicate with other nodes via topics. A topic is a crucial element in the communication with ROS. It works like a bus for the exchange of message between nodes. A node is able to publish data to any number of topics and have subscriptions to others. This moves the reader to the third concept, the publisher. It is a node which sends a message to the ROS graph. This message is expected to be received in other node. To get this result, it is needed that the node class is created and the topic to which it is going to send the message is defined. On the other hand, the subscriber is the node whose function is to receive the message. In the same way than before, it is necessary to create a the node class and to define to topic that it is going to send it the message. Additionally, services work in a similar way as publishers and clients work in a similar way as subscribers. The main difference is that, in this case, the client is the node which in the first place sends a request. And then, the service, is the node that responds to this request.

All these relations between the main elements of the ROS graph is shown in Figure 4.1

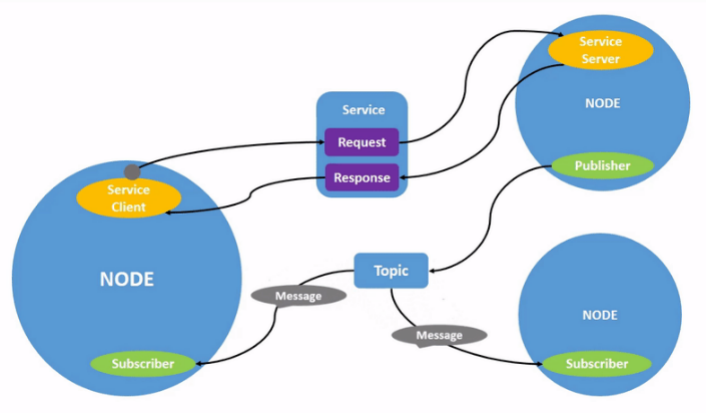


Figure 4.1: Typical ROS graph [49].

In this system, as explained in the previous chapters, IMUs are going to send data to a microprocessor which is going to stimulate motors depending on the information received. For this task, two publishers and two subscribers have been created. *ImuPublisher* is the node which is going to send the position data of legs and chest to the Raspberry Pi. For it, five topics are used: *GaitStimulator_IMU_1*, *GaitStimulator_IMU_2*, *GaitStimulator_IMU_3*, *GaitStimulator_IMU_4* and *GaitStimulator_IMU_5*. *ImuSubscriber* is the node in charge of receiving in the Raspberry Pi all the information which comes from the IMUs to do its appropriate processing. In the same way, it is a subscriber of the five topics mentioned above. For this Master's Thesis, it is going to be used a computer instead of the Raspberri Pi for the processing of the signal to simplify the number of tasks that the microprocessor has to do, as it is going to be explained in the Section 4.2.

On the other hand, once the signal is processing, two more nodes are used. *MotorActivator* is the one which is going to send a 1 or a 0 depending on the motor that should be activated. For this task, eight topics are going to be used, one per motor: *GaitStimulator_MUSCLE_QL*, *GaitStimulator_MUSCLE_HSL*, *GaitStimulator_MUSCLE_SL*, *GaitStimulator_MUSCLE_TAL*, *GaitStimulator_MUSCLE_QR*, *GaitStimulator_MUSCLE_HSR*, *GaitStimulator_MUSCLE_SR* and *GaitStimulator_MUSCLE_TAR*. On the contrary, *MotionRecorder* is a node that is going to be used to receive this binary signal and, based on it, activates the corresponding motors. It is also going to use the same eight topics.

A graph which shows the ROS elements of our system better is shown in Figure 4.2. Nodes are represented in green and topics in blue.

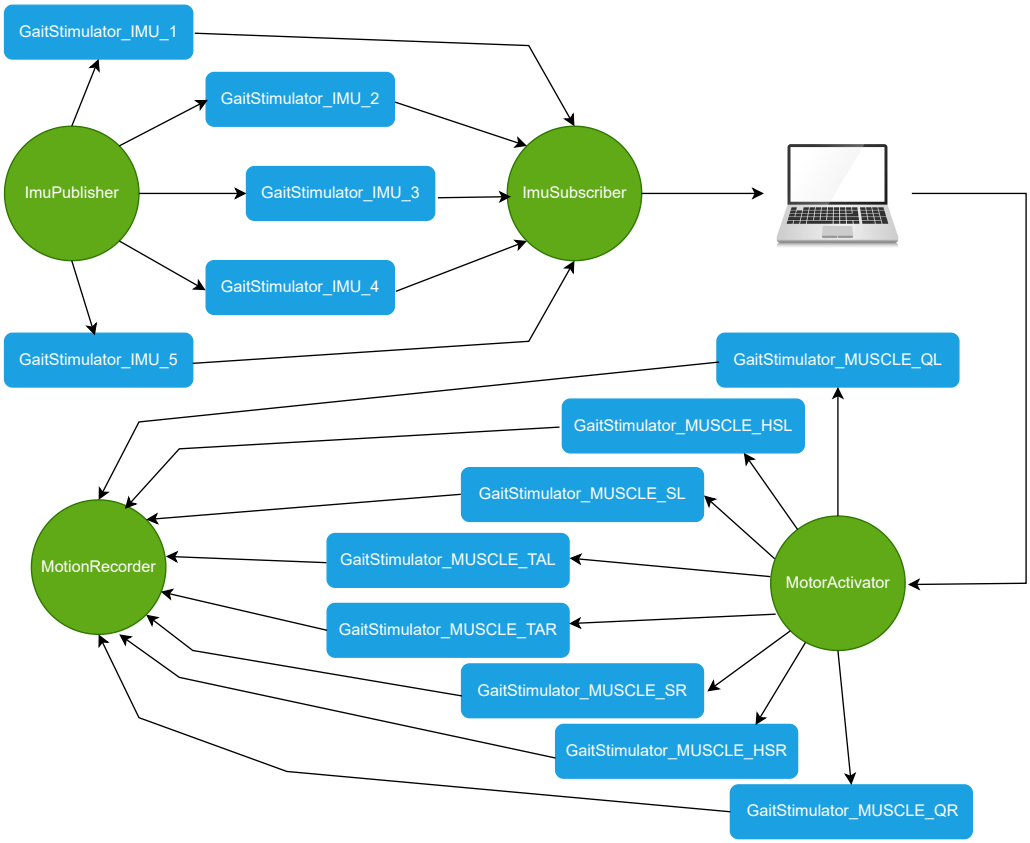


Figure 4.2: System ROS graph.

4.2. Treatment of the signal

The aim of this stage is to obtain the gait cycle graph and, based on it, determine the percentage of the gait in which the patient is and what muscles should be activated at this moment. For this task, it is going to be used a program develop by Tom Busink, a Dutch student of the University of Twente Master's Degree in Biomedical Engineering who has worked on this part of the project.

In Figure 4.3, it is shown how is the typical graph of a gait cycle. To get it, it has been used the angular velocity data provided by the IMUs, specifically, from the IMUs located in the lower leg. Before the process starts, there are five seconds of calibration. Then, the detection of peaks starts. For this purpose, three important peaks must be considered that can be better seen between seconds seven and eight. The first minimum, represented with and orange circle, corresponds to the moment in which the heel starts to be in contact with the floor. The second important peak, the relative maximum marked in black, corresponds to the moment in which the transverse arch and the fingers touch the floor and the complete foot is in contact with it. Finally,

the third peak, the second minimum represented with a yellow circle, determine the exact moment in which the heel starts to be in the air, lose its contact with the floor and the next step starts. This last peak also specifies the complete time considered for a step.

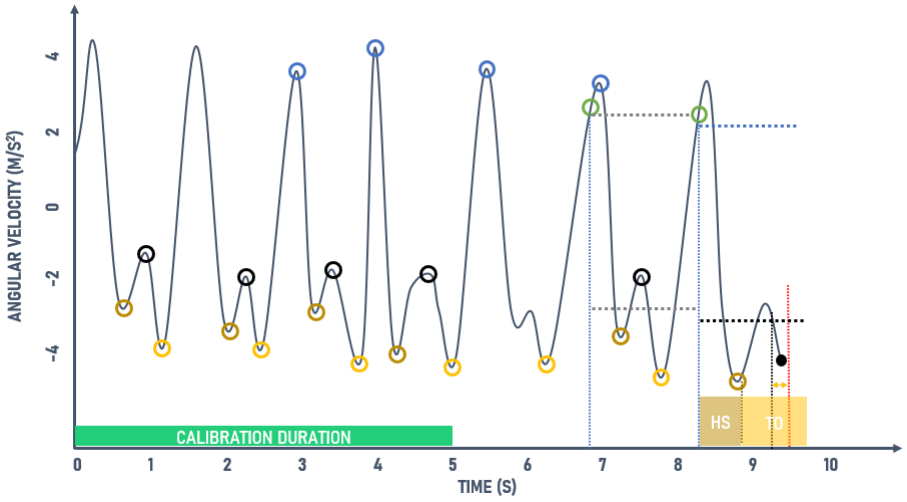


Figure 4.3: Gait cycle graph.

For the acquisition of the previous signal, some elements are needed. The first ones are the IMUs, that recollect the angular velocity in m/s^2 and send all this data in a vector to ROS. Then, the computer used for the processing, receives this information and a BPF of order 1 (to avoid delays, as it is expected that the system works in real time) is used to visualize better the signal. For this experiment, the Band Pass Filter has been defined from 0,1 to 4 Hz. These values have been chosen because in general, the walking patterns goes from 0 to 5 Hz but there are information that is redundant for us. Nevertheless, for specific purposes it could be interesting to increase a little bit the bandwidth and to have a BPF from 0 to 7 Hz.

Furthermore, a predictor is used to detect the important moments in the gait cycle. As it has been explained, there are five seconds of calibrations in which the system is focused on three tasks. Firstly it checks if it is able to detect all the top peaks and mark them in blue. Then, in the same manner, it checks if it is able to detect the relative minimums and mark them in orange and yellow (the yellow mark is going to be considered the total moment, when the step has finished and a new one starts). And, finally, it detects if it is able to detect the relative maximums and marks them in black. Once the calibration is done, it defines the thresholds, one for differentiating the top peaks and a second one to differentiate the relative maximum from the lowest peaks. To to define the threshold for the top peaks, it take into consideration the previous top peaks detected, do its average and, in the 80 % of this average, the threshold is located. It works in the same way for the lower part threshold. As it can be imagined, the threshold is going to take different values because once we advance along the signal, the average of the previous detected peaks changes. With

this threshold defined, it is easier to determine where are the peaks. Once the peaks are located, the prediction takes place. For this task, it is important to take into account that there are 40 frames per second, so it can be concluded that the distance between blue and orange circles is around 10 frames, between blue and black circles is 20 frames and the distance between blue and yellow 30 frames. Then, the brown circles corresponds to our predictor. As it can be seen, they differ a bit from the real values but they are very close to it. By knowing that between those two brown circles it should be 40 frames, if for example, there is a distance of 10 frames or a similar value between a brown circle and an orange predicted circle, it can be concluded that the prediction is correct.

After the prediction, an AFO starts to work. It is an adaptive frequency oscillator whose function in the system is to determine the moment in the gait cycle in which the vibration motors should be activated. It has two inputs signals, the filtered IMUs signal and a binary value that takes the value of 1 (when the total moment takes place) or 0 in the rest of the cases. It follows the signal received from the sensors and when it receives a 1, it translate it into a new start of this signal. In this way, it is able to use the frames to calculate the percentage of the gait cycle in which the patient is. With this information, it is going to be possible to stimulate the motors a period of time in which it is expected that their corresponding muscles should be activated.

The percentage of gait cycle in which each muscle should be activated and its duration is shown in Table 4.1 [22]. Moreover, the percentage in which we are going to stimulate each muscle and the duration of this stimulation are shown. To make the motors vibrate, a 1 is sent to the corresponding ROS topic. For example, it we want to activate the left quadriceps, a 1 is transmitted to *GaitStimulator_MUSCLE_QL* and, after the 60 % of the gait cycle, a 0 is sent to the same topic.

Muscle	**Normal gait cycle**		**Used during trial**	
	Initiation (% of gait cycle)	**Duration (% of gait cycle)**	**Start vibration (% of gait cycle)**	**Duration (% of gait cycle)**
Quadriceps (Q)	86	24	85	25
Hamstring (HS)	86	24	85	25
Soleus (S)	10	50	10	50
Tibialis Anterior (TA)	58	54	60	55

Table 4.1: Initiation and duration of muscle activity during a normal gait cycle and percentages used in the trial to perform synchronized vibration.

4.3. Graphical User Interface (GUI)

Once the system is working in the desired way, a graphical interface has been designed. Until this moment, the activation and deactivation of the system was controlled with some command windows. The aim of this section is to create an interface that could make easier the use of this system for the medical staff.

The code has been implemented using HTML and JavaScript. HTML has been used for the structure of each screen of our application. This include tabs, images and buttons that have a specific functionality in the the interface. On the contrary, JavaScript has been used to define the functionality of each element of the application, that is, what happens when we press a button and the dynamic update of the elements.

Furthermore, NodeJS has been used as a runtime environment. Among its advantages, it stands out that it is open source, what means that the source code of NodeJS is public available and maintained by contributors from all the parts of the world; it is cross-platform, that is, it can work in any operating system like Windows, macOS or Linux; and, it is controlled by events, which allows to manage multiple connections at the same time.

With these elements in mind, the interface structure and some functionalities can be created (see Figure 4.4). Specifically, this screen is shown to register all the patients, the different tests that they do and their results.

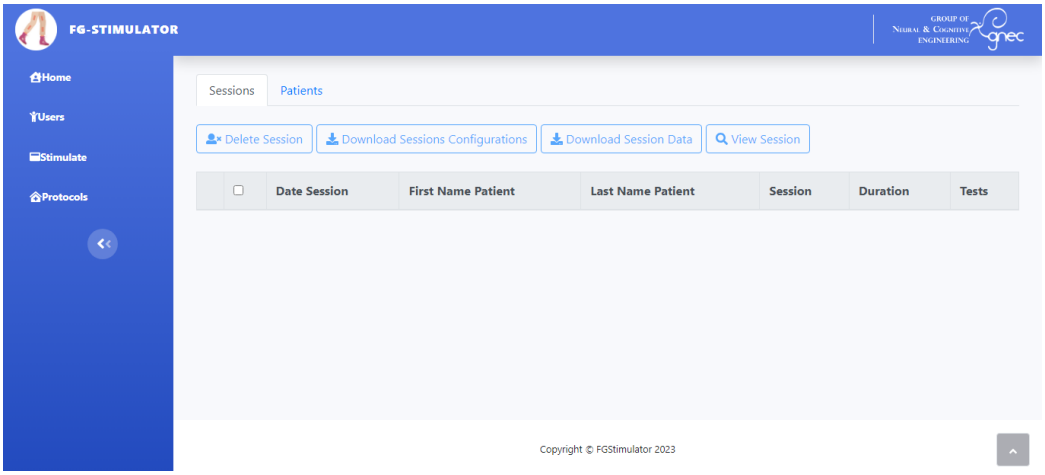


Figure 4.4: Interface: Users.

The stimulation screen has been created with the aim that doctors can select to activate and deactivate specific motors when they want. This can be seen in Figure 4.5. For this task, ROS has been used in the same way as it has been explained in previous chapters. It is important to take into account that we are going to create a server with the Raspberry Pi and the application is going to connect to this server, so an additional element is needed to use ROS in the web interface. For this task, two options are available: to use a predefined bridge created to be used with ROS, or to use Sockets. The second option has been chosen. Sockets have been used as a bridge between the Server created by the Raspberry PI and the navigator.

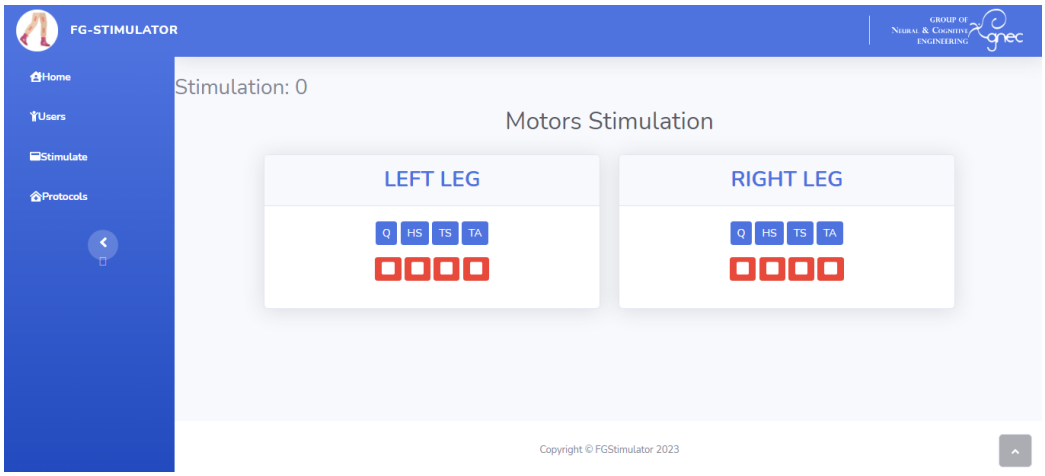
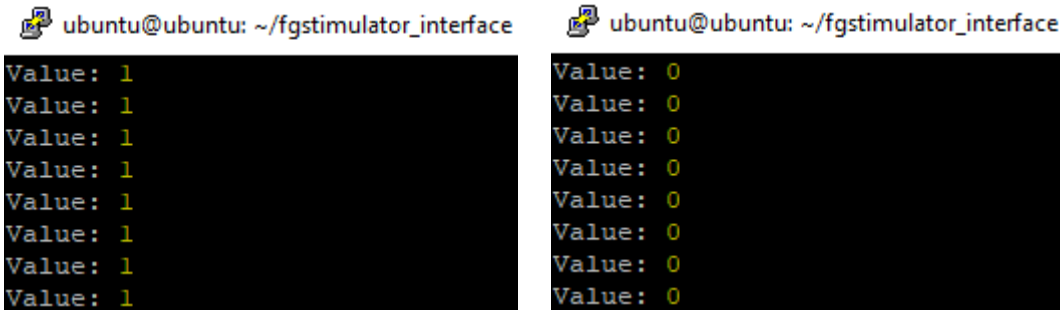


Figure 4.5: Interface: Stimulate.

Finally, when the doctors want to stimulate, for example, the left quadriceps, they only have to press on the button "Q" of the "Left Leg" block to make the motor works. At this moment, a 1 is sent to the topic *GaitStimulator_MUSCLE_QL* and the motor vibrates. Then, to stop it, they only have to press on the button to stop and a 0 is transmitted to the same topic, as it is shown in Figure 4.6.



(a) Message transmitted to stimulate (b) Message transmitted to stop stimulation

Figure 4.6: Messages transmitted in ROS to stimulate and stop stimulating the motors.

To conclude, as next steps, it has been though that it would be interesting to

implement a protocols tab where doctors could select the different protocols they want to perform to their patients. One protocol could be composed by some tests, so the idea is that doctors could create their protocols within this tab in an easy way and execute them. For example, as it is shown in Figure 4.7, doctors can define a protocol to analyze the static posture of a patient during different periods of stimulation in their muscles. For the creation of the protocol, they only have to drag the muscle that they want to stimulate to the bar below and specify the time they want to stimulate it. Finally, it could be desirable to add an image element where they could see IMUs data on the screen to analyze what is the effect of each protocol in the posture and walking patterns of the patients.

Figure 4.7: Example of the creation of a protocol.

Chapter 5

Results

To conclude this study, it is important to validate that this system works in different situations and it would be suitable for different types of patients. For this purpose, two study designs have been defined to test the system with patients. Both are thought to be tested initially with healthy people and, in the future, with Parkinson's Disease patients. In this Master's Thesis only healthy subjects have participated in the studies. The first study design aims to analyze the influence of single and multi-muscle or multi-tendon stimulation of patients' posture and their tendency to make a step. On the other hand, the second study design has been realized to test if the whole system is able to work in different situations that could take place with real patients.

Before performing the tests, the documentation and permissions needed to realise these type of tests must be considered. In this case, patients will be explained what this study is about and what are their role on it. Later, they must sign a consent form in which they confirm that they have understood what the research is about and what are the risks of their participation in the study. By singing this document, they also give us permission to record and take photos if needed and to use their results in the study designs for the research (see Appendix A).

5.1. Study design 1. Healthy person standing with variable vibration duration on upper and lower leg muscles and tendons

As aforementioned, the aim of this study was to measure the influence of the vibration in different parts of the upper and lower leg muscles and tendons to determine what are the best parts of the body to place the vibration motors.

To perform this study, two actuators and three IMUs were used. The decision of using only two actuators is because it is easier to analyze the results for each part of the leg, as the two legs are going to be stimulated at the same time. They are going to be placed in eight different positions that can be seen in Table 5.1. Regarding the IMUs, only three are needed for this study. Their position can be seen in Table 5.2

Vibration Motors	Location	
Quadriceps (Q)	**Muscle**	Fastened over the muscle belly approximately 15–20 cm above the knee joint
	Tendon	Fixed to the quadriceps tendon as close to the patella bone
Hamstring (HS)	**Muscle**	Fastened over the muscle belly approximately 15–20 cm above the knee joint
	Tendon	Fixed to the semimembranosus tendon 5 cm above the knee joint
Soleus (S)	**Muscle**	Fixed to the center of the Soleus belly
	Tendon	Fixed to the Achilles tendons, at the level of the ankle joint
Tibialis Anterior (TA)	**Muscle**	Fixed on the center of the Tibialis belly
	Tendon	Fixed on the tendons of TA, 3–5 cm above the ankle joint

Table 5.1: Location of the vibration motors on the muscles and tendons.

IMUs	Location
Trunk (TR)	5 cm below the cranial end of the sternum
Thigh (TH)	15 cm above the knee joint
Shin (SH)	15 cm above the ankle on the center of the shin bone

Table 5.2: Location of the IMUs in the body.

Furthermore, with the aim of measuring the position of the patients in a more accurate way, the P-600 force plate from BTS Bioengineering [50] was used apart from the IMUs. This system measures ground reaction forces and movement during human movement. Due to the orientation of the sensors, forces can be measured in three axes (see Figure 5.1). In this case, we are interested in Z-axis force, as we want to analyze the inclination of the patient according to the stimulation received.

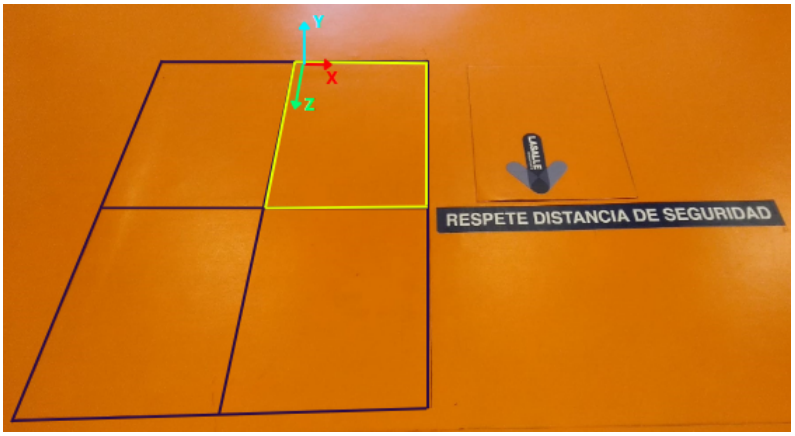


Figure 5.1: Force plate and distribution of forces used in IRF La Salle.

For this study, healthy subjects were asked to stand on the leveled force plate shown above, without additional balancing aid. They had to keep their eyes closed and their arms crossed in front of their thorax during the complete trial. Additionally, their heels had always to be in contact with the ground without shifting during the trial. Firstly, the subjects were asked to squad by bending the knees 3 times in a row, as an indicator for the start of both the IMU measurements as the vibratory stimulation. Then, they were asked to stand still with a straight posture for 30 seconds without stimulation. After this initial posture period, the subjects were given the instruction

not to resist the applied perturbation. Next, during a period of 3 minutes and a half, the subjects received 4 periods of 10 seconds of vibrations followed by a period of non-vibrations with a random duration at one muscle group at a time (see Figure 5.2). The same muscle group was stimulated on both the right and left leg simultaneously. Finally, after the last vibration period, the recording was extended by 20 seconds to be able to analyse the recovery after vibrations.

Once the trial was finished, the actuators were placed in another location shown in Table 5.1 and the process started again. It was performed eight times, one per location of the actuators.

Figure 5.2: Stimulation intervals during in each trial of the first study design.

Four healthy patients from ages between 21 and 44 years old participated in this study design. The subjects performed the entire experimental protocol on one day and each session lasted around 1 hour per subject.

Furthermore, the four subjects were asked about their perception of their motion. To analyze them, we are going to go deeper in the four periods of ten seconds of stimulation, as they appear to have a relevant influence in the position of the patients. For this analysis, the legend shown in Figure 5.3 is going to be used.

Figure 5.3: Perception legend.

Figure 5.4 shows the baselines of the four subjects. In Figure 5.5 the changes of position of the four subjects with stimulation in their hamstring muscles are shown. Additionally, we asked them about their motion perception, which is shown in Figure 5.6. As we can see, there was a significant change of position when the stimulation took place for Subject 1. In the case of Subject 2, we can see that the patient moved forward just before the stimulation and with the stimulation he, in general, corrected his position. In Subject 3, posture data does not show any relevant difference between the posture of the patient with hamstring stimulation and the baseline. Finally, in Subject 4, we can see motions forward. According to these results, the four patients felt that their body was moving forward.

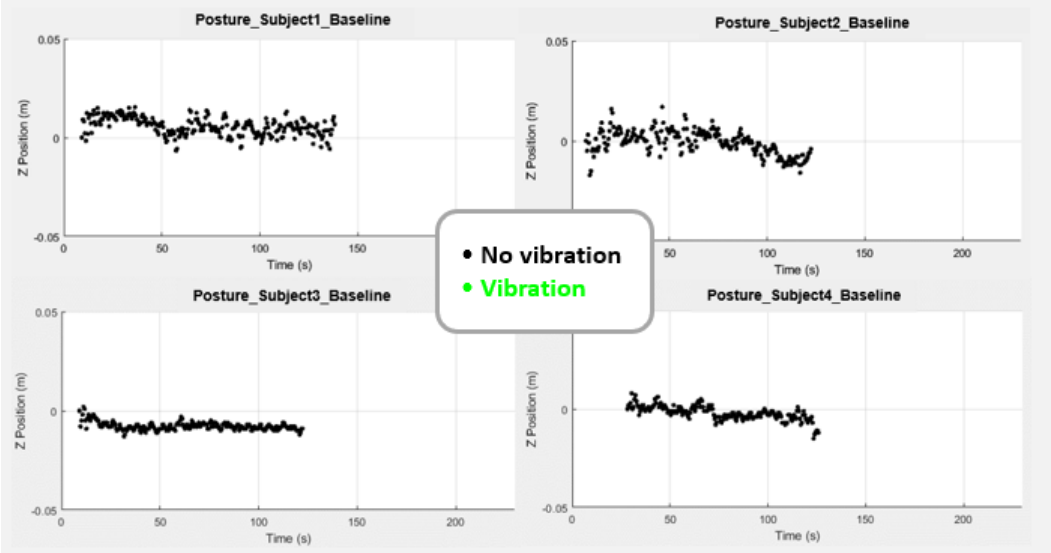


Figure 5.4: Subject baseline 1.

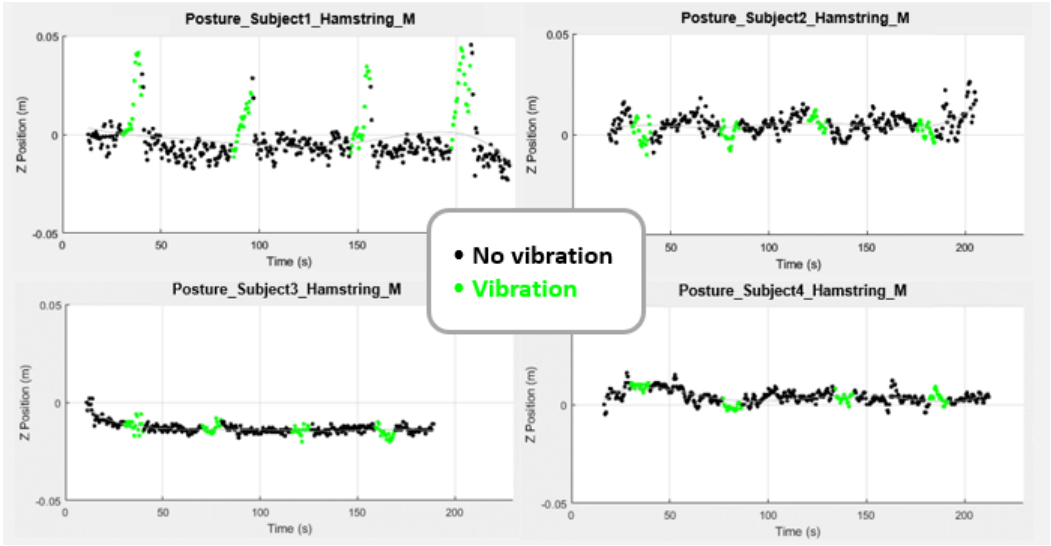


Figure 5.5: Posture of the four subjects with stimulation in their hamstring muscles.

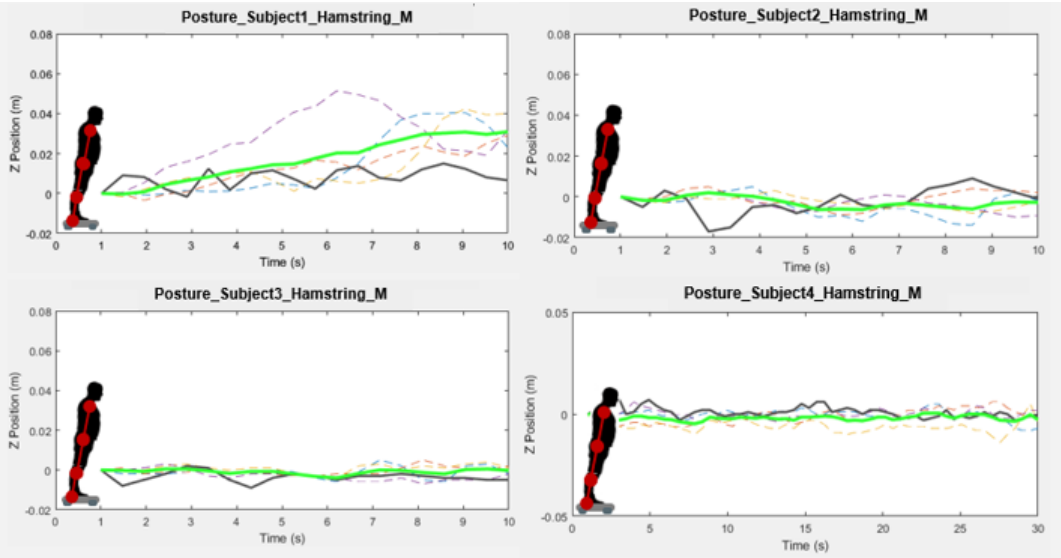


Figure 5.6: Perception of motion of the four subjects with stimulation in their hamstring muscles.

Figure 5.7 and Figure 5.8 show the posture of the four subjects with stimulation in their hamstring tendons and their perception of motion with this type of stimulation, respectively. Despite we can see some movements forward and backwards in the Subject 1, she did not feel any motion. In second place, Subject 2 shows more coherent results because we can see motions forward, especially at the end of the trial, and he also felt it. For Subject 3 we see a function of movement without important changes. However, he felt motion forward and that the system made him to band his knees. Lastly, we can see a little motion backward at the end of the trial for Subject 4 that he also perceived it.

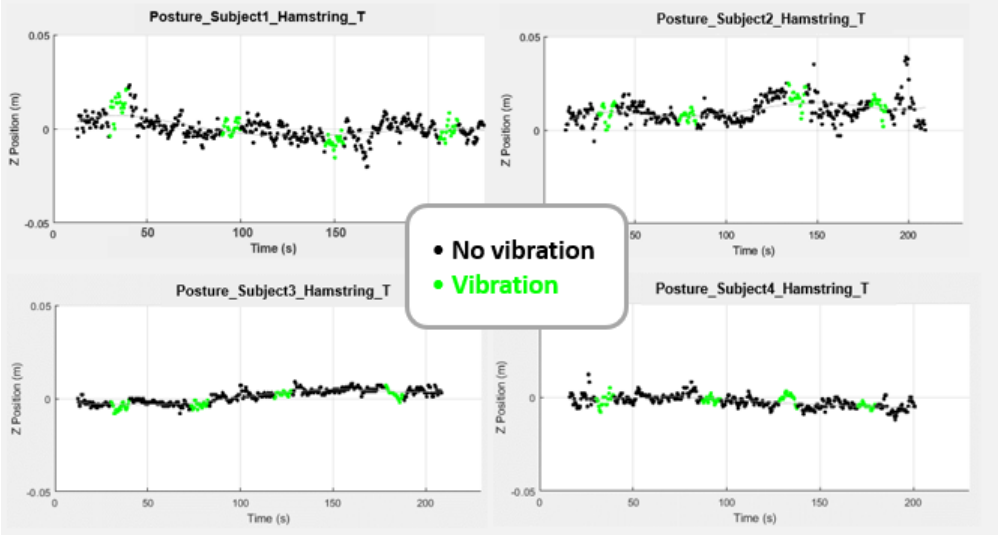


Figure 5.7: Posture of the four subjects with stimulation in their hamstring tendons.

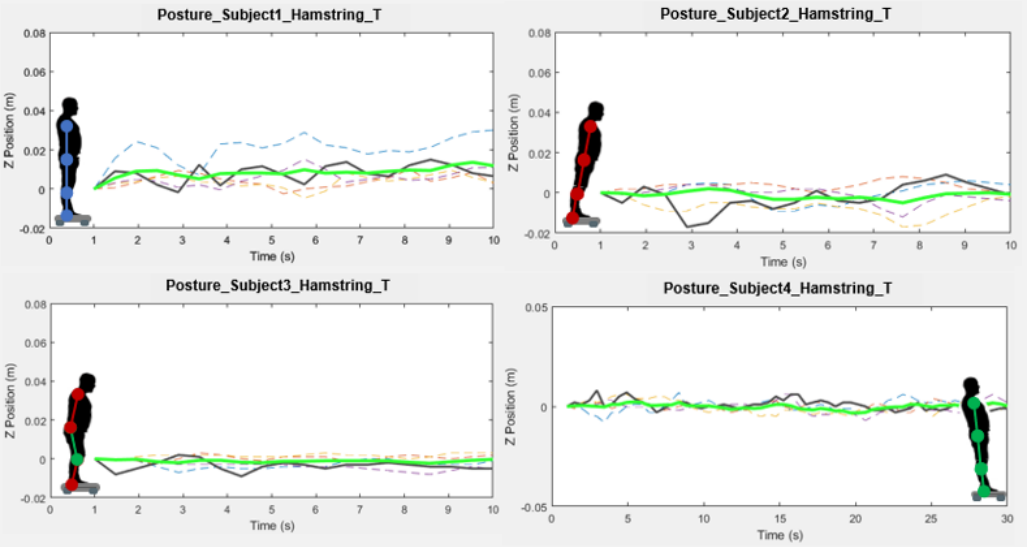


Figure 5.8: Perception of motion of the four subjects with stimulation in their hamstring tendons.

As shown in Figure 5.9 and in Figure 5.10, the results were the same for the Subject 1 with a stimulation in her soleus muscles. In the Subject 2, we can see an important movement backwards that the patient could feel. And Subject 3 and Subject 4 experimented movements forward and backwards that Subject 3 felt as motion forward and Subject 4 as motion backwards.

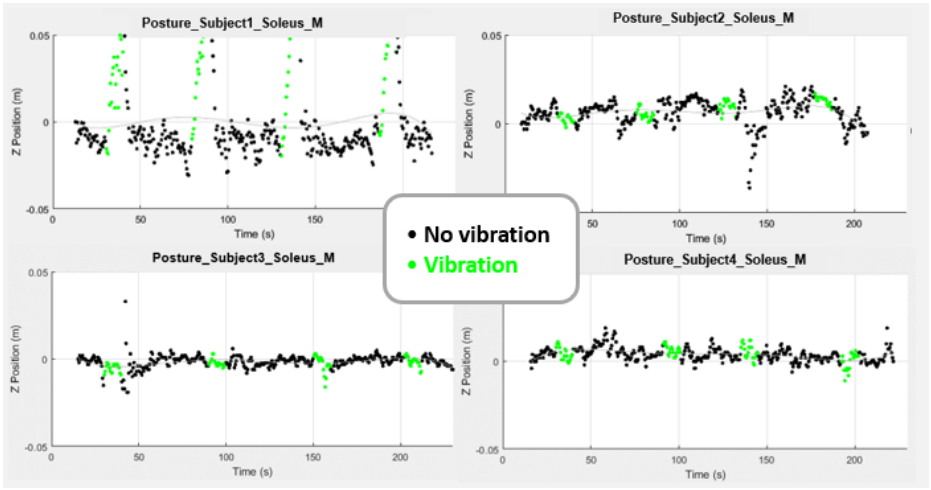


Figure 5.9: Posture of the four subjects with stimulation in their soleus muscles.

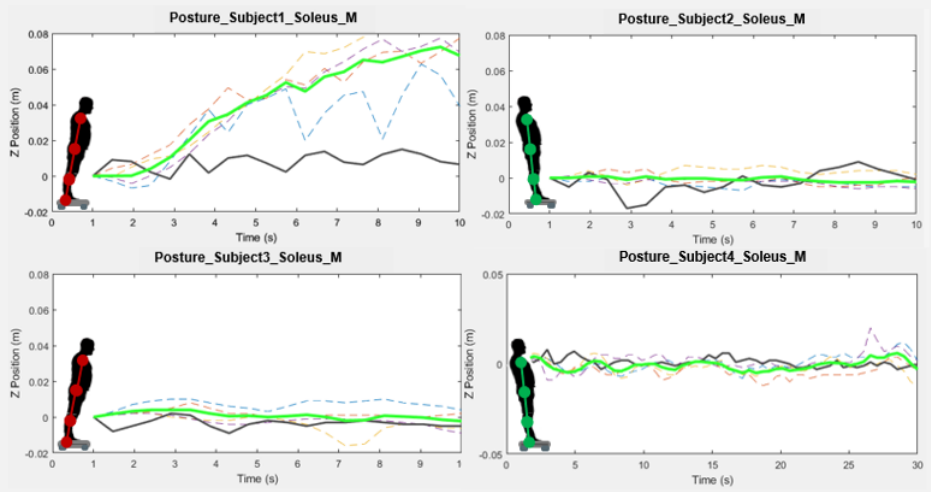


Figure 5.10: Perception of motion of the four subjects with stimulation in their soleus muscles.

Figure 5.11 and Figure 5.12 show the posture of the four subjects with stimulation in their soleus tendons and their perception of motion with this type of stimulation. As we can see, Subject 1 experimented movement forward synchronized with the vibration whereas Subject 2 had movements forward in the beginning of the trial and movement backwards at the end, however, any of them felt anything. On the contrary, Subject 3 felt a motion backwards that is represented at the end of the trial. Finally, we can consider that Subject 4 had a stable behaviour, so he did not feel any movement.

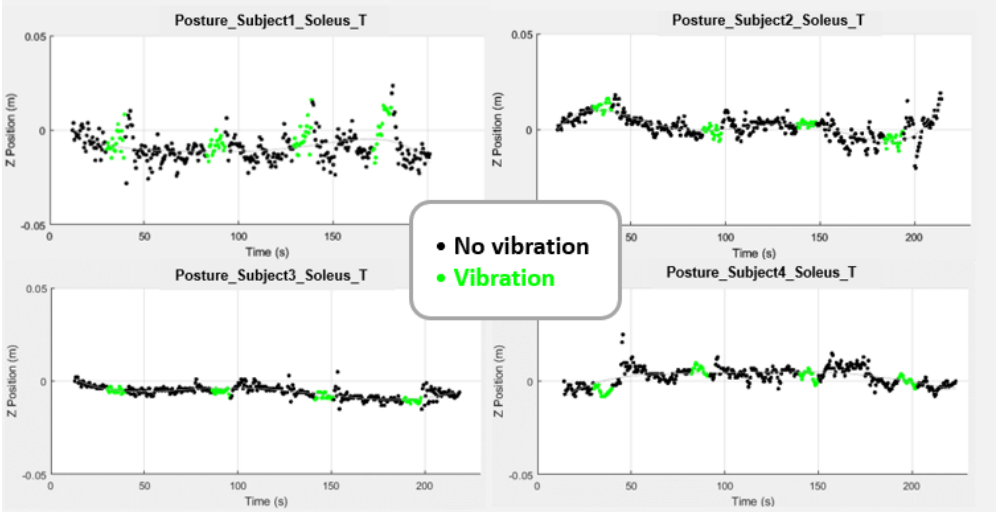


Figure 5.11: Posture of the four subjects with stimulation in their soleus tendons.

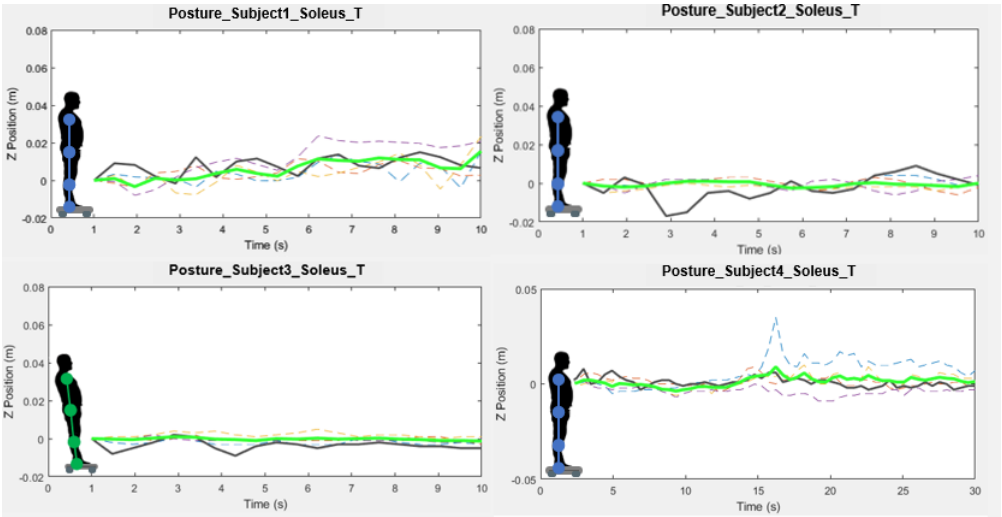


Figure 5.12: Perception of motion of the four subjects with stimulation in their soleus tendons.

As shown in Figure 5.13 and in Figure 5.14, due to a failure in the force plate system, we only have results for three of the subjects for the stimulation in the quadriceps muscles. As we can see, the results are very coherent for the Subject 2 and the Subject 3, as they felt motion forward when it is produced. However, we can see this type of movements also for Subject 4, but, in this case, he did not feel anything.

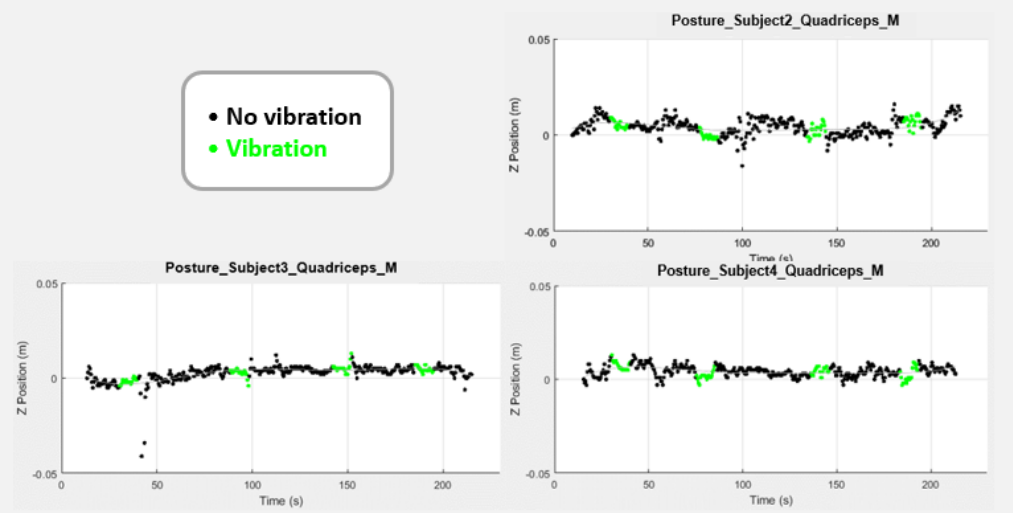


Figure 5.13: Posture of the four subjects with stimulation in their quadriceps muscles.

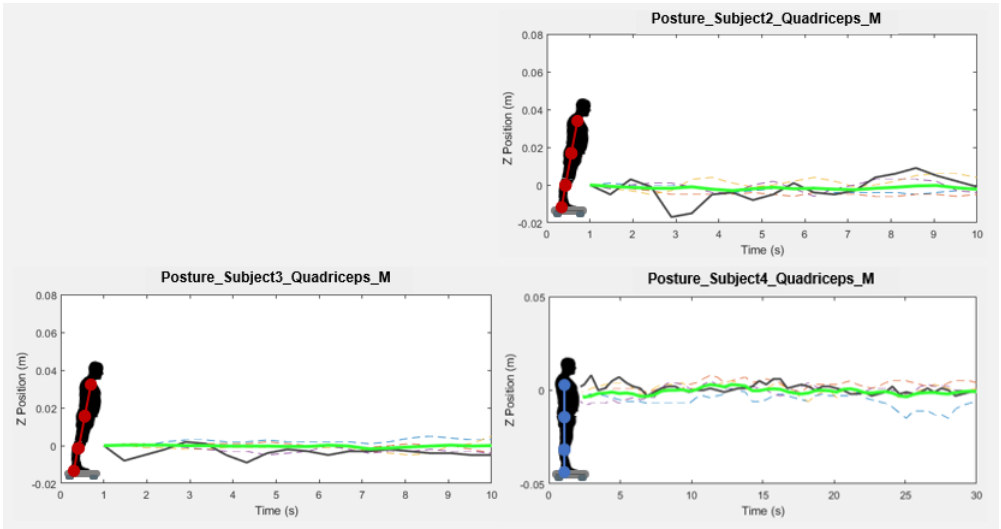


Figure 5.14: Perception of motion of the four subjects with stimulation in their quadriceps muscles.

Figure 5.15 and Figure 5.16 show the posture of the four subjects with stimulation in their quadriceps tendons and their perception of motion with this type of stimulation, respectively. As we can see, Subject 2 experimented movement forward during and after the stimulation, and he could felt it. Subject 3 had smaller movements forward during the stimulation and he also felt it. But, Subject 4 had motion forward during the trial and he did not feel it.

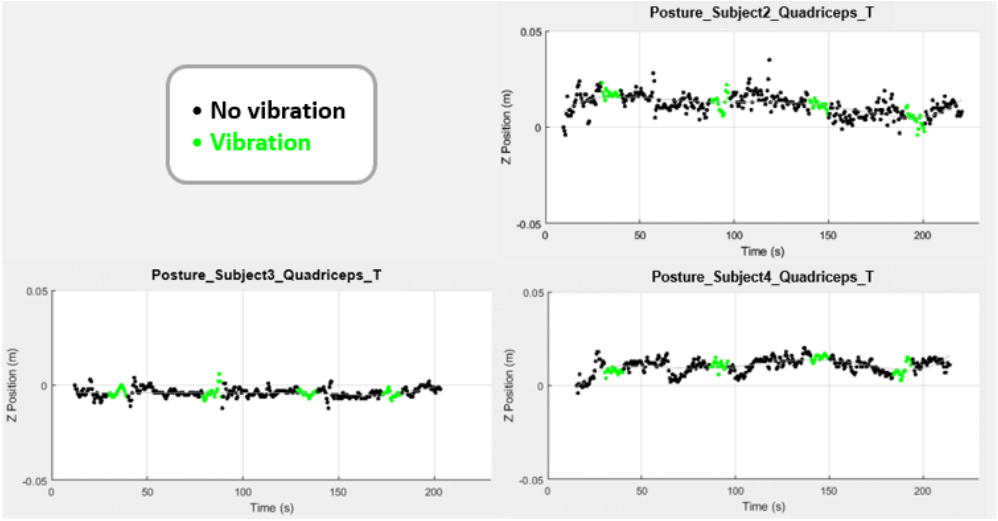


Figure 5.15: Posture of the four subjects with stimulation in their quadriceps tendons.

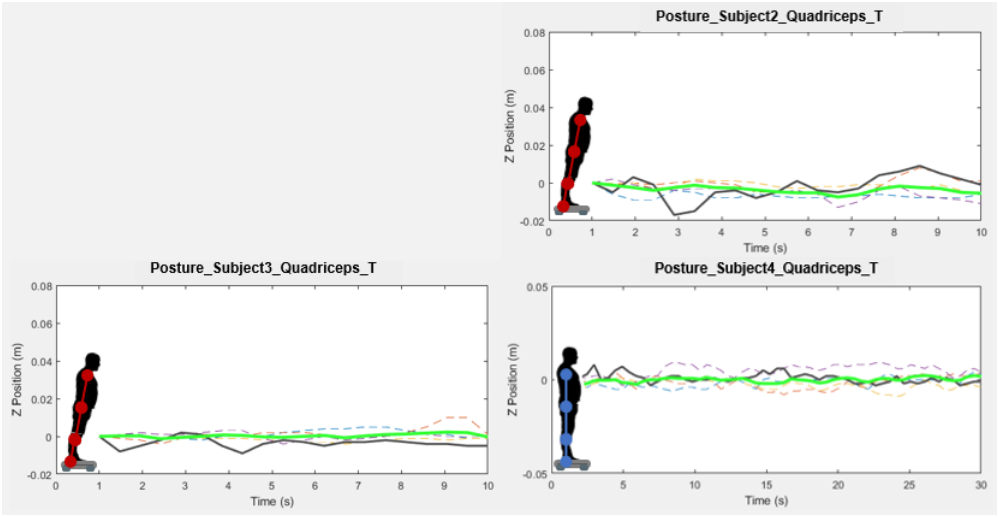


Figure 5.16: Perception of motion of the four subjects with stimulation in their quadriceps tendons.

As shown in Figure 5.17 and in Figure 5.18, for tibialis anterior muscles stimulation, Subject 1 experimented some movements forward that he felt with a banding of her knees. Subject 2 had a little motion forward but his behaviour was, in general, stable, so he did not feel any motion. Subject 3 had a more stable behaviour and, in fact, he did not perceive movements. And finally, Subject 4 experimented some movements forward that he could feel.

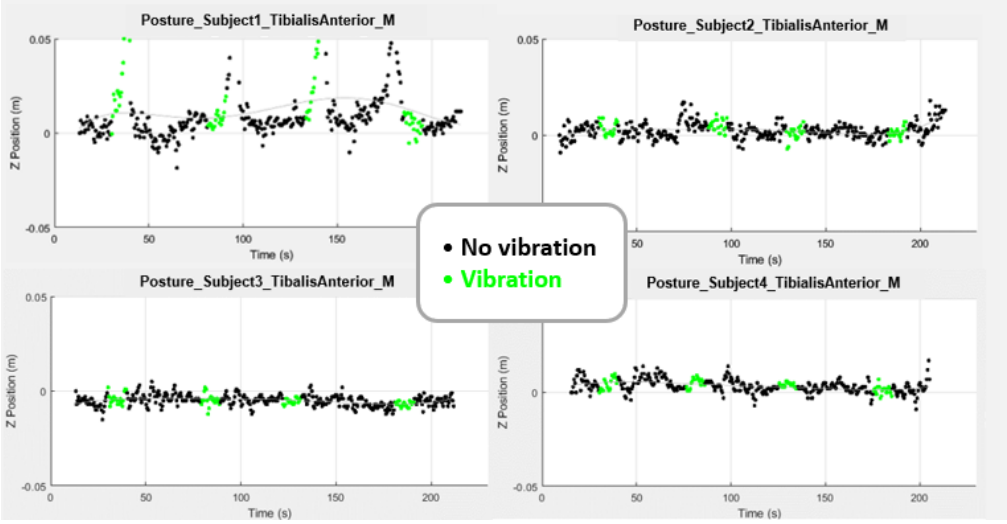


Figure 5.17: Posture of the four subjects with stimulation in their tibialis anterior muscle.

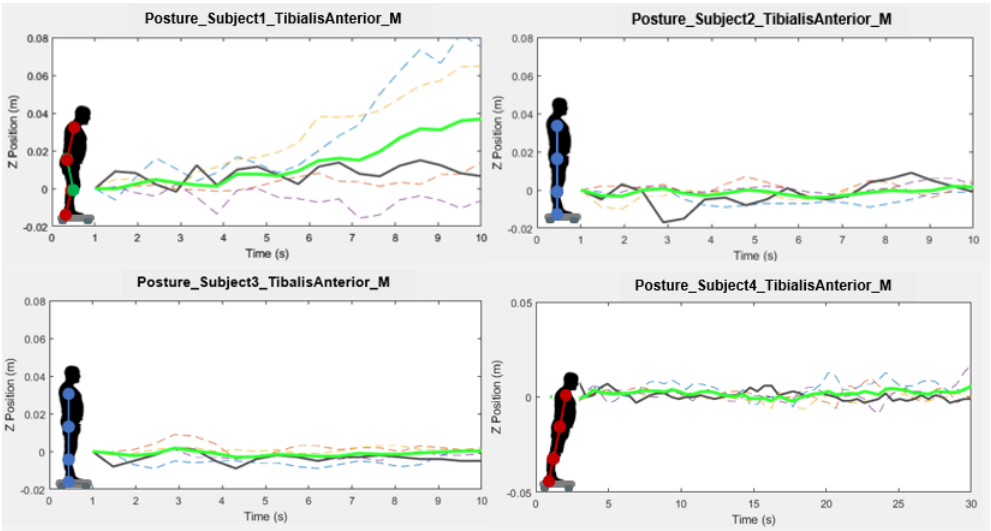


Figure 5.18: Perception of motion of the four subjects with stimulation in their tibialis anterior muscle.

Finally 5.19 and Figure 5.20 show the posture of the four subjects with stimulation in their tibialis anterior tendons and their perception of motion with this type of stimulation, respectively. Subject 2 experimented a lot of movement forward and backwards but he did not feel anything. Subject 3 started with a stable behaviour and he finished the trial with a motion forward that he felt apart from a movement backwards in the beginning of the trial. And Subject 4 did not perceive any movement in spite of he moved forward and backwards.

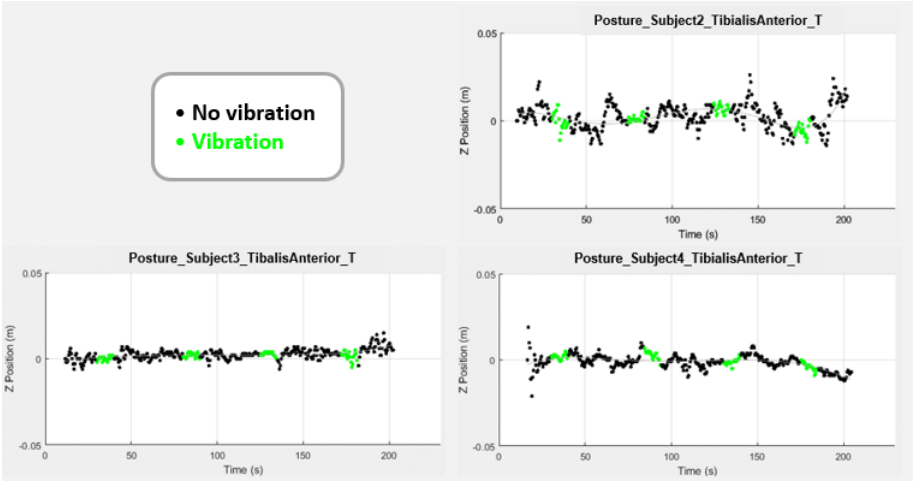


Figure 5.19: Posture of the four subjects with stimulation in their tibialis anterior tendons.

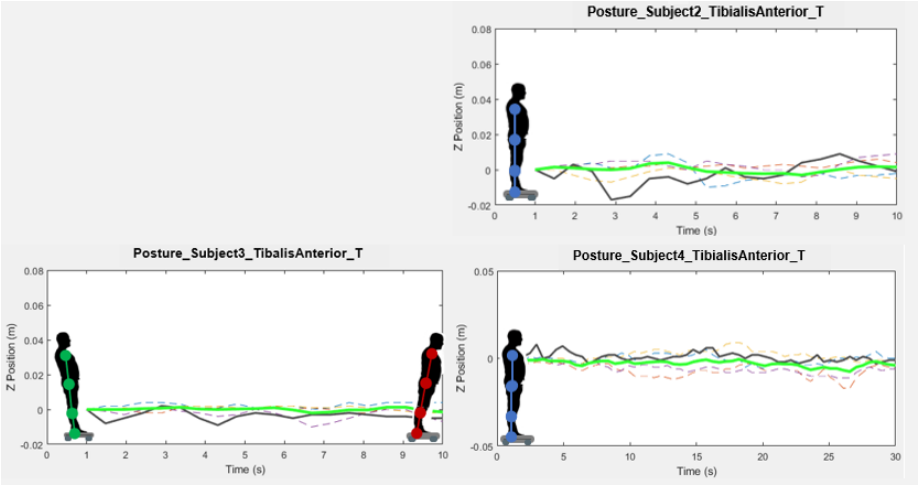


Figure 5.20: Perception of motion of the four subjects with stimulation in their tibialis anterior tendons.

5.2. Study design 2. Healthy subject walking with variable vibration duration on both leg muscles

To validate technically the final system, a subject tested it in different situations to guarantee that it is able to detect the peaks of the signal, determine the percentage of the gait cycle in which the patient is and stimulate the motors in the correct moment. For this purpose, five tests were done by the subject. These tests correspond to the most typical walking patterns in patients with Parkinson's Disease. They are: normal walking, walking by changing the speed, shuffling along, shuffling along on one foot and tiptoe.

Firstly, normal walking was analyzed. As shown in Figure 5.21, the peak prediction worked very well and all the peaks were detected successfully. This can be translated into an appropriate stimulation in all the muscles in the exact moment as it should be applied. It can be seen in Figure 5.22, where the squares represent the motors stimulation and, as it is shown, they fit perfectly with the waves of all the muscles.

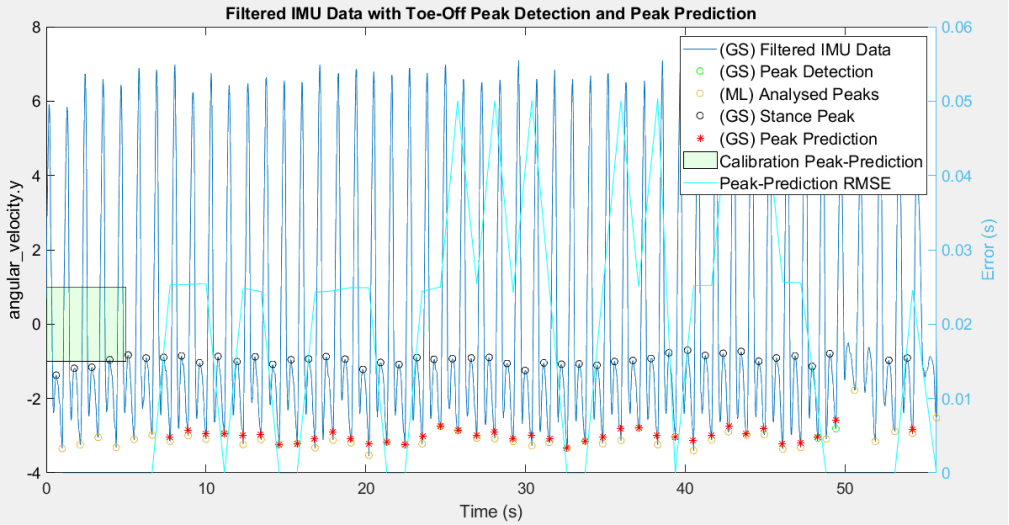


Figure 5.21: Filtered IMU Data with Toe-Off Peak Detection and Peak Prediction with normal walking.

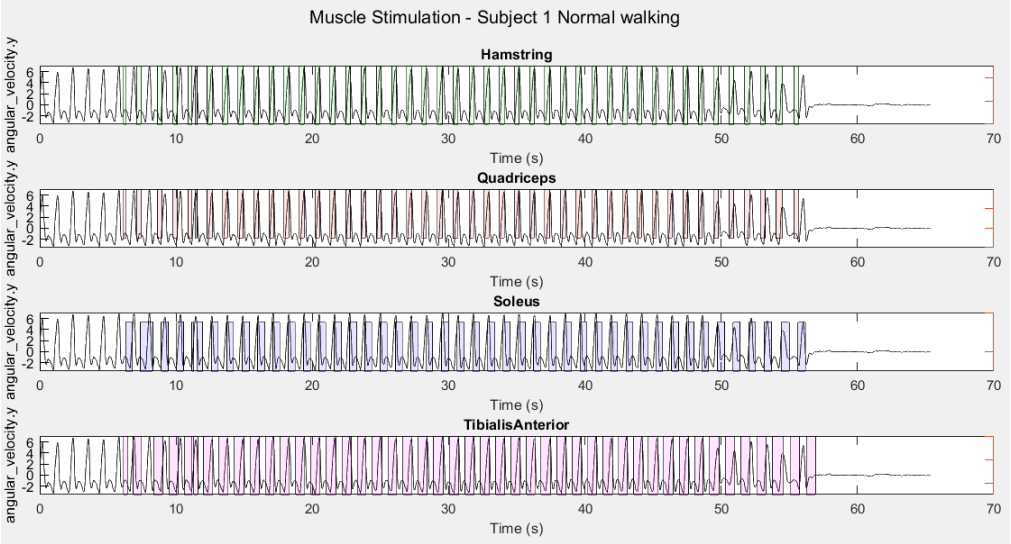


Figure 5.22: Muscle Stimulation with Normal Walking

Secondly, test consisted in walking with different speeds. For this trial the subject started walking with a normal rhythm. Then, he increased his speed. Next, he returned to his normal rhythm. Finally, he walked slower and normal again. It can be seen in Figure 5.23, where these changes of speed can be seen by focusing on the distance between the peaks. From the second 10 to 20, the peaks in the graph are closer whereas from second 45 the distance between them is bigger. In this case, the prediction failed in some cyles, which was translated into stimulations in different moments as expected that can be easily observed in the stimulation for hamstring and quadriceps in Figure 5.24.

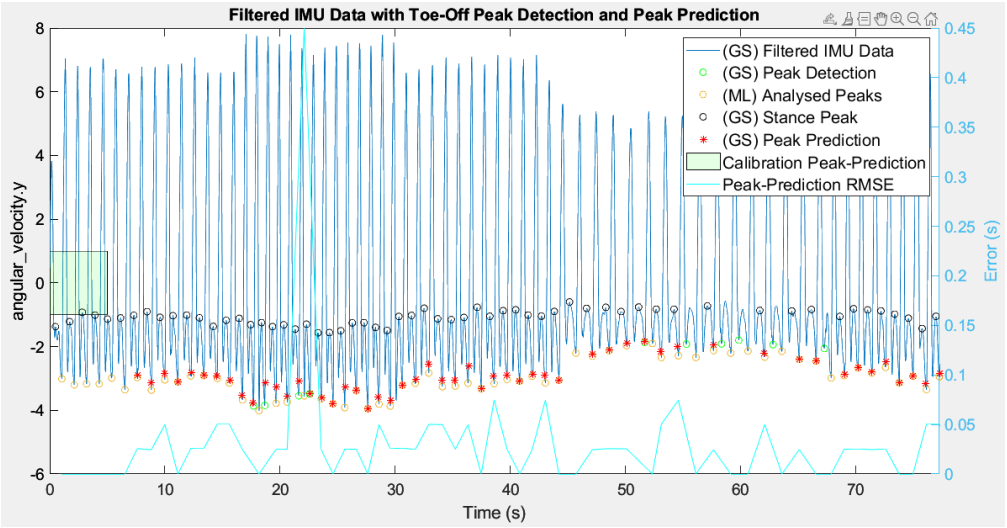


Figure 5.23: Filtered IMU Data with Toe-Off Peak Detection and Peak Prediction walking by changing the speed.

Figure 5.24: Muscle Stimulation Walking by changing the speed.

Later, the system was tested while the subject was shuffling along. As it can be seen in Figure 5.25, the prediction in this situation is worse and more peaks are not detected. In the same manner as the previous test, there were problems with the moment in which hamstring and quadriceps are stimulated (see Figure 5.26).

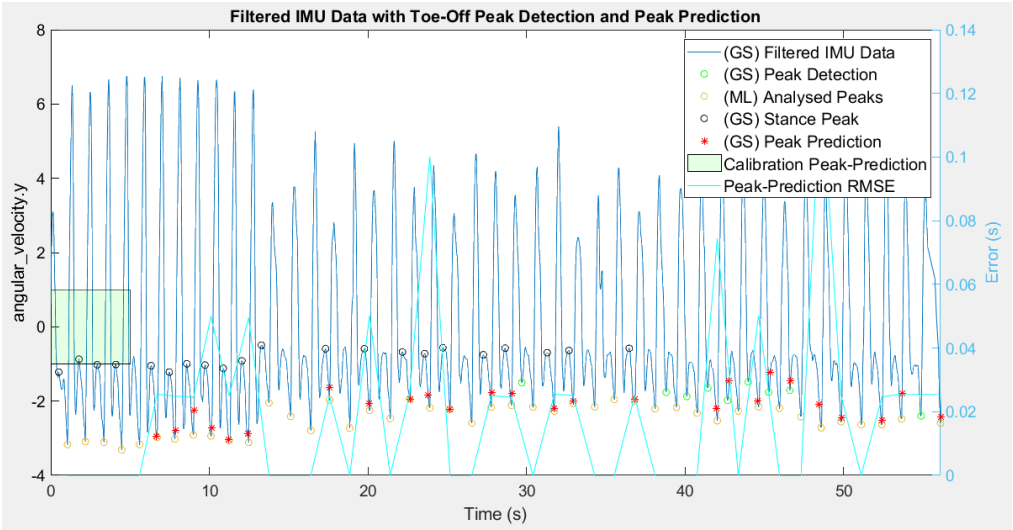


Figure 5.25: Filtered IMU Data with Toe-Off Peak Detection and Peak Prediction Shuffling along.

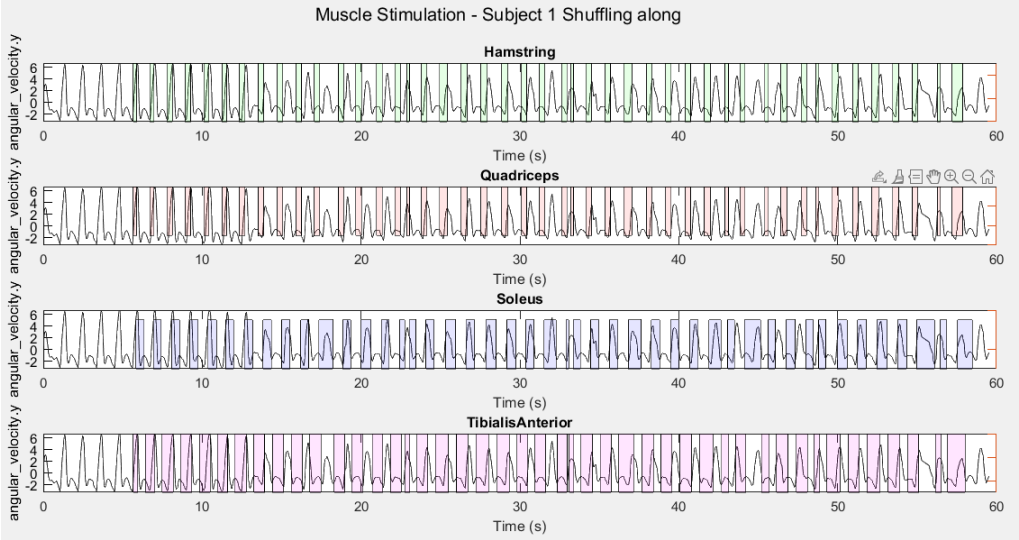


Figure 5.26: Muscle Stimulation Shuffling Along.

In the next trial, the system was tested while the subject was shuffling along on one leg. The results were very similar as shuffling along (see Figure 5.27 and Figure 5.28).

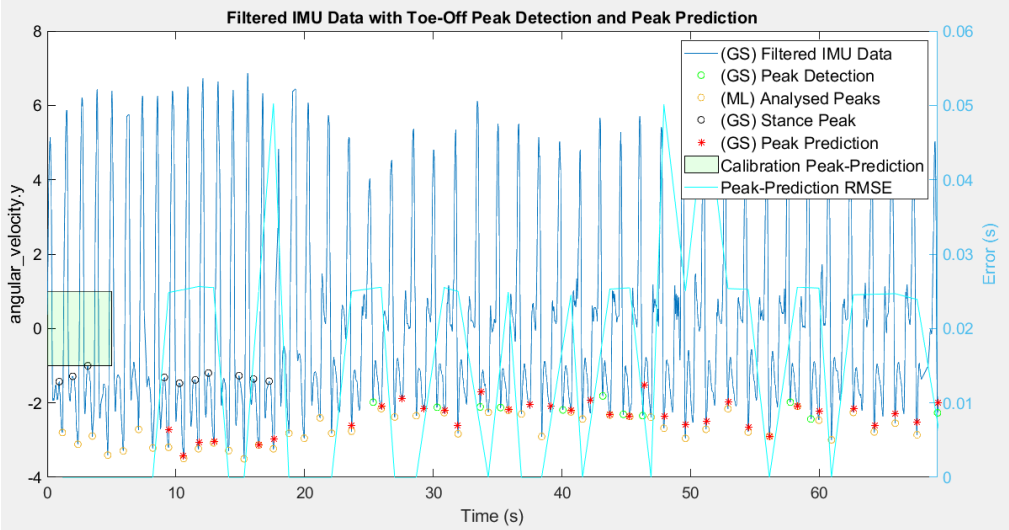


Figure 5.27: Filtered IMU Data with Toe-Off Peak Detection and Peak Prediction Shuffling along on one foot.

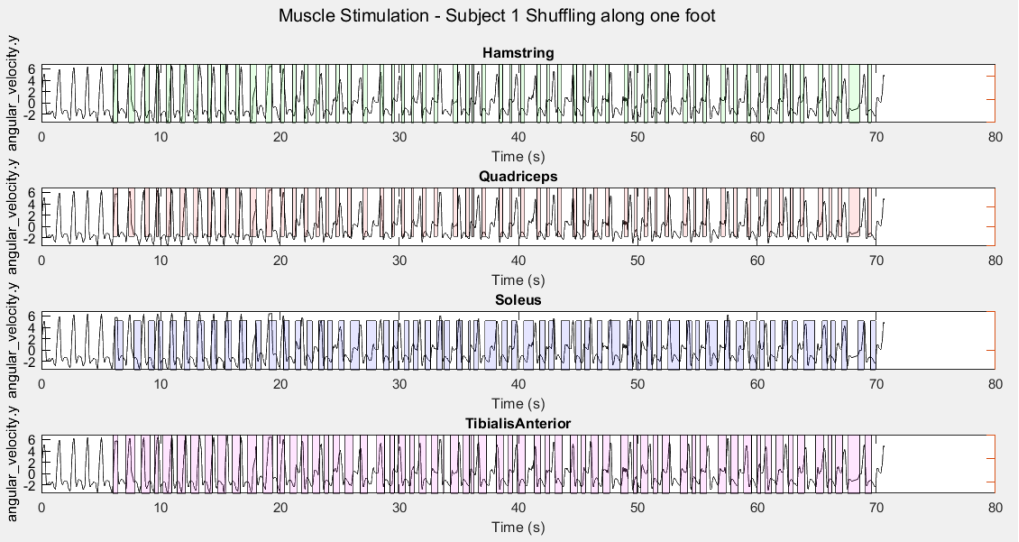


Figure 5.28: Muscle Stimulation Shuffling Along One Foot.

Finally, the system was tested while the subject was tiptoeing. As shown in Figure 5.29, the prediction was very good and practically all the peaks were detected. Due to this accurate prediction, the muscles stimulation is correct for all the muscles (see Figure 5.30).

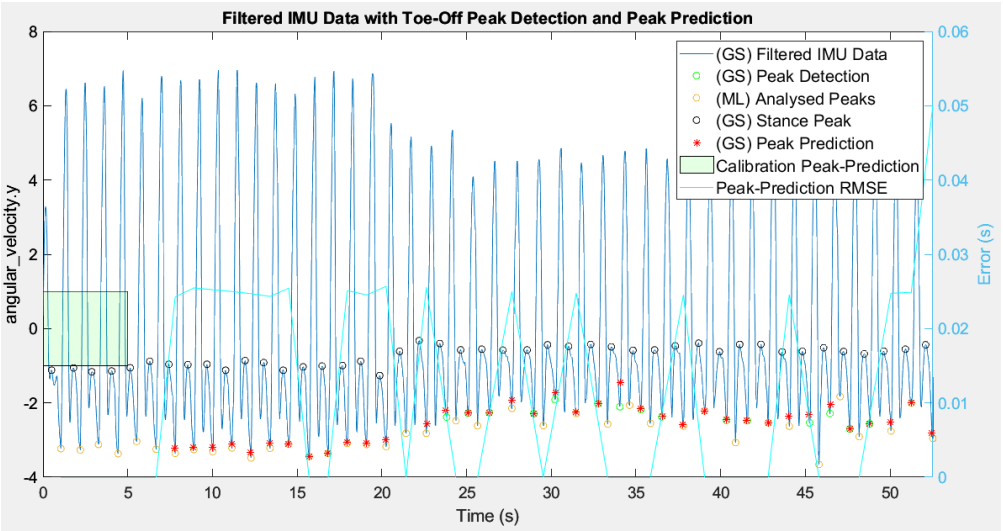


Figure 5.29: Filtered IMU Data with Toe-Off Peak Detection and Peak Prediction Tiptoe.

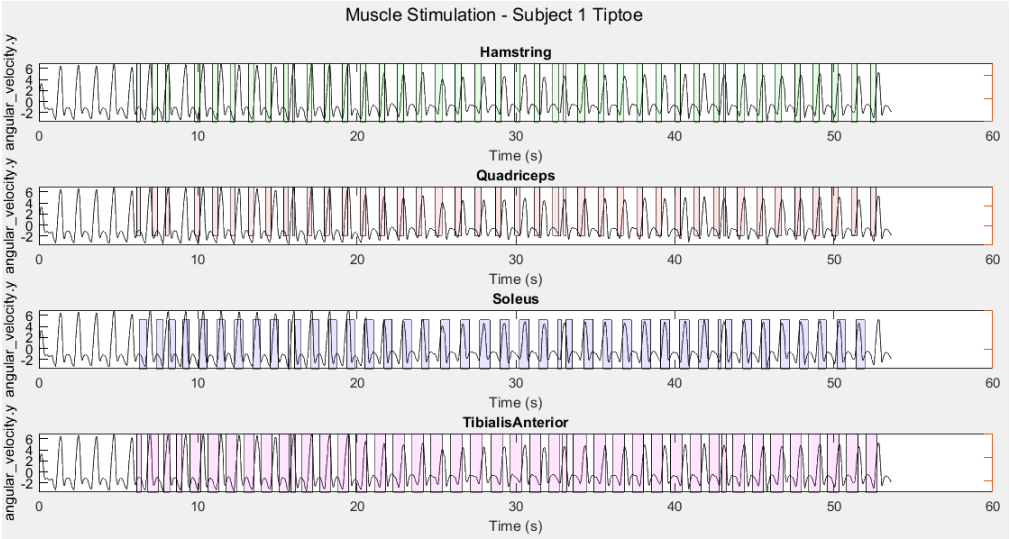


Figure 5.30: Muscle Stimulation Tiptoe.

Chapter 6

Conclusions and next steps

6.1. Conclusions

In this Master's Thesis, the aim was to create a portable afferent stimulation system that could be efficient in the treatment of freezing of gait that patients with Parkinson's Disease suffer. Despite it could not be possible to test the system with patients, the results obtained invite us to be optimistic and continue working on this line of research.

To reach the final solution, firstly, it was necessary to do some research work to find out more about the disease and the symptoms that were expected to be treated. Secondly, numerous components were analyzed in order to see which ones could be more suitable for our system and six designs were tested before getting our final system. In this step, some problems appeared with the stimulation of as many actuators as possible at the same time and at the expected vibration frequency.

Furthermore, there were problems with the treatment of the signal that made more difficult the activity of detecting each stage of the walking patterns. To solve them, it was needed to adjust the filtering and that the thresholds used for detecting the peaks change their values automatically during the gait cycle. On the other hand, a graphical user interface was implemented to make easier for the medical staff the use of this system. Additionally, a new tab was proposed with the aim that doctors can define the protocols that they need to perform with patients.

Finally, two study designs were performed with healthy subjects. The first one was intended to discover what are the parts of the body that, with stimulation, could make easier for patients to walk. The aim of the second one was to validate technically the final system. After having analyzed the results, it can be concluded that, the best parts of the body to place the actuators are hamstring muscle, quadriceps muscle and tendon and soleus muscle, as they were the places in which more patients felt a motion forward. Furthermore, after having done different tests walking with the system, despite it has limitations, we can affirm that it would be able to work with real patients with Parkinson's Disease.

6.2. Next steps

The future lines of work proposed based on the existing afferent stimulation system are the following:

To start with, taking into account that the system has not be tested with patients with Parkinson's Disease, it would be important to perform tests with them as soon as possible. With these tests, we would be able to know the limits of our system and to do the final adjustments to improve the prediction of the percentage of gait cycle in which the patient is. As result, we would be able to do a more accurate muscle stimulation which is going to help to analyze if this would help with the reduction of freezing of gait events and their duration.

Once, it has been demonstrated that afferent stimulation during the gait cycle has a real influence in the occurrence of freezing of gait events, it would be interesting to test if we would be able to change walking patterns with the system. Specifically, if we are able to make the patients to walk faster or slower by stimulating their muscles an instant before or after they should be activated. If we have success with this study, the possibility of using this system in the treatment of other diseases could be considered.

Finally, it would be advisable to create a more complete graphical user interface which allows medical staff to do a better follow up of patients and to design new protocols to perform with them. Additionally, an interesting improvement for the actual system would be to make new wires that could guarantee a stable signal and to create a case to carry all the components with the aim of achieving a more robust system.

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Appendix A

Consent Form

In this Section, the consent form that patients signed before taking part in the study designs is shown. There are two versions, one in Spanish and a second one in English because some participants were from Spain but others were from other parts of the world.

A.1. Spanish Version

Descripción del estudio GaitStimulator:

La enfermedad de Parkinson, que se estima que afecta a entre 7 y 10 millones de personas en el mundo, se define como una enfermedad no transmitible sujeta a numerosas comorbilidades y con una alta carga económica para los pacientes, sus familias y el sistema sanitario. No existe una cura para esta enfermedad.

El tratamiento está orientado a que el paciente pueda vivir de manera independiente el máximo tiempo posible mientras que se intenta minimizar su discapacidad. El tratamiento más utilizado y efectivo hasta el momento contra el Parkinson es la medicación. Sin embargo, la naturaleza crónica y progresiva de la enfermedad obstaculiza la eficacia de los tratamientos farmacológicos existentes a largo plazo. Si se tiene en cuenta que los medicamentos no son efectivos con el 50% de los pacientes y que la tolerancia a estos medicamentos decrece con la edad, sumado a que no es posible aplicar terapias invasivas en personas de la tercera edad, se antoja necesaria una investigación más profunda para encontrar nuevas opciones terapéuticas que permitan manejar los síntomas del Parkinson de una manera más efectiva.

La congelación de la marcha es uno de los síntomas más incapacitantes de la enfermedad de Parkinson. En función de la fase de la enfermedad, entre un 20 y un 60% de los pacientes sufren estos episodios. La congelación de la marcha es un síntoma motor caracterizado por periodos transitorios, de varios segundos de duración, en los que el intento de ambulación se ve afectada. Progresivamente está aumentando el número de personas que experimentan esta congelación de la marcha y van reduciendo

su nivel de actividad física para evitar sufrir este síntoma.

Con este estudio se pretende investigar cómo afectan los estímulos vibratorios de los músculos inferiores de la pierna en la mejora de los patrones de la marcha de personas con Parkinson. Además, se pretende contrastar cómo estos estímulos afectan a reducir los episodios de congelación de la marcha y la duración de aquellos que se produzcan. La estimulación vibratoria se producirá con un sistema compacto y autónomo posteriormente referido como "GaitStimulator".

El GaitStimulator es un sistema prototipo autónomo compuesto por múltiples sensores inerciales (IMU) y actuadores vibratorios. Las IMUs se colocan en distintas partes del cuerpo para detectar la postura y analizar el ciclo de la marcha en tiempo real. Los actuadores vibratorios se colocan en cuatro músculos de la parte superior e inferior de las piernas (isquiotibiales, cuádriceps, sóleo y tibial anterior), tanto de la pierna izquierda como de la derecha. Los actuadores vibratorios transmiten vibraciones a los vientres musculares con una frecuencia de 80 Hz mediante control de tensión. Las IMUs se fijan al cuerpo mediante correas de velcro elásticas y ajustables. Los actuadores vibratorios se fijan a las piernas mediante bandas elásticas. Una fuente de alimentación portátil alimenta todos los componentes electrónicos. El peso total del sistema de control y energía es de unos 2 kg y el sujeto puede transportarlo en una mochila.

Se trata de un estudio observacional in situ, de una sesión donde se tomarán distintas medidas. Dicha sesión durará 2 horas y constará de cuatro fases: Introducción, Preparación, Recogida de datos y Retroalimentación.

Autorización

Por este documento solicitamos su autorización para realizarle el procedimiento, así como a usar imágenes e información de su Historia Clínica con fines docentes o científicos, ya que está siendo atendido en un Hospital Universitario. Su anonimato será respetado.

Declaración y firmas

Antes de firmar este documento, si desea más información o tiene cualquier cuestión, no dude en preguntarnos.

Relativo al paciente

D./D.ª ..... con D.N.I ..... He sido suficientemente informado del proyecto GaitStimulator, cuyas pruebas serán desarrolladas en el Hospital Niño Jesús / IRF La Salle, y en las que voy a prestar mi colaboración, realizando actividades relativas a "ensayos para evaluar el rendimiento en la marcha utilizando un sistema de estimulación aferente"; explicándoseme sus riesgos,

complicaciones y alternativas, lo he comprendido y he tenido el tiempo suficiente para valorar mi decisión. Por tanto, estoy satisfecho con la información recibida. Por ello, doy mi consentimiento para que se me realice dicho procedimiento por el médico/investigador responsable. Mi aceptación es voluntaria y puedo revocar este consentimiento cuando lo crea oportuno, sin que esta decisión repercuta en mis cuidados posteriores. Sé que estoy siendo atendido en un Hospital Universitario. AUTORIZO la utilización de imágenes e información de la Historia Clínica resultante del procedimiento con fines docentes o científicos, tratándose de forma confidencial y anónima según dispone la legislación vigente.

En caso de cancelación, rectificación, o cualquier duda, dirigirse al equipo de investigación: Jorge Quijorna Santos (jorge.quijorna.santos@alumnos.upm.es) o Tom Busink (t.busink@student.utwente.nl).

Firma del paciente Fecha:

Relativo al investigador

D./D.ª ..... he informado al paciente y/o tutor o familiar del objeto y naturaleza del procedimiento que se le va a realizar, explicándole los riesgos, complicaciones y alternativas posibles.

Firma del investigador Fecha:

Relativo a los familiares y tutores

El paciente D./D.ª ..... no tiene capacidad para decidir en este momento.

D./D.ª ..... con D.N.I ..... y en calidad de ..... he sido informado/a suficientemente del procedimiento que se le va a realizar. Por ello, doy expresamente mi consentimiento. Mi aceptación es voluntaria y puedo retirar este consentimiento cuando lo crea oportuno.

Firma del familiar Fecha:

CONSENTIMIENTO INFORMADO DE LA VIDEOFILMACIÓN

D./D.ª ..... con D.N.I ..... domiciliado en ....., por la presente,

AUTORIZO

Al investigador, a la utilización de mi imagen en grabación audiovisual, tomada con fecha ....., para su uso por el/ella o por terceros con fines exclusivamente científicos.
En ....., a ..... de 20 .....
Firma:

Protección de datos personales

Todos los datos recopilados se manejarán y almacenarán con la mayor confidencialidad posible y se utilizarán exclusivamente para los fines del proyecto GaitStimulator. El consorcio tomará todas las medidas necesarias para garantizar que los voluntarios comprendan completamente los motivos de la recopilación de datos, el tipo de datos que se recopilarán y los detalles del uso de los datos.

Todas las actividades de prueba y evaluación en un conjunto representativo de personas sin relevar la identidad ni ningún otro dato personal a cualquier parte externa se realizarán en el Hospital Niño Jesús (Madrid) e IRF La Salle (Madrid), en colaboración con el CSIC. Los procedimientos se ajustan a las leyes y reglamentos de la Ley orgánica 15/1999, December 13, "de protección de datos de carácter personal".

Se le pedirá a los participantes en las pruebas de usuario que den su permiso por escrito para el uso de la información de edad, altura, peso y sexo con fines estadísticos. Los datos personales no serán registrados en el proyecto. Con el fin de garantizar la privacidad y protección de los datos:

- Se aplicará un código a cada usuario. La identificación entre el código y el usuario solo estará presente en el consentimiento informado, y esta relación nunca existirá en forma electrónica (es decir, si se escanea el consentimiento informado, la relación entre el usuario y el código se borrará en el proceso de escaneo).
- El código será el único medio para acceder a los resultados de los ensayos y a los datos del usuario. Los datos del usuario nunca incluirán su nombre o cualquier forma de identificación (DNI o número de pasaporte)
- Se garantizará la confidencialidad de los datos de los usuarios.
- El CSIC designará un responsable de custodia de los datos.

- Solo las personas relacionadas con el proyecto GaitStimulator podrán acceder a los datos.
- Todos los datos personales serán destruidos en un máximo de diez años después de la finalización del proyecto.

Los documentos recogidos en el proyecto (como cuestionarios o logs en Focus Groups o Living Labs) serán destruidos en un máximo de 10 años tras la finalización del proyecto por una persona designada por cada socio.

También se tendrán en cuenta la Directiva 95/46/CE sobre protección de datos y privacidad, y el artículo 29 del Grupo de trabajo de protección de datos WP 131 (establecido en virtud del artículo 29 de la Directiva 95/46/CE).

Los resultados se compartirán con los participantes si solicitan la información, pero solo después de que se complete el análisis de datos. Los resultados solo se compartirán entre el personal de investigación calificado dentro del Hospital Niño Jesús, IRF La Salle y/u otros socios de GaitStimulator. Si el participante o su tutor está interesado en ver los datos recopilados, se le entregará un resumen de los datos analizados. El personal de investigación explicará e interpretará las observaciones.

A.2. English Version

GaitStimulator study design description:

Parkinson's disease (PD), which is estimated to afflict 7 to 10 million people all over the world, is defined as Non-Communicable Disease (NCD) subject to numerous comorbidities and with a huge economic burden to patients, their families, and to the healthcare system. There is no known cure for PD.

The overall management is directed toward keeping the patient functioning independently as long as possible while minimising disability. The standard and most effective treatment of Parkinson is medication. Nevertheless, the chronic and progressive nature of the disorder hampers the efficacy of the available pharmacological treatments for long-term use. If we consider that the drugs used are not helpful in 50% of patients and that patient's tolerance to drugs decreases with age, coupled with the impossibility of applying invasive therapies in elderly patients, further research and new therapeutic options are needed to manage Parkinson symptoms more effectively

Freezing of Gait (FOG) is one of the most disabling features of PD. Depending on the stage of the disease, between 20-60% of individuals with PD suffer from episodic freezing of gait. FOG is a motor phenomenon characterized by transient periods, usually lasting several seconds, in which attempted ambulation is halted. Progressively more people who experience FOG restrict their walking and reduce their level of

physical activity to avoid triggering the motor disorder

The aim of the study is to investigate whether vibrations on different muscles bellies of the lower leg improve the walking pattern of PD patients. In addition, we would like to investigate whether these same vibrations might reduce the number of freezing of gait (FOG) and their durations. The vibratory stimulation is given via a compact, stand-alone system, hereafter referred to as GaitStimulator.

The GaitStimulator is a standalone prototype system consisting of multiple inertia sensors (IMUs) and vibrating actuators. The IMUs will be placed on various locations of the body to detect both the posture of the body as well as analyse the gait cycle in real-time. The vibrating actuators are placed on four upper and lower leg muscles (Hamstrings, Quadriceps, Soleus, Tibialis Anterior) of both the left and right leg. The vibrating actuators transduce vibrations to the muscle bellies with a frequency of 80 Hz using voltage control. The IMUs are attached to the body using elastic, adjustable Velcro straps. The vibrating actuators are attached to the legs using elastic bands. A handheld powerbank powers all the electronics. The total weight of the control and energy system is about 2 kg and can be carried in a backpack by the subject.

This is an on-site, one-session observational study using a within-subject repeated measures design. This is an on-site, single-session, observational study with different subject measures design. This session will take about 2 hours and involve four phases: Introduction, Preparation, Data collection, and Feedback.

Authorisation

We hereby request your authorisation to perform the procedure, as well as to use images and information from your medical history for teaching or scientific purposes, as you are being treated in a University Hospital. Your anonymity will be respected.

Declaration and signatures

Before signing this document, if you require any further information or have any questions, please do not hesitate to ask us.

Concerning the patient

Mr./Mrs. ..... with ID ..... I have been sufficiently informed about the GaitStimulator project, whose tests will be carried out at the Hospital Niño Jesús / IRF La Salle, and in which I am going to collaborate, carrying out activities related to "trials to evaluate walking performance using an afferent stimulation system"; having been explained its risks, complications and alternatives, I have understood it and have had enough time to evaluate my decision. I am therefore satisfied with the information received. I therefore give my consent to have this procedure performed by the responsible physician/investigator.

My acceptance is voluntary and I may revoke this consent at any time without this decision affecting my further care. I know that I am being treated in a University Hospital. I AUTHORISE the use of images and information from the Clinical History resulting from the procedure for teaching or scientific purposes, being treated confidentially and anonymously in accordance with current legislation.

In case of cancellation, rectification or any doubt, please contact the research team: Jorge Quijorna Santos (jorge.quijorna.santos@alumnos.upm.es) or Tom Busink (t.busink@student.utwente.nl).

Patient's Signature Date:

Concerning the investigator

Mr./Mrs. ..... I have informed the patient and/or legal tutor or relative of the purpose and nature of the procedure to be performed, explaining the risks, complications and possible alternatives.

Researcher's Signature Date:

Concerning relatives and legal tutors

The patient Mr./Mrs. ..... does not have the capacity to decide at this stage.

Mr./Mrs. ..... with ID ..... and as ..... I have been sufficiently informed of the procedure to be carried out. I therefore expressly give my consent. My acceptance is voluntary and I may withdraw this consent at any time.

Relavive's Signature Date:

INFORMED CONSENT TO VIDEO FILMING

Mr./Mrs ..... with ID ..... domiciled at ....., hereby,

I AUTHORISE

To the researcher, for the use of my image in an audiovisual recording, taken on the date ....., for use by him/her or by third parties for exclusively scientific purposes.
At ....., ... de 20 .....
Signature:

Personal data protection

All data collected will be handled and stored as confidentially as possible and used exclusively for the purposes of the GaitStimulator project. The consortium will take all necessary steps to ensure that volunteers fully understand the reasons for data collection, the type of data that will be collected and the details of data use.

All testing and evaluation activities on a representative set of individuals without disclosure of identity or any other personal data to any external party will be carried out at the Hospital Niño Jesús (Madrid) and IRF La Salle (Madrid), in collaboration with CSIC. The procedures are in accordance with the laws and regulations of the Ley Orgánica 15/1999, Diciembre 13, "de protección de datos de carácter personal".

Participants in the user tests will be asked to give written permission for the use of age, height, weight and gender information for statistical purposes. Personal data will not be recorded in the project. In order to ensure privacy and data protection:

- A code will be applied to each user. The identification between the code and the user will only be present in the informed consent, and this relationship will never exist in electronic form (i.e. if the informed consent is scanned, the relationship between the user and the code will be erased in the scanning process).
- The code will be the only means of accessing test results and user data. User data will never include the user's name or any form of identification (ID or passport number).
- The confidentiality of user data shall be guaranteed.
- The CSIC will designate a data custodian.
- Only people working on the GaitStimulator project will be able to access the data.

- All personal data will be destroyed within a maximum of ten years after the end of the project.

Documents collected in the project (such as questionnaires or logs in Focus Groups or Living Labs) will be destroyed within a maximum of 10 years after the end of the project by a person designated by each partner.

The Data Protection and Privacy Directive 95/46/EC and Article 29 of the Data Protection Working Party WP 131 (established under Article 29 of Directive 95/46/EC) will also be taken into account.

Results will be shared with participants upon request, but only after data analysis is completed. Results will only be shared among qualified research staff within the Hospital Niño Jesús, IRF La Salle and/or other GaitStimulator partners. If the participant or their legal tutors are interested in viewing the collected data, a summary of the analysed data will be provided. Research staff will explain and interpret the observations.

Appendix B

Ethical, economic, social and environmental aspects

The aim of this Master's Thesis has been to design and implement a neuroprosthesis for the treatment of freezing of gait by afferent stimulation. Its purpose was to have a functional system that could help to understand this pathology and contrast if by the use of this system it would be possible to reduce or remove freezing of gait and have an effect in the gait cycle patterns.

This Thesis has a huge social impact because it is going to help in the treatment of freezing of gait, a symptom that does not have a established solution for the moment. The main aim of this project is to reduce freezing of gait events and their duration. Moreover, it would be interesting to contrast if by vibration stimulation it is possible to produce changes in the walking patterns.

In terms of the economic impact, one of the advantages of this project is that the prize of the components used to make the system is not too much expensive, as it can be seen in the Appendix C. By this way, it is easier that more investigators are prone to research in this field. Additionally, despite for the moment this project is only experimental, if in the future this research has a positive outcome and it is commercialized, its prize should be as low as possible to make its purchase easier for all the patients who need it.

Finally, the environmental impact in the manufacturing of the components is unknown due to all of the components are made in China. It uses a power supply to work, so the whole consumption of energy goes out from it. The only thing to take into account is to recycle in an appropriate way the power supply when it stops to work properly. Moreover, the lyfe cicle of the components, if they are used in a responsible way, ir very high.

Appendix C

Budget

This Thesis has been realized in Robotics and Control Laboratory at Escuela Técnica Superior de Ingenieros de Telecomunicación (Universidad Politécnica de Madrid) and at Robotic and Automatic Centre (CSIC) in a period of 9 months. For the preparation of the budget needed, it has been analyzed personnel costs and materials costs, as it is shown below:

- **Personnel**:

	Hourly cost (€)	**Hours**	**Total (€)**
Project leader	60	30	1800
Supervisor	40	200	8000
Master's student	30	600	18000
TOTAL			**27800**

Table C.1: Personnel costs.

- **Material costs**:

	Lifetime (years)	**Units**	**Cost (€)**	**Amortization (€/month)**	**Use (months)**	**Total (€)**
IMU	5	5	202.7	3.38	9	30.41
Raspberry Pi 4	5	1	129.95	2.17	9	19.49
Motor	5	8	54.32	0.91	9	8.19
Driver	5	8	44.55	0.74	9	6.66
I2C Multiplexer	5	2	19.24	0,32	9	2.88
Power Supply	5	1	39.99	0,67	9	6.03
TOTAL						**73.66**

Table C.2: Material costs.

	Cost
Personnel costs	27,800€
Material costs	73.66€
Subtotal	27,873.66€
IVA	5,853.47€
Total	33,727.13€

Table C.3: Total costs.