Universidade do Minho
Escola de Engenharia

Helena Raquel Gouveia Silva Gonçalves

Functional Feedback Vibrotactile System for Patients with Parkinson's Disease: Freezing of Gait

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DECLARAÇÃO

Nome: Helena Raquel Gouveia Silva Gonçalves

Endereço eletrónico: a68371@alunos.uminho.pt Telemóvel: 968723092

Cartão do Cidadão: 14238754

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Assinatura:

Do not pursue success. Become a good engineer and success will pursue you.

"3 Idiots" - Rajkumar Hirani

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"Do not forget to thank!", one of the indications you gave me since I was a child. Well, Mum, thank you for being the first to believe in me and to be my emotional pillar in this fight. I owe you everything.

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ABSTRACT

Parkinson's Disease (PD) is a **neurodegenerative disorder** of the Central Nervous System (CNS) affecting the nigrostriatal system, with **motor and non-motor symptoms**. One of the most critical gait disturbances are the "freezing" episodes, denominated by **freezing of gait (FOG)**. FOG corresponds to **a temporary, sudden and involuntary disability to ongoing motor movement**. To overcome FOG, two approaches can be considered: the pharmacological and non-pharmacological methods. Regarding to the **pharmacological method**s, firstly, there have been **no significant scientific advances and these methods do not alter the course of PD symptom, and consequently, do not prevent FOG**. Thereby, this pharmacological barrier has encouraged new researches based on **non-pharmacological approaches.** In fact, the non-pharmacological methods **are a non-invasive and efficient solution for patients to overcome FOG**, with an increasingly innovative character. However, some non-pharmacological methods are more efficient than others and in particular, pa**tients present less difficulties in overcoming FOG when using feedback and especially Neurofeedback Systems.** In particular, Vibrotactile Neurofeedback can be perceived in any environment and easily accepted by patients. However, the **current Vibrotactile Neurofeedback Systems have some limitations for the patients**: are not ergonomic or robust, constrain the freedom of movement, are uncomfortable and not easy to use.

Therefore, in this thesis, it is presented a solution, aiming to develop and validate a **Wearable Neurofeedback Vibrotactile Device in order to help PD patients to overcome FOG**. The developed system is composed by a sensory acquisition system, a processing unit and an actuation system (the vibrotactile motors). The **sensory acquisition system** includes an accelerometer which data is used to detect the gait event. **When this event is detected, the actuation system is activated and provides the vibrotactile feedback.**

The implemented system was validated **in healthy and in PD patients in Hospital of Braga**. The results allowed to conclude that the system i**s able to provide vibrotactile Neurofeedback according to the motion of each user and, more importantly, the patients showed a good acceptability in using the system while walking.**

KEYWORDS: PARKINSON'S DISEASE, FREEZING OF GAIT, NEUROFEEDBACK SYSTEMS, VIBROTACTILE FEEDBACK

RESUMO

A doença de Parkinson (DP) é uma doença neurodegenerativa do Sistema Nervoso Central (SNC) que afeta o sistema nigrostriatal, **com sintomas motores e não motores**. Um dos distúrbios de marcha mais críticos são os episódios de "congelamento", denominados pelo *freezing of gait* (FOG). O FOG corresponde a uma i**ncapacidade temporária, repentina e involuntária de oferecer continuidade ao movimento**. Para superar o FOG, duas abordagens podem ser consideradas: os métodos farmacológicos e não farmacológicos. Em relação aos **métodos farmacológicos**, em primeiro lugar, n**ão houveram avanços científicos significativos e esses métodos não alteram o curso do sintoma de DP** e, consequentemente, **não impedem o FOG**. Deste modo, esta barreira farmacológica incentivou novas pesquisas baseadas em abordagens **não farmacológicas**. De fato, os métodos não-farmacológicos são **uma solução não-invasiva e eficiente para que os pacientes superem FOG**, com um caráter cada vez mais inovador. No entanto, alguns métodos não farmacológicos são mais eficientes do que outros e, em particular, **os pacientes apresentam menos dificuldades em ultrapassar o FOG ao utilizar feedback, especialmente através de Sistemas de *Neurofeedback***. Em particular, o *Neurofeedback* Vibrotátil pode ser percebido em qualquer ambiente e facilmente aceito pelos pacientes. No entanto, o**s atuais sistemas de Neurofeedback Vibrotátil têm algumas limitações para os pacientes:** não são ergonômicos ou robustos, limitam a liberdade de movimento, são desconfortáveis e não são fáceis de usar.

Portanto, nesta tese, é apresentada uma solução, **com o objetivo de desenvolver e validar um Dispositivo *Wearable* de *Neurofeedabck* Vibrotátil para ajudar pacientes PD a superar FOG.** O sistema desenvolvido é composto por um sistema de aquisição sensorial, uma unidade de processamento e um sistema de atuação (os motores vibrotáteis). O **sistema de aquisição sensorial** inclui um acelerómetro, onde os dados adquiridos são usados para detetar um evento da marcha em particular. **Quando este evento é detetado, o sistema de atuação é ativado e fornece o feedback vibrotátil.**

O sistema implementado foi validado e**m pacientes saudáveis e em pacientes com DP no Hospital de Braga**. Os resultados permitiram concluir que o sistema **é capaz de fornecer *Neurofeedback* vibrotátil de acordo com o movimento de cada usuário e, mais importante, os pacientes mostraram uma boa aceitação no uso do sistema durante a caminhada.**

PALAVRAS-CHAVE: DOENÇA DO PARKINSON, FREEZING OF GAIT, SISTEMAS DE NEUROFEEDBACK, FEEDBACK VIBROTÁTIL

ÍNDICE

LIST OF FIGURES

List of Tables

LIST OF ABBREVIATIONS AND ACRONYMS

CNS	Central Nervous System
DESC	Discrete Event-driven Sensory feedback Control
ERM	Eccentrical Rotation Motors
FF	Foot-flat
FOG	Freezing of Gait
FSR	Force Sensitive Resistors
HO	Heel-off
HS	Heel-strike
IMU	Inertial Measurement Unit
MST	Mid-stance
PD	Parkinson’s Disease
RAS	Rhythmic Auditory Stimulation
RQ	Research Question(s)
TO	Toe-off

CHAPTER 1 – INTRODUCTION

This dissertation presents the work developed over the fifth year of the Integrated Master in Biomedical Engineering, more precisely, in Medical Electronics Branch. The project was developed in the Biomedical & Bioinspired Robotic Devices Lab (BiRD Laboratory) at the Center for MicroElectroMechanical (CMEMS) established in University of Minho. In addition, the culmination of the proposed work was achieved through the validation of the developed system at the Hospital of Braga in collaboration with the Clinical Academic Center (2CA).

The knowledge assimilated in the development of the thesis addresses the assisting and rehabilitating of abnormal gait patterns areas presents in a wide range of neurological diseases. In fact, the main goal of my thesis is the development of a wearable neurofeedback system for patients with Parkinson's disease (**PD**) in order to account for one of the gait abnormalities caused by this disease: the Freezing of Gait (**FOG**). This system provides vibrotactile feedback to patients with PD, so that they can integrate it into their normal gait physiological system, allowing them to overcome the freezing episodes and thus improve their gait impairments. The system is based on the user-centered principle, considering the end-user driven, multitasking and less cognitive effort concepts.

Thereby, in this dissertation, all steps taken, studies in the literature, critical analyzes, implemented procedures and obtained conclusions are presented in this dissertation.

1.1 Motivation

PD is a **neurodegenerative disorder** of Central Nervous System (**CNS**), which affects the motor and non-motor system and for which there is still no cure [1]–[3]. Being the most prevalent disease in the world, it was estimated to be around 20.000 persons in Portugal suffering from PD, reaching more than 1 in 100 persons in Europe [1] and affects approximately 1 million Americans [2].

Even tough PD itself is not fatal, this disease cause hard complications and his origin is not yet known, but is assumed to result from a combination of environmental and genetic factors. Interestingly, one of the genetic mutations, that origin PD, is more frequent in Portugal than in the other Europe countries or even in United States [2], [3].

PD’s symptoms include a continuous loss of motor control as stiffness, slow movement, postural instability, resting tremors and a wide range of **gait disorders**. Furthermore, non-motor symptoms can be pointed out, as depression, loss of sense of smell, gastric problems, cognitive damages and many others[1]–[6]. It was noted that symptoms of PD begins often after 55 years old and being the rarest cases diagnosed before 40 years old [3].

One of the most critical gait impairments caused by PD are the **FOG events**, which corresponds to a **temporary, sudden and involuntary disability to ongoing motor movement** [7]. These FOG episodes can occur at any time and, consequently, to **complicate the patients' quality of life** [8]. Besides that, there is a **danger of falling**, once the beginning and the end of these episodes are **unpredictable**, which is very dangerous for older patients [6], [8]–[10].

In order to overcome FOG, two approaches can be considered: the **pharmacological and non-pharmacological methods** [11]–[13]. Regarding to the pharmacological methods, there are **no significant advances** and, usually, the **patients become dependent on the medication** [12], [13]. Thereby, this **pharmacological barrier** has encouraged to **new researches** aiming develop devices more effective.

In fact, the non-pharmacological methods are **non-invasive and efficient solutions** for patients to overcome FOG avoiding the habituation phenomenon [13]. Nonpharmacological studies, devices and methods were presented in [13] and [14] such as generals training exercises, physiotherapy, treadmill, robotic gait training, mechanical assistive devices, methods with virtual reality, systems based in neurofeedback, among others. In particular, it was founded that the **patients present less difficulties in overcoming FOG when external cues are provided through the use of Neurofeedback Systems** [13]–[19].

Sensory cueing systems can be defined as the use of temporal and spatial external stimulus aiming to improve gait dysfunctions. There are three main cueing systems: visual, auditory and vibrotactile systems [12], [13], [20], [21]. On one hand, the visual systems can only be used in a rehabilitation context or in places where FOG occurs frequently, not avoiding the unpredictability of these events. The use of auditory systems is compromised in noisy environments [20], [21]. On the other hand, **the vibrotactile feedback is able to be perceived in any environment and easily accepted by patients**. Indeed the vibrotactile neurofeedback systems have proven to be the most promising method to help PD patients to overcome the freezing events [14]–[19].

Haptic bracelets, podotactile systems, headbands and trunk vibratory systems are devices developed able to provide vibrotactile feedback [14]–[19]. Haptic bracelets have only been validated with a small number of patients [15] and the users accused some discomfort when using the podotactile systems [17], [19]. Headbands and trunk vibratory systems have only been used in a rehabilitation context [14], [18]. In general, the current vibrotactile systems present some limitations that should be improved: **do not consider feedback control strategy, ergonomics, robustness, freedom of movements, patients' comfort and thus have low user acceptability**.

1.2 Problem Statement

If on the one hand, vibrotactile systems have proven to be a promissory non-pharmacological approach to aid PD patients to combat FOG, on the other hand, it is important to overcome the limitations of the previous mentioned vibrotactile systems. Thus, it is necessary **to develop a vibrotactile neurofeedback system** that focuses on the **principles of patient use** and require **low cognitive effort**, so that the developed system **must be embedded in the user's daily life**.

The sensitivity of the skin varies from zone to zone in the human body. Thus, firstly, it is required **to identify the best body zone** to provide vibrotactile feedback without the wearable system compromises the patients' freedom of movement in their daily tasks. Once the best body zone has been identified, it is necessary **to define the feedback control strategy to adopt**, with the ultimate goal that the vibrotactile feedback must **integrate the patients' motor physiological system**. Therefore, it is imperative to **tune the vibrotactile feedback with the gait events of each patient**, being required to use sensors to detect the moment of each gait event. Thus, combining the gait data acquired in real time, it is possible to provide a synchronized vibrotactile pattern for each patient. However, in order to develop a system that can be embedded into the users' daily lives, the required sensors should be embedded onto the system.

These are requirements that are the key **to the development of a wearable system based on vibrotactile stimulus to aid PD patients**, presenting an innovative character and allowing **to improve some issues** of the **actual vibrotactile systems** developed.

1.3 Goals and Research Questions

The main goal of this thesis is **to develop a vibrotactile neurofeedback wearable system** in order to **help PD patients to overcome FOG**, decreasing the number or the duration of freezing episodes. The system will be validated in healthy and through the definition of inclusion and exclusion criteria as well as clinical protocols, some key requirements will be validated with PD patients in a *hospital context*, in order to enable a design user-driven.

In order to achieve this main goal, it is required to understand a set of notions, from the knowledge of physiological concepts, to the integration of the electronic system developed in this thesis. For instance, it is important to gather knowledge about the sensorial system in humans' body, specifically in patients with PD, and their sensorial feedback during the gait cycle. Additionally, it is important to perform a critical study on other vibrotactile systems already developed, in order to identify the most efficient feedback strategy to provide.

Thus, this main aim is divided into several goals, in order to represent all the methodological steps established to attain the ultimate goal, as follows:

- **Goal 1:** the first goal aims to **study about PD** and more specifically, about on the **FOG**, one of its motor symptoms. The culmination of this goal, is to analyze it is possible to **overcome FOG**;

- **Goal 2:** the second goal is to make an **extensive analysis about the several studies, techniques and devices already developed**, based on **vibrotactile feedback systems** and related with PD, specially used to overcome FOG. This state of art aims to understand how the **interaction and integration between systems and patients works**. Also, as a second goal, it is **intended to identify the limitations** in the existing vibrotactile devices aiming **to propose new solutions**, bringing up the requirements that the system must attend;

- **Goal 3:** the third goal is to understand how the **human skin perceives the vibrotactile stimulus**, in order to identify the **ideal body zone to provide vibrotactile feedback**. In addition, this goal will make it possible **to establish the frequency range of vibration** to provide, in accordance with the range of skin perception. Also, it will enable **to propose an ergonomic and wearable system** that can **be integrated in the daily tasks of each patient**;

- **Goal 4:** the fourth objective is to establish **how will be performed the bridge between the patients' sensory motor system and the feedback to be provided**. With this goal it is required to realize **the importance of detecting the gait events** and some technical constraints such as the need of **synchronize the real-time gait detection and providing the vibrotactile stimulus**. It is also imperative to define the **feedback strategy** (continuous *vs* discrete event-driven) in order to avoid the **phenomenon of**

habituation without requiring too much **cognitive effort** from users. It is important that **the proposed feedback is able to integrate the users' motor physiological system, replacing the missing capabilities**.

- **Goal 5:** the fifth goal is **the design of the project**, namely the exploration and identification of the materials to be used in the system in order to guarantee a robust, universal and adaptable system for each patient. Furthermore, it will be identified the electronic components required for the sensory data acquisition system, the data processing unit, the control system of vibrotactile motors and the wireless communication unit. This goal will **define the vibrotactile system specifications**, the real-time gait acquisition, implement the gait events detection and a state machine for gait events transitions and synchronous integration of the electronic system to collect the gait signals and control the vibrotactile units.

- **Goal 6:** the sixth goal aims to validate the developed system **by carrying out a set of experimental tests**. Thereby, it is required **to define the experimental tests and clinical protocols** (participant **inclusion and exclusion criteria**) in accordance to the actual state-of-art of clinical tests with PD patients and in particular PD patients with FOG, addressing for instance typical situations that trigger freezing episodes. Furthermore, it will be important **to establish a set of metrics to evaluate continuously the patients** in each test session; and

- **Goal 7:** following the previous goal, at this point, it is intended to carry out a **critical analysis of the collected data** in order to optimize the system designed and verify the raised hypothesis.

Once the goals have been defined, then the research questions (RQ) of this project are presented, being expected to be answered in the present work:

- **RQ 1:** What are the symptoms associated with FOG episodes and how it manifests in PD patients? Which is the best approach to help PD patients improve motor symptoms? These RQs are addressed in Chapter 2.

- **RQ 2:** Which the non-pharmacological methods with greater potential to help PD patients to overcome FOG? Which kind of stimulus can overcome FOG episodes? Which feedback should be provided to patients? These RQs are addressed in Chapter 3.

- **RQ 3:** What is the frequency range of vibration perceived by the mechanoreceptors of the skin in the human body? Where is the ideal location of the delineated system to provide vibrotactile feedback in human body? How many vibrotactile units are needed to provide the required stimulation and were should be place? These RQs are addressed in Chapter 4.

- **RQ 4:** How will it be possible to integrate the feedback provided in each patients' motor sensory system? How important is the detection of gait events for the feedback strategy to adopt? Should this strategy be continuous or discrete time driven? These RQs are addressed in Chapter 4.

- **RQ 5:** Which are the electronic components required to provide the appropriate vibrotactile feedback? Which are the control mechanisms necessary to control the vibrotactile motors? Which are the sensors with greater potential to acquire the gait signal and be integrated in the developed system? These RQs are addressed in Chapter 5.

- **RQ 6:** What is the frequency of vibration that should be provided in the vibrotactile feedback? How long should the vibrotactile stimulus be given? How to obtain a robust algorithm for gait event detection through the acceleration in lower trunk? How to incorporate this algorithm with the control system of the vibrotactile units in a synchronized way? These RQs are addressed in Chapter 6.

1.4 Contribution to Knowledge

A wearable system based in Vibrotactile Neurofeedback was implemented, being a safe and stable device for help PD patients to overcome FOG. In particular, the main contributions of this work are:

- Detection of the best perceived frequency around the abdomen and identification of the minimum interval to perceive vibrotactile feedback in healthy and PD patients;
- Implementation and Validation of an algorithm for gait detection in real-time through a sensor built into the developed system for healthy subjects and PD patients. The gait detection is performed by the single-axis acceleration measured in the lower trunk. Also, in this scope, an algorithm to estimate gait parameters was implemented, based on the gait segmentation.
- Development of a wearable system able to provide vibrotactile feedback in a time-discrete manner and synchronized with a gait event. It was designed for to be adapted for each person, allow freedom of movements which is essential for multitasking and require low cognitive effort.

1.5 Publications & Oral Presentations

The accomplished work allowed the publication of **two conference papers** and **three conference oral presentations** as follows:

- **Helena Gonçalves**, Graça Minas, Ana Rodrigues and Cristina Santos. **"Functional Feedback Vibrotactile System for Patients with Parkinson's Disease-Freezing of Gait"**, 2017 IEEE 5th Portuguese Meeting in Bioengineering (ENBENG), February 16-18, Coimbra. **– *Oral presentation.***

- **Helena Gonçalves**, Inês Lima, Graça Minas, Ana Rodrigues and Cristina Santos. **"Literature Review of Vibrotactile Systems Addressing Freezing of Gait in Parkinsonians"**, 2017 IEEE 17th International Conference on Autonomous Robot Systems and Competitions (ICARSC), April 26-28, Coimbra. **– *Oral presentation and Paper.***

- **Helena Gonçalves**, Graça Minas, Ana Rodrigues and Cristina Santos. **"Neurofeedback Vibrotactile System for Parkinsonians Overcome Freezing of Gait: First Steps in Detecting the most Perceived Frequency",** 2017 IEEE Climbing and Walking Robots and Support Technologies for Mobile Machines (CLAWAR), September 11-13, Porto. - ***Oral presentation and Paper***.

Furthermore, in addition, **two journal pape**r are being written:

- Detection of the best Frequency perceived around the Abdomen in patients with Parkinson’s Disease; and
- Real-time Gait Events Detection and Gait Parameters Estimation through the Lower Trunk Acceleration in patients with Parkinson’s Disease.

Lastly, the thesis was applied for the **Fraunhofer Portugal Challenge 2017 – Idea Contest**, having passed to the second phase of the contest that is currently unfolding.

1.6 Thesis Outline

This dissertation is organized as follows.

Chapter 2 presents the motivation of the present thesis, describing several points about PD, namely epidemiology, risk factors, causes, symptoms and treatments. Subsequently, FOG is defined, as well as how it manifests itself and what are the consequences for the patients and possible causes of this motor symptom. Finally, it is described **how it is possible to overcome the FOG episodes**, making a relevant contrast between **pharmacological and non-pharmacological approaches**.

A **general overview of the non-pharmacological methods** used in the scope of PD, aiming to improve the motor symptoms and, in particular, the FOG is made in **Chapter 3**. Also, a **critical comparison** between each of the presented methods is made, highlighting their limitations in order to propose a solution that will allows patients to overcome FOG.

In **Chapter 4** it is explained how works the interaction between the provided vibrotactile feedback and the human sensory system. Thus, in this chapter it is explored the **human vibrotactile frequency discrimination** in skin and for different body zones. Lastly, it is analyzed the **feedback control strategy** that must be followed in order to allow the integration of the vibrotactile feedback in the patients’ sensory system.

In **Chapter 5** is presented the **developed solution**, discussing the importance of each of its components, specifying their functions, in order to explain all the systems that make up the global system developed: a **vibrotactile neurofeedback system for PD patients to overcome FOG**.

Chapter 6 presents the **validation** of the developed system, explaining the implemented experimental tests. A **system overview** of the implemented system, the **methods** and **validation**, the obtained **results** and the **discussion** are discriminated for each of the tests accomplished.

The **conclusions** of this work are made in **Chapter 7**. Finally, the **proposals to continue** this work in the **future** are written in this chapter too.

Note: In the figures which are presented videos, for the print dissertation format it is possible to view the videos in question using the QR code that is next to the respective figures.

CHAPTER 2 - PARKINSON’S DISEASE: FREEZING OF GAIT

In this chapter is made a contextualization about **PD,** describing the epidemiology, risk factors, causes, symptoms and treatments. On this thesis, one of the major symptoms of this disease is addressed, the **FOG**. Thus, a FOG definition is presented, as well as how it is manifested and which are the consequences for the patients and possible causes of this symptom. Finally, it is described how it is possible to overcome FOG episodes, making a relevant contrast between a pharmacological and non-pharmacological approaches.

2.1 Parkinson’s Disease

In 1817, the English doctor *James Parkinson* made the first description of patients with PD, however, there are older documents that refer to symptoms already potentially caused by this disease. Later, it was the French neurologist *Jean-Martin Charcot* who gave a more detailed description of the PD symptoms and proposed for the first time the name of "Parkinson's Disease" [3].

PD is the second most common **neurodegenerative brain disorder**, being estimated that affects 20000 persons in Portugal, more than 1 in 100 persons in Europe [1], approximately 1 million Americans [2], reflecting approximately 1% of the world's population [3]. Figure 2.1 depicts the number of persons who died with PD worldwide in 2009. In this figure it was used a measure denominated DALY – the disability-adjusted life year – which corresponds a measure of overall disease burden, expressing the number of deaths per year due to ill-health, disability or early death [22].

PD does not directly increase the risk of mortality. However, it should be emphasized that this disease is associated to hard complications that indirectly increase the risk of mortality (**gait disorders**, dementia, urinary infections, among others) [3].

The PD main risk factor is the age, which means that the likelihood of developing the disease increases with aging. Other potential risk factor is the family history and some studies suggests that PD is slightly more frequent in men even though this conclusion is not consensual [2]–[4].

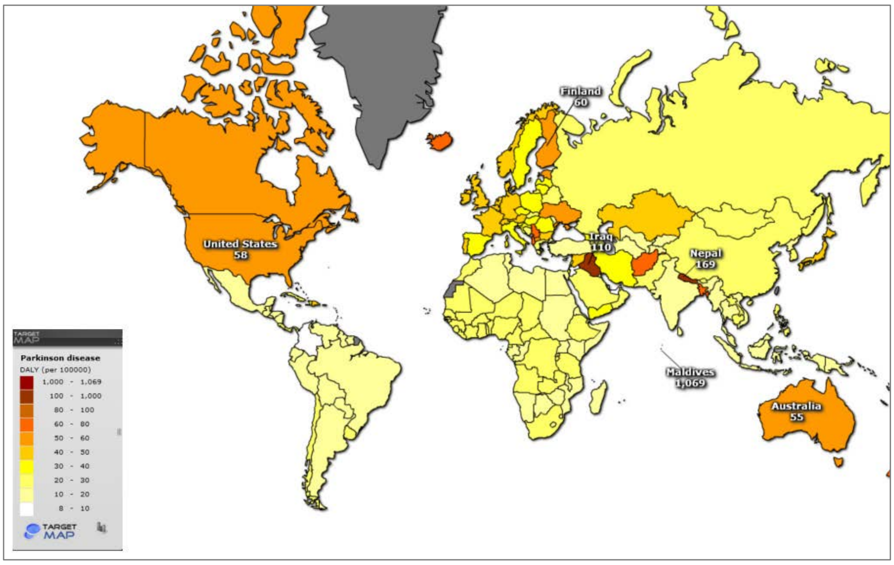


Figure 2.1 - Number of persons who died with PD worldwide in 2009. Adapted from [22].

Although **PD's origin is not yet known**, it is assumed to result from a combination of **environmental and genetic factors** [4]–[6]. Interestingly, one of the genetic mutations, that origin PD, is more frequent in Portugal than in the other Europe countries or even in United States [2], [3].

Even so, it is known that the PD motor impairments are caused by the **degeneration of a neurotransmitter called dopamine** in the substantia nigra, a brain area responsible for producing dopamine neurons. Effectively, many PD patients lose 80% or more of their dopamine-producing cells.

Figure 2.2 expresses the dopamine route in the brain. The substantia nigra contains the dopamine which provides nervous signals that will travel to brain regions - the thalamus, the striatum and the globus pallidus - responsible to trigger the production of brain signals in these regions to control the motor movement and balance in persons [6]. Therefore, the significant decrease of dopamine, leads to **make it impossible to the patients to execute their normal motor tasks** and thus, to appear the first symptoms in patients with PD [6], [23]. However, it is important to point out that even though the dopamine's cause of degeneration remains uncertain, many studies have identified the presence of common cellular characteristics on the brain of PD patients: the accumulation of Lewy bodies and Lewy neurites (abnormal and dense clumps of proteins that grow inside of the nerve cells) in neurons of the substantia nigra, which may interfere with the transmission of nerve signals or other important neuronal functions, including the correct production of dopamine [6].

On one hand, PD is considered a devastating disease, but one the other hand, PD's progression may take 20 years or more. However, in some persons, the disease progresses much

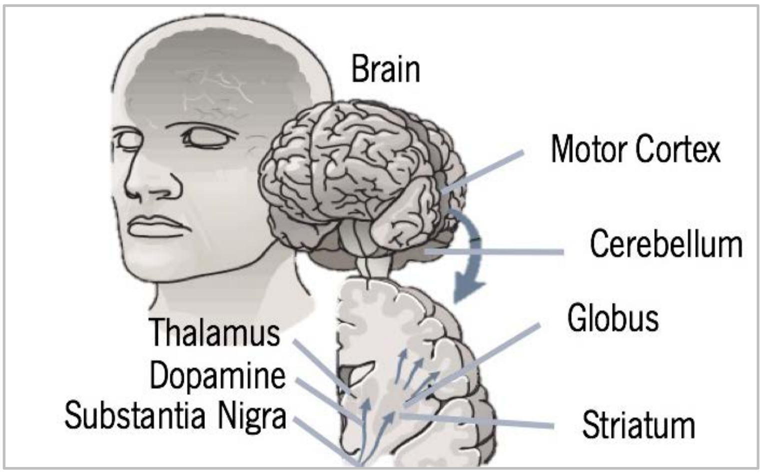


Figure 2.2 - The dopamine pathway in the brain. Adapted from [6].

more quickly and it was noted that PD's symptoms begin often after 55 years old and in the rarest cases was diagnosed before 40 years old [1]–[4], [6].

Currently, there is no standard test for diagnosing PD and usually the PD diagnosis is based on symptoms, medical history and results of some clinical examination [1]–[6]. Symptoms usually do not develop until 80% of the dopamine in the brain is damaged. In the early stages the symptoms are milder and the diagnosis is difficult [6].

Table 2.1 corresponds to a common system used to describe how the symptoms of PD progress and the subsequent features, called Hoehn and Yahr scale [4], [6].

Table 2.1 - Hoehn and Yahr scale of PD [4], [6]

Stages	Symptoms and Signs	Features most known
I	Signs and symptoms on one body side only Symptoms mild Symptoms inconvenient but not disabling	Usually presents tremors in one limb Social environment have noticed changes in posture, gait and facial expression
II	Symptoms are bilateral Minimal disability Posture and gait affected	-
III	Significant slowness of body movements Early impairment of equilibrium on walking or standing up	Generalized dysfunction that is moderately severe
IV	Severe symptoms Can still walk but with a limited extent Rigidity and bradykinesia	No longer able to live alone Tremors may be less than earlier stages
V	Cachectic stage Complete invalidism Cannot walk or stand	Requires constant nursing care

Besides this scale, another scale usually used is the Unified Parkinson's Disease Rating, being considered a scale more complicated with more ratings which measure mental behavior, functioning, mood, daily tasks and motor function. Either Hoehn and Yahr scale or Unified

Parkinson's Disease Rating scale are important to measure how PD patients are faring and how much treatments are helping them [2]–[4], [6].

The motor and non-motor systems are affected, causing hard complications and lowering the patients' quality of life. Cognitive impairments, apathy, depression, psychosis, panic attacks, anxiety, hallucinations, excessive salivation, speech impairments, loss of sense, sweating, gastric problems, sexual alterations, urinary problems or constipation, pain and fatigue are PD's non-motor symptoms that can be pointed out. In the motor symptoms, it is common to verify **a continuous loss of motor control**. In fact, PD interferes with motor movement more and more as time goes on, including akinesia (difficulty in starting a movement) or even bradykinesia (slowness of movement), rigidity, postural reflexes instability, resting tremors (rhythmic movement of the extremities in the resting position) and a **wide range of gait disorders** [2]–[6].

The akinesia and the bradykinesia are experienced as the difficulty and slowness to open and close hands, to hold a glass, to get up from a chair, to start the gait and difficulty in writing that tends to become smaller (micrography). The rigidity consists of a resistance to passive mobilization of a segment of the human body (neck, trunk and limbs), contributing in the long term to osteoarticular problems (e.g. arthrosis) and muscular atrophy [3], [4]. The postural instability is a consequence of postural reflexes perturbations due to the bradykinesia, and usually, there is a direct correlation of postural instability with the greater severity of the disease and other motor symptoms, such as the rigidity or cognitive disturbances [3]–[5]. The resting tremors are essentially more noticeable on the hands, face and lips and tend to appear asymmetrically, progressing to both sides with the worsening of the disease. Some patients during their gait present small steps (festination), impaired balance (especially with difficulty to stabilizing the arms), poor foot elevation in gait cycle, sometimes an involuntary increase in walking speed and freezing episodes at the beginning or during walking presenting a difficulty to restart gait [3].

2.2 Freezing of Gait

With regard to the motor symptoms, one of the most cardinal gait disorders are the freezing episodes, denominated by **FOG.** Indeed, many PD patients, already in a middle-stage of PD, experience freezing episodes [11], [24], [25] more precisely it occurs in 50% of patients with advanced PD [12].

The FOG corresponds to **a temporary, sudden, transient, unpredictable and involuntary disability of movement of people performing gait** [11]. Usually these episodes last few seconds [13] and are associated with a unique feeling described as: the patient feels that his feet are glued to the ground, causing him to remain in the same place, despite making a concerted effort to overcome the motor block and move on [7]. Curiously, it is noted that these episodes do not affect only walking, can also occur during the speech moments and even in repetitive tasks involving the upper limbs, such as writing [12].

It is possible to distinguish three types of freezing manifestation: **1 - leg trembling –** while the feet are still on the ground, knees move slightly, making legs tremble; **2 - shuffling –** slow movement once the lifting of the feet from the ground is locked and it is characterized by producing unusually small steps; and **3 - complete akinesia –** the feeling of total rigidity and immobility, i.e. a complete inability to move on (it most occurs in the initiation of movement) [12].

In general, the freezing episodes often happen when something interrupts or gets in the way of a normal sequence of movements, giving an unpredictable feature for these episodes and consequently, increasing the danger for the patient.

Although these events may occur at any time, tend to typically occur **at the start or end of the gait, while walking in tight spots, crossing gates, to turn a corner, to turn around, to circumvent objects, when the floor changed or even when patients are doing multitasks**. Furthermore, these episodes can result from stressful situations or when PD patients are **surrounded by crowds** [13]. In Figure 2.3, it is presented a short video of an older PD patient suffering some freezing episodes, representing some of the situations that trigger a FOG episode – crossing a carpet, turning around and crossing a gate [26].

Figure 2.3 - An older PD patient suffering some freezing episodes, while crossing a small carpet. Adapted from [26].

There are PD patients who do not have FOG episodes, but the patients who suffer from these episodes present a **high risk of falling** since their balance is affected, which is very dangerous for older patients. In addition, as PD progresses, freezing is more likely to happen.

Thereby, the episodes of freezing **drastically affect the patients' daily motor tasks, decreasing their quality of life** [11], [12].

Currently, it is not possible to point an exact cause for these episodes and, in fact, **the neurological and pathological root of FOG events is unknown**.

A previous study analyzed video recordings and revealed that FOG events are often associated with shaking legs when the PD patients endeavor to overcome the blockages of FOG, speculating that it **is an atypical form of dystonia of the legs or dystonic tremors** (involuntary contractions and spasms) [24]. In fact, a laboratory studied the values measured with pressure sensors placed in the insoles of patients, which demonstrated an increase in high frequency components (2-6Hz) during an episode of freezing. These measured values may represent an attempt to overcome the episode, **from the nerve messages through the neural network**, which interferes with normal gait patterns [25]. Studies performed about the steps carried before a FOG showed that there is a cumulative loss of stride length, accelerative cadence and an abnormal time of the tibialis anterior and gastrocnemius muscle activation, suggesting **a central deficit in rhythmic control of the gait during the FOG events** [11], [25]. Despite these neurological studies do not identify the reason that causes a patient to suffer blockages during gait, it is possible to suggest that **there is a failure to forward the nerve message that allows the motor system to be controlled** [23]–[25].

Indeed, even though the FOG pathological cause is unknown, some widespread changes in the brain structure and function in PD patients have been associated with this pathology, since during FOG events occur motor, cognitive and postural impairments. As a matter of fact, some studies were performed about functional metabolism involving patients with PD, who have experienced FOG and non-freezing counterparts, in order to compare the acquired information in brain during walking. As a result, some alterations at the brain level were detected: blood flow modifications in the orbitofrontal and the parietal brain areas, an abnormal concentration of glucose and high levels of dopamine in brain regions of the striatum and parietal. The researchers also verified that certain functional alterations in specific areas of neural networks are associated with FOG events: frontopariental area (area between the frontal and parietal lobe), visual occipital-temporal (area between the occipital and temporal lobe) and a brain supplementary motor area involved in the mobility process[27], [28]. In spite of the various methodological and technical paradigms used in these studies, it is possible to claim that **a dysfunction of higher-order brain centers** together with **the midbrain and brainstem regions** (involved in the dynamic and rhythmic control of gait and other movements) are involved in the FOG events [28]. Therefore, the pathological reason for FOG is directly related to the **characteristic brain damage of PD, the degeneration of dopamine** [6], [8], [23]–[25], [27], [28].

2.3 Overcome a Freezing Episode: Pharmacological *vs* Non-pharmacological Approach

PD is a very heterogeneous disease, **with a wide variability from patient to patient**, not only in terms of initial clinical symptoms, but also in terms of response to medication and the number of motor complications [6].

The first drugs to be used in the treatment of PD were composed with an anticholinergic effect (substances extracted from plants or synthetically produced). However when the doctor *Hornykiewicz,* in the early 1960s, discovered that PD patients had a decrease in the chemical dopamine (neurotransmitter) in some areas of the brain, this discovery opened the door for the use of the drug levodopa (which degrades in dopamine). In fact, in 1961, the neurologist *Birkmayer* injected for the first time into patients levodopa (provided by *Hornykiewicz*) with an undisputed beneficial effect. The marketing of levodopa tablets and other antiparkinsonian drugs continued in the following decades. More recently, a new breakthrough has occurred in the treatment of the disease with the introduction of new surgical techniques. Although there have been descriptions of brain surgeries since the early 20th century, it was in 1987 that *Alim-Louis Benabid* first used deep brain stimulation surgery (electrode placement in the brain) for the treatment of these patients [3], [4], [6].

Nowadays, **a pharmacological approach is always followed**, with **Levodopa** being the most prescribed medication. The improvement of motor symptoms through pharmacological treatment depends on the stage of the disease and the response initially. After the clinical diagnosis, during the first 3 to 5 years, most patients have a "honeymoon" phase, where antiparkinsonian medication can control the symptoms. However, with **the course of the disease** there is a loss of efficacy of medication related to several factors: the **need for larger doses of medication, shorter time of medication effect, worse control of motor symptoms and even increased incidence of side effects of the medication itself**. One of these side effects are the motor fluctuations, which develop after 5-10 years of medication and is a situation that occurs to more than half of the patients medicated. These **motor fluctuations** refer to changes in the patient's clinical status throughout the day, with periods in which motor symptoms are well controlled (referred to as periods **ON**) and periods in which these symptoms reappear (designated **OFF**) and in which patients may suffer motor symptoms such as FOG [4], [6], [11].

In fact, for more than 20 years, the researchers have been actively seeking a drug that delays or reverses PD and its symptoms [3]. Some medications show efficacy in delaying the progression of motor symptoms, but the effect is constant for everyone: **as the disease progresses, the effectiveness of the medication is reduced and at present there is no marketed drug that has shown delay or reversal of the progression of the disease** [3], [4], [8], [11].

With regard to the surgical treatment, the deep brain stimulation allows motor improvements similar to those obtained with levedopa, but with almost disappearance of motor fluctuations. Regardless of the stage of the disease, it is verified that the patients get their symptoms controlled for a few years, disappearing the unpredictability of the OFF periods. In fact, the patients are able to obtain more improvements and somehow increase their quality of life, when they follow a surgical treatment comparing to a drug treatment [3], [11].

However, over time, even patients who have undergone a surgical treatment, have motor symptoms that improve, but after came back. In addition, the surgical interventions carry an inherent risk during surgery: there is a high risk of cerebral hemorrhage during surgery, which can lead to permanent neurological damage and it occurs in 2% of cases [3].

Thereby, like medication, **the surgical interventions do not cure or alter the course of P**D [3], [6], [8], [11]–[13].

Indeed, in order to overcome the freezing episodes, instead a pharmacological approach can be followed. However, as mentioned above, this approach **does not allow to change the course of the disea**se, not preventing FOG. Further, in the last years, there has been **no scientific progress that reverses this situation**. In this way, this **pharmacological barrier has driven to follow other approaches in order to defeat these limitations** [8], [11]–[13].

Thus, non-pharmacological approaches have been heavily explored by researchers, revealing their innovative character [13], [29]. **Physiotherapy, treadmill and robotic gait training, mechanical assistive devices, systems based in virtual reality and neurofeedback devices** have been the most explored methods in the proposed non-pharmacological apporaches [13].

Contrastingly, these **non-pharmacological methods have proven to be effective** in ensuring a **continuous improvement of motor symptoms** and, in particular, **helping patients to overcome or to prevent the freezing episodes**. Consequently, it has been possible **to**

improve patients' quality of life so that they can easily perform their daily motor tasks **more autonomously and without difficulty** [12], [13].

2.4 Discussion & Conclusions

A contextualization about the PD, **a neurodegenerative disorder** of **CNS** which affects the **motor and non-motor system** was presented. Then, one of the most critical gait PD motor symptoms, the "freezing" episodes, denominated as freezing of gait (FOG), was discriminated. FOG can be described as a **temporary, sudden and involuntary disability to ongoing motor movement**.

To overcome FOG, two approaches were presented: **the pharmacological and non-pharmacological methods**.

Regarding to the **pharmacological methods**, firstly, there have not been **significant scientific advances**. Furthermore, these methods are **invasive** and **do not alter the course of PD symptom** and consequently, **do not prevent the freezing episodes**. As a result, the **patients' quality of life is limited**.

Thereby, this pharmacological barrier has encouraged to new researches based on non-pharmacological approaches. In fact, the **non-pharmacological methods** are **non-invasive and efficient solutions for patients overcome FOG**, with an increasingly **innovative character**. Thus, the patients present a continuous **improvement of PD symptoms**, allowing **to reduce the number and/or duration of freezing episodes** and consequently, **increase their quality of lif**e. Table 2.2 presents these considerations on the two approaches that can be followed to help patients improve their motor symptoms and in particular to overcome episodes of freezing.

Table 2.2 - Final considerations about Pharmacological vs Non-pharmacological approach

Approach			Considerations
Pharmacological	Medication	Levodopa	✘ Without significance scientific advances ✘ Invasive method ✘ Does not alter the course of PD symptoms ✘ Does not prevent FOG
	Surgical interventions	Brain deep stimulation	
Non-pharmacological	Physiotherapy Treadmill and Robotic gait training Mechanical assistive devices Virtual reality systems Neurofeedback systems		✓ Increasingly innovative character ✓ Effective and non-invasive ✓ Increase patients' quality of life ✓ Continuous improvement of PD symptoms ✓ Reduce the number/duration of FOG

In view of the above, it is possible to conclude that in order to aid PD patients, the approach that should currently be followed is to develop a non-pharmacological system **centered on patients**.

CHAPTER 3 - LITERATURE REVIEW OF NON-PHARMACOLOGICAL SYSTEMS ADDRESSING FREEZING OF GAIT IN PARKINSONIANS

In this chapter is presented a general overview of the non-pharmacological methods used in the scope of **PD**, aiming to improve the motor symptoms and, in particular, the **FOG**. Thereby, a critical analysis is performed about each one of the methods, comparing them and identifying their main limitations, in order to delaine a system that allows patients to overcome FOG.

3.1 Introduction

The non-pharmacological methods have received much attention in the last years, since are an **effective approach** in **increasing patients' quality of life**. Indeed, in [13] was presented an analysis of nonpharmacological methods, showing they are **capable to improve the gait performance**, **patients' autonomy** and, in general, **PD symptoms**.

In fact, there are multiple techniques and methods for improving PD motor symptoms that have much potential to aid patients in their daily tasks. The **general training exercises, physiotherapy, treadmill, robotic gait training, mechanical assistive devices, methods with virtual reality and systems based in neurofeedback** have been pointed out [13], [30].

However, **some methods are more effective than others to overcome the freezing events** and it was founded, for instance, that patients usually **have less difficulties with movement when external stimuli (sensory cues) are provided through the neurofeedback systems** [13]. Thus, it is necessary to a review all non-pharmacological methods that allows discuss the current non-pharmacological limitations. In this chapter, this point is addressed, providing a review on non-pharmacological methods and raising up critical issues.

3.2 General training exercises and Physiotherapy

The **training exercises** and **physiotherapy** aim at re-education and maintaining physical activity, enabling that the treatment has a better efficiency and also a social and psychological improvement of the PD patient [31]. Furthermore, general exercises and physiotherapy are the strategy most applied to improve stability in patients [13] and a personalized program of physical therapy can help postural problems, deformities and gait disorders [32].

In 2006, the *American Academy Neurology* presented some efficient physiotherapeutic modalities to PD patients: multidisciplinary rehabilitation with physiotherapy components; treadmill train with partial suspension of weight; balance and high intensity resistive train; music therapy; and yoga [13], [27], [31]. In addition, it is included in the program passive and active exercises, walk training, development of daily activities, heat and ice treatments, electrical stimulation and hydrotherapy [32]. The models of rehabilitation use multiple compensatory strategies as therapeutic approach [13].

Since these disease is progressive, exercise sessions should not only be carried out in a short time, but must become a lifestyle for patients. Many clinicians claim that it is very important to start training sessions from the moment it is established the diagnosis of disease in order to prevent muscle atrophy among other deficiencies on muscle tone [33][28]. [28] states that the exercise sessions when are held at an early stage of the disease, allow motor control closer to the physiological motor control which consequently favors the more advanced stages of the disease. Besides that, physical therapists work with patients with the main goal to improve range of motion, exercise tolerance or endurance, and overall motor function. It is especially helpful to improve axial or midline motor function such as difficulties in gait, arising from a poor posture and reduction in the balance [31].

In fact, among the many consequent benefits of training, stands out the increase of tonus and strength muscular involved in the gait, as well as improvements in the balance of the steps, where there was an increase in the length of steps. In addition to these benefits, it was shown that it is possible to get a better biomechanical posture alignment [32]. In [13] it was alleged that, on exercising patients with PD in a randomized control trial, it was showed positive changes in functional axial rotation and functional reach. Furthermore, the used exercises resulted in lower rates of fall and consequently higher quality of life.

So many aspects as the proper functioning of musculoskeletal system and exercises adapted to the severity of the disease are important for being considered in regards the regular and functional exercises in order to improve motor symptoms and quality of life in PD patients. Thus, if the correct functioning of the exercises is no longer possible due to the motor impairments of patients, the exercises should take into account the current state of the patients' motor abilities. Therefore, it is necessary to have regular contact with a therapist who can assess the functional status of the patient and according to this assessment to develop an appropriate set of exercises [28].

The physiotherapists generally intervene in four stages:

- **Stage 1 - Pre-habilitation:** This stage corresponds to a prevention phase, where the program of exercises starts even before the patients present motor symptoms (balance disturbed, stiffness or movement disabled). Generally, the physical therapists, in the first months after diagnosis of the disease, have a considerable scope to teach patients the strategies to optimize the locomotor performance and tricks to accomplish physical activities before starting the medication. At the time of the diagnosis, the disease progression is usually minimal, which provides to the physiotherapists an opportunity to take an advantage of the patients' capacity for motor skill learning of patients.

- **Stage 2 – Rehabilitation:** In this disease's phase, patients already present symptoms. Furthermore, the freezing episodes begin to occur at this point, so it is very important the physiotherapists indicate a set of measures to be taken in these situations. Thus, it is still possible to take steps to fix these problems. There are some techniques for correcting posture, balance issues, strengthen of some muscles, reduce the number of falls and combat the freezing episodes. Additionally, at this stage, it is necessary to adjust the type and time of medication to the motor symptoms experienced by each patient and the severity of each symptom.

- **Stage 3 – Preservation:** At this stage, the main goal is to preserve all the work that has been done up to this point, in order not to worsen certain motor symptoms.

- **Stage 4 – Prevention:** Over time and the older of patients, the physiotherapists show a less emphasis on the treatment of impairments of the body's structure and postural, unless these impairments are the reason of particular problems such as pain, complications in swallowing or even difficulties in breathing. At this point, usually are involved training nurses or family members to minimize some activity limitations such as to help patients to move from one position to another or to perform daily activities (eating, dressing, moving, among others).It is important to highlight that, as in the previous stages, but more than ever, the physiotherapists must work in partnership with the patients' families, other medical members and with the patient [28], [34].

The exercises more important refers to the flexibility, aerobic and strengthening. Furthermore, there are crucial exercises for walking, turning and falls prevention. As for flexibility, the most suitable exercises are stretching tips: standing stretches (chest, back and shoulder stretches); seated stretches (neck, chest, hamstring, overhead, rotation stretches and ankle circles); and lying stretches (shoulder and rotation stretches). The aerobic exercises involve jogging, dancing, swimming, biking and chair aerobics. These exercises, not only aim to improve motor functions, but also to allow to overcome cardiovascular problems. Regarding the strengthening exercises, it is included six types: wall slides; quad strengthening; shoulder blade squeeze; and on-the-ground strengthening exercises (bridge, quadruped and back extension) [34]–[36]. Figure 3.1 depicts some of these general exercises: a flexibility, an aerobic and a strengthening exercise.

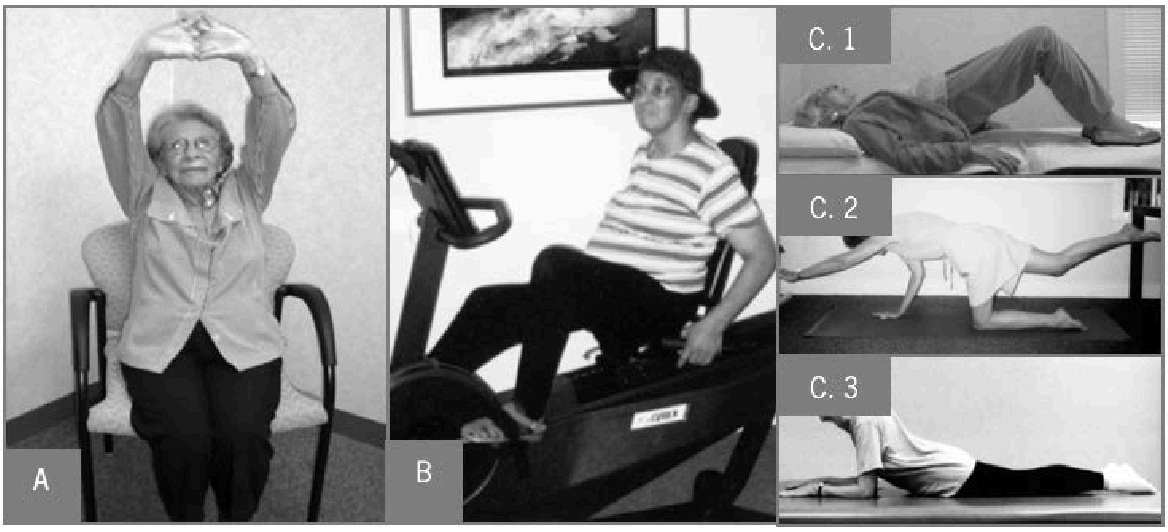


Figure 3.1 - Examples of general exercises: A. Flexibility Exercise – seated overhead stretch; B. Aerobic Exercise – chair aerobic exercise; and C. Strengthening exercises – C.1 bridge; C.2 quadruped and C.3 back extension. Taken from[11].

In short, the general training exercises and physiotherapy have several types of treatment for various PD symptoms, being the largest concern the rigidity due to the loss of range of motion and the lack of balance in locomotion. Thus these strategies are safe, effective and affordable methods in order to improve balance, posture, self-esteem, well-being and quality of life of patients [32]. Finally, knowledge about the rehabilitation of people with PD is increasing, but there is still a need to improve and verify patients' awareness for a possible better life [28].

However, it should be emphasized that this non-pharmacological method **"obliges" the patients to be directed to the training sessions**, requiring a **commitment from patients**.

Another important factor is that in many countries physical therapy sessions are **monetarily inaccessible** to many people [37].

3.3. Treadmill and Robotic Gait Training

As a potential intervention, the electromechanical devices have been suggested to assist the patients' gait. In 2010, in [38] *Cochrane's* review stated that the treadmill training has no effect on cadence and the effects on the walking are not clear in PD patients. However, in the last years, it was reported the efficiency of task-specific, intensive and forced use of gait rehabilitation programs based on treadmill training, improving the walking distance, gait speed and stride length in patients with mild to moderate PD [13], [39]. Advantageously, the speed of treadmill can be adjusted according to the severity degree of the patients' illness [39]. In addition, robotic gait training, specifically robotic treadmill training, provides long and safer duration walking and improve walking capacity, stride length, fatigue and gait speed in PD patients [39], [40]. Frequently in the last years, it was preferred used treadmill with robotic assistive than without them [13], [39]–[41].

When comparing effects of **robotic gait training v**ersus equal intensity **treadmill training** and conventional physiotherapy on walking ability in patients with mild to moderate PD, it is possible to explore some conclusions about that. [40] aims to compare the effects of these points. Sixty patients with mild to moderate PD were randomly assigned into three groups equals: robotic gait training group underwent robot-assisted gait training; treadmill training group performed equal intensity treadmill training; and physiotherapy group underwent conventional gait therapy according to the proprioceptive neuromuscular facilitation concept. All patients performed 45-minutes treatment sessions, three days a week, for four consecutive weeks and patients were evaluated before (T0), after (T1) and 3-months post-treatment (T2). Regarding to the results on the primary outcome (T0), not statically significant difference was found between the robotic gait training group and the treadmill training group. However, after the treatment, on the primary outcomes (T1), a statically significant improvement was founded in favour of robotic gait training group, compared with the treadmill training group and physiotherapy group. Finally, on the last evaluation (T2), the last results were confirmed. These results support the fact that robotic gait training improve walking more efficiently, when it is considered the post-treatment, than physiotherapy and treadmill training [13], [40].

Picelli in [41] presents a study which aim was to determine whether robotic gait training could have a positive influence on postural stability in patients with mild to moderate PD. In this study, thirty-four patients with mild to moderate PD were randomly allocated into two groups: robotic training group underwent robot-assisted gait training; and physiotherapy group experienced a training program not specifically aimed at improving postural stability. The treatment sessions lasted 40-mintues, three days a week, during four weeks. They were performed by patients' groups and they were evaluated before, immediately after and 1-month post-treatment. In favor of the robotic training group, a significant improvement was found after treatment and all improvements were maintained at the last evaluation. Therefore, it was concluded that robotic gait training improves postural instability in patients with mild to moderate PD [13], [41], as described in [40].

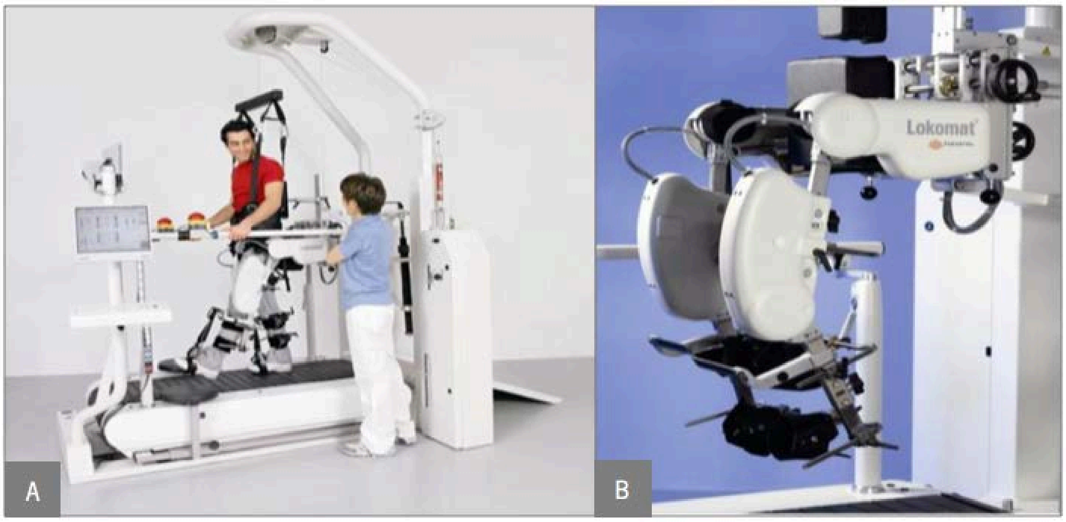


Figure 3.2 - The Gait Trainer GT1 (Reha Stim, Berlin, Germany). Taken from [109].

In these studies, in the robotic gait training groups, the patients were treated with Gait Trainer GT1 (Reha Stim, Berlin, Germany) – Figure 3.2, which is a static suspension system. The use of the GT1 allows a robot-assisted propulsion of gait, stimulating the swing and stance phase. This system consists in two-motor-driven footplates, thus the participants were secured in a harness with their feet on footplates, while movements of the center of mass were controlled in a phase-dependent manner by ropes attached to the harness. Concerning to the gait parameters, it was evaluated with the GAITRite system (CIR System, Havertown, PA) [40], [41].

Another study used the Lokomat for the robotic treadmill training, depicted in Figure 3.3, a driven gait orthosis that automates locomotion therapy offering mechanical guidance of lower extremity trajectories. In this study, seventy PD patients were evaluated during their

Figure 3.3 - The Lokomat: A. Automated gait orthosis on a treadmill with a body weight-support system; and B. Lokomat leg orthosis. Taken from [40].

robotic treadmill training sessions and, again, the patients demonstrated to improve their motor symptoms and consequently their gait performance [42]. It is important to accentuate that the Lokomat allows to decrease the number of FOG episodes, since the system uses a dynamic body weight-support organization in order to sustain the patient above a motorized treadmill synchronized with the Lokomat [43].

In summary, the robotic gait training was useful to improve the functional mobility, the walking capacity, the motor symptoms and provided a transient improvement in the PD patients' quality of life. In addition, when compared with the conventional physiotherapy sessions, there are further improvements in motor symptoms. Two other strong points of these sessions are the fact that it is possible to directly measure patients' gait allowing a more thorough evaluation and to relieve the hard work of physiotherapists [13], [39]–[41].

However, just like the physical therapy sessions, the **treadmill and robotic gait training sessions** require the **patients to move to a specific site for treatments**, not addressing the **daily patients' tasks** [44].

3.4 Mechanical Assistive Devices

In the past few decades, the **mechanical assistive devices** have gained wide impact in its utilization in PD patients, allowing to enhance patients' mobility, assisting them to maintain balance and giving them a self-freedom to execute their daily routines [45].

With the advancement of technology, there are a wide variety of mechanical assistive devices that can help patients with PD and some of them correspond at the standard devices used in geriatric and physical medicine. This way, the standard assistive devices also can be used in PD patients with a special adaptation to the case of the patient [45], [46].

It is possible distinguish three general types of mechanical assistive devices indicated to improve PD patients' gait: canes and walking sticks; walkers; and power wheelchairs [45].

Canes and walking sticks, generally are used in patients with moderate level of illness. Although a simple single cane may prevent or reduce falls in patients without balance, a four-legged (quad) cane can provide a greater support (Figure 3.4).Modern canes are light-weight, strong, easy adjustable for proper height and can have a variety of grip styles [45]–[47]. Recently, it was developed an interesting cane, a laser-cane: this system consists in a device attached to the cane that projects a red laser light beam horizontally across the floor in front of the patient, providing a visual cue that might help patients to overcome the starting of hesitation and freezing (Figure 3.5) [45].

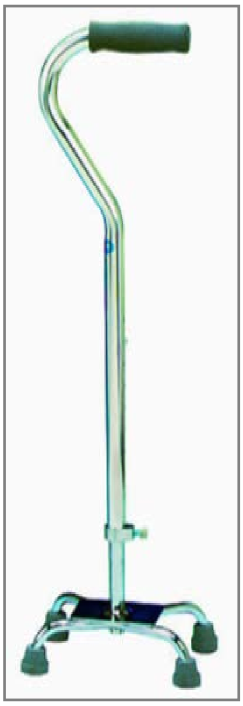


Figure 3.4 - Four-legged (quad) cane. Taken from [42].

Figure 3.5 - Laser cane. Taken from [42].

Concerning to the walkers, these systems are used when the canes cannot provide the adequate support. Even though the traditional four-legged aluminum walker can be useful in PD patients, stabilizing patients and increasing confidence, many patients fall over backwards still holding their walker. Thus, a good solution was presented by placing wheels on the walker legs – wheeled walker. In the last years, novels wheeled walkers as three-legged, four-legged and U-shaped designs have been presented (Figure 3.6) [45], [47]. These modern walkers are more lightweight, fold easily for placement into a vehicle and more comfortable for the hand's support. By the same token that happens with laser-cane, a laser can be attached to the walker and project a red laser light beam to help patients in the same terms of laser-cane [45].

Figure 3.6 - Walkers: A. Three-wheeled walking stabilizer; B. Four-wheeled walking stabilize; and C. U-shaped walking stabilizer. Taken from [42].

With regard to the last type of mechanical assistive devices, when the patients cannot ambulate long distances, due to many disturbances in gait as FOG, other specific motor symptoms or imbalance, it is adequate to use a power wheelchair, allowing to the patients more independence, specially outside in houses. Although in the last decades it was developed a wide variety of power wheelchair's designs with a hand control, it is very important to adapt the system to the patients' symptoms (such as tremors or bradykinesias) (Figure 3.7) [45].

Currently, few scientific studies have been done on the efficiency and risks of these mechanical assistive devices for the gait of PD patients. Thus, it is only possible to assess

Figure 3.7 - Power wheelchair with hand-controller. Taken from [42].

something based on clinical experience and, in fact, it was verified that these devices allow to aid the PD patients' gait during their daily tasks, obtaining a greater autonomy [45].

In general, the canes and walking sticks are ideally used for PD patients at a milder stage; the walkers are very useful for people with moderate gait deficiency (PD motor symptoms at an intermediate stage) and at a later stage for patients with severe gait deficits, the motorized devices, as power wheelchairs, are ideal to provide this autonomy in lost mobility [45]–[47]. An important aspect to consider is that the use of tools such beams, which present visual cues, reduce the periods of freezing, such as the laser-cane [45] or feedback system that will be discussed.

However, in spite of the mechanical assistive devices' potential benefits, some studies have shown that **30–50% of people abandon their devices soon after receiving them**, raising questions about the **effectiveness**, **appropriate selection** and **risks** that these devices may present [45]. Some reports have pointed out that assistive devices may actually **increase the risk of falling** by a variety of mechanisms and thus can sometimes worsen gait in PD patients: the presence of any disturbance in the environment in which the patient is walking, such as a carpet, causing balance problems [45], [46].

Another limitation is pointed, the need for patients to **allocate an adequate cognitive** and **attentional resources** to control an assistive device. This cognitive weight is detrimental for patients with cognitive impairments, besides to make impossible to perform **multitasking** [45].

3.5 Virtual Reality

In last years, the **virtual reality** training has been also considered for improving balance deficits for different types and ages of population [13].

Espay in [48] developed a device constituted by a virtual augmented reality goggles and earphones. The virtual augmented reality goggles contain built-in LCD screen, which projects floor tiles while patient are moving, and earphones produce sound step-matched cue as determined by on attached sensor. The device is constituted by three main systems can be seen in Figure 3.8: a small measurement-computation unit attached to the patients' clothing; earphones; and head-mounted microdisplay.

The open-loop devices can improve gait and balance impairments but it is considered that these devices may be unreliable in FOG in some patients. Therefore, the development of a wearable virtual reality device, driven through inertial sensors that delivers earth-stationary visual feedback, offered the hypothesis to examine a closed-loop sensory (visual-audio) feedback system. This system displays a life-size virtual checkerboard-tiled floor superimposed on the real world through specialized goggles, in closed-loop. Likewise, the rhythm of auditory cue is determined through the rhythm of the steps [49].

Figure 3.8 - Virtual reality goggles, containing a built-in LCD screen between the visors and earphones, attached at the belt. Taken from [49].

Espay focused in assessing the efficacy of a wearable, closed-loop, visual-auditory cueing device in patients with PD in an off-stage (baseline values) and after two weeks. It was concluded that this closed-loop sensory feedback when used an at-home training program, is on effective and desirable intervention to improve gait, able to decrease FOG, and consequently increases the quality of life of PD patients [48], [49].

Another system that uses virtual reality to assistance PD patients is the *Nintendo Wii*, which has been considered a good alternative in the motor rehabilitation [13], [50]. The use of virtual reality by Nintendo Wii allows an interaction that develops physical, auditory, visual, cognitive, psychological and social tactics during the activities, working with the aim to improve functional performance and gait [50]. With the objective of studying the effect of virtual sensorimotor activity on gait disorder in patients with PD, fifteen subjects were evaluated performing activities with Nintendo Wii virtual platform into three categories: aerobics, balance and Wii plus exercises. All subjects carried out separate virtual exercises twice a week, for 40-minutes, performing a total of 14 sessions. All patients demonstrated a continuous improvement in gait performance, with an increase in stride length and gait speed, and a reduction in motor impairment, especially in the items of rigidity and flexibility of the lower limbs. In fact, in the last evaluations, patients manage to do the Nintendo Wii activities without help, with rhythm and upper limbs control, and performed the exercises in less time [50]. In the same study, it was claimed that a 69-years-old patient who underwent three different Nintendo Wii Fit exercises twice a week for 8-weeks, showed a high improvement in functional performance and gait speed. Additionally, it was stated that Nintendo Wii Fit^{TM} is useful to practice not only motion exercises but also cognitive abilities in order to help patients to maintain, reaffirm and learn cognitive functional techniques [13], [50].

Some similar studies that allowed to compare virtual reality balance training, conventional balance training and untrained group have been done in the last years [13], [48]–[50]. Some of them showed that virtual reality training improves patients' balance with more efficacy than other training sessions. However, some of these studies reported that virtual reality trainings have a similar impact to conventional balance trainings. Even so, virtual reality training proved be a feasible, safe, and powerful technique to improve gait performance [13], [48]–[50]. However, nowadays, these devices still present a **low degree of acceptance** on the part of patients, are often considered **uncomfortable** and "**weighted" cognitively** and are **expensive** equipments [49], [51].

3.6 Neurofeedback Systems

In [13] was presented an analysis of nonpharmacological methods, showing they **are capable to improve the gait performance and consequently the patients' quality of life** and such methods show that **patients usually have less difficulties with movement when some kind of external cue is provided** [12], [13], [20], [52], [53]. In fact, it is possible to affirm that techniques based in **sensory cueing can be efficient for overcoming FOG events**, allowing **patients to improve motor functions** and **decrease the number of freezing episodes or its severity** [12]. Sensory cueing can be defined as **the use of external temporal or spatial stimuli to facilitate movement, gait initiation and continuation** [12].

There are four main systems of cueing: **visual cueing** (include for instance perpendicular stripes on the floor, walking sticks, rhythmic flashing light mix on glass frames or even a laser beam mounted on a chest or shoes and virtual reality); **auditory cueing** (metronome is the most used in Rhythmic Auditory Stimulation – RAS); and **tactile cueing** (haptic system) [12], [23], [49], [50], [53], [54]. A fourth system of cueing can be considered, it consists in **a mix** of the previous other systems [12], [55], [56].

Rosemarie in [53] analyzed the effect of provide sensory cueing in PD patients who already have experienced FOG. It was compared five different sensory cues on the duration of freezing episodes: vibratory alert, auditory alert, vibratory rhythm, auditory rhythm and visual cue. The vibratory alert was constituted by three vibration pulses delivered at the right calf slightly below the knee joint and auditory alert by three binaural beeps of 1 s duration with breaks of 1 s in between. Regarding to the vibratory and auditory rhythm, the signal was composed by ten vibration pulses and ten binaural beats, respectively. The visual cues were presented through two parallel stripes projected on the floor.

Seven PD patients, regularly suffering FOG episodes, participated in the experimental tests, where they had to walk a predefined course repeatedly and two seconds after FOG episode's cues were always triggered (Figure 3.9). The course contained elements that typically evoke freezing and consisted of the following tasks: 1 - Standing up from a chair and getting a glass of water from the kitchen; 2 - Going with the glass to the bathroom and leaving the glass on the washbasin; 3 - Walking to the bedroom and picking up a clothes hanger from the cupboard; 4 - Carrying the clothes hanger to the washing room and leaving it there; 5 - Going back to the chair; and 6 - Performing tasks 1-5 in reverse order starting with task 5.

In order to evaluate the effect of provided cues, the average duration of freezing episodes under the different cueing conditions was determined. All freezing episodes with duration of 2 s or more were taken into account for further analysis. It was considered a freezing episode when the patient stops and/or hesitates until the next was accomplished.

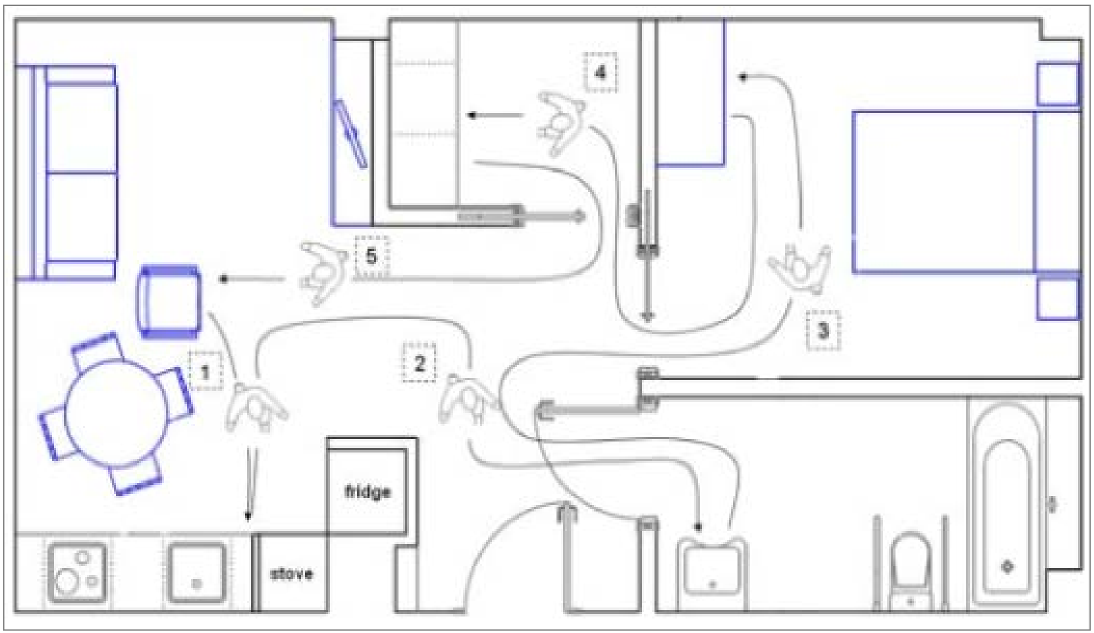


Figure 3.9 - Course and tasks performed by the participants under different cueing conditions in an observation laboratory: 1-Standing up from a chair and getting a glass of water from the kitchen; 2- Going with the glass to the bathroom and leaving the glass on the washbasin; 3- Walking to the bedroom and picking up a clothes hanger from the cupboard; 4 -Carrying the clothes hanger to the washing room and leaving it there; 5 – Going back to the chair; and 6 – Performing tasks 1-5 in reverse order starting with task 5. Taken from [50].

The values measured showed that the best decrease of the average duration of freezing, comparing with the value baseline (7.9 s), was obtained with visual cue (5.3 s) and vibratory rhythm (6.3 s). The subjective individual evaluation provided by patients through questionnaires, curiously, affirmed that the audio alert and vibratory signals had a better effect in reducing their freezing duration. Although the results have not been coherent t, it is possible affirm that the s**ensory vibratory cue allows high improvements in the patients' gait**, specifically, in the events FOG [53].

3.6.1 Visual Cueing

When episodes of **FOG often occur in the same places at home or even in a rehabilitation session**, **visual cueing** could be an efficient method to help patients overcome a freezing episode [57].

Some techniques used in patients with PD are presented in figures 3.10 to 3.14: floor strips (verticals and horizontals); an assistive carpet; placing obstacles or colored things of the floor; and digital visual cueing tests [12].

In [21], [58] was reported two studies that evaluated the duration of FOG in seven PD patients when they walked a predefined course in the presence of situations that might trigger a freezing episode. Comparing the sessions with visual cues in form of stripes projected on the floor with the baseline sessions, without visual cues, it was verified a decrease on the average duration of freezing episodes. Another study was carried out in order to investigate the effect of visual cues in PD patients assessing some gait parameters: the stride length and gait speed [59]. In this study was used two types of visual cue, a taped step length markers on the floor and an individualized subject-mounted light device projected to the ground. After performing experimental tests with 14 PD patients, it was verified that in the baseline conditions (without visual stimuli), the stride length and gait speed were reduced in patients. By contrast, both of

Figure 3.10 - Floor stirps: A. vertical and B. horizontal. Taken from [12].

these parameters increased using visual cues in the experimental tests. It is noteworthy that the reaction time was also measured while performing specific tasks and it was obtained better results through the use of the subject-mounted light device. Lastly, the main finding of this study is that the stride length can be regulated using stationary visual cues without increasing patients' perceived effort [59].

Despite the benefits of using visual cues, as mentioned above, their use has limitations since are **only recommended in a rehabilitation context or in places and situations that often trigger freezing episodes.** Thus, these visual neurofeedback systems do not address the issue of **multitasking**, limiting the **autonomy** of patients in performing their daily tasks [57].

Figure 3.11 - Assistive carpet. Taken from [12].

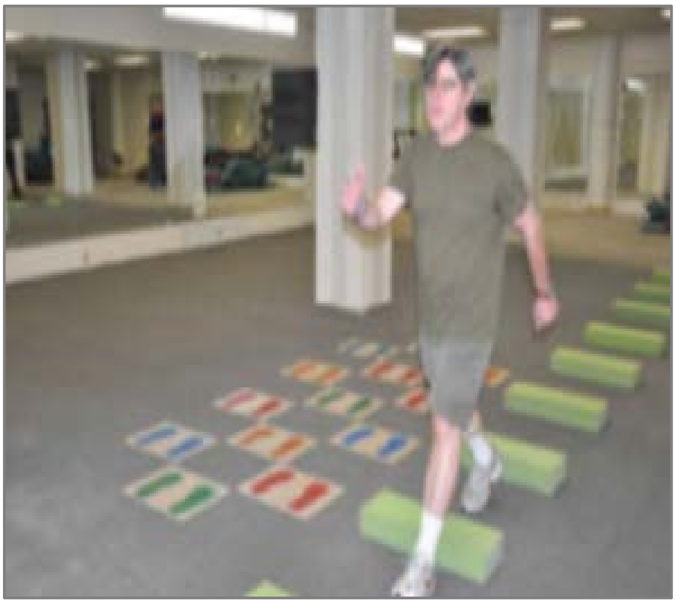


Figure 3.12 - Walking with obstacles. Taken from [12].

Figure 3.13 - Visual cueing test. Taken from [12].

Figure 3.14 - Visual cueing with colored stars. Taken from [12].

3.6.2. Auditory Cueing

Auditory cues are another form of stimulation helpful for improving gait in PD patients [60]. In [23] was summarized studies that demonstrate the effects of Rhythmic Auditory Stimulation (RAS) on improving gait deficits in parkinsonians. In fact, the auditory cueing, specifically RAS, such as playing marching music or simple songs, has been proven to be an inexpensive, safe and an effective method in assist patients, improving their motor deficits in a variety of movement disorders.

Several studies were published comparing music and metronome in gait rehabilitation sessions in healthy persons: while one study affirms that healthy young adults exhibit a speeder gait with music than with metronome cues, another similar study reported a significantly increase in cadence with both music and metronome cues. Although, these studies demonstrated that music has the same or better effect than metronome at increasing velocities, a third study showed that metronome cues favor a better gait synchronization and speed. Similarly, familiar songs also result in less stride variability and faster gait velocity, due to the fact that it requires less cognitive demands in synchronizing footsteps with familiar beats [23].

In [54] was proposed the use of a smartphone device, coupled with external accelerometers, as a system for providing RAS (through earphones or headphones) when FOG episodes are detected. The biggest challenge for the researchers was to develop a system that only provided RAS cues when FOG episodes were detected through external accelerometers. In addition, the system was intended to be unobtrusive and portable, since the use of permanent RAS could be uncomfortable for patients during their daily routines. Therefore, they called their system FOG-Assist which consists in an Android application package, Bluetooth-enable accelerometers and pre-trained classification models (Figure 3.15): the FOG-Assist software enabled to any Android smartphone to act as the main core of system. With this system, it was

Figure 3.15 - The FOG-Assist system on a Nexus One smartphone with external accelerometers. Taken from [51].

eliminated the need for dedicated hardware while providing context-aware RAS to patients in an unobtrusive manner [54]. In [61] it was validated the efficiency of this last presented device in detecting FOG events, demonstrating that it is able to detect these freezing events and provide the correct and corresponding auditory cue.

In 2014 [62] and 2015 [63], other devices with the same idea were developed and studied. The development of these wearable systems, through a smartphone-built architecture to detect online FOG events and provide auditory cues in order to improve gait, allowed to increase the acceptability and usability for the patients. Thereby, it was possible decrease the number of FOG events.

A wide variety of devices have been developed to provide fixed-time RAS, for instance: the Listenmee®, an intelligent and portable goggles' system containing built-in headphones that delivers RAS while patients are walking in order to improve gait; the Walk-Mate, an interactive RAS device which used pressure sensors in shoes that feed gait timing data into a computer system and adjust the metronome cueing beat in real-time; and the D-Jogger which is a system that the music displayed is adjusted with patients' gait rhythm [23]. All these studies and developed devices prove the fact that auditory cueing is an effective method to improve motor symptoms in patients with PD, since it allows to increase the gait cadence and synchronization [23], [54], [60]–[63]. Yet, it is important to refer that the use of these auditory neurofeedback systems bring complications when their use involves **noisy environments** where auditory feedback may not to be clear.

3.6.3. Vibrotactile Cueing

Human skin can convey vibrotactile messages that are carried to the brain via afferent nerves, being recognized as a receptor for communicating sensorial information. For instance, vibrotactile feedback can be utilized to encode vibration measurements from an assistive device to the skin of the user [20].

In 2011, a gait rehabilitation study using tactile cueing was developed considering an early pilot study which presented a Haptic Bracelets for wrists and ankles. The Haptic Bracelets was designed and built as a self-contained wireless device containing a computer Wi-Fi chip, accelerometers, crisp and low-latency vibrotactile with a wide dynamic range (Figure 3.16). It is important to salient that, in this primary study, the vibrotactile units can be felt in six milliseconds and through the in-built accelerometers collet gait data and storage and later analyze it, using live streaming via Wi-Fi.

In order to improve the pilot skills study and around gait impairments, it was studied three novel modes of Haptic Bracelets use. The first mode consists in the use of two bracelets as a vibrotactile metronome, one on each leg. It was proposed this mode because it was acclaimed previously that tactile cueing demonstrates similar benefits to an auditory cue. This could be beneficial, for instance, when the use of earphones may compromise the security of the user. The second mode corresponds to a flexible interactive pace stimulation with the aid of a therapist: environmental obstacles, as changing slopes in situations where patients stumble, made impossible to them keep in phase with a fixed beat; thus, the therapist could beat an appropriate pulse for the patients' haptic bracelets through a communicating pair of bracelets. On the last approach, the bracelets were used in the patients' ankles, the gait asymmetry was continually monitored and was provided a tactile metronomic guidance.

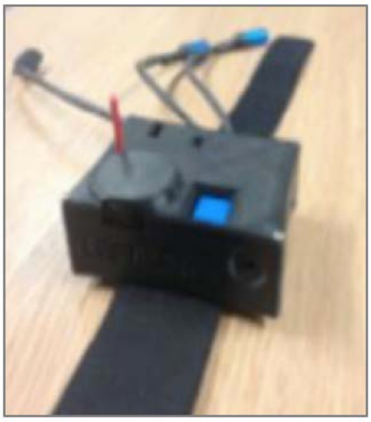


Figure 3.16 - Haptic Bracelet. Taken from [15].

Only the two first modes were tested and this study has been tested in post-stroke. However, the members of the study, including therapist, still reported that Haptic Bracelets were great for PD, and tactile cueing was capable to help patients to overcome FOG [15].

Shull and *Damian* in [20] at the year of 2015 synthesized a set of the haptic wearable research for clinical applications involving motor sensory impairments referring their usage in PD patients. In 2016, *Maculewicz* in [30] summarized the systems for gait rehabilitation based on instrumented footwear contextualizing to their usage in PD through auditory and haptic cues.

Not only *Shull* and *Damian*, but also *Maculewicz*, pointed to a study [16], which presented its progress in developing a wearable electronic tactile display that provides stimulations through vibrations on the mechanoreceptors in the foot sole.

This work builds up on a previous prototype, proposing a technologically improved second device and with new optimized tactile patterns.

The first prototype of the shoe-integrated tactile display was developed in 2008 to investigate how people understand information through their feet. It consists of a 16-point array of actuators (vibrators) integrated in a commercial inexpensive foam shoe-insole (providing axial forces up to 13 mN and vibrating frequencies between 10-55Hz) and each actuator was independently controlled (Figure 3.17). It is important to refer that this first prototype was meant to be used on the right foot and it was controlled by a computer through an electronic unit and all subsystems were connected by cables.

Figure 3.17 - First prototype of shoe-integrated tactile display (16-point array of actuators). Taken from [16].

Experimental studies with the first prototype indicated that patients understand information displayed on the plantar surface of the foot, but then it was noted that this information was complex since the foot was not capable of making a precise discrimination with many actuators. Therefore, in a new study, it was suggested that the information displayed to the feet must be encoded as short structured vibrating patterns and is not necessary to

Figure 3.18 - Second prototype of shoe-integrated tactile display (4-point array of actuators). Taken from [16].

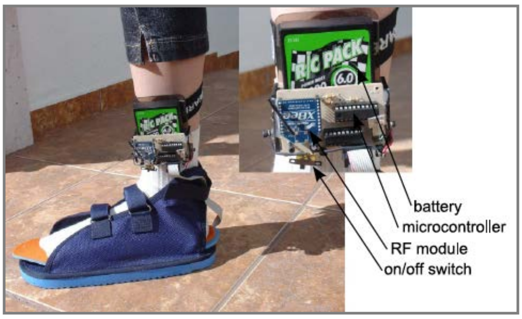


Figure 3.19 - Fully wearable device with wireless connection. Taken from [16].

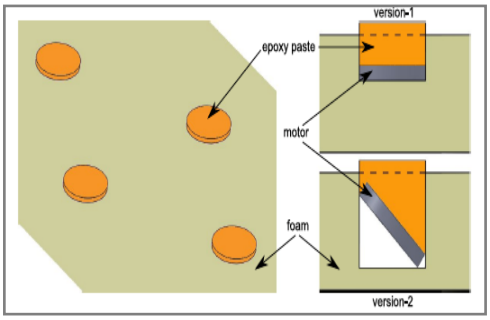


Figure 3.20 - Arrangements of vibrating motor in both prototypes: Version 2: transmits vibrations of higher amplitude to the foot sole. Taken from [16].

integrate a large number of actuators. Thus, the new prototype only integrates four vibrators as is represented in Figure 3.18. Besides this novelty, a major improvement is the fact that all wires were eliminated through the use of a radio-frequency transmission module, which allows simple and reliable point-to-point communication between electronic structures. Since the number of vibrators units was reduced, it was possible to integrate on-board the power supply battery (Figure 3.19). Note that the first prototype motors were perfectly adjusted on the foam but in the second prototype, the motors were set with an angulation of a 45º, as depicted in Figure 3.20, to allow that vibrations are only transmitted to the epoxy paste sole and patients feel vibrations without damages.

The main goals of the study experiences with the second prototype in 20 healthy subjects were three: first evaluate new tactile patterns encoded in only four actuators; secondly, verify whether background is relevant for podotactile recognition; and third determine any significant difference between wearing the tactile display on the left and right foot. The results showed that the use of few actuators was enough to patients easier understand directional and patterns information and it is simpler and fast to design. Moreover, tactile-foot feedback was easier to be recognized for relevant backgrounds and it was concluded that there is no significant difference between the right and left foot perception. The obtained results confirm the pertinence of these advances and show the proposed device potential for patients with PD [16].

In 2012, another study [17] was pointed by *Shull* and *Damian*, in which the effects of vibrotactile feedback training in PD patients were investigated. In this study, it was investigated the effects of one training session with real-time vibrotactile feedback comparing with a similar session of non-biofeedback training in PD patients.

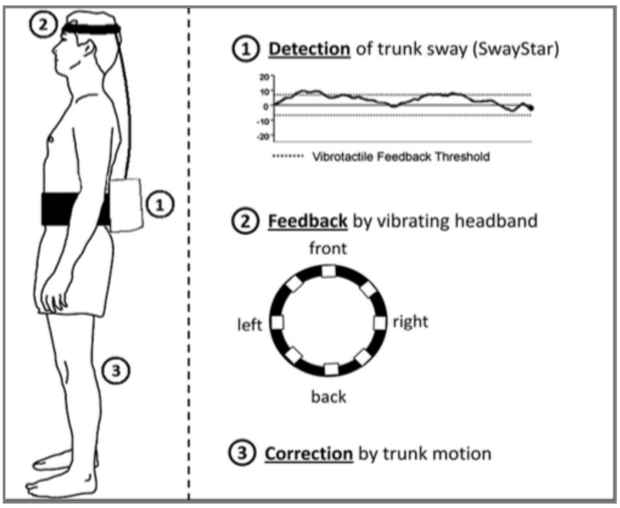


Figure 3.21 - Schematic representation of SwayStar and biofeedback system: 1- Detection of trunk sway; 2 – Feedback by vibrating headband; and 3 – Correction by trunk motion. Taken from [17].

The central point of these tests was to quantify trunk sway during everyday stance and gait balance tasks. Using a balance biofeedback (BalanceFreedom, Balance International Innovations GmbH, Switzerland), was possible to provide the biofeedback, through a headband that is connected to the angular velocity sensors at the lower trunk. The vibrotactile feedback was provided at a frequency of 250 Hz by eight vibrotactile sensors spaced equally around the headband. When the trunk sway exceeds the anterior-posterior or mediolateral sway threshold, the feedback is provided in the corresponding direction of the movement, allowing the patients to correct their posture. The vibrotactile feedback was felt until trunk sway is back within threshold values. In Figure 3.21 it is possible to analyze the referred system.

During the experimental tests, in training sessions, the subjects were asked to correct their sway by moving the trunk away from the direction indicated by the vibrator unit until the trunk sway is back within threshold values, and no more feedback vibrations would be given. After the experimental tests, it was concluded that the use of vibrotactile feedback in training sessions may be more beneficial for balance in PD patients comparing to conventional balance training exercises. In spite of this study has been focused in the balance training, it was possible to affirm that this vibrotactile feedback system seems to support PD patients to overcome freezing episodes, since the balance was a physical condition observed in FOG.

Still in 2012, in [18] was presented a vibrotactile neurofeedback training system for PD patients in order to reduce the number of falls. In this study has been used a body sway analysis provided by the Vertiguard-RT device (Vesticure GmbH, Germany) during fourteen everyday life stance and gait conditions.

This device corresponds to a body-worn fixed on the lateral and antero-posterior planes at the center of body mass (hip) under well-defined sensory motor conditions. It was used gyrometers that measure the trunk sway while the subjects are asked to carry out the Stand Balance Deficit Test (SBDT). This neurofeedback system contains a battery driven main unit (120x76x32 mm, 190g) which is fixed on a belt at the hip and four vibration stimulators on the front, back, left and right side. The vibration stimulators are mounted on the same belt as the main unit.

Based on the body sway analysis, the individual feedback was calculated and stored in the main unit for each patient. Continuously, the main unit also determined the force during body movements in lateral and antero-posterior direction by inbuilt gyroscopes and compares those values with individual pre-set thresholds in order to afford the stimulator activation in the specific directions.

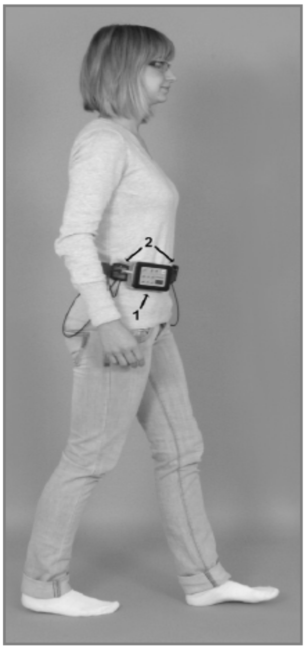


Figure 3.22 - Vertiguard-RT vibrotactile neurofeedback system: 1 - main unit; and 2 - vibration pads. Note: only two of the four stimulators are visible in the figure (each arranged at 90º around the hip). Taken from [18].

Daily training was performed under a physician supervision over two weeks. After the training phases, was observed a significant reduction in falls during patients' daily life and consequently an increase of its quality of life.

Similarly to the last presented study, though the Vertiguard-RT has been developed for training sessions, it can improve the imbalance that is one of the main points of FOG, reducing the number of falls caused by freezing episodes [18].

In [30], *Maculewicz* also pointed to another work: a wireless vibratory feedback system, called PDShoe. The approach developed, presented two aims. Firstly, to design and to accomplish tests about the synchronization between the gait steps and vibratory stimulations PDShoe. The second purpose was test the efficacy of vibration provided by the PDShoe. In fact, they hypothesized that PDShoe could be able to resolve differences in gait between healthy and PD patients who experienced FOG.

The components used in the developed prototype were chosen based on the performance of the desired function. The system comprises: a pair of water shoes used as a platform to house the actuator and electronics; three force sensors used in each shoe placed at the heel, ball and toe foot; three vibrators unit at the heel and toe foot; a unit for data processing; and a logic control trough an Arduino microprocessor. Figure 3.23 depicts the described system.

Figure 3.23 - The PDShoe system developed. Taken from [19].

Three Engineering Acoustics Inc.2 C-2 tactor vibrators were attached to each shoe by Velcro: two vibrators at the heel and one at the toe, which are activated when the force on the corresponding sensors exceeds a threshold value (Figure 3.24).

The Arduino microprocessor has been programmed such that, when the pressure sensors report a value that exceeds a threshold (22.5 N, the best value judged by the researchers), the correspondent vibrators units was activated and started vibrating at a predetermined frequency 175 Hz – low enough to minimize auditory feedback and high enough to be sensed by all users. When the heel contacted the ground, the heel force sensor detected a value that overlapped the threshold value and the heel vibrator unit provided the vibrational stimulation. In the same way, when the ball and toe foot detected a value that exceeded the pre-set threshold, the toe vibrator unit began to vibrate. If both pressure sensors determined a value above the threshold, both vibrators units were activated.

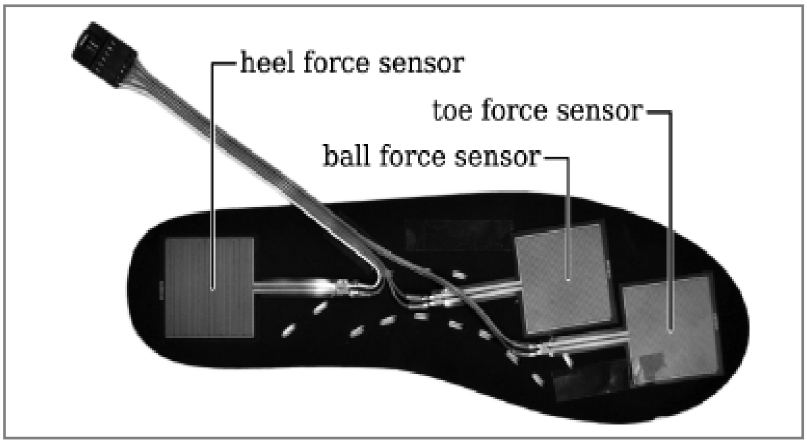


Figure 3.24 - Three sensors used in each shoe, placed in the heel, toe and ball of the foot. Taken from [19].

The system was validated with two subjects, one subject with PD who experienced freezing of gait (FOG), and one subject with PD with an implanted deep brain stimulator. The obtained results enabled to conclude that the PD patient that experienced FOG showed significant changes to all measures. Also, they verified that this patient presents a decrease in the duration of the transition from stance to swing phase, which is a positive sign that may reflect a less severity of shuffling when walking. All subjects showed an improvement in gait indices and clinical measures after wearing the PDShoe for one week [19].

A recently study, in 2015, presents a wearable biofeedback system for detecting body sway through an analysis about the plantar force and provides to the users a corresponding haptic cue [14].

The objectives are threefold. The first one was to present a wearable biofeedback system, that measures and analyses the changes in plantar forces and wirelessly sends control signals to vibrators units located on the trunk. The second objective was to notify the findings of an experiment directed to evaluate the effects of using this system on static balance, assessed through the measurements of the center of pressure movements. The last one was to study if this wearable device could improve balance in daily routines.

The vibrotactile biofeedback system implemented consisted in a plantar force acquisition unit and a vibration feedback unit. The plantar force acquisition unit, attached to a pair of flat insoles with adhesive tapes. Consisted of six thin-film force sensors, a microprocessor unit, a wireless transmitter module and a rechargeable battery. All electronic components (except force sensors which are located at the heels) in the plantar force acquisition unit were fastened to the lateral side of the lower leg by an elastic strap. The vibration feedback unit consisted of four vibrators (XY-B1027-DX), a wireless receiver module and a battery. The vibrators units (10 mm diameter and 2.7 mm height each) were placed at the anterior, posterior, left and right side of subjects' upper trunk by adhesive tapes and the vibration frequency and strength were 220 Hz and 1G, respectively, which was able to be recognized by human skins. The force data were acquired at the foot soles through the plantar force sensors and then were delivered the appropriate processed signals to the vibration feedback unit via Bluetooth. Based on the processed vibrating signals, the vibration feedback unit activates the vibrators. Therefore, if the detected forces exceeded the pre-set thresholds, full intensity of vibrations would be evoked at the corresponding vibrator. In Figure 3.25 is presented the system described.

This study found that the device improved the static balance and posture of participants which may serve as a source for a new development to attack the unstable postural in FOG experienced by PD patients [14].

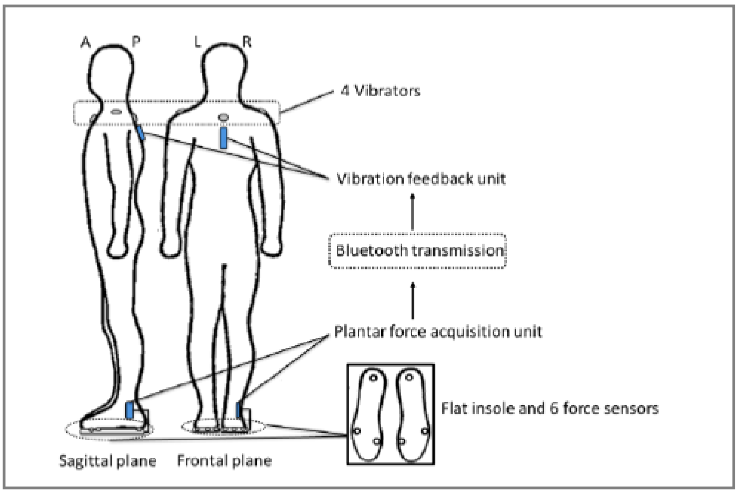


Figure 3.25 - The vibrotactile system, consisted of a plantar force acquisition unit, a vibration feedback unit, four vibrators and six force sensors attached to a pair of flat insoles. Taken from [14].

3.6.4. Mix Cueing

As referred previously each cue alone can provide the stimulation that can help patients with PD to overcome FOG events, but **simultaneous multisensory cues could have a stronger combined effect** [23].

Several studies have been proved that matching footsteps to visual cues and delivering auditory cues improves gait and reduces FOG. Nevertheless, replicating clinical scenarios with auditory and visual stimulations sometimes could be unfeasible for patients who wish to train at home in a daily task and an interactive system would be a better solution. Therefore, an ideal cueing system would include both visual and auditory stimuli. These systems take us back to virtual reality [48], [23]. The virtual augmented reality goggles presented in sub-section **3.5 Virtual Reality**. The system besides being constituted by the glasses was also constituted by earphones, that could provide additional auditory feedback from the patient’s own steps. Patients hear the auditory cue in a continuous manner so long as patients are walking steadily, producing a rhythm based on their gait pattern [48].

Another study presented the design of a wearable audio-tactile underfoot feedback targeted at patients with PD, denominated SoleSound: this footwear system is capable of delivering audio-tactile underfoot feedback to the patients by means of a real-time feedback apparatus. This sensory information was provided through piezo-resistive and inertial sensors installed at the feet. In Figure 3.26 is presented the described system.

The system was constituted by two footwear and a belt unit: each footwear unit mediates the kinematic data and pressures under the foot trough the Inertial Measurement Unit (**IMU**) and four piezo-resistive force sensors, respectively; a single-board computer was attached to the users' belt, powered by a small Li-Po battery and an USB sound card. Furthermore, both units used a Xbee module for the inter unit communication. The auditory and vibrotactile feedback was provided using two channel audio amplifier boards to drive a loudspeaker mounted inside the amplifier box and five vibrotactile transducers embedded inside de the of the shoe.

In this study, it was preferred not to use the headphones for being obtrusive and does not resemble real walking conditions. The loudspeaker system generate sound at foot level (auditory cue) by the interaction between the shoe sole and the ground. Based on the data of the two piezo-resistive sensors and the inertial sensor which is sent to the belt unit, a corresponding signal was used for both auditory and vibrotactile feedback. The experimental results tested in

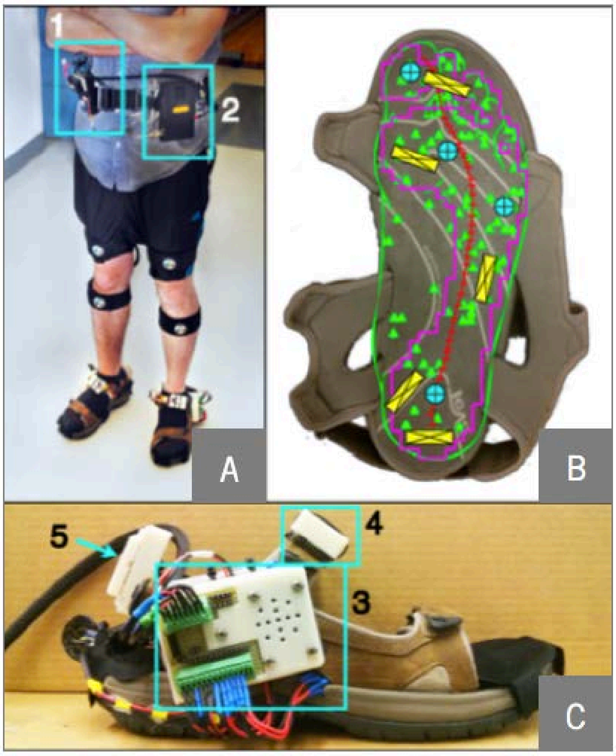


Figure 3.26 - SoleSound system: A. A subject wearing the belt unit: 1 – single-board computer, battery pack and Xbee module and 2 – USB sound card; B. The Nominal locations of actuators (yellow rectangles) and of piezo-resistive sensors (cyan circles), the Map of cutaneous mechanoreceptors in foot sole (in green), the Areas where the highest pressures are expected during walking (magenta outline) and the Path of the centre of pressure (red curve) ; and C. A close-up of shoe unit: 3 – amp box, loudspeaker case and shoe battery, 4 – ADC and Xbee module and 5 – IMU and Xbee module. Taken from [55].

three healthy persons indicated that this system can alter the natural gait pattern of subjects since that it effectively in modulates the perception of the ground surface during on gait [55].

In summary, when sensory cues are combined and synchronized could give the opportunity to develop a system more complete and effective.

3.7 Discussion & Conclusions

In this chapter was done a **review of the non-pharmacological methods** that can be followed to assist patients with PD since they have been proven to be **effective in improving their quality of life**.

Some methods are more efficient than others and in fact, by analyzing Table 3.1, which presents all the considerations raised about these methods, it is possible to conclude **that neurofeedback systems based on vibrotactile cueing allows a continuous improvement in PD motor symptoms and helping them to overcome FOG**.

The **general training exercises** and **physiotherapy** and the **treadmill** and **robotic training exercises do not address the daily patients' tasks** and **forces the patients to go to the training sessions** and limits the patients in performing **multitasking**. On other hand, the **degree of acceptability, comfort and cognitive effort requirements** are some of the main limitations pointed to the **mechanical assistive devices** and **systems based in virtual reality**. Thus, it is reasonable to claim that the **neurofeedback systems allow to overcome some of these limitations**. Indeed, it was considered that the patients present less difficulties in motor tasks using sensory cues through the neurofeedback systems, allowing improve some PD motor symptoms. Among the four types of existing neurofeedback systems, it has been found that **vibrotactile systems**, besides of **helping PD patients to overcome FOG**, advantageously **are suitable for any type of situation and environment**. In contrast, when using **visual and auditory cueing** it is demanded **dedicated environments** since these are affected by **noisy environments**. All these considerations are discriminated in Table 3.1.

Concerning to the vibrotactile neurofeedback systems, the **haptic bracelets, podotactile systems, headbands and trunk vibratory systems** are devices able to provide vibrotactile feedback, being constituted by a **sensory acquisition system** and a **processing unit** to control the **vibratory units**. The potential of these vibrotactile neurofeedback systems comparatively to the other systems rises up another important question**: the development of wearable systems**. In fact, the **wearable systems allow their integration into patients' daily tasks, making possible the accomplishment of multitasks.**

Table 3.2 summarize all these vibrotactile systems developed since 2012 until 2015, discriminating the main components of the implemented systems and highlighting the gait integration, detection of FOG and inclusion of PD patients in experimental tests.

The haptic bracelets only have been validated with a **small number of (non-PD) patients** and the users accused some **discomfort** when using the podotactile systems. In addition, in general, the systems presented **poor robustness** and thus **low user acceptability**.

Thus, it is necessary to **identify the best body zone to provide vibrotactile feedback**, aiming develop a system more **robust, functional, ergonomic and considering the patients' comfort** and **acceptability**.

Table 3.1 - Final considerations about Non-pharmacological Systems addressing FOG

		Approach	Considerations
General Training Exercises and Physiotherapy		Rehabilitation	✘ Does not address the daily patients' tasks ✘ Forces the patients to go to the training sessions ✘ Some training sessions are monetarily inaccessible in some countries
Treadmill and Robotic Training Exercises		Rehabilitation	✘ Does not address the daily patients' tasks ✘ Forces the patients to go to the training sessions
Mechanical Assistive Devices		Assistive	✘ Elevated degree of abandonment ✘ May increase the falling risk (environmental disturbances ✘ Requires some cognitive and attention effort
Virtual Reality Devices		Rehabilitation and Assistive	✘ Low acceptability degree ✘ Uncomfortable ✘ Requires cognitive effort ✘ Expansive apparatus
Neurofeedback Systems	Visual Cueing	Rehabilitation and Assistive	✘ Only recommended in a rehabilitation context or in places and situations where often FOG occurs
	Auditory Cueing	Assistive	✘ bring complications when their use involves noisy environments
	Vibrotactile Cueing	Rehabilitation and Assistive	✓ Continuous improvement of PD symptoms ✓ Reduce the number/duration of FOG
	Mix Cueing	Rehabilitation and Assistive	✘ Requires some cognitive and attention effort

Table 3.2 - Vibrotactile neurofeedback systems developed from 2012 until 2015 and discrimination of used vibration motors, sensors, wireless communication, presence of gait integration and PD tests performed

Vibrotactile Neurofeedback System	**Vibration motors**			**Sensors**		**Wireless Communication**	**FOG Detection?**	**Gait Integration?**	**Testing with PD patients?**
	Location	Number	Frequency	Measure	Location				
Haptic Bracelets (2011)	Wrist and ankles	-	-	Accelerometers	Wrist and ankles	Wi-Fi	No	No	No
Podotactile System (2011)	Foot sole	4	10-55 Hz	-	-	Radiofrequency	No	No	No
Headband (2012)	Head	8	250 Hz	Gyroscope	Lower Trunk	No	No	Yes	Yes
Vertiguard-RT (2012)	Lower Trunk	4	-	Gyroscope	Hip	Bluetooth	No	Yes	Yes
PD Shoe (2013)	Toe and heel Foot	2	175 Hz	3	Toe, ball and heel Foot	X-Bee	No	Yes	Yes
Upper Trunk Vibration (2015)	Upper trunk	4	220 Hz	6	Foot sole	Bluetooth	No	Yes	No

CHAPTER 4 – PROBLEM DESCRIPTION

Up to the moment, it has been concluded that vibrotactile neurofeedback systems, a non-pharmacological approach, are efficient in helping **PD** patients to overcome **FOG**. Further, were raised the limitations of the current developed systems, so it is mandatory to study how works the interaction between the provided vibrotactile feedback and the human sensory system.

Thus, in this chapter it is explored the human vibrotactile frequency discrimination in order to identify the range vibration frequency that must be provided to be perceived by persons. Furthermore, it is studied the tactile discrimination in different body locations and then focusing the waist zone. Lastly, it is analyzed the feedback control strategy that must be followed in order to allow the integration of the vibrotactile feedback in the patients' sensory system.

4.1. Introduction

Before developing any biomedical system, which aims to be integrated into peoples' daily lives, it is necessary to study their interaction between the human-system.

In humans, the cutaneous **mechanoreceptors** are essential for vibrotactile sensory perception [64]. The cutaneous mechanoreceptors can be distinguished in four sub-groups: the **Meissner**, **Merkel** and **Pacinian corpuscles** and **Ruffini ending** [64]–[66]. It was verified that the **vibratory perception depends essentially on the Pacinian corpuscles**, **which responds to a determined vibration frequency range.** Furthermore, the **cerebral cortex discriminates the vibrotactile information provided at a different frequency range**. Thus, it is possible **to define a vibration frequency range t**hat considers the range of the skin and cortex motor [64].

In addition, the vibratory sensitivity in the skin has different characteristics depending on the **body region** that receives stimulation [65]. Therefore, according to the end use of the system that is intended to be developed, it is necessary to perform a frame between the zone to provide the vibrotactile information and its ability to discriminate the vibratory signal [65], [67].

Ideally when we provide for vibrotactile feedback, it is expected that it occurs on **integration into the humans' sensory system**. The **motor tasks are divided into subtasks** since the **CNS responds with a different nervous command for each subtask** [68]–[70].

4.2. Human Vibrotactile Frequency Discrimination

The **tactile sensory system** is mediated by the **cutaneous mechanoreceptors**, which are involved in touch sensitivity, pressure, vibration and sense of position. The mechanoreceptors are usually sensitive to the deformation or stretching and are presented in various parts of the body, including the skin, muscles, tendons, blood vessels and various viscera [64] .

The **sensory system**, when stimulated**, transmits information** such as location, intensity, duration, frequency and even the density of the stimulated receptors. This information is **encoded** in subgroups of receptors, axons and neurons that activate the primary and secondary somatosensory cerebral cortex. Therefore, these **receptors** and **their connection to the central pathways** and t**arget areas in the cerebral cortex** constitute the **vibratory sensory system**. In fact, each receptor and fiber nerve is activated primarily by a stimulus, which establishes specific connections with the CNS [64], [65].

Generally, the receptors respond to a form of energy, whether mechanical, chemical, thermal or electromagnetic. Thus, each sensory receptor, according to its specific modality, acts as a transducer converting the perceived information into action potentials. In this, skin receptors intervene in the tactile sensitivity [64]–[66].

Many receptors participate in the vibration sensitivity perception, **depending primarily on the stimulus frequency**. In addition to the receptors, it is necessary to consider the pathways that lead the vibration sensitivity information to the cerebral cortex. In the cerebral cortex, a different level of decoding in the cortical areas is required. Thus, the specific characteristics of the vibrotactile stimulus, such as **frequency** and **amplitude**, are very important for the **decoding** of sensory information [64].

The physiology of vibratory sensitivity is complex and involves several receptors in different parts of the body. Few studies have been performed to understand its functioning, whereas even among clinical members it is poorly understood [64]–[66].

4.2.1. Anatomy and Physiology of Cutaneous Mechanoreceptors Responsible for Vibrotactile Perception

It is possible to distinguish four types of mechanoreceptors found in human skin: **Meissner Corpuscles, Merkel Corpuscles, Pacinian Corpuscles and Ruffini ending**s [64]–[66]. Table 4.1 shows these four types of mechanoreceptors and their main characteristics as receptivity field, frequency range of detection, sensibility to temperature, spatial and temporal discrimination and local perception and movement of vibrations. The information in the table was organized considering the mechanoreceptors depth in the skin, their capacity of perception of stimuli and slow or fast adapting.

Table 4.1 - Types of mechanoreceptors in human skin and their main characteristics, according with their skin depth and capacity of perception of stimuli [64], [65]

	Fast-adapting	**Slow-adapting**
Superficial skin	Meissner Corpuscles (FAI): ▪ small receptivity field; ▪ detection at frequencies of 20-50 Hz; ▪ no temperature sensitivity; and ▪ spatial and tactile perception.	Merkel Corpuscles (SAI): ▪ small receptive field; ▪ detection at frequencies of 5-15 Hz; ▪ temperature sensitivity; ▪ no spatial and temporal discrimination; and ▪ discrimination of the tactile form and its roughness.
Deeper tissue	Pacinian corpuscles (FAII): ▪ wide receivers field; ▪ detection at frequencies of 60-400 Hz; ▪ temperature sensitivity; ▪ spatial and temporal discrimination; ▪ deep pressure and vibrations perception; and ▪ perception of external events.	Ruffini ending (SAII): ▪ wide field of receptivity; ▪ detection at frequencies of 15-400 Hz; ▪ temperature sensitivity; and ▪ not present in glabrous skin.

Adaptation refers to how mechanoreceptors respond to sustained skin indentation [66] and there are receptors able to perceive the intensity of the stimuli for a prolonged time, being known as mechanoreceptors of slow-adapting. On the other hand, mechanoreceptors of fast-adapting respond only to the begin or the end of the stimulus. These two modes of adaptation allow the detection of different stimulation patterns in time and space [65], [66].

Regarding to the receptive field, this characterization refers to the area of skin that will generate a response in a sensory neuron when stimulated, being this area dependent of the stimulus intensity [66]. As it is possible to observe in Table 4.1, the receptive fields of Pacinian corpuscles and the Ruffini endings are larger than the receptive fields of the Meissner corpuscles and the Merkel disks.

For these reasons and considering their skin depth (Figure 4.1): the fast-adapting type I mechanoreceptors (FAI) terminate in Meissner corpuscles; the fast-adapting type II (FAII) mechanoreceptors end in Pacinian corpuscles; the slow-adapting type I (SAI) mechanoreceptors terminate in Merkel disks; and the slow-adapting type II (SAII) mechanoreceptors end in Ruffini endings, more deep [66], [71].

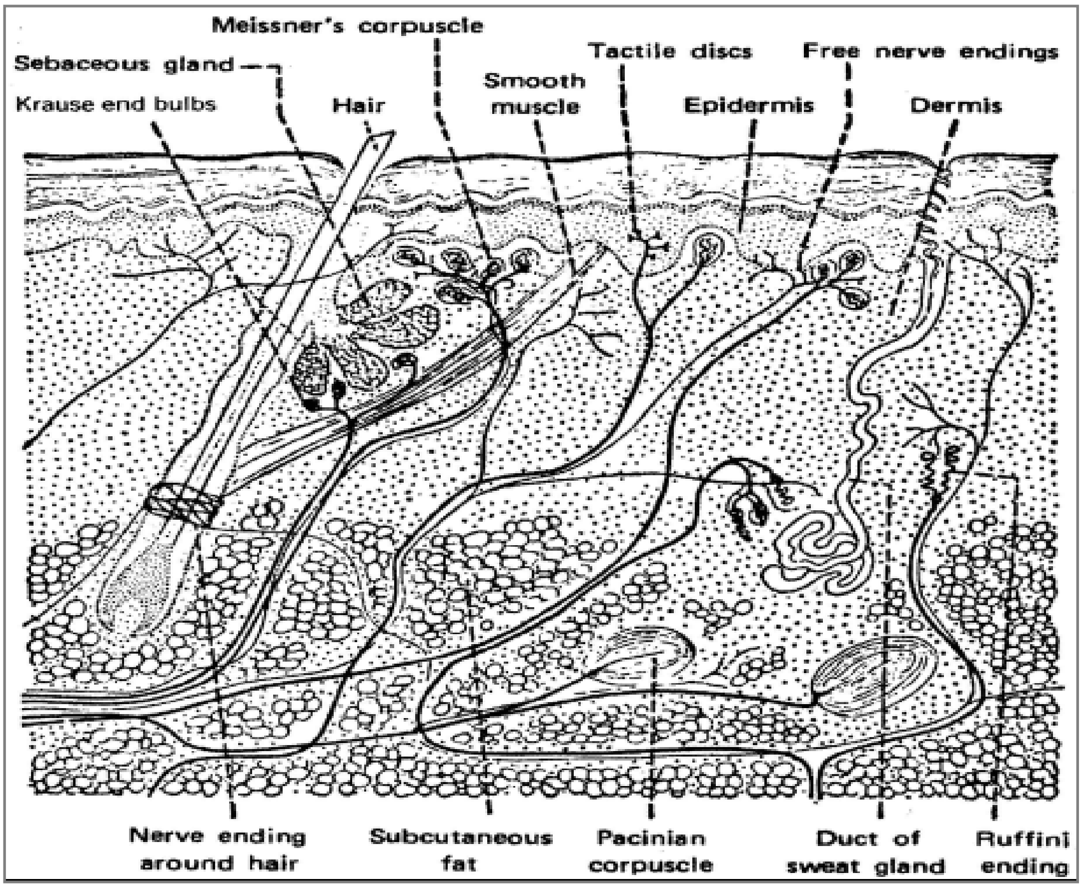


Figure 4.1 - Cross section of human skin. Taken from[63].

Regardless of the type of stimulus being provided, the entire neuronal population that is involved in the stimulus perception has the function to detect, firstly, its **presence** and consequently, its **begin**, **duration** and **end**. Besides that, **a continuous and persistent activation causes the perception to be attenuated**, leading to the phenomenon of **habituation** [64].

It is also important to note that there are significant differences in the vibratory detection between the glabrous skin and the skin with hairs. In hairy skin the vibratory threshold is higher compared to glabrous skin due to the different receptors and afferent fibers that are stimulated in these two areas of the skin [64]–[66].

The lower frequencies depend on the sensory fibers associated with the hair follicles in the hairy skin (5-80 Hz) and the Meissner corpuscles on the glabrous skin.

The higher frequencies (60-400 Hz) depend strongly on Pacinian corpuscles, which are present in the glabrous skin. In fact, the Pacinian corpuscles are the largest mechanoreceptors that exist and are encapsulated, presenting 20 to 70 layers: the roller of its capsule and the inner core function as a mechanical filter at high frequencies [64], [66]. Thus, **the vibratory perception depends essentially on the Pacini corpuscles** [64].

The mechanoreceptors respond to a stimulus within their "receptivity" field, as described in Table 4.1, but when a larger area is stimulated, a greater number of receptors are recruited in adjacent areas. Thus, an area of high receptor density upon stimulation will provide a response with high spatial detail [66].

4.2.2. Vibrations as Sensory Modality

The entire body has elastic mass that has the ability to vibrate and the vibrations are associated with mechanical oscillatory stimuli [64]–[66].

In the biological systems, the vibrations can be felt as a result of a sinusoidal oscillation of the skin, and this oscillation is then captured by the mechanoreceptors that respond to each oscillation with a **code of pulsations that triggers action potentials**. Thus, the vibratory frequency will trigger the action potentials generated by these sensory nerves. Thereby, it is possible to state that the vibration detection capacity depends of stimuli thresholds, once they are submitted to synchronized activations with the action potentials [64], [65].

The vibration detection, for **skin** in general, ranges from **80-300Hz** range [64]. It is important to note that the amplitude of the vibratory mechanical wave does not depend on frequency and the perceived amplitude is between 17 and 30 dB [64].

The **nerve impulse degrades progressively** in each neuronal “level” until it reaches the cerebral cortex, due to a progressive decrease of the “firing” frequency. The cerebral cortex, more precisely the somatosensory cortex, becomes saturated when it reaches a plateau of relatively low frequencies. Hence, the frequency discrimination capability of the human body is between **80-250 Hz** [64]–[66].

In face of this, it is necessary to distinguish the perceptual capacity of the mechanical receptors and the discrimination capacity of the sensorial information of the cerebral cortex, relative to the somatosensory system. **Thus, although the skin can achieve vibration**

detection thresholds between 80-300 Hz, the cerebral cortex only discriminates frequencies between 80 and 250 Hz, as is described in the follow figure [64].

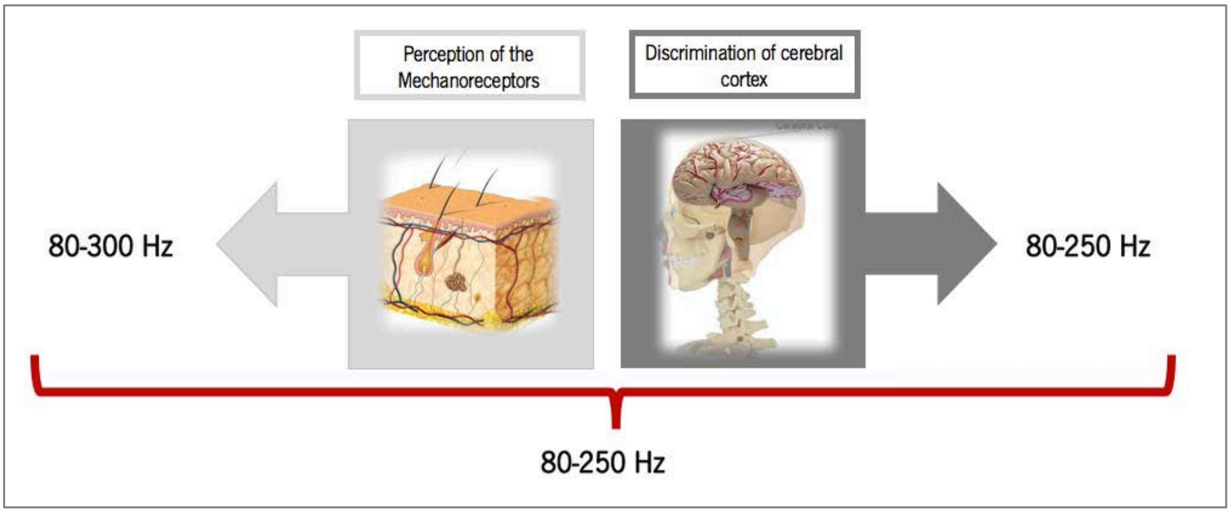


Figure 4.2 - Representation of the frequency discrimination in human body.

4.3. Tactile sensitivity in the body sites

As described before, the mechanoreceptors afferents characteristics and their distribution throughout the skin reveal why the perceptual resolution and sensitivity of the skin vary at different body locations [66].

Table 4.2, presents in descending order the body sites with the highest sensitivity, considering the sensitivity to the spatial location, the vibration and the pressure and the discrimination between two points [65].

Table 4.2 - Body sites listed in order of most sensitive to least sensitive for tactile sensitivity measures [65]

Tactile and Sensitive Measures	Body sites
Spatial Location	Face, fingers, hands palms, abdomen, arms, legs (bottom), chest and thigh.
Vibration Sensitivity	Hands, foot soles, region of the larynx, abdomen, head region and buttocks.
Pressure Sensitivity	Face, trunk, fingers and lower extremities.
Two-Point Discrimination	Tongue, lips, fingers/hands palms, toes feet, face and lower trunk.

As previously stated, **the areas of the skin without hair**, the **glabous skin**, are more **sensitive** to vibrations. So as we can confirm in the previous table, the hands and the soles of the feet are the areas of the body with greater vibration sensitivity [65].

In [65] was presented a review that discusses the tactile modality, specifically measures of tactile sensitivity for the human body. It was founded that the women present more pressure sensitivity comparing to the men and the sensitivity was generally the same for both the left and right sides of the body. Furthermore, in particular regions, the elderly and obese persons have higher vibration sensitivity thresholds.

Despite this discrimination of the vibrational sensitivity between the different body zones, it is necessary to be aware that the parameters of the vibrotactile signal can also influence the sensitivity and the perception of tactile stimuli in the different body sites. For instance, the tactile time response for the **trunk** is **4 μsec at 200 Hz**, but this value can be increased or decreased, depending on the **inter-stimulus interval** (discrete *vs* continuous signal), **amplitude** and **frequency**. Therefore, it is important to define two concepts that should be taken in account when considering vibrotactile sensitivity: adaptation and masking.

Adaptation is a phenomenon that occurs when a stimulus is presented for a lengthy amount of time (a continuous signal in a long term of time). This phenomenon is characterized by a reduction in the perceived intensity of the vibration signal and the adaptation stimulus can increase the threshold for the succeeding stimulus. Thereby, the adaptation can be avoided if the vibration stimuli is presented for shorter lengths of time with a discrete signal.

Masking is another phenomenon that happens when the perception of a precise vibrotactile stimulus is overlapped in time and/or space with other stimulus, and thus interferes with the ability to discriminate the correct vibration signal [65].

When it is intended to develop a neurofeedback system that provide vibrotactile information, it is necessary to consider both the **vibrotactile sensory discrimination** in humans and **the end use** of the system. For instance, in 2004, *Tsukada* and *Yasumura* developed a wearable device named Active Belt, that allow the users to get directional information through tactile sensory. This system consisted: in two sensor systems to detect the users' localization and orientation – GPS and directional sensor; eight vibrotactile units attached to wearable device named Active Belt, that allow the users to get directional information through tactile sensory. This system consisted: in two sensor systems to detect the users' localization and orientation – GPS and directional sensor; eight vibrotactile units attached to the belt separated at regular intervals; and a microcontroller to control the device. In the following Figures 4.3 and 4.4 is showed the prototype active Belt and it main components. It was considered appropriate to implement a belt to transmit directional information via tactile, since **the lower trunk is good for transmitting directional information and the persons can distinguish directions with high precision based on vibrations in the trunk** [71].

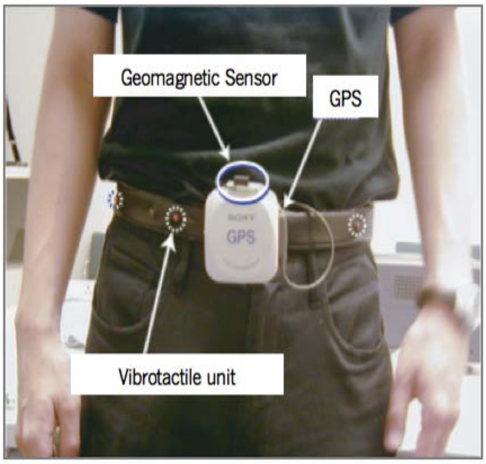


Figure 4.3 - The ActiveBelt system. Adapted from [69].

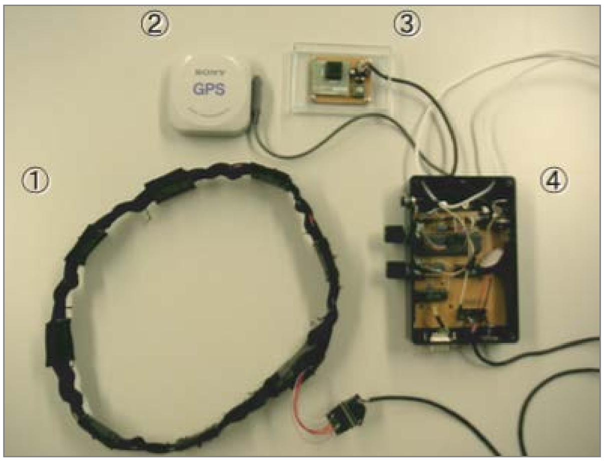


Figure 4.4 - Active Belt main components: 1-Active Belt Hardware; 2-GPS; 3- Direction Sensor; and 4-Microprocessor. Taken from[69].

Another system was developed in 2006, in order to study the tactile display and the vibrotactile pattern recognition on the torso. Thus, it was designed and tested a vibrating navigation aid system, which was consisted of a 4x4 matrix of vibrotactile units, mounted on a waistband to stimulate the lower trunk back (Figure 4.5). Theoretically, it was chosen to study vibrotactile stimulation in the trunk, because it is the zone of the body with the **greatest extension of skin** (half the surface of the human body), possessing hundreds of mechanoreceptors, so it is great to provide haptic feedback. In addition, it is considered the **second area with the highest sensitivity**. Further, once they have designed a navigation system, the trunk allows navigation with the **hands free** [67].

Figure 4.5 - 4x4 matrix vibrotactile units mounted in a waistband. Taken from [65].

Analyzing these studies, it can be concluded that the trunk, in particular **the waist zone**, is an ideal zone to provide vibrotactile feedback through the implementation of **wearable systems**, since it allows to perceive the stimuli with high sensitivity and addresses the requirements of **multitasking** and **freedom of movement** for the user.

4.4. Vibratory location in waist: space discrimination

The **number of vibrotactile units** and their **disposal**, specifically the distance between them, are a determining factor for human perception of vibrotactile signs when using neurofeedback systems. Thus, it is very important to realize the effects of the location and space of vibrotactile feedback, more precisely, in the lower trunk, at the waist.

In 2004, [67] was explored the main conditions for the precise location of vibration stimuli presented to the waist. It was intended to identify the vibrotactile location thresholds in the zones around the abdomen, through the implementation of a belt with vibrotactile units. It was chosen to implement a belt because its use in the abdomen zone allows the patients, during motor tasks, such as walking, to have their hands free. Apart from that this is the zone of the body that is strongly related three-dimensionally with the space capacity.

Before carrying out the experimental tests, in the first place it was conducted a study for the detection of vibrotactile thresholds around the abdomen. This detection was tested at 6 equidistant sites around the abdomen, using a belt 2.5 cm above the navel. The detection was performed for each site with two forced-choice alternatives. These choices consisted of indicating the time interval to which the vibrotactile stimulus was applied. From two options, two intervals of 500 msec were considered, with 1 sec of separation and on one of the 500 msec intervals the vibratory stimulations were provided. The subject would have to indicate, through a two-button keyboard, in which of the intervals the stimulation would have been applied to. If the interval was incorrectly identified, the intensity of the vibration was increased by 1dB in the next trial, but if three followed intervals were correctly identified, the intensity of the stimulation decreased by 1dB. Each session consisted of six blocks of trials, one for each frequency: 25, 50, 80, 160, 250 and 320 Hz. Each subject performed the tests twice and used headphones to focus on the test. The threshold for each frequency was then calculated from the last seven dB changes.

It was founded that the spine and navel were the areas with most sensitive to higher frequencies and the lower back also showed higher sensitivity to higher frequencies, albeit with lower values. The belly zone showed the highest sensitivity at higher frequencies compared to the other areas of the abdomen. However, it was found that the sensitivity in the abdomen for the different frequencies did not differ greatly from zone to zone.

Another three experiences were carried out. The first experience allowed to determine the best way to locate 12 equidistant vibrotactile units in a belt around the abdomen, with on average distance between the vibrotactile units of 74 mm.

Four sessions of 5 blocks of 60 trials were performed: each vibrotactile unit was stimulated 5 times, at random. This way, it was created a cylindrical keyboard that allows participants to identify the units that are being stimulated easily and to measure the response time of each participant: the opposite end of the keyboard corresponded to the navel and the end closest to the participants' spine (Figure 4.6). The participants pressed the button of the cylindrical keyboard corresponding to the zone of the vibration and the participants were asked to respond as quickly as possible.

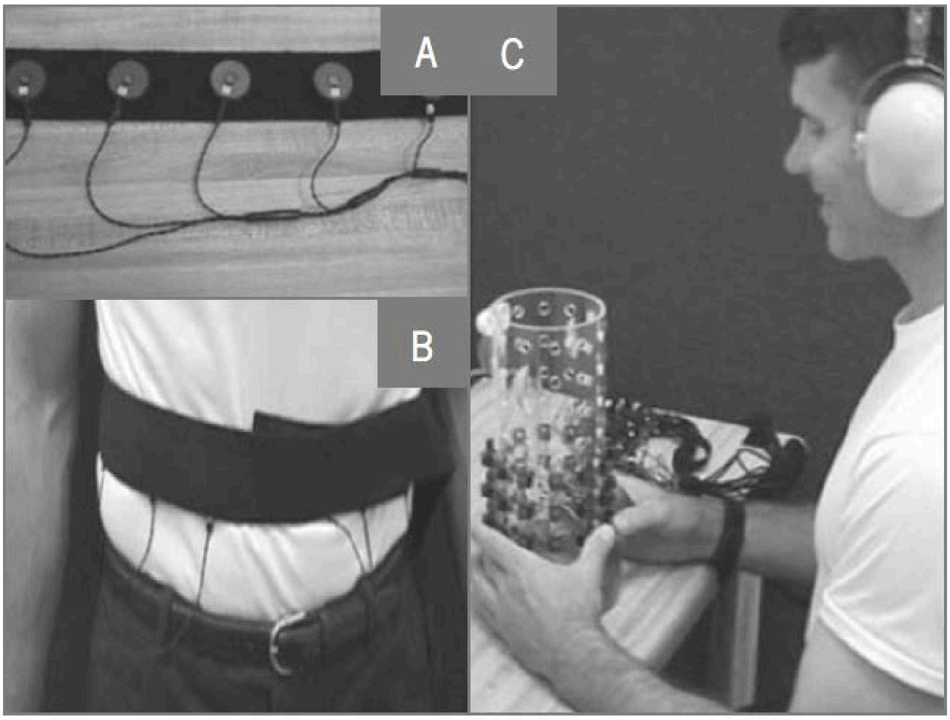


Figure 4.6 - A. Electromechanical tactors attached on the velcro belt used in experiences 1-3; B. The velcro belt with the vibrotactile units equidistant; and C. The response device - a cylindrical keyboard, isomorphic with the belt of tactors. Adapted from [65].

It was concluded that the ability to vibrotactile detection was almost perfect on the spine and navel and in places most adjacent to these reference points. Since the spinal and navel stimuli were easily identified, when stimulation was performed to the more adjacent areas, these sites were soon excluded from their options. It was also found that there was a similar pattern of detection on the front and back of the body, as well as detecting a similar bilateral detection pattern. Finally, it was verified that when the participants missed the vibrotactile detection in the zones of the navel, column, right and left side, the participants indicated the opposite zone. Whereas in the zones between those previously mentioned, the area next to the wrong one was wrongly indicated. However, despite these errors the percentages of detection were high.

Still in this first experiment it was thought that if the sessions were performed periodically, for some time, it would be possible to improve the performance measured in each session. For each session, there was a 2% improvement in the detection of vibrations, but without significant improvements among the 12 vibrotactile units.

In the second experience, it was determined the best form to locate 8 and 6 vibrotactile units, in the belt, in an equidistant way. Thus, since the number of vibrotactile units was reduced to 8 and 6 units, the space between the units was increased to 107 and 140 mm, respectively. Thereby, the increase of space between the vibrotactile units was evaluated. It is important to note that, for each of 8-orientation and 6-orientation, the influence of the arrangement of the vibrotactile units on the navel and the spine was compared and evaluated, where two provisions were considered: the placement of units in the navel and spine and another without placing the units in these zones (Figure 4.7). As in the first experience, four sessions of 5 blocks of 60 trials were performed and a cylindrical keyboard was used, with the corresponding keys only.

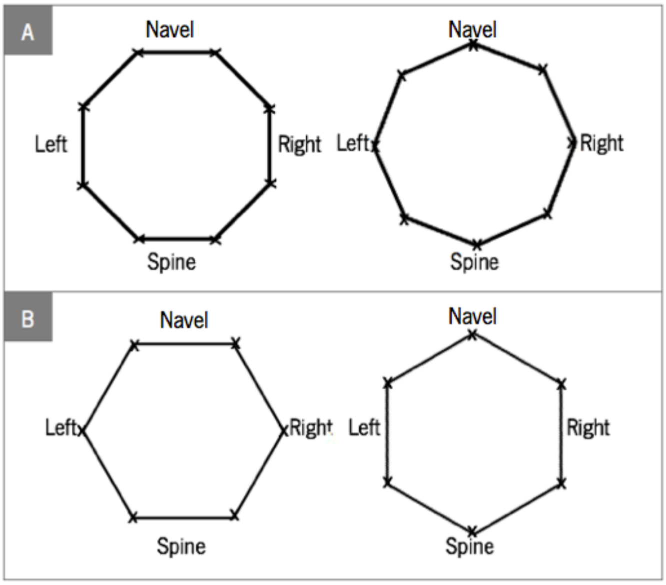


Figure 4.7 - Representation of the vibrotactile units placement around the abdomen (top view) when using: A. 8 units (107 mm of distance); and B- 6 units (140 mm of distance). In both images, at the left when not considered the placement of a vibrotactile unit at the navel and spine and at right when not considered the placement at these zones.

In this experiment, better results were obtained by reducing the number of vibratory units, obtaining better values for 6 vibrotactile units (97% accuracy). Once more, the spine and navel presented a higher percentage of accuracy, but nonetheless, the detection of vibratory stimulation in all zones was detected more easily, with a marked increase in percentages. It should be noted that the increase in the distance between the units favored an increase in the percentage. Finally, in situations where the vibrotactile units were not placed in the spine and navel, for 6 and 8 units, the results worsened because the reference areas were not directly stimulated.

In the third experience, 7 vibrotactile units were used in a semicircle around the abdomen and the ability to detect the stimulations provided with this arrangement was tested. In this case, the distance between the vibrotactile units was the same as in the first experiment (74 mm), but the participants were subdivided into two groups. In the first group the vibrotactile units were arranged by making a semi-circle, to the left and right side - left *vs* right; on the other hand. In the second group, the vibrotactile units were arranged in a semicircle at the front and at the back of the abdomen – front *vs* back (Figure 4.8). For this experiment 5 blocks of 70 trials were performed, following the same evaluation line as the previous experiments.

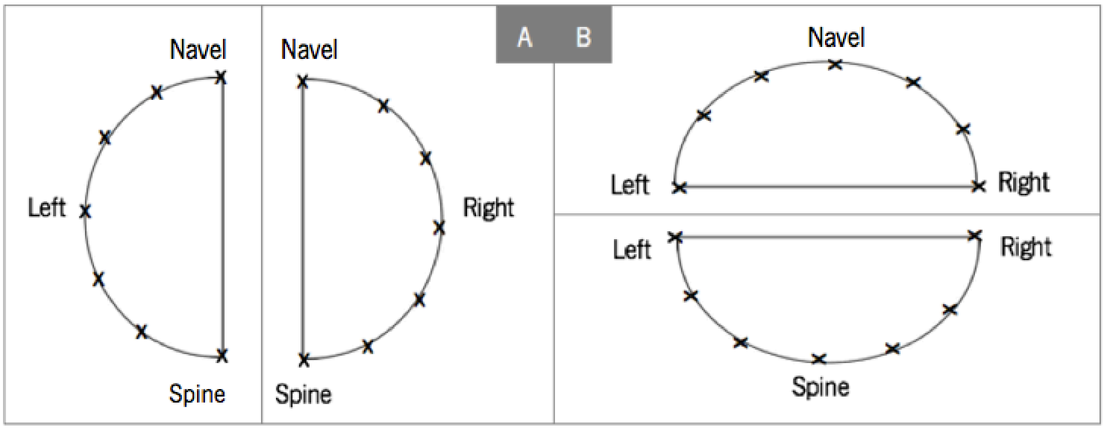


Figure 4.8 - Representation of the vibrotactile units placement around the abdomen (top view) when using 7 units (74 mm of distance): A – the first group left vs right side (using the placement of vibrotactile units in the navel and spine at the limit of the belt); B- the second group front vs back (not using the placement of vibrotactile units in the navel and spine at the limit of the belt).

For the group that studied the left *vs* right side, similar results were verified in both sides. Even between the stimulated zones, there were no major discrepancies unlike in experience 1, with the same spacing between the units. However, a higher percentage for the areas near the spine and the navel and less percentage for the more distant areas.

Regarding to the group that contrasted the front *vs* back side of the body, some significant differences were verified, with a higher percentage for the front. Also in comparison with experience 1 and even with the other group, the results were improved, since the reference areas did not correspond to the units that were at the extremes of stimulation.

Overall, it has been found that by reducing the number of units, the percentage of detection increases, also because the “choice” option is smaller, since it involves lesser cognitive effort. Further, it is important to consider the use of the vibrotactile units in the reference areas, navel and spine.

In summary, by reducing the number of units by increasing the space between the units, the detection results were better (12, 8 and 6 vibrotactile units to 72 mm, 107 mm and 140 mm, respectively). In fact, in the last experiment, when the number of units decreased from 12 to 7, but keeping the same distance between units, the results were similar to those with more units. Therefore, it is important and necessary **to reduce the number of units,** in order to increase the space between them. Also in the third experiment, the influence of the use of the stimulation on the anatomical reference areas, the navel and the spine, was verified. When the motors were placed only in the right or left part, these units were located at the stimulation ends and it was verified that the results were worse. This fact has also been verified by the response time, which is longer when these areas are stimulated at the extremities. In fact, **biologically, these zones are considered as anatomical references presenting high precision** [67].

4.5. Feedback Control Strategy

When it is intended to develop a system that provides feedback to people so that it can work integrated with their sensory system, it is **necessary to define a feedback control strategy**, especially when it comes to motor tasks such as walking. Thus, this control strategy showed consider both **the nervous signals of the human body involved in the motor tasks** and the **feedback signals provided**, in order to allow on interplay between them.

4.5.1. Detection of specific motor tasks transitions

The peripheral sensory events, which are used for applying specific control signals to perform tasks and progression of its phases, are supervised by the CNS through a sensory predictive feedforward control. In fact, the CNS integrates all the dynamism of the control processes and the implementation of all predictive actions of the sensorimotor system, allowing it to act appropriately in the course of each motor action [72]. Therefore, it is reasonable to affirm that the somatosensory feedback, specifically through receptors on the skin and muscles in the legs, is crucial in the control of the balance and movement of the human, for instance, to ensure that the sensorimotor system responds according to the physical properties of the floor, such as irregularities, slippery, slope, among others [73].

It is possible to distinguish two temporal scales of action of the control predictive feedforward: when the somatosensory afferent system triggers compensatory actions to respond perturbations in the course of action, allowing its progress through commands that let you respond to discrete mechanical events that occur on a faster time scale. This type of sensory control predictive feedforward is referred to as Discrete-event Driven Sensory. On the other hand, in a longer time scale, there are motor action commands that are triggered according with acquired experiences, to allow an adjustment of engine controls, mainly related to the afferent information about the physical properties - that capacity to standardize responses is called Anticipatory Parameter Control [72].

In humans, **the motor tasks can be organized in phases characterized by specific muscle activities and tuned according to mechanical events in discrete times**, since for each event, muscle activity is different and suited to respond every need. *Johanssson* and *Edin* proposed a model called **Discrete Event-driven Sensory feedback Control** (**DES**), claiming that "this model posits that motor tasks in humans, such as object manipulation, are organized in phases characterized by specific coordinated muscle activity and delimited by means of sensory encoded discrete events (…) Such events are often represented in a multimodal fashion, but at other times they exclusively evoke activity in tactile afferents. That is, the task evolves in an open-loop fashion where the successful completion of each phase is signified by specific combinations of temporally correlated sensory signals" [68], [69].

In order to explore the applicability of **DESC** model, *Ciprini* formulated a paradigm in which healthy people operate an artificial robot hand performing simple tasks - grasping, lifting and repositioning an object. These tasks are mechanical events that are crucial for use by the sensory feedback system. To this end, *Ciprini* developed **a system that acts based on events, through vibrotactile feedback**. With short duration, these events allow the progression of grip-load-replacement tasks of an object with the hand, **determining whether the artificial feedback has been properly integrated into the system of sensorimotor control of each participant** through the **implementation of delays in the vibrotactile stimulation**. Four phases can be distinguished: grip phase, load phase, hold phase and replacement phase. Hence, for instance, when one of the digits of the robotic hand touches the object, a vibration in the corresponding digit is transmitted, which is verified on the grip phase (contact and grasp phase the object) [68]–[70]. Therefore, the participants received discrete vibrotactile stimuli, that marked transitions from one phase to another. With this study, *Ciprini* achieved results consistent with the DESC model, finding that **CNS monitors peripheral sensory events**, specifically **marking the transition between the phases of a motor task**, **using these events to apply control signals in the course of a task**. It was then found that the participants were able **to integrate artificial sensory feedback in motor control tasks, responding appropriately to delays in feedback** [68].

In summary, it was highlighted the division of motor tasks into subtasks and the importance of detecting transitions between phases of subtasks, each one corresponding to a different action commanded by the CSN.

4.5.2. Human Walking: Gait phases and events

In humans, the act of walking requires a periodic movement of each foot from one position of support to the next and sufficient ground reaction forces, applied through the feet, to sustain the body. These two requisites are necessary for any form of bipedal walking to occur, no matter how distorted the pattern may be by the underlying pathology and this periodic leg movement is the essence of the cyclic nature of human gait [74].

Indeed, the human gait cycle presents a sequence of gait phases, divided in two main moments denominated **stance** and **swing phase**. The stance phase corresponds to the period the foot is on the ground (from 0% to 60% of gait cycle). In the swing phase the same foot is no longer in contact with the ground (from 60% to 100% of gait cycle), allowing the advance of the leg and body progression. These two major gait phases are sub-divided in sub-phases, which are represented in Figure 4.9 and discriminated in Table 4.3 [74], [75].

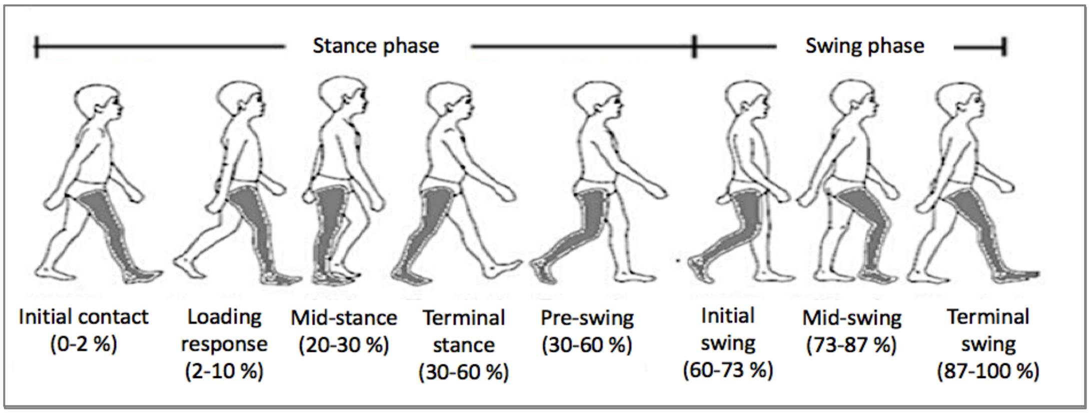


Figure 4.9 - Gait cycle, highlighting the stance and swing phase and its respective gait phases. Adapted from [72].

It is important to note that the gait phases terminology in Figure 4.9 refers to the right leg, thus the same nomenclature is applied to the left leg, which for a normal gait cycle is a half cycle behind/ahead of the right leg [74].

The transition between each sub-phase corresponds to a gait event, as described in Figure 4.10. It is possible to distinguish four major events: **the heel strike, foot flat, heel-off and toe-off**. By definition, the gait cycle **begins and ends with the heel strike event**, which is described as the first ground contact of the leading leg. When all the foot plantar surface of the leading leg touches the floor, is occurs the foot flat event. Then, the heel lifts from the ground corresponding to the **heel-off** event, and ending with the **toe-off** event, the moment that the foot leaves the ground. The **toe-off event marks the transition to the swing phase** and, as described in Figure 4.10, the **stance phase** is initiated with the **heel strike** event and finished in the toe-off event. [74], [75].

Other two events can be considered during the swing phase: the acceleration and deceleration. The acceleration begins as soon as the foot leaves the ground from the toe-off event and the deceleration describes the action of the muscles as they slow the leg and stabilize the foot in preparation for the next heel strike and move on to a new gait cycle [74]. It is important to note that **mid stance** and **mid swing** also can be considered gait events and correspond to opposite events in gait cycle.

Table 4.3 - Gait cycle sub-phases description and some pointed considerations [75]

Gait Cycle Phases	Gait Cycle Sub-phases	Description	Considerations
Stance phase	Initial contact	First moment the leading leg foot touches the ground	-
	Loading response	Begins with initial floor contact of leading limb and continues until the other foot is lifted for swing phase	Responsible for shock absorption Provides forward propulsion and stability
	Mid stance	Starts when the other foot lifts and continues until the body weight is aligned over the forefoot	Provides progression and trunk stability
	Terminal stance	Begins with the heel rising of the leading limb and only ends when the other foot strikes the ground	Transference of body weight for the ahead of the forefoot
	Pre-swing	Starts with the initial contact of the opposite limb and ends when the foot leaves the ground	Transitions moment from stance to swing phase
Swing phase	Initial swing	Begins with a lift of the foot from the ground and continues until the swinging foot is opposite to the stance foot	Contributes for foot clearance of the floor
	Mid-swing	When the swinging leg passes the opposite stance leg	-
	Terminal swing	When the leading leg is decelerated in preparation for the stance phase.	Ends when the heel strikes the floor

Thus, when a foot is in mid stance, the other foot is in mid swing [74], [75]. In summary, ordering the gait events, as shown in Figure 4.10, we obtain: 1 **– Heel-strike (HS)**, 2 **– Foot flat (FF)**, 3 **– Mid stance (MST)**, 3 **– Heel-off (HO)**, 4 **– Toe-off (TO)**, 5 **– Acceleration**, 6 **– Mid swing** and 7 **– Deceleration** [74], [75].

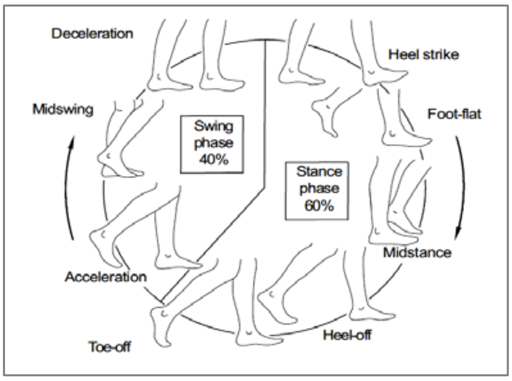


Figure 4.10 - Gait events during one gait cycle. Taken from [72].

Thereby, it is possible to verify that the **gait cycle can be divided into phases and that the transition between phases corresponds to an even**t. The **CNS controls the motor system** with **different responses** according to each event and sub phase [74], [75]. Thus, the **detection of specific gait-phase transitions** is relevant in order to **synchronize** with the **sensory and functional feedback to convey the vibrotactile stimuli**.

4.5.2. Providing Time-Discrete Gait Information

For each gait-phase, the CNS uses knowledge of environmental properties combined with information about the current state of the system around, in order to predict motor commands. The CNS generates predictions about the sensory inferences of the motor output and includes sensory signals associated with the mechanical events. These behaviors are possible through the **comparison of the predicted and the actual sensory feedback** and allow the **monitoring of the course of the motor tasks**. **When a mismatch or an erroneous in the predictions occurs, the brain, or more precisely the CNS, can convey signals about learned tasks, specific phase corrective actions** and a **better adjustment for the predictive control in the subsequent phase of the task** [68], [73].

This information about the predictive feedback control system was studied by Crea in [73], claiming that the "predictions about the terminal sensory state of each action phase provide initial state information for the next action-phase of controller" and "in the absence of such predictions, this state information would have to be obtained by peripheral afferent signal at the start of each phase". *Crea* append that these predictions state information "would prevent smooth transitions between action phases because of substantial time-delays in sensorimotor control loops". Therefore, *Crea* developed a novel feedback system strategy relied **on the detection of specific gait-phase transitions** of the lower-limb amputees, **using vibrating elements that are activated in a time-discrete manner.** The novelty introduced in his study was **the use feedback synchronized with specific gait-transitions**, once it was proposed to overcome some limitations of time-continuous stimulation presented in previous studies [73]. In fact, when providing a time-continuous high-power stimulation, the **users felt stifling, uncomfortable and unacceptable for the user** and, when using a time-continuous low-power stimulation, occurred the **adaptation phenomenon**, which usually results from a prolonged mechanical stimulation of skin receptors [68], [70], [73]

CNS is minded to control the motor behaviors through processing by incorporating time-discrete somatosensory information. Thereby, *Crea* proposed that the lower-limb amputee can **incorporate the feedback in a discrete manner in his control system**. Furthermore, this allows to develop the ability of **integrate the physiological gait pattern, without having to pay continuous attention to the signals**, which happens in time-continuous stimulation. Thus, *Crea* has presented a new device with the purpose of partially replace somatosensory information, useful for the control of the amputee lower limb gait. In order to confirm that, tests were realized with healthy subjects, concluding that the system has excellent usability, **time-discrete feedback is easily perceptible by humans** and, potentially, can assist control of gait kinematics [73].

For these reasons, providing time-discrete gait information was deemed appropriate to ensure the perception of stimulations without excessive stimulation of the skin surface.

4.6. Discussion & Conclusions

In this chapter, it was studied how the interaction between the vibrotactile feedback and the patients' sensory system will be performed.

In skin, the cutaneous mechanoreceptors are responsible to perceive the vibrotactile information that is provided. Indeed, many mechanoreceptors participate in the vibration sensitivity perception, depending primarily on the stimulus frequency. However, the vibration sensitivity depends strongly on the Pacinian corpuscles, one of the four types of mechanoreceptors – Meissner, Merkel and Pacinian corpuscles and Ruffini ending - that exist in the skin. All these cutaneous mechanoreceptors have a vibration frequency range for perception and it was discovery that, in general, the vibration detection for skin ranges from 80-300Hz.

In addition to the receptors, it is necessary to consider the pathways that lead the vibration information to the cerebral cortex. Indeed, the vibrotactile information that is perceived in skin mechanoreceptors is deteriorated until it reaches the brain, more precisely, the cerebral cortex, which, consequently, is able to discriminate a range of 80-250 Hz.

Therefore, it is concluded that the vibration frequency range that must be considered is 80-250 Hz in order to belong to the human perception interval of vibrotactile feedback.

All body zones present different responses to the vibration feedback. In order **to develop a wearable system to address a multitasking requirement and the patients' freedom of movement**, **the waist body zone, in lower trunk, gather the necessary conditions to provide vibrotactile feedback**, being pointed out as an area **capable of easily perceiving this type of stimulus**.

In human, the **motor tasks can be organized in phases** characterized by **specific muscle activities** and **adjusted according to mechanical events in discrete time**s, because for each event, muscular activity is adequate to respond to all needs. The **CSN actuates in the transition of each motor subtasks**, commanding the muscular activity involved in the different motor actions in all human sensory system. Thus, it is relevant **to detect the transition between each phase of motor tasks in order to integrate the vibrotactile feedback provided in the patients' physiological sensory system**. Since it is intended to address a PD motor symptom, the FOG, the vibrotactile feedback to be provided will have **to be synchronized with the gait events transitions**. Thus, when an episode of freezing occurs, in order **to replace the failure in the forwarding of the nervous message commanded by the CSN in the transition between each motor subtask**, it is expected that the **vibrotactile feedback is incorporated in the command of these actions**, making it possible for the **patient not to block**.

It has also been found that the CNS has the ability to control the motor behaviors through the processing and incorporation of sensory information in **discrete time**. Thus, the vibrotactile information to be provided must follow a discrete-time approach, allowing patients to incorporate a pattern into their motor system, without having to demand a **high cognitive weight** and avoid the **phenomenon of adaptation.**

Table 4.4 - Main considerations highlighted in the present chapter and respective requirements

	Answer	Requirement
Frequency range of vibrational perception	80-250 Hz	Interaction sensorial system and feedback provided
Best body zone to provide vibrotactile feedback	Waist zone – Lower Trunk	Wearable Free hand concept Multitasking
Vibrotactile feedback control strategy	Detection of gait events transitions	Incorporation of vibrotactile pattern into the patients' sensory system trying to replace missing capabilities
	Time-discrete information	Adaptation phenomenon Less cognitive effort

These conclusions raise up all the requirements that the proposed system must complete. The following table presents the answers that have been presented in the chapter, highlighting the innovative character of the proposed system in order to achieve all the requirements addressed.

CHAPTER 5 – SOLUTION DESCRIPTION: THE WAISTBAND

Once accomplished the critical literature research and carried out all the major requirements to be met, in this chapter is presented the proposed solution.
Thus, it is discussed the importance of each used components, specifying their functions, in order to explain all the systems that make up the global system developed: a vibrotactile neurofeedback system for **PD** patients to overcome **FOG** – a waistband solution.

5.1. Introduction

The non-pharmacological methods allow to overcome the pharmacological barrier that is imposed when it is intended to improve the parkinsonian gait and specially to attack the FOG.

The critical review about non-pharmacological methods, held in **Chapter 3**, emphasizes the **use of Neurofeedback Systems** to help PD patients to reduce the number/duration of freezing episodes. In particular, it was observed that the use of vibrotactile cues in neurofeedback systems enable their use in any type of situation and environment in patients' daily tasks. Also in Chapter 3, the limitations of the current vibrotactile systems were pointed out and in fact, some of these systems were not tested with PD patients, were considered uncomfortable by some users or/and presented poor robustness and low acceptability. Therefore, in this chapter, it is presented a new non-pharmacological solution, constituted by a **Vibrotactile Neurofeedback System**.

Considering the vibrotactile discrimination at the skin level and all the required nervous system to perceive the transmitted information, it was founded that, humans, in general, are able to discriminate a **vibratory frequency range of 80-250 Hz**.

Also, it was verified that the **lower trunk** is a body zone able to perceive the vibrotactile feedback with high sensibility and, in addition, the development of a wearable device to use in this body zone addresses the multitasking and free hands concepts.

Furthermore, the vibrotactile feedback to provide must be synchronized with gait events and in **time-discrete** since the motor tasks can be subdivided in phases characterized by specific muscle activities and the **CNS** executes a discrete time motor control in the **transitions** of each sub phase.

Thus, the Vibrotactile Neurofeedback System presented in this chapter, is implemented through a **waistband** which allows to provide vibrotactile information at the lower trunk zone, more properly at the **navel**, **right**, **spine** and **left zones** in a **discrete-time** and in accordance with **one gait event transition**.

In Figure 5.1 is depicted the thought line and steps followed until the definition of the solution developed: a vibrotactile neurofeedback system for PD patients - the waistband.

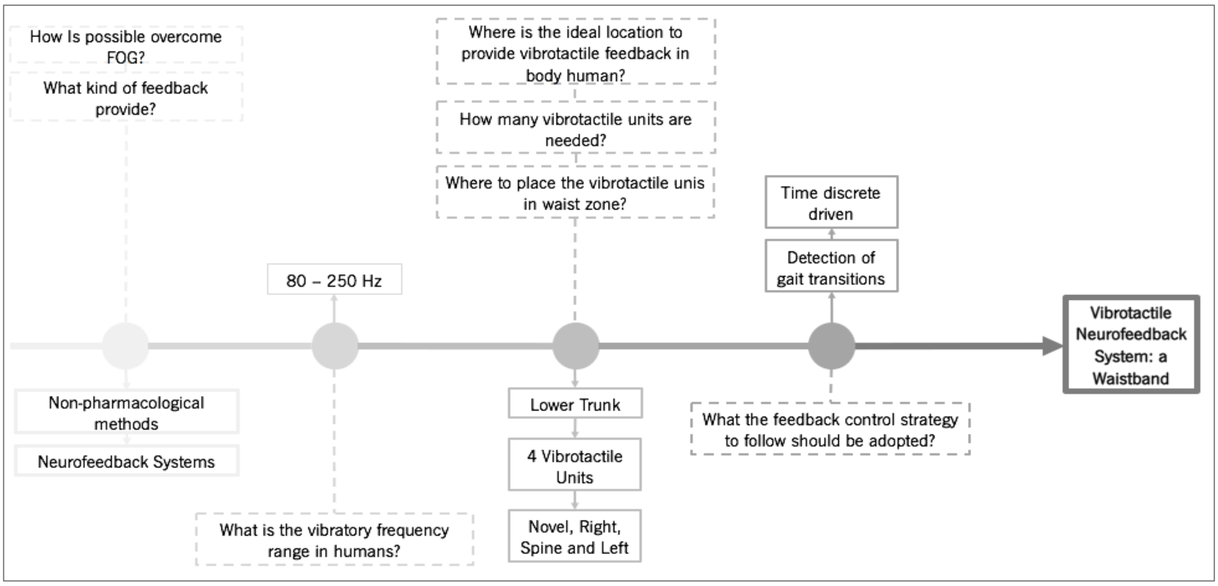


Figure 5.1 - Thought line and steps followed until the definition of the solution developed: a vibrotactile neurofeedback system for PD patients: the waistband.

5.2. General Overview

A first prototype was implemented: a belt. Figure 5.2 shows 4 views of the developed belt: front, right, back and left view.

Figure 5.2 - The developed belt system in four views: front, right, back and left.

The belt system is more discriminated in Figure 5.3: in the larger bag (marked with green) are located the majority of the electronic components, the **processing unit**, the **wireless communication component** and the **power supply system**; and in the longest bags (marked with red) are placed the **haptic drivers** and **the vibrotactile units**. The belt can be **adjusted to any abdominal diamete**r and the adjustment of the longer bags always allows the placement

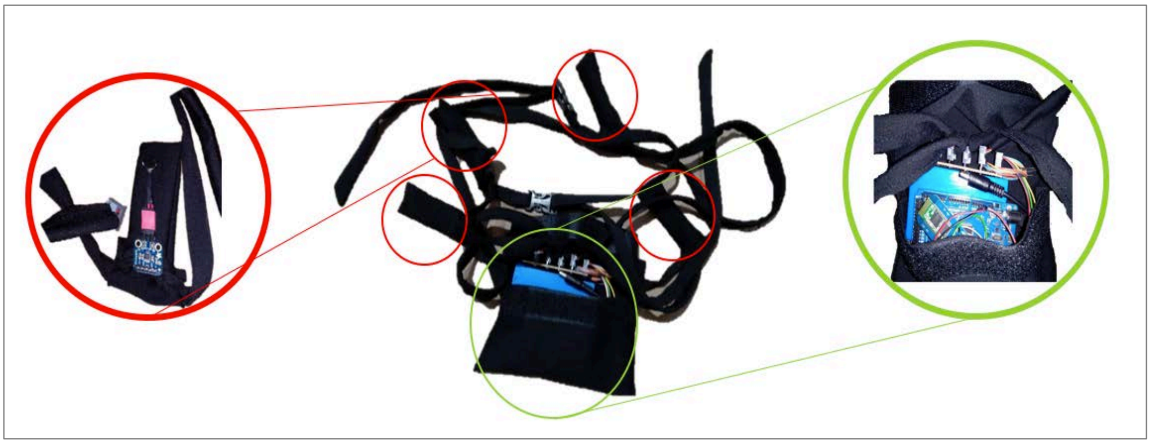


Figure 5.3 - Belt system discrimination: the processor unit, the wireless communication component and the power supply system allocated at the larger bag, demarcated at green; and the four actuation system, with the vibrotactile units, placed at the longest bags.

of the vibrotactile units in the zones previously specified.

Although this belt system allows to provide vibrotactile feedback in the waist zone, **the users perceived poorly the feedback** since the vibrotactile units are not continuously in contact with the users' body and, besides that, the system presents low robustness.

The next step required to specify measures to overcome the limitations presented by this one: the development of the waistband represent in Figure 5.4.

The **waistband**, besides **ensures the continuously contact of the vibrotactile units with the users' body** and **present more robustnes**s, is a **wearable device** able to provide **vibrotactile feedback at the navel, right, spine and left waist body zones** and is **adjustable to any users' abdominal diameter**.

All the electronic components are placed in the waistband, as is possible to verify in Figure 5.5: the majority of the electronic components are allocated in the blue bag (demarcated in grey) and the four vibrotactile units are fixed to the waistband (demarcated at red).

All the systems which compose the waistband are detailed described in the following section, highlighting their key features.

Figure 5.4 - The developed belt system in four views: front, right, back and left.

Figure 5.5 - The waistband: at top, an inside view, highlighting the vibrotactile units (demarcated at red) and in down, an outside view, emphasizing the majority electronic components (demarcated at grey).

5.3. System Architecture

The implemented system was composed by five main systems: the **Processing Unit**, the **Lower Trunk Acceleration Acquisition System**, the **Data Storage System**, the **Wireless Communication System** and **Graphical Interfaces.** These main systems and the respective components are displayed in the Figure 5.6. The system was power supplied by a **Lithium-Ion Researchable Covert Battery** with 12V.

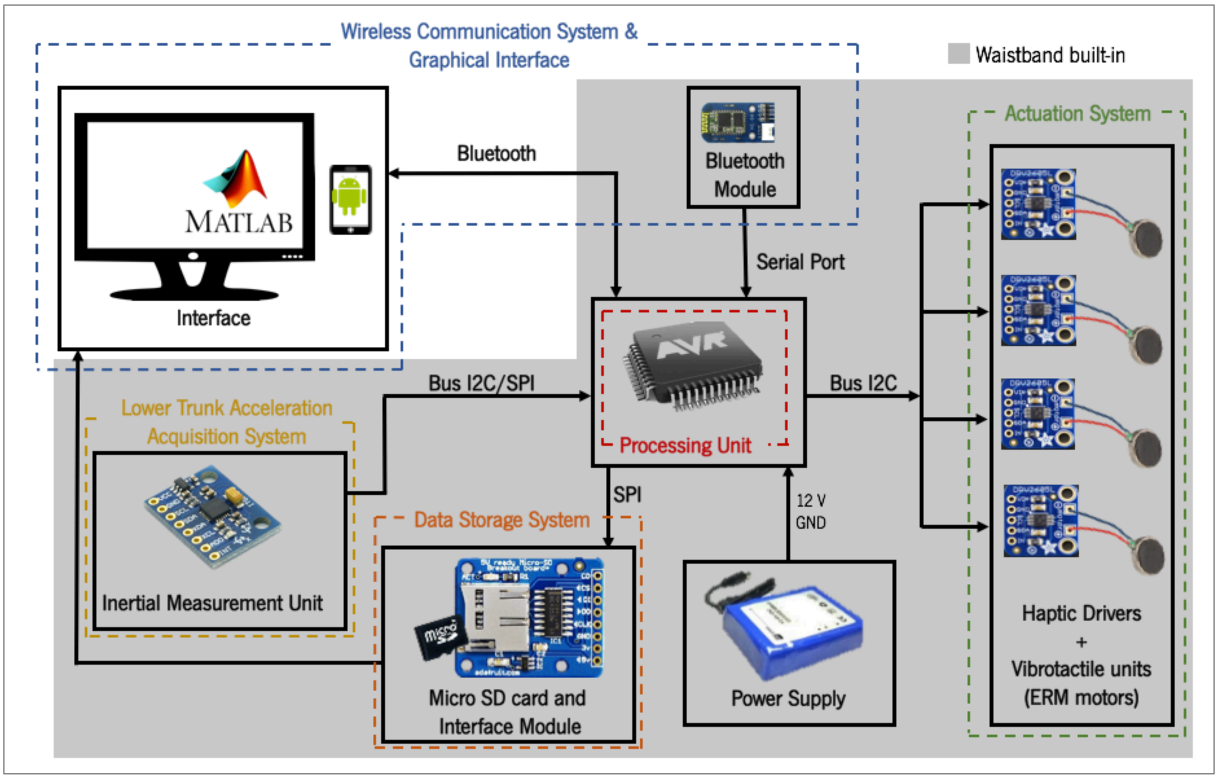


Figure 5.6 - The systems architecture overview, illustrating the main systems with the respective components and interfaces between them: the processing unit (delimited at red); the lower trunk acceleration acquisition system (delimited at yellow) constituted by an IMU; the data storage system (delimited at orange) composed by a micro SD card and the respective interface module; the actuation system (delimited at green) with the haptic drivers and the vibrotactile units (ERM motors); the wireless communication system – a Bluetooth module – and the graphical interface in MATLAB and android (delimited at blue); and the power supply battery.

The **lower trunk acceleration is collected** through the **IMU** and the **processing unit receives this information**, in order to **process** the acquired data. Based on the processing, the **processing unit delivers signals** to the **haptic drivers to control the vibrotactile units** and provide the **vibrotactile feedback**. The **micro SD card** and the **respective interface module** allow **to store the lower trunk acceleration** and the **Bluetooth module** permits the **wireless communication** between the processing unit and the developed **graphical interfaces**.

5.3.1. Processing Unit

The processing unit selected for the project was the **Arduino Mega 2560** given a low power consumption and an extensive range of enhanced Input/Output signals and peripheral features. The microcontroller used by the Arduino Mega is the ATmega 2560, which presents flexible features, many important to this project: a fast clock speed of 16 MHz; a wide range of PWM outputs and analog inputs; supports I2C and SPI communication; the microcontroller has two 8-bit timers (Timer 0 and 2) and four 16-bit timers (Timer 1,3,4 and 5); and presents three serial ports, a one-built-in LED, a reset button, a power jack and an USB connection. The board can operate on an external supply of 6 to 20 V, but it is recommended a range of 7 to 12 V, thereby all the system is power supplied by 12V through the battery above mentioned. Some of these features are depicted in Figure 5.7 illustrating the Arduino Mega 2560 board [76], [77].

The I2C pins allow the communication with the IMU to process the acquired lower trunk acceleration and with the Haptic driver to control the vibrotactile motors, in a **PWM mode** through the use of the PWM output pins. Also, the SPI pins enable the communication between the SD card Module Interface and the Arduino board. The use of the power jack ensures the portability of the system since it is possible to power supply the board with a researchable battery.

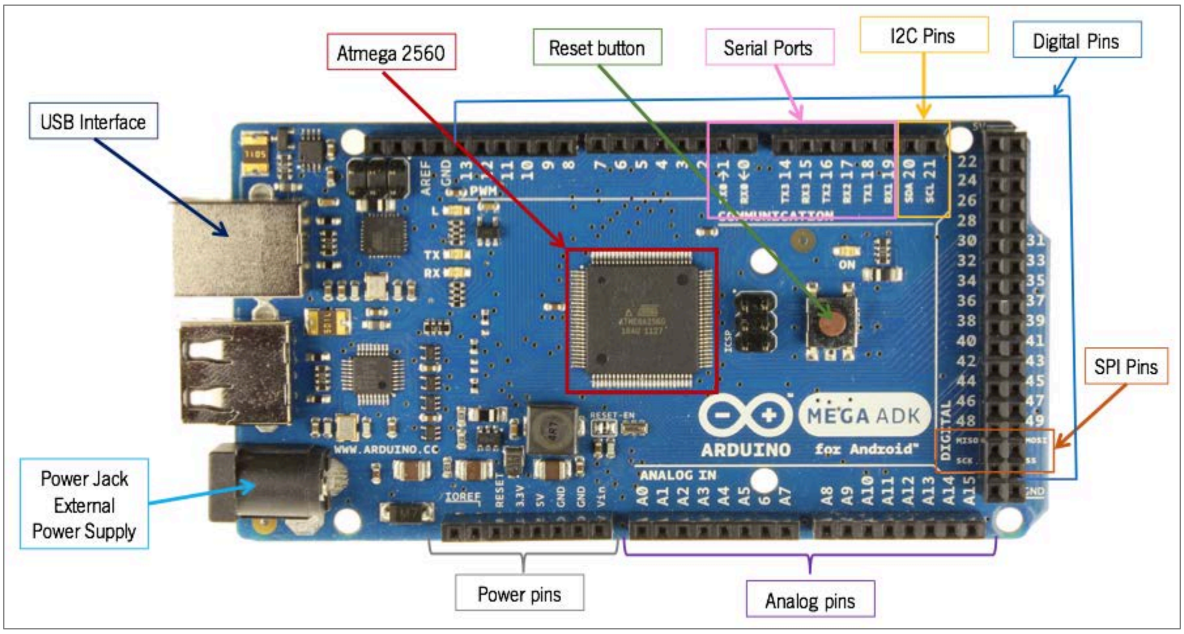


Figure 5.7 - The Arduino Mega 2560 board. Adapted from [77].

5.3.2. Lower Trunk Acceleration Acquisition System

Previously, force platforms, stereo photogrammetric systems, optical bars, or video-analysis have been used to analyze the human gait [78], [79]. However, these devices present limitations making them feasible for measurements on daily-life situations: do not allow a complete analysis of the entire gait cycle and require long post-processing, especially when used for subjects with gait abnormalities [78]. **Wearable sensors**, such as **IMUs**, are an optimal alternative since they allow to evaluate gait in real-time without these restrictions. Furthermore, with the technological advances, these sensors are lighter and smaller, making them suitable to record gait information and be embedded in wearable devices for outdoor ambulatory applications [79]. Thereby, in particular, it was chosen to use an IMU attached to the waistband, in order to allow acquire the gait in lower trunk (at spine level).

The **MPU-6050**, which was the world's first integrated 6-axis motion tracking device, combining 3-axis gyroscope and 3-axis accelerometer in a small 4x4x0.9 mm package was used. The MPU-60X0 is also designed to interface with multiple non-inertial digital sensors on its I2C port, being this the communication protocol implemented. Figure 5.8 depicts the implemented connections between the processing unit and the IMU.

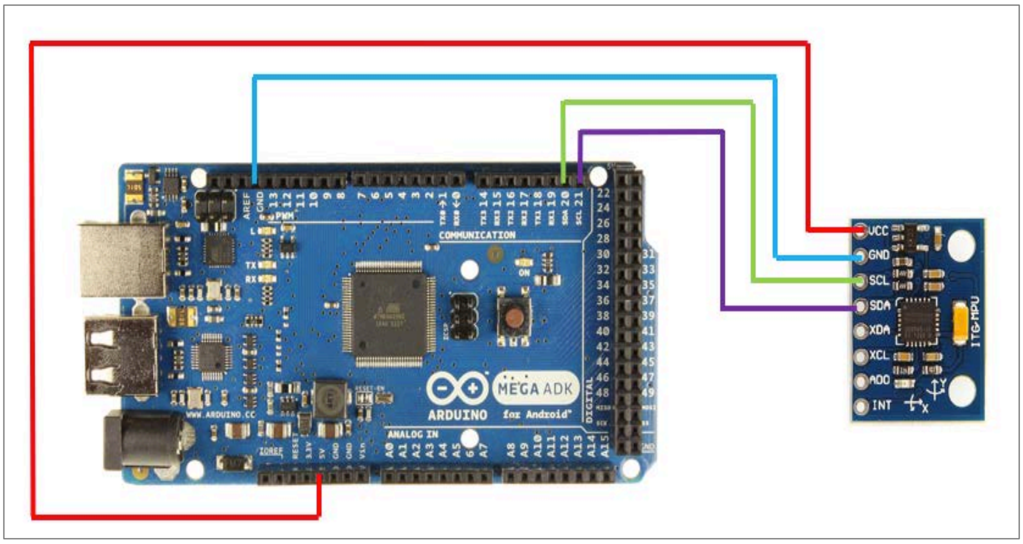


Figure 5.8 - Implemented connections between the processing unit and the IMU.

In this particular system, it was only necessary to collect the vertical acceleration data along the sagittal plane. The accelerometer data was analyzed, with a full-scale range of ± 2g (enough to detect gait events through a lower trunk acquisition) [80].

Figure 5.9 represents the localization of the IMU in the lower trunk, highlighting the implemented sensor and the accelerometer axes orientation used.

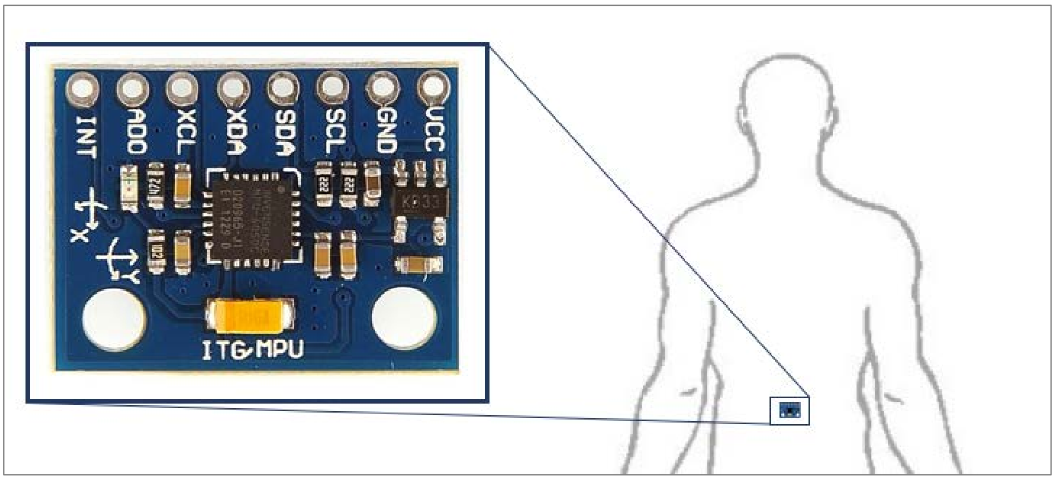


Figure 5.9 - Implemented sensor, IMU, (in the dark blue frame) attached in the waistband located in the lower trunk.

5.3.3. Actuation System

The actuation system consists of the Haptic Drivers and the respective vibrotactile motors.

Regarding to the haptic drivers, it was used the **Adafruit Industries' DRV2605 Haptic Driver**, which allows to obtain an extremely adjustable haptic control of actuators, Eccentric Rotating Mass (**ERM**) and Linear Resonance Actuator (LRA), over a shared I2C-compatible bus. This driver contains a smart-loop architecture, which provides a reliable motor control, a consistent motor performance and a feedback-optimized ERM drive providing automatic overdrive and braking that is important to simplify the input waveform paradigm. The DRV2605 Haptic Driver was composed by five pins: the supply pin (VDD), being recommend use to 2.5-5.5V; the two I2C-compatible bus pins (SCL and SDA): and the multi-mode input

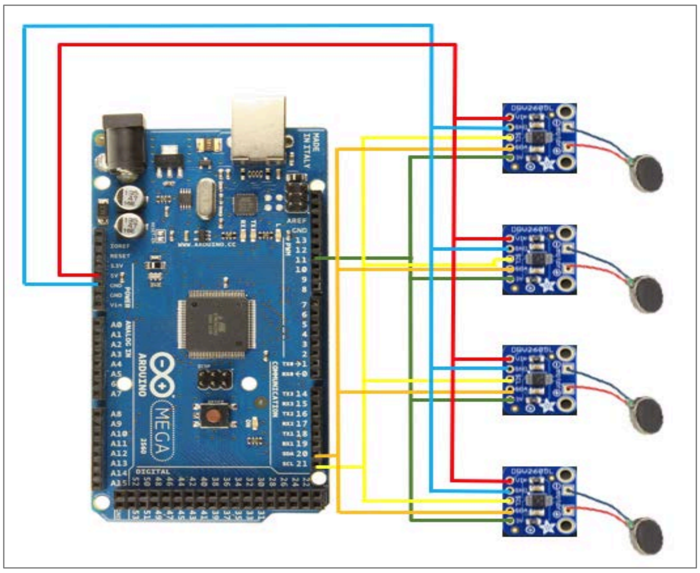


Figure 5.10 - Implemented connections between the processing unit and the haptic drives with the respective vibrotactile motors.

I2C selectable pin (IN/TRIG). In the four haptic drivers was used the PWM (Pulse-Width-Modulation) mode, by the pin IN/TRIG to provide the PWM sign [81]. Figure 5.10 represents the implemented connections between the processing unit and the haptic drivers with the respective vibrotactile motors.

The vibrotactile units are mini vibration motors 2.0mm (Seed Studio Electronic), a special type of **ERM motors**, coin vibration motor, also known as pancake vibrator motors [82]. Due to their small size and enclosed vibration mechanism, coin vibrating motors are a popular choice for many different applications.

In the following figure is presented the whole constitution of a pancake motor. In the flat flexible PCB, a 3-pole commutation circuit is laid out around an internal shaft in the center. In the next layer, there are two voice coils and a small mass that are integrated into a flat plastic disc with a bearing in the middle, which sits on a shaft. Two brushes on the underside of the plastic disc make contact to the PCB commutation pads and provide DC tension to the voice coils which generate a magnetic field. Then, this field interacts with the flux generated by a disc magnet (NdFeB neodymium) that is attached to the motor chassis. The disc rotates and, due to the built in off-centered eccentric mass, the motor vibrates.

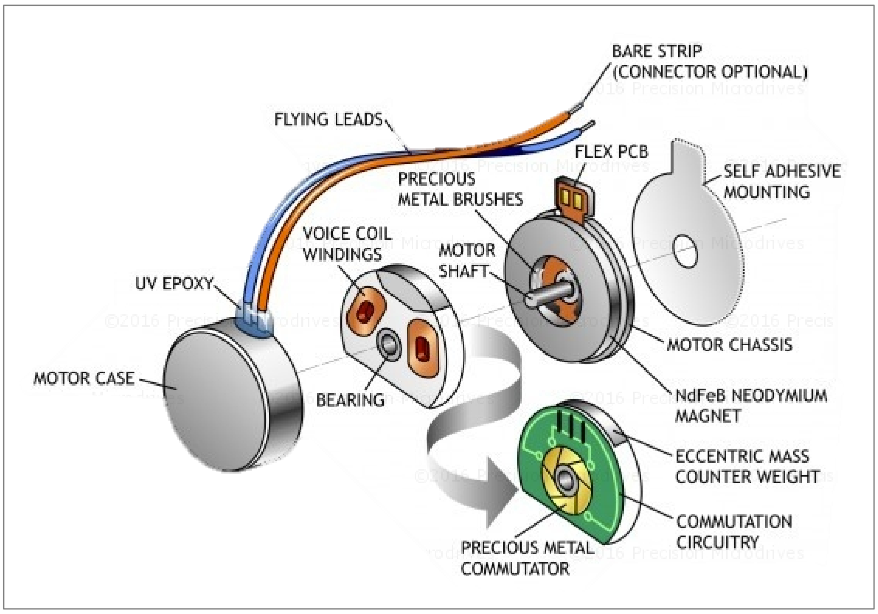


Figure 5.11 - ERM, the pancake motor constitution. Taken from [110].

Since these motors work with DC voltage, the simplest manner to drive they, is to connect the leads to a constant voltage DC source, at the motor’s rated voltage. A constant voltage will drive the motor at a constant speed, and hence at a constant frequency and vibration amplitude, until the supply is switched off. In fact, these motors are driven by an over range of voltages, however there is a “start voltage” which corresponds to the lowest voltage that must be applied to ensure the rotation of the motor, and consequently the vibration. From the "start voltage", as the applied voltage is increased, the vibration frequency increases almost-proportionally. In this way, it was necessary to construct a graph that allowed to relate the frequency of vibration with the voltage applied to each motor. Indeed, the DC tension is be

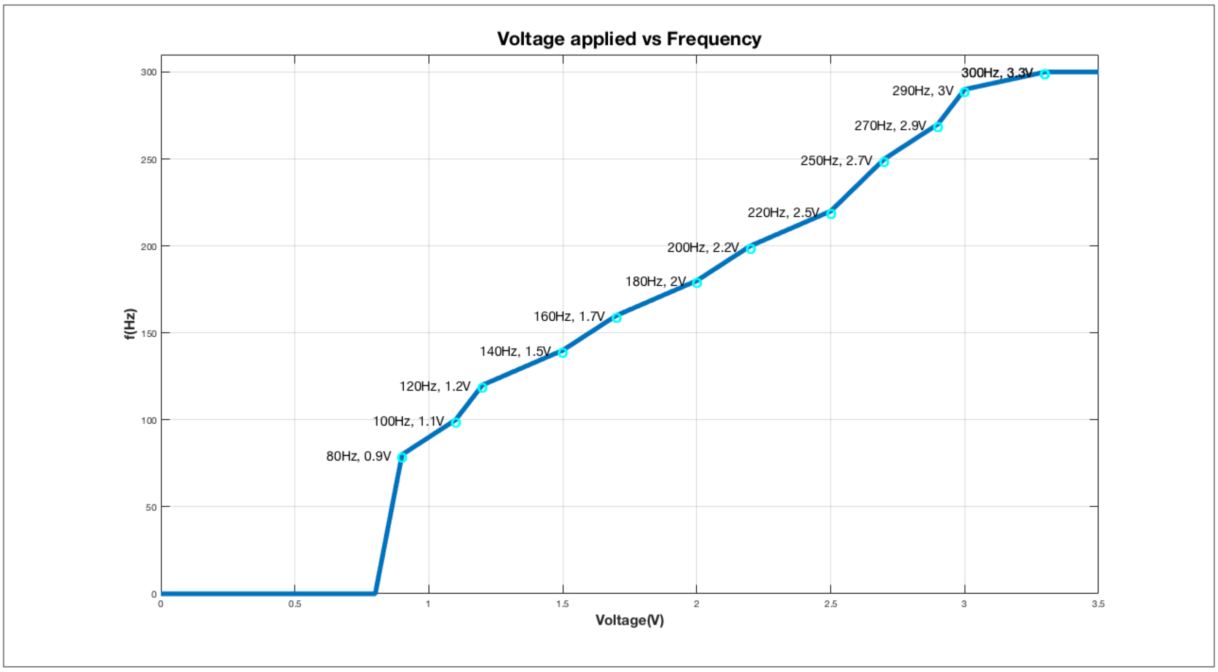


Figure 5.12 - Obtained graph with the relation between voltage applied vs frequency of vibration.

given by the duty cycle of the PWM provided by the processing unit to the haptic drivers and, consequently, to the motors.

Therefore, since these vibrotactile motors rotate an inner disc around a determined axis, an analog accelerometer was attached to the motor for studying the frequency as a function of the applied voltage. The period of the signal obtained by the acceleration of the motor rotation axis, indicates the frequency value. Figure 5.12 shows the obtained graph, where it is possible to conclude that the "starting voltage" for the used motors is 0.9 V. It should be noted that the tests were only carried out for a maximum voltage limit applied to the motor, 3.5 V. Furthermore, the verified range of frequencies is in accordance with the skin vibratory perception range.

5.3.4. Data Storage System

In order to store the acquired gait data during the experimental tests, an SD card with sufficient memory was used to store the data over a large period of time. Note that, even though the microcontroller in the processing unit contains non-volatile memory, 4 kB of EEPROM and more 256 kB in flash memory, this is a limited amount of built-in storage for the current propose and, consequently, it was used a SD card, as an alternative.

For a sampling period of 10 ms, duration of tests of 14400 s (4 h) and considering collecting 3 samples per each sampling (acceleration in the three axes), it is necessary a card memory able to store a a minimum value of 8.24Mb, approximately.

The interface chosen to write in the memory card and to communicate with the processing unit was the **Adafruit Module**. There are two ways to interface with SD cards: SPI mode and SDIO mode. The SDIO mode is faster, but is more complex and this module only supports SPI [83]. Figure 5.13 depicts the used connections between the processing unit and the micro SD card in the Adafruit Module.

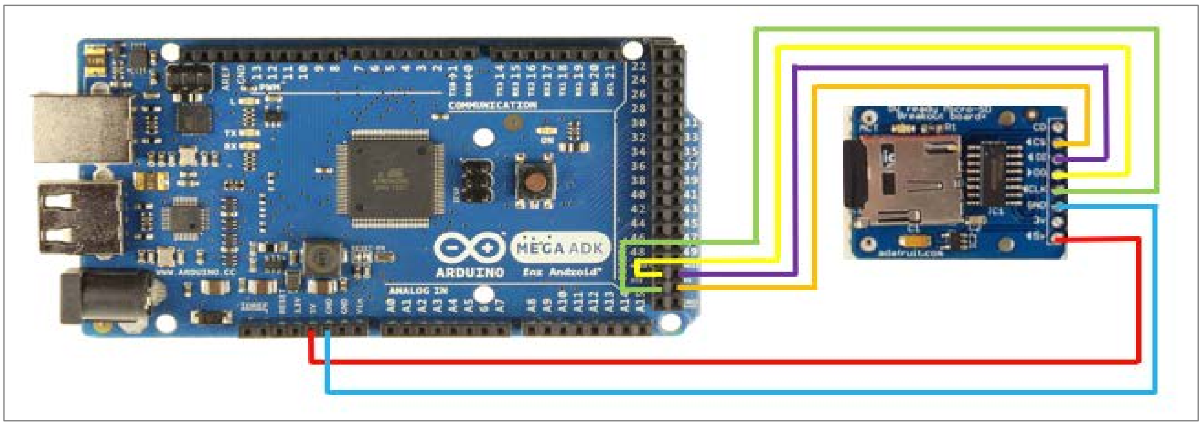


Figure 5.13 - Implemented connections between the processing unit and the micro SD card in the respective Adafruit Module.

5.3.5. Wireless Communication & Graphical Interface

To obtain a wireless communication, it was used a **Bluetooth Module**, the **HC-06 Itead Studio**. This module uses the Bluetooth 2.0 allowing a range of 10m of wireless communication and communicate with the processing unit through the serial port. Figure 5.14 shows the implemented connections between the processing unit and the Bluetooth Module.

The graphical interfaces were created in **MATLAB®** and **Android**. MATLAB® interfaces are easy to deploy and enable offline data processing. Similarly, the interface in Android allowed greater practicality during the test phases, once it was implemented in a mobile phone, a smaller device. With these interfaces, it is possible to select the experimental tests parameters and to communicate with the main device, the waistband, via wireless. The developed interfaces are presented in the following Chapter in order to enable a better explanation according to the performed experimental tests

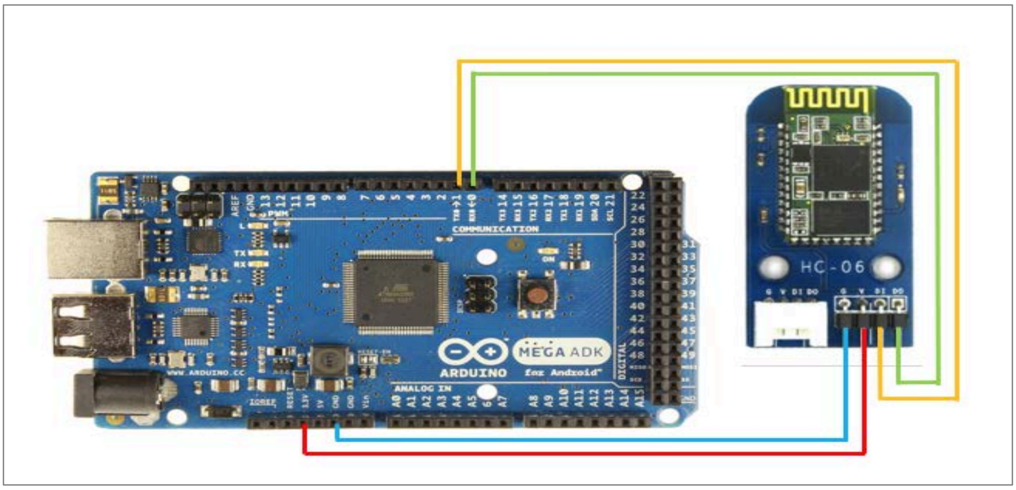


Figure 5.14 - Implemented connections between the processing unit and the Bluetooth Module.

5.3.6. System Integration

The final system was implemented in a **PCB** which allows to allocate all the components linked to the processing unit, previously presented, with a stronger connection. Figure 5.15 presents the designed PCB in the **Eagle software**. The integration of all the components in this PCB allowed to reduce the space occupied by all the electronic components and to increase the

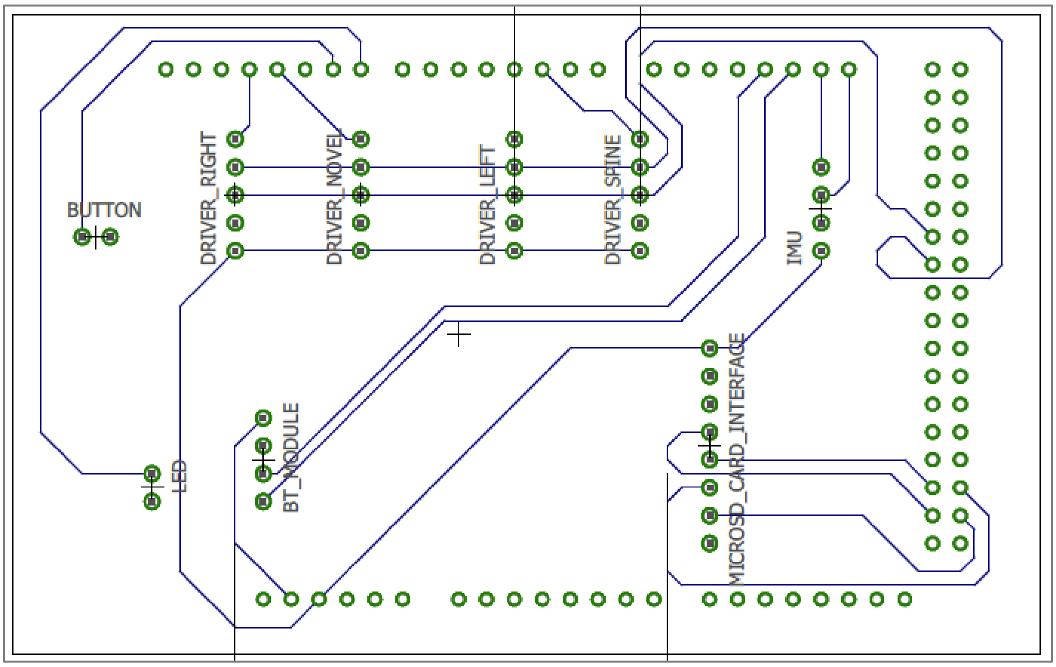


Figure 5.15 - Designed PCB in the Eagle software.

5.4. Conclusions

In this chapter, the implemented hardware and software for the development of a waistband was presented, which allows to **acquire, process** and **store** the **human gait in the lower trunk**, to **provide vibrotactile feedback** and to receive information **via Bluetooth** by **graphical interfaces**. To this end, several electronic circuits and graphic interfaces were implemented.

Thereby, the developed device is composed by a **Gait Acquisition System (IMU), a Processing Unit (Arduino), an Actuation System (Haptic Drivers and Vibratory ERM motors), a Wireless Communication System (Bluetooth Module)** and a **Data Storage System (Micro SD card and respective module)**. In addition, **Graphical Interfaces** have also been developed in **Android** and in **MATLAB**.

CHAPTER 6 – WAISTBAND VALIDATION

After developing the hardware and the software required to implement the proposed system, experimental tests were carried out to validate the waistband. These experimental tests followed a set of phases in the development of the project. In this chapter is presented for each of these tests, a system overview of the implemented system, the methods and validation, the obtained results and the discussion until reaching the final system validation. Finally, the conclusions and other considerations to be followed are presented.

6.1 Introduction

In the development of any project, the phase that follows the system implementation corresponds to the validation of each subsystem until a final verification of the general system.

In this project, the validation of the system comprises three major phases:

1 - In the first phase, were performed experimental tests to d**etect the best perceived frequency around the abdomen**;

2 - The second phase referred to the **gait events detection and parameters calculation through the acceleration acquired in the lower trunk**; and

3 – Lastly, the **system will be evaluated in a closer context to the final objective**, **considering the best frequency detected** through the first test and **integrating the gait detection** performed in the second phase.

Based on these steps, it was defined the **protocols** and **experimental methods** to follow, the necessary **inclusion and exclusion criteria** and the **relevant variables** for **analysis** and **evaluation**.

6.2 Detection of the best Frequency perceived around the Abdomen

After a critical research on the literature and the identification of the frequency vibratory range of perception in humans, it was necessary **to detect the best frequency perceived** either by healthy individuals and PD patients, with a temporal and spatial context.

Therefore, for the first test, it was intended to detect the best perceived frequency to be used in the final system. For this, three types of tests were performed: **1 – Time interval *vs* Frequency; 2 – Pattern *vs* Frequency; and 3 – Time interval and Pattern *vs* Frequency.**

Time interval *vs* Frequency test examines whether the subjects can perceive the vibrotactile stimuli provided during certain time intervals in order to obtain an evaluation in a **temporal context**. **Pattern *vs* Frequency test** allows to observe if the subjects can actually perceive the vibrotactile stimuli in the four zones to which the stimuli are being provided (navel, right, spine and left body zones) **– spatial context**. **Time interval and Pattern *vs* Frequency test** analyzes if the provided vibrotactile feedback is perceived in a short time interval and for all the stimulated zones, being evaluate the detection of the best frequency in a context not only **temporal**, but also **spatial**. In addition, during the last test it was **detected the minimum time interval required for perception**, which is important to provide the vibrotactile feedback in the final system

6.2.1 System Overview

These tests demanded the developed system and applications depicted in Figure 6.1, namely: the **Processing Unit**, the **Actuation System** with the **Haptic Drivers** and the **Vibrotactile Motors**, the **Wireless Communication System**, via Bluetooth, and the **Graphical Interfaces.**

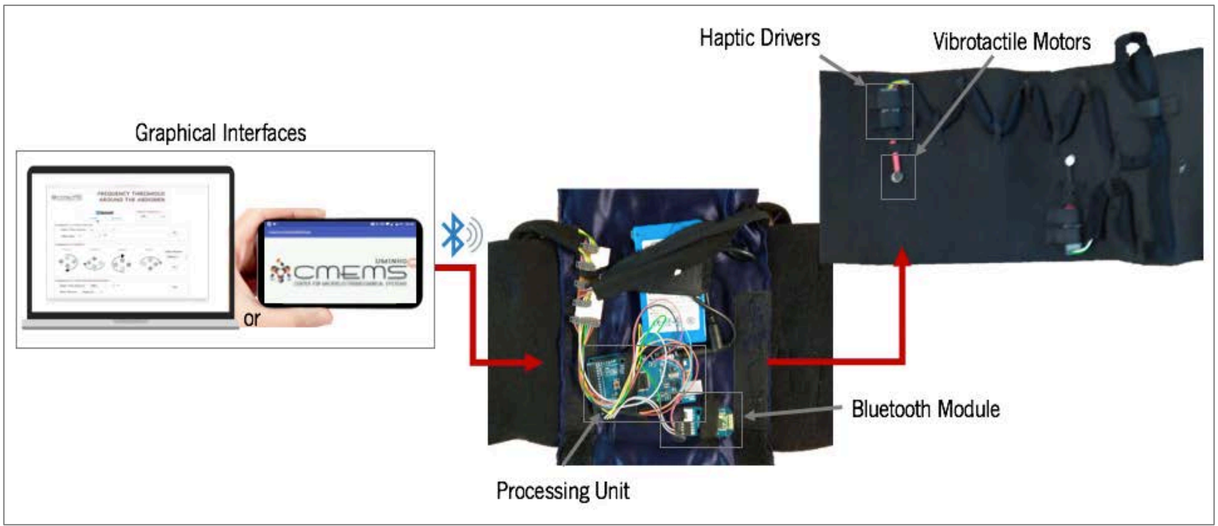


Figure 6.1 - Implemented system highlighting the Graphical Interfaces in MATLAB® and Android, the Processing Unit, the Bluetooth Module, the Haptic drivers and the vibrotactile motors.

The developed graphical applications allow to select the evaluated test parameters and pair with the Bluetooth module to send the data to the processing unit and carry out the experimental test. The following videos in Figure 6.2 show the develop graphical applications.

Figure 6.2 - Representation of the implemented graphical interfaces: on top – MATLAB® Interface and in down – Android Interface.

6.2.2 Methods & Validation

The validation of the proposed system involved 15 healthy subjects and 5 PD patients. Table 6.1 and 6.2 presents their gender, mean age, mean weight and mean height of the healthy subjects and PD patients, respectively. It should be noted that all patients had **an autonomous gait** and **were not at a dementia stage of illness.** The **phase of the medication was also controlled**, that is, all the patients were in the **ON phase**, where the medication had the desired effect. These are **inclusion and exclusion criteria** used in the experimental tests.

Table 6.1 - Morphological characteristics (number, gender, mean ± SD age, mean ± SD weight and mean ± SD height) of the involved healthy subjects in the proposed validation.

Number	**Gender**		**Age**	**Weight**	**Height**
	Female	Male			
15	6	9	25.07 ± 1.59 years old	67.5 ± 5.58 kg	175 ± 6.75 cm

Table 6.2 - Morphological characteristics (number, gender, mean ± SD age, mean ± SD weight and mean ± SD and height) of the involved PD patients in the proposed validation

Number	**Gender**		**Age**	**Weight**	**Height**
	Female	Male			
5	2	3	71.6 ± 2.23 years old	72.2 ± 1.39 kg	163.6 ± 3.08 cm

It should be noted that the studied frequencies **belong to the range of human perception**, 80 to 250 Hz, and was discriminated as: **80, 100, 120, 140, 160, 180, 200, 220 and 250 Hz**. Further, **all subjects repeat the experimental tests three times** in order to obtain more reliable results.

The following sub-sections describe the methodology followed for each of the tests carried out for the first phase. After the accomplishment of these tests, it was carried out a questionnaire for each participant.

6.2.2.1 Time Interval *vs* Frequency

Since the vibrotactile feedback will be provided in short time intervals according to the transition of the gait phases, it is important to detect the best perceived frequency in a short time.

Therefore, in this test there is a **trial capture interval** where half of the interval corresponds to an **OFF phase (without stimulation)** and the other half to an **ON phase (with stimulation)**. During the ON phase, vibrotactile stimuli were supplied considering the frequencies in test. The order of each of these OFF/ON phases is selected in each test. The participant only **indicated in which of the intervals he/she perceived the stimulation**. The tests were carried out for ON/OFF intervals of **4 s** and **2 s**. These intervals were chosen based on the literature in clinical protocols already performed [65]. The participant was **warned of the beginning of each trial capture** and it was demanded **to use headphones** during the experimental tests to ensure that they were unaffected by any external influence of the surrounding environment or even some sound from the vibrotactile motors. Note that **all vibrotactile units vibrated at the same time and with the same frequency under analysis**.

The participants **repeat the tests three times** for each time interval of capture (2 and 4 s). Figure 6.3 represents this test for a time interval of 2 s, where the blue line corresponds to the OFF-phase and the red line to the ON-phase. Note that, although in this representation the first half of the capture interval corresponds to the OFF phase, **these phases were alternated between each test**. The capture intervals should never be too close, with a minimum of 20sec between each trial.

In the graphical interface, the tester selected **the capture time interval (2 or 4 s), the half of it interval was provided the vibrotactile feedback** and the **frequency to analyze**.

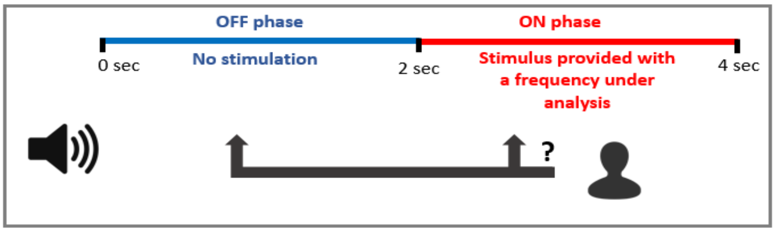


Figure 6.3 - Representation of the Time Interval vs Frequency test, for a timer interval of 2 s. Blue line corresponds to the OFF phase and red line to the ON phase.

6.2.2.2 Pattern *vs* Frequency

It is important to verify if the vibrotactile feedback is perceived in all the vibrotactile units in the same way for each one of the frequencies, despite their location.

Thus, in this test, **four vibratory patterns were provided** (pattern U, D, C and D), which are disclosed in Figure 6.4 (with description of the order of each vibratory pattern). These patterns were randomly selected and **each vibrotactile unit vibrated for 2 s**, for in respective

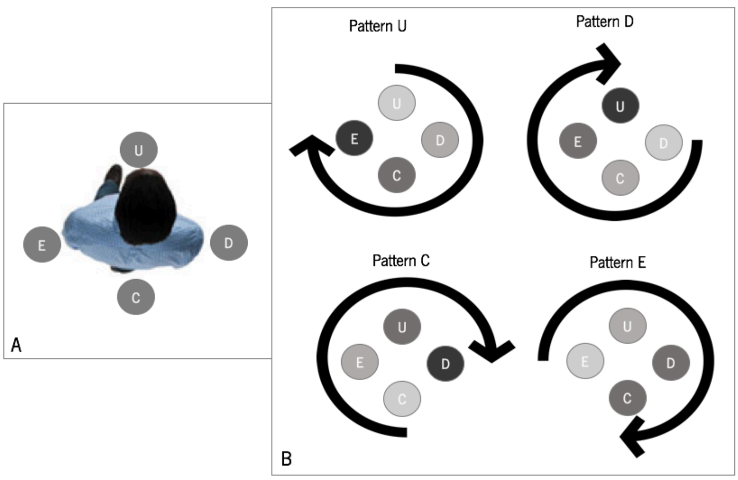


Figure 6.4 - Representation of the Time Interval vs Frequency test, for a timer interval of 2 s. Blue line corresponds to the OFF phase and red line to the ON phase.

pattern order, at the frequency of the test. The participants **indicated which pattern they perceived** and as previously described, the participants used headphones for the same purpose.

6.2.2.3 Time Interval and Pattern *vs* Frequency

In order to ascertain the frequencies perception in a short time interval, on a scale of milliseconds, for all the vibrotactile units, it was detected the best perceived frequency according to the **spatiotemporal context** at the same time.

The represented patterns in presented Figure 6.4 were used and the vibrotactile units vibrates for five intervals of study **– 100, 250, 500, 750 and 1000 ms –** according to the pattern's order, at the frequency of the test. Likewise, the participants **indicated the pattern perceived** for each and used phones to avoid environmental interferences. These time intervals are chosen **taking into account that the normal gait cycle** is approximately 1.15 s and **the minimum duration for gait events** is 115 ms [107]. It was important to identify these test time intervals since in this test it is intended **to detect which minimum interval the feedback should be given according to the gait event**s. However, it is important to highlight that in this test, it was only tested the frequencies of 200, 220 and 250 Hz, since for frequencies below 200 Hz, the vibrotactile motors can not effectively vibrate for the lower time intervals of 100 and 250 ms.

Finally, the participants had to fill in a questionnaire with the following questions presented in Figure 6.5.

Questions	Scores (1-Nothing, 2-Little, 3-Moderate, 4-High and 5-Very High)
Frequencies perception	
Time interval perception	
Vibrotactile unit perception at navel	
Vibrotactile unit perception at right	
Vibrotactile unit perception at spine	
Vibrotactile unit perception at left	
Comfort	

Figure 6.5 - Self assessment questionnaires performed.

6.2.3 Results and Discussion

The obtained results for the first experimental test, **Time interval *vs* Frequency**, are indicated in Table 6.3, where the percentage of healthy and pathological subjects that correctly identified the stimulation interval is highlighted.

By analyzing Table 6.3, it is verified that the **lower the vibration frequency**, **lower the number of subjects who correctly identified the stimulation intervals**, both for the **healthy subjects** and **patients with PD**. However, the **greatest decrease** in the percentages of correct identification was obtained for the **PD patients group**.

Table 6.3 - Percentage (mean ± SD) of healthy subjects and PD patients who correctly identified the stimulated interval for each of the frequencies tested to the time intervals of 2 and 4 s

Time interval (s)	Frequency (Hz)	Percentage (%)	
		Healthy subjects	PD patients
4	80	81.25 ± 10.83	33.33 ± 33.33
	100	81.25 ± 10.83	33.33 ± 33.33
	120	87.50 ± 12.50	58.33 ± 30.05
	140	93.75 ± 10.83	66.66 ± 33.33
	160	100.00 ± 0.00	91.66 ± 8.33
	180	100.00 ± 0.00	100.00 ± 0.00
	200	100.00 ± 0.00	100.00 ± 0.00
	220	100.00 ± 0.00	100.00 ± 0.00
	250	100.00 ± 0.00	100.00 ± 0.00
2	80	78.46 ± 15.14	16.66 ± 16.66
	100	82.38 ± 14.57	33.33 ± 33.33
	120	87.59 ± 12.56	33.33 ± 33.33
	140	96.75 ± 14.83	58.33 ± 30.05
	160	96.66 ± 18.10	66.66 ± 33.33
	180	100.00 ± 0.00	91.66 ± 8.33
	200	100.00 ± 0.00	100.00 ± 0.00
	220	100.00 ± 0.00	100.00 ± 0.00
	250	100.00 ± 0.00	100.00 ± 0.00

In fact, **regardless of the stimulation time (2 or 4 seconds)**: **higher the vibration frequency**, **better the frequency perception**. Even so, the **percentages of correct identification declined more for a shorter stimulus interval**. Indeed, for the **4 s stimulation intervals**, the frequency at which **healthy** and **pathological subjects** start to correctly respond to the stimulation interval was **160 Hz** and **180 Hz**, respectively. Whereas, for the **2 s stimulation intervals**, the frequency at which all **healthy subjects** and **PD patients** began to correctly respond to the stimulation interval increased to **180 Hz** and **200 Hz**, respectively.

Nevertheless, the frequency value for which all participants correctly began to identify the stimulation interval did not differ significantly between healthy and pathological subjects, as well as between the time intervals tested, 4 and 2 s.

For the second experimental test, **Pattern *vs* Frequency**, the acquired results are pointed out in Table 6.4, where, likewise, is discriminated the percentage of subjects that correctly answered the provided pattern.

Table 6.4 - Percentage of healthy subjects and PD patients who correctly identified the provided pattern for each of the frequencies tested in the four patterns (U, D, C and E)

Pattern	Frequency (Hz)	Percentage (%)	
		Healthy subjects	PD patients
U	80 and 100	100.00 ± 0.00	98.66 ± 12.33
	120, 140, 160	100.00 ± 0.00	98.66 ± 12.33
	180 and 200	100.00 ± 0.00	98.66 ± 12.33
	220 and 250	100.00 ± 0.00	100.00 ± 0.00
D	80 and 100	98.66 ± 12.33	98.66 ± 12.33
	120, 140, 160	100.00 ± 0.00	98.66 ± 12.33
	180 and 200	100.00 ± 0.00	100.00 ± 0.00
	220 and 250	100.00 ± 0.00	98.66 ± 12.33
C	80 and 100	91.66 ± 18.33	98.66 ± 12.33
	120, 140, 160	98.66 ± 12.33	98.66 ± 12.33
	180 and 200	100.00 ± 0.00	100.00 ± 0.00
	220 and 250	100.00 ± 0.00	100.00 ± 0.00
E	80 and 100	95.15 ± 6.65	98.66 ± 12.33
	120, 140, 160	100.00 ± 0.00	98.66 ± 12.33
	180 and 200	100.00 ± 0.00	98.66 ± 12.33
	220 and 250	100.00 ± 0.00	98.66 ± 12.33

As verified by the experimental tests, through the analysis of Table 6.4, the **percentages of correct identification** of the given patterns declined to the **lower vibration frequencies** for the **healthy** and **pathological subjects**, although with greater accentuation for PD patients (except in the U pattern).

However, it is important to note that the lower percentages of correct identification by the **healthy subjects** and **PD patients** were obtained for **C and E patterns**, respectively. To the lowest percentage in the C pattern, for the healthy subjects, can be justified by the physiology of the column of each person, since for a more curved column the vibrotactile unit located there was not directly in contact with the body of the user, decreasing its perception in such zone. On the other hand, the low percentages of the E pattern in PD patients may be due to the fact that the left body side, at the waist level, is not an area which is used as a natural anatomical reference and thus may require some cognitive effort for its perception. Lastly, it should be noted that the frequency for which all subjects responded correctly to the provided pattern was **120 Hz for healthy subjects** and **180 Hz for PD patients**.

Finally, concerning to the last tests which evaluate the Time Interval and Pattern vs Frequency, it was observed that **the subjects' perception decreases for lower stimulation time intervals** and **for the C pattern**, regardless of the group of subjects (although lower percentages were obtained with PD patients). In fact, only for the stimulation **time interval of 250 ms**, the healthy subjects detected all patterns for any frequency analyzed. Also, in general, the same was verified for patients with PD. All these results discussed are presented in Table 6.5.

Table 6.5 - Percentage (mean ± SD) of healthy subjects and PD patients who correctly identified the provided pattern in a shorter time interval of vibration for each of the frequencies tested (200, 220 and 250 Hz)

Time interval of vibration (ms)	Pattern	Frequency (Hz)	Percentage (%)	
			Healthy subjects	PD patients
100	U	220 and 250	100.00 ± 0.00	58.33 ± 30.05
	D	200	100.00 ± 0.00	58.33 ± 30.05
	C	200 and 220	91.66 ± 8.33	42.10 ± 20.75
	E	200	95.15 ± 6.65	58.33 ± 30.05
250	U	200	100.00 ± 0.00	100.00 ± 0.00
	D	200, 220 and 250	100.00 ± 0.00	100.00 ± 0.00
	C	200	100.00 ± 0.00	98.95 ± 16.65
	E	220	100.00 ± 0.00	100.00 ± 0.00
750	U	220	100.00 ± 0.00	100.00 ± 0.00
	D	200	100.00 ± 0.00	100.00 ± 0.00
	C	200 and 220	100.00 ± 0.00	100.00 ± 0.00
	E	220 and 250	100.00 ± 0.00	100.00 ± 0.00
1000	U	200	100.00 ± 0.00	100.00 ± 0.00
	D	200	100.00 ± 0.00	100.00 ± 0.00
	C	200, 220 and 250	100.00 ± 0.00	100.00 ± 0.00
	E	220	100.00 ± 0.00	100.00 ± 0.00

Regarding to the **questionnaires**, they allowed to subjectively evaluate the participants' opinions on all the parameters analyzed in the experimental tests. The scores obtained are pointed out in the Table 6.6.

The **healthy subjects** evaluated the **perception of frequencies** and **time intervals** with a **high level**.

For the **perception of each vibrotactile unit**, **these values varied between healthy subjects and PD patient**s. Since the navel and the spine are considered natural anatomic references, it was expected that the vibrotactile units placed at these body zones were the best perceived. However, the vibrotactile unit placed at the spine received lower scores from the healthy subjects and, as aforementioned, this lower perception can be explained since there was no permanent contact of the vibrotactile motors with the body of the user due to the column curvature of each person. In addition, the PD patients scored the vibrotactile unit located on the left body side with a lower score. Nevertheless, this observation is very subjective, since it is only possible to indicate the cognition of each patient as a justification for it.

Lastly, all subjects, healthy and PD patients, **did not consider the use of the waistband uncomfortable**, considering possible to perform their daily tasks and while perceiving the provided vibrotactile stimuli. Indeed, the PD patients showed great interest and acceptability of the developed system.

Table 6.6 - Scores of the self-assessment questionnaires (mean ± SD)

Questions	**Scores** **(1-Nothing, 2-Little, 3-Moderate, 4-High and 5-Very High)**	
	Healthy subjects	PD patients
Frequencies perception	4.75 ± 0.25	4.66 ± 0.33
Time interval perception	4.75 ± 0.25	4.33 ± 0.33
Vibrotactile unit perception at navel	4.75 ± 0.25	4.66 ± 0.33
Vibrotactile unit perception at right	4.75 ± 0.25	4.66 ± 0.33
Vibrotactile unit perception at spine	2.75 ± 0.48	4.66 ± 0.33
Vibrotactile unit perception at left	4.00 ± 0.41	3.33 ± 0.67
Comfort	4.81 ± 0.12	4.66 ± 0.33

6.2.4 Conclusions to Future Considerations

Experimental tests were performed to detect the best vibratory frequency perceived by PD patients and healthy subjects. The detection of this frequency was carried out taking into account a spatial and temporal context and the conjugation of the two through the accomplishment of three experimental protocols denominated of **Time interval *vs* Frequency, Pattern *vs* Frequency** and **Time interval and Pattern *vs* Frequency**. These tests allowed to detect the best perceived frequency around the waist zone in a shorter time interval for all the body zones in which the vibrotactile units are placed.

The detected frequency threshold (frequency from which the perception of all the group subjects under analysis was complete) for the two firsts tests (**Time interval vs Frequency** and **Pattern vs Frequency**) are highlighted in Table 6.7. Based on these results, it was possible to conclude that, in the final system, **the frequency to be used should be above 160 Hz**, in order to be perceived with higher sensibility.

Also in this Table, it is possible to compare the threshold frequencies detected between the tests. Since the obtained threshold frequency was smaller for the Pattern vs Frequency test, it is possible to conclude that the **all subjects have more spatial precision than temporal**.

Table 6.7 -Obtained mean vibratory frequency threshold around the waist zone with the experimental tests: Time interval vs Frequency and Pattern vs Frequency

	Subjects	**Test**	**Best Frequency Perceived (Hz)**
	Healthy	Time interval vs Frequency	>160
		Pattern vs Frequency	>120
	PD Patients	Time interval vs Frequency	>180
		Pattern vs Frequency	>180
Mean			>160 ± 14.14

It is important to emphasize that the third test allowed to detect the minimum time interval that the vibrotactile feedback should be provided in order to be clearly perceived. Thus, it was observed that **above 250 ms** of stimulation time interval, the healthy subjects and almost all PD patients detected all patterns for any frequency analyzed.

Summary, in these tests was clarified the **minimum vibratory frequency**, **above 160 Hz**, that should be provided in the final system. Besides that, it was identified the **minimum threshold time of vibrotactile feedback**, **250 ms**.

6.3 Detection and Estimation of Gait Events and Parameters through the Lower Trunk Acceleration

Walking is one of the most common human physical activities and plays an important role in our daily tasks. The term "gait" is used to describe the way of walking, consisting in consecutive cycles subdivided in a sequence of events which mark the transitions from one gait phase to another [84].

For most people walking, is fully subconscious and requires no cognitive burden, but for PD patients the activity of walking is affected and does not flow with normality [84]–[89].

In fact, a study in 2008 [86] investigated the gait dynamics and kinematics in PD patients and correlate these features with the predominant clinical features, concluding that the **walking velocity and stride length were reduced significantly** in parkinsonians. Also, in 2010, it was performed a research comparing the spatiotemporal and kinematic parameters between PD patients and healthy elderly subjects. It was observed statistically differences between the PD patients and the healthy elderly subjects: the PD patients presented a **decrease in the cadence** and a **gait cycle time higher** than the healthy elderly subjects [88].

Similarly, another study [87] divided the PD gait disturbances in two types, continuous and episodic. The episodic gait disturbances occur occasionally and periodically, appearing apparently in a random and inexplicable manner. By contrast, the continuous changes refer to alterations in the walking pattern that appear to be more or less consistent from one step to the next. Indeed, concerning to the continuous impairments it was described that PD patients presents a **longer double limb support**, spending more time with both feet on the ground and consequently an impaired postural control. This is justified by the inability of the patients to generate sufficient stride length and a reduced gait speed.

Lastly, a recent review [89] was performed to analyze the biomechanical aspects of walking in PD individuals. It has been argued that parkinsonians have **difficulty to regulate**

gait in a spatiotemporal context, reducing the step length, increasing the step frequency, and thereby **growing the double foot support phase** on the ground. In addition, these gait alterations promote **gait asymmetries** and a **reduction in walking speed** followed by **postural instabilities** and **loss of motor control**.

All these gait disturbances suffered by PD patients meant that it becomes imperative to develop gait analysis methods for monitoring their walking behavior. As a result, so far, to evaluate the gait in PD patients, force insoles, wearable inertial sensors in the feet and shank and video based motion analysis systems have been used [90]–[94].

Although the use of wearable inertial sensors has been subject of many studies, none of the developed systems for gait analysis in parkinsonians was used in the lower trunk. In this way, the **innovative character** of the implementation of the gait acquisition system in the lower trunk, through the use of an **IMU** attached to the developed waistband, is accentuated. In this section, it is proposed, implemented and validated a gait monitoring system mounted in the lower trunk, embedded in the waistband. This system is able to detect and determine the gait events and parameters.

6.3.1 Background: Gait Acquisition Systems in Lower Trunk

In the last years, several systems have been developed that acquire the lower trunk acceleration through the use of IMUs in order to detect gait events and temporal and spatial parameters [95]–[106]. Table 6.8 provides a review of some of these systems from 2001 to 2016, highlighting some main features of their implementation, namely, real-time detection, acceleration orientation used, discrimination between right and left foot, sample frequency used, processing method and algorithm implemented and which gait events and parameters were detected and calculated, respectively.

The development of these detection systems requires the use of sophisticated algorithms specially for real-time contexts, which are actually very important for gait laboratories and outside of rehabilitation environments towards assisted living environments. By analyzing Table 6.8 only two of these systems provided a real-time detection of gait events, namely the heel strike and toe-off [96], [97]. In addition, it was discovered that the implemented algorithms varied greatly from system to system and in general, **heuristic role**s and **wavelet-based approaches** were the most used [95], [97], [99], [101], [104].

Table 6.8 - Lower trunk acceleration acquisition systems developed from 2011 to 2016

Ref	Year	Real-time Implementation	Acceleration orientation	Detection Right/Left foot	Sample Frequency (Hz)	Full-scale acceleration range (g)	Processing	Algorithm	Gait Events detected	Gait Parameters detected
[96]	2001	-	Vertical	-	50	-	-	Based in a sum of FFTs	HS, FF, MST and TO	Stride time, Step asymmetry, Stride length and Gait speed
[99]	2002	-	Antero-posterior	-	200	-	-	Comparing with a ground truth – Footswitches	HS and TO	-
[101]	2002	-	Vertical	-	200	10	-	-	HS and TO	Gait speed, Cadence, Step length and Step time
[104]	2002	-	Antero-posterior	✓	100	-	-	-	HS and TO	Stride duration, Step length and Gait speed
[98]	2004	-	Vertical	-	-	-	Low-pass Butterworth filter before (4th order zero-lag at 20 Hz)	-	Heel strike, Foot flat, Mid stance and Toe-off	Step length and Gait speed
[94]	2009	✓	Antero-posterior	-	-	-	FIR filter (11th order)	Location of zero crossings	HS and TO	-
[95]	2012	✓	Vertical and Antero-posterior	-	-	-	FIR filter (30th order zero-lag at 2.5 Hz)	Heuristic roles	HS and TO	Step length
[100]	2012	-	Vertical	-	-	-	-	Wavelet-based approach	HS, FF, MSR and TO	Step length and Gait speed
[103]	2013	-	Vertical	-	-	2	-	-	HS and TO	Step length and Gait speed
[93]	2015	-	Vertical	-	200	2	FIR filter (30th order zero-lag at 2.5 Hz)	Heuristic roles	HS and TO	Step length and Gait speed
[97]	2015	-	Vertical	-	100	8	-	Wavelet-based approach and Heuristic roles	HS and TO	Step length, Gait speed and Gait asymmetry
[102]	2016	-	Antero-posterior	-	128	6	-	Wavelet-based approach	HS and TO	Stride, Step and Stance time Step length

Further, it was possible to verify that most of the algorithms were constructed based on the **vertical acceleration** along the frontal plane [95], [97]–[101], [103], [105]. Also, it was noticed that that the used sampling frequency diverged from 50 to 200 Hz [95]–[106].

This literature analysis allowed to study the acceleration signal in the lower trunk which is depicted in the Figure 6.4. In this figure, is presented the gait segmentation pointing out its events of the stance phase, for the right and left foot can be estimated using the vertical acceleration: **heel strike**, **foot-flat**, **toe-off**, **mid-stance** and **heel-off**.

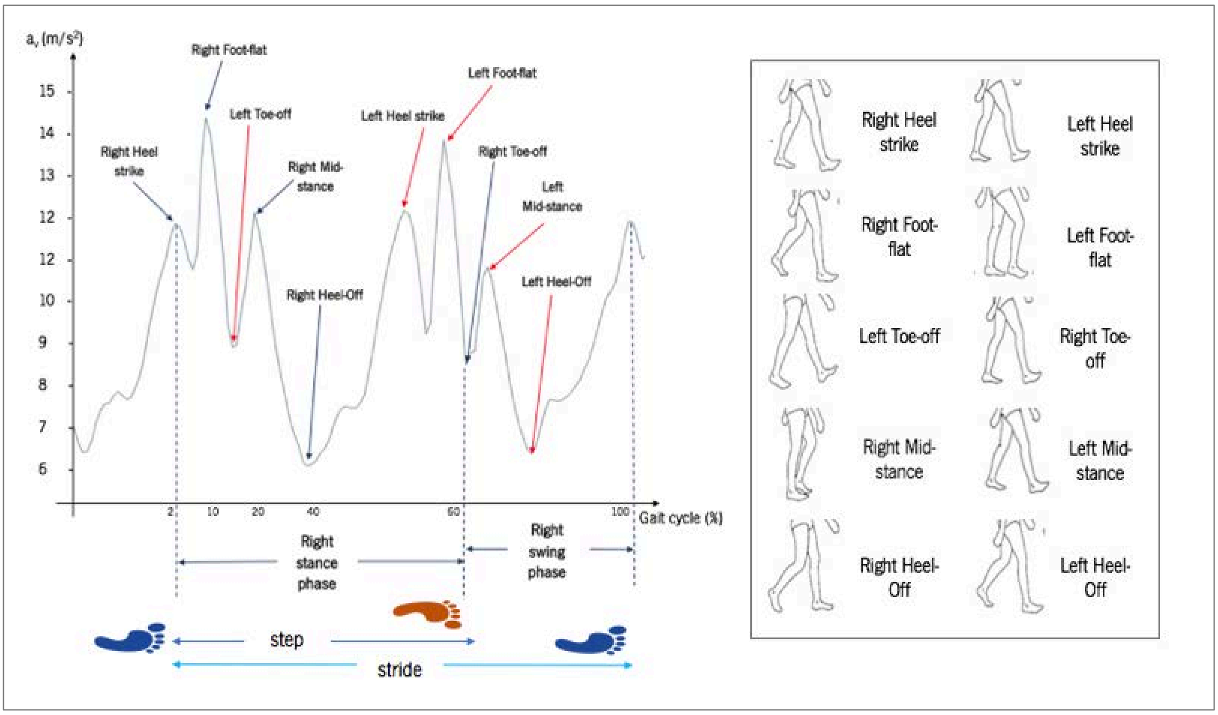


Figure 6.6 - Vertical acceleration over one stride. Adapted from [98].

Furthermore, it was concluded that it is possible **to calculate the temporal, spatial** and **spatiotemporal gait parameters**.

Concerning to the time parameters, **step and stride durat**ion are calculated as follows [98], [99]:

Eq. 1: *Step duration(s)* = $t_{\text{Left Toe-off}} - t_{\text{Right Toe-off}}$

Eq. 2: S*tride duration(s)* = $t_{\text{2nd Left/Right Toe-off}} - t_{\text{1st Left/Right Toe-off}}$

Where, the $t_{\text{Left Toe-off}}$ and $t_{\text{Right Toe-off}}$ correspond to the time where occurs the left and right toe-off and the $t_{\text{2nd Left/Right Toe-off}}$ and $t_{\text{1st Left/Right Toe-off}}$ are the time where occurs the second and first left/right toe-off, respectively.

Regarding to the **spatial gait parameter,** the **step length**, the most direct way to estimate this parameter is through the double integration of the acceleration signal. However, the errors of this methodology grow quadratic in time, so it becomes impractical. A solution presented is the use of the inverted pendulum method, which is based on the assumption that the vertical movement of a center of mass during a step (between the left and right toe-off) is equal to that described by a point mass suspended at the end of an inverted pendulum, as represented in Figure 6.7.

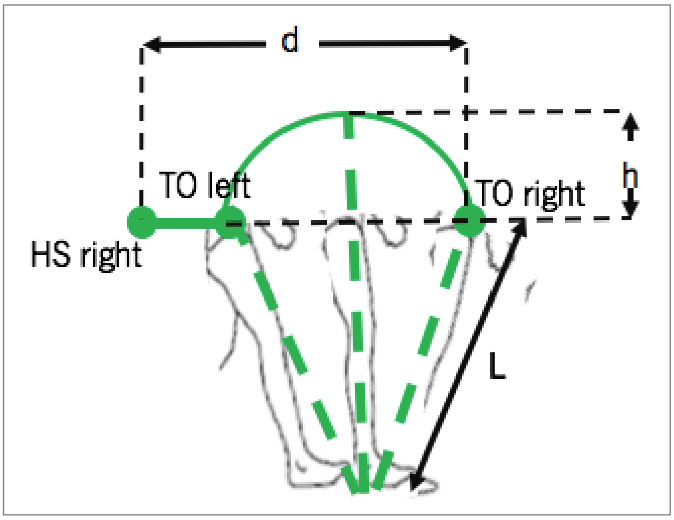


Figure 6.7 - Inverted Pendulum Method applied for the human body over one step (HS – Heel strike TO – Toe-off). Adapted from [98], [99].

The **inverted pendulum model** is able to determine the **step length** (**d**) which needs the height from the floor to the place where the sensor is placed (**L**) and the height of the center of mass during the step (**h**), which can be obtained by the double integration of the vertical acceleration. Therefore, the **step length** can be estimated by the following equation [98]:

Eq. 3: $\textit{Step length (m)}\ d = 2\sqrt{2\mathrm{Lh} - \mathrm{h}^2}$

Once estimated the step length and the step time it is possible to calculate the **gait speed**, a spatiotemporal gait parameter, which is obtained by dividing the step length by the step time, as follows [99]:

Eq. 4: $\textit{Gait speed}\ (\mathrm{m/s}) = \frac{\textit{Step length}}{\textit{Step time}}$

6.3.2 System Overview

In order to validate the gait segmentation and gait parameters estimation through the vertical acceleration in the lower trunk, it was implemented an acquisition sensory system in the developed waistband, as is discriminated in Figure 6.8. As a ground truth, it was used two **FSR sensors** (from Interlinks Electronics®) placed on the heel and toe foot of each subject. This strategy was very effective to determine the performance of identification of heel-off and toe-off events. In addition, it was used a system to storage the acceleration data in each experimental test for an offline evaluation.

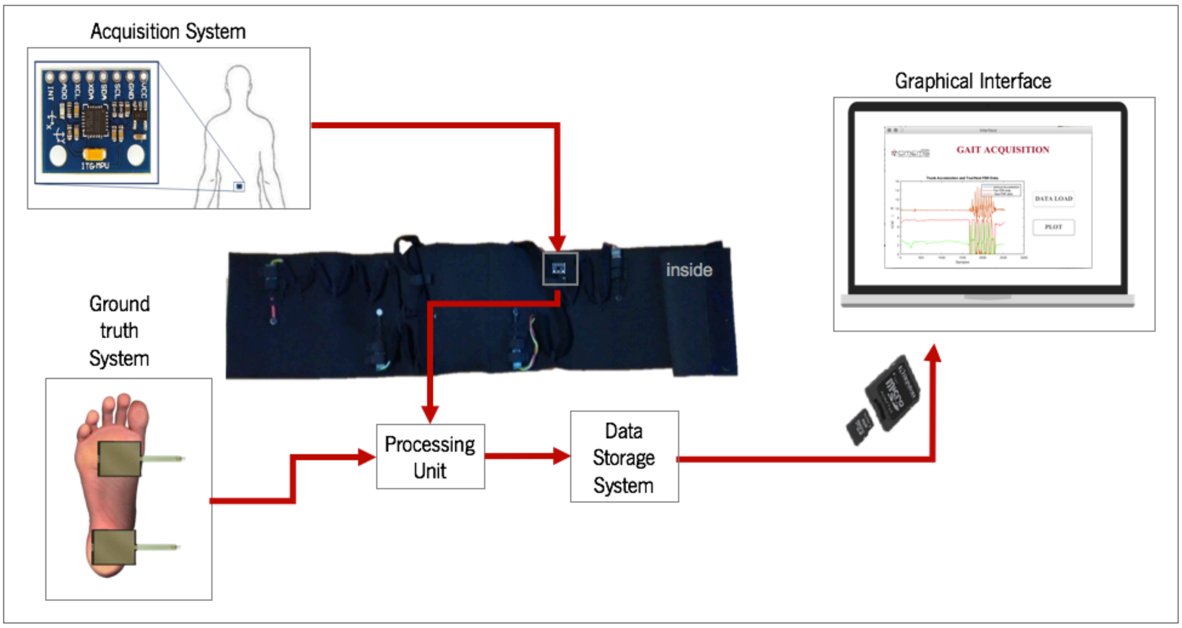


Figure 6.8 - - Implemented system highlighting the Acquisition system, the Ground Truth System, the Processing Unit, the Data Storage System and the Graphical Interfaces in MATLAB®.

Therefore, for the validation tests of the gait segmentation and parametrization in real-time and offline, it was used a **Processing Unit**, an **Acquisition System** (IMU), a **Ground Truth System** (FSRs) and a **Data Storage System** (mini SD card and respective Module to interface it). Besides the hardware implemented, it was also performed a **MATLAB® interface** to better visualize the acquired signals already segmented, with the respective identification of the gait events and the estimated gait parameters. All these systems, hardware and software are represented in Figure 6.8. The developed graphical interface and its functioning are depicted in Figure 6.9.

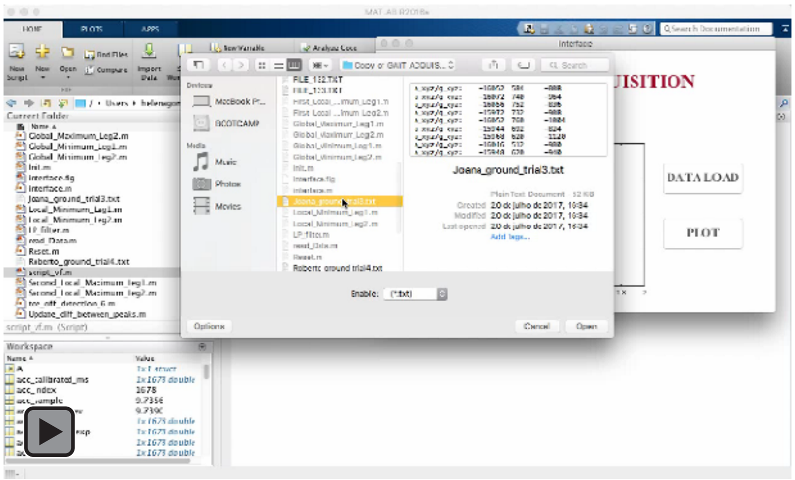


Figure 6.9 - Representation of the implemented graphical interface in MATLAB®.

6.3.2.1 Proposed algorithm to detect the gait events

The proposed algorithm consists in five stages: **acquisition, calibration, filtering, 1st derivative computation** and **finite state machine**.

For the **calibration routine**, are **captured 1500 samples** which are used **to calculate an offset** that is withdrawn from each of the samples subsequently acquired. Then, each acquired sample ($sample_n$), after calibrated, is filtered with an **exponential filter**, which is ideal for a real-time implementation based on heuristic rules, since it **does not cause delays in the signal** and **smoothes the samples**. Thus, each sample was filtered based on the following equation:

$$\textbf{Eq. 5: } sample_{n_{filtered}} = \alpha . sample_n + (1 - \alpha) . sample_{n-1}$$

Where, α is the smoothing factor (0 < α < 1) and $sample_n$ corresponds to the current sample and $sample_{n-1}$ to the previous sample. After performing some tests, it was chosen that the data was better filtered for α=0.5.

After **filtering the sample** ($sample_{n_{filtered}}$), the **1st derivative is determined** to detect when the **acceleration increases, decreases,** or **remains constant** and, in order to deal with the noise, t**he derivatives below a threshold (near to zero) are assumed as null**. This allows to detect only the major variations, that usually are associated with the local peaks. The calculation of the 1st derivative was performed based on the following equation:

$$\textbf{Eq. 6: } sample_{n_{diff\_derivated}} = sample_{n_{filtered}} - sample_{n-1_{filtered}}$$

Once the 1st derivative ($sample_{n_{diff\_derivated}}$) is calculated, **it follows the FSM** implemented by means of a switch case statement, which changes the states in accordance with the decision rules. All these stages are presented in the flow chart depicted in Figure 6.10

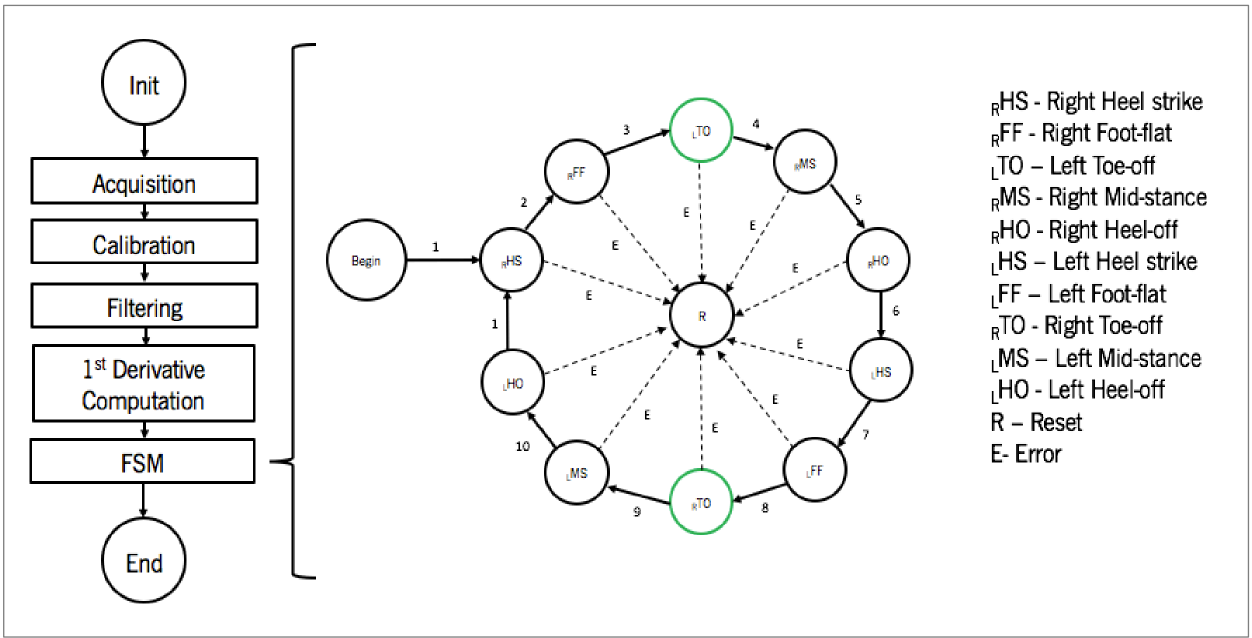


Figure 6.10 - Flow chart (left) and FSM (right) used to detect the gait events.

Also in Figure 6.10 it is possible to verify that the state machine is constituted by **eleven states that correspond to ten gait events and one of reset**. Each of these events correspond to a peak in the signal characteristic of the acceleration acquired in the lower trunk, as represented in **Figure 6.6** . Thereby, in Table 6.9 is indicated the **gait event corresponding to the peak in the acceleration signal**. To detect each of these events, **ten decision rules have been implemented** that allow to pass from one state to other, which are also presented in the same table.

Table 6.9 - Gait events detected and corresponding signal acceleration peaks

Gait event	Signal acceleration Peak	Decision Rules
Right Heel strike	1st Local Maximum	$(sample_{n_{diff\_derivated}} < 0)$ & $(sample_{n-1_{diff\_derivated}} > 0)$ & $(sample_{n-1} > \text{th}_{\text{1st max local 1}})$
Right Foot-flat	Global Maximum	$(sample_{n_{diff\_derivated}} < 0)$ & $(sample_{n-1_{diff\_derivated}} > 0)$ & $(sample_{n-1} > \text{th}_{\text{max global 1}})$
Left Toe-off	Local Minimum	$(sample_{n_{diff\_derivated}} > 0)$ & $(sample_{n-1_{diff\_derivated}} < 0)$ & $(sample_{n-1} < \text{th}_{\text{min local l 1}})$
Right Mid-stance	2nd Local Maximum	$(sample_{n_{diff\_derivated}} < 0)$ & $(sample_{n-1_{diff\_derivated}} > 0)$ & $(sample_{n-1} > \text{th}_{\text{2nd max local 1}})$
Right Heel-off	Global Minimum	$(sample_{n_{diff\_derivated}} > 0)$ & $(sample_{n-1_{diff\_derivated}} < 0)$ & $(sample_{n-1} < \text{th}_{\text{min global 1}})$

Left Heel strike	1st Local Maximum	$(sample_{n_{diff\_derivated}} < 0)$ & $(sample_{n-1_{diff\_derivated}} > 0)$ & $(sample_{n-1} > th_{1st\ max\ local\ 2})$
Left Foot-flat	Global Maximum	$(sample_{n_{diff\_derivated}} < 0)$ & $(sample_{n-1_{diff\_derivated}} > 0)$ & $(sample_{n-1} > th_{max\ global\ 2})$
Right Toe-off	Local Minimum	$(sample_{n_{diff\_derivated}} > 0)$ & $(sample_{n-1_{diff\_derivated}} < 0)$ & $(sample_{n-1} < th_{min\ local\ l\ 2})$
Left Mid-stance	2nd Local Maximum	$(sample_{n_{diff\_derivated}} < 0)$ & $(sample_{n-1_{diff\_derivated}} > 0)$ & $(sample_{n-1} > th_{2nd\ max\ local\ 2})$
Left Heel-off	Global Minimum	$(sample_{n_{diff\_derivated}} > 0)$ & $(sample_{n-1_{diff\_derivated}} < 0)$ & $(sample_{n-1} < th_{min\ global\ 2})$

To increase the robustness of the algorithm, the **thresholds** ($th_{1st\ max\ local\ 1}$, $th_{max\ global\ 1}$, $th_{min\ local\ l\ 1}$, $th_{2nd\ max\ local\ 1}$, $th_{min\ global1}$, $th_{1st\ max\ local\ 2}$, $th_{max\ global\ 2}$, $th_{min\ local\ l\ 2}$, $th_{2nd\ max\ local\ 2}$, $th_{min\ global\ 2}$) used in the decision rules were **adaptively calculated** every three gait cycles and the first thresholds were set empirically. Also, after the occurrence of three gait cycles, each of these peaks was detected based on its respective peak of the previous cycle, and must belong to a **cadence** calculated every three gait cycles. In this way, the peaks were only valid if they belonged to this calculated interval. Furthermore, in each state it was verified if the person was only **standing,** without taking a step and **in such case the reset state was activated**.

It is emphasized that the filtering, as well the calculation of the 1st derivative and the decision rules depend on the previous sample acquired, so this is always stored at the end of each stage. For the first sample acquired, it is assumed that the previous sample is zero at each of the different stages of the algorithm.

6.3.3 Methods & Validation

The gait events detection was accomplished in real-time and offline and gait parameters estimation was performed offline. Thus, the validation of the adaptive system of detection and estimation for the gait events and parameters was accomplished in three conditions:

1 – Offline on a treadmill;

2 - Offline on the ground; and

3 – Real-time, on the ground.

Globally, all steps performed by the subjects were analyzed and each gait event detection was evaluated regarding its **accuracy percentage (correct event detection)** and p**ercentage of detections that occurred with delay (delayed detection) and advance (earlier detection)**, as well the **duration of that delays and advance**s.

The gait events detected were compared with the signals from the FSR in each gait cycle, defined as ground truth. However, it is important to highlight that there was a greater concern in the correct identification of the toe-off event, because in the final system, this is the gait transition event chosen to provide the vibrotactile feedback.

Being this project carried out with the clinical partnership of the Neurology Service in the Hospital of Braga, it was agreed that it is necessary to estimate the following gait parameters so that an evolutionary evaluation of each patient can be obtained: **stride and step time, step length and gait speed**. Thus, the obtained estimation of the gait parameters was compared with the values of a normal gait and in the tests performed in the treadmill, the estimated gait speed was compared with the speed actually performed.

6.3.3.1 **Offline** Detection of gait events and Estimation of gait parameters **on a treadmill**

The estimation of gait parameters depends directly on the validation of the detection of gait events in offline mode. In this way, 7 healthy subjects (which morphological characteristics are presented in Table 6.10) had to walk on a treadmill at six different speeds: 2.5, 3, 3.5, 4 and 4.5 km/h (0% of slope). For each condition, the participants performed 3 trials for 60 seconds.

Table 6.10 - Morphological characteristics (number, gender, mean ± SD age, mean ± SD weight and mean ± SD height) of the involved healthy subjects in the proposed validation

Number	Gender		Age	Weight	Height
	Female	Male	23.86 ± 0.59 years old	66.33 ± 3.80 kg	170.29 ± 3.98 cm
7	2	5			

6.3.3.2 **Offline** Detection of gait events and Estimation of gait parameters **on the ground**

The validation of the gait events detection in offline, on the ground, involved 6 healthy subjects and the same 5 PD patients who participated in test – Detection of the best Frequency perceived around the Abdomen - section 6.2. The morphological features of these participants are presented in Table 6.1 and 6.11, respectively. In these experimental tests, the subjects had to **walk a distance of 20m, in an unobstructed hallway, three times, at a desired comfortable speed and freely**.

Table 6.11 - Morphological characteristics (number, gender, mean + SD age, mean + SD weight and mean + SD height) of the involved healthy subjects in the proposed validation

Number	Gender		Age	Weight	Height
	Female	Male	23.83 ± 0.7 years old	65.5 ± 4.34 kg	175 ± 6.74 cm
6	4	2			

6.3.3.3 **Real-time** Detection of gait events **on the ground**

The real-time validation, it was performed with 4 healthy subjects and 2 PD patients, which morphological characteristics of each group are presented in Tables 6.12 and 6.13. As in the previous test, all patients presented **an autonomous gait**, **without dementia** and were in the **ON phase of medicatio**n.

Table 6.12 - Morphological characteristics (number, gender, mean + SD age, mean + SD weight and mean + SD height) of the involved healthy subjects in the proposed validation

Number	**Gender**		**Age**	**Weight**	**Height**
	Female	Male			
4	3	1	22.50 ± 0.96 years old	58.75 ± 3.12 kg	165.50 ± 5.04 cm

Table 6.13 - Morphological characteristics (number, gender, mean + SD age, mean weight and mean + SD height) of the involved PD patients in the proposed validation

Number	**Gender**		**Age**	**Weight**	**Height**
	Female	Male			
2	1	1	74.00 ± 1.00 years old	69.00 ± 1.00 kg	164.5 ± 9.5 cm

The methodology applied in these experimental tests was exactly the same that followed for the offline validation on the ground, so the subjects walked a distance of 20 m in on unobstructed hallway three times, at a comfortable speed.

In the following figures, Figure 6.11 and 6.12, the present validation with one healthy subject and one PD patient is, respectively, disclosed.

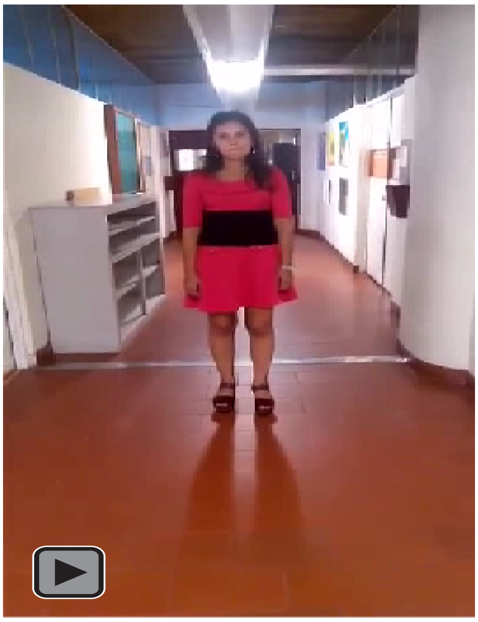


Figure 6.11 - Experimental test of validation of the proposed system with a healthy subject.

Figure 6.12 - Experimental test of validation of the proposed system with a PD patient.

6.3.4 Results and Discussion

The versatility and robustness of the proposed algorithms for different walking conditions is highlighted in the following sections.

6.3.4.1 **Offline** Detection of gait events and Estimation of gait parameters **on a treadmill**

The accuracy of the correct identification of the toe-off event (considering both foot), in percentage, is provided in Table 6.14. Besides the accuracy percentage, it is also presented the percentage of delayed and advanced detection and the delay and advance delay times. Note these results were compared with the signals from the FSR.

Table 6.14 - Algorithm performance in terms of accuracy, percentage of occurrence and duration of delays (delayed detection) and advances (earlier detection) for toe-off gait event (in offline on the treadmill)

Gait event	**Treadmill speed (km/h)**	**Accuracy (%)**	**Delay (mean ± SD)**		**Advance (mean ± SD)**	
			%	ms	%	ms
Toe-off (right and left)	4.5	100	5.39	1.36 ± 0.32	1.94	2.03 ± 0.07
	4	99.96	9.44	1.9 ± 0.15	3.90	1.73 ± 0.18
	3.5	97.79	8.63	1.98 ± 0.24	6.19	2.17 ± 0.06
	3	93.72	14.46	2.37 ± 0.07	7.01	2.20 ± 0.20
	2.5	75.37	18.79	2.42 ± 0.27	9.04	2.80 ± 0.25

By analyzing Table 6.14, it is concluded that the **proposed algorithm for gait detection** is **accurate** in the detection of the toe-off for gait speeds above 3km/h, with an accuracy above **93.75%.** In fact, for a gait speed of 2.5km/h the accuracy decreases until 75.37% since the amplitude of the signals decreases for lower speeds and the algorithm has empirical initial thresholds not sensible to these values.

Regarding the **percentage of occurrences of delays and advances**, it is observable that the **worst results were obtained for lower speeds**. This observation is due to the fact that the method is susceptible to the variations of cadence and the algorithm detects local maximums that are very close to the global maximum, mainly for smaller speeds, where the amplitude of the signal in the local and global maximum peaks is very closer.

The estimation of gait parameters depends directly on the correct identification of gait toe-off events. Therefore, the gait parameters were estimated for treadmill velocities of 3.5, 4 and 4.5 km/h because these velocities presented high percentages of accuracy. Also, it was established a term of comparison with the standard values that are presented in the literature, which are discriminated in Table 6.15.

Table 6.15 - Human standard spatiotemporal parameters [107]

Gait Parameters Estimated	Literature's valor (Mean)
Step time (s)	0.54
Stride time (s)	1.15
Step length (m)	0.79
Gait speed (km/h)	4.25

Table 6.16 presents the gait parameters estimated (mean ± SD) for the different treadmill speeds. In addition, indicates the error relatively to the treadmill speed in percentage.

Table 6.16 - Gait parameters estimated and measured error (percentage mean error)

Treadmill speed	Gait Parameters Estimated	Estimated Value (mean ± SD)	
4.5 km/h	Step time (s)	0.61 ± 0.55	
	Stride time (s)	1.21 ± 0.32	
	Step length (m)	0.78 ± 0.02	**Error (treadmill)**
	Gait speed (km/h)	4.53 ± 0.16	0.66 %
4 km/h	Step time (s)	0.49 ± 0.55	
	Stride time (s)	1.12 ± 0.32	
	Step length (m)	0.55 ± 0.02	**Error (treadmill)**
	Gait speed (km/h)	3.98 ± 0.16	0.50 %
3.5 km/h	Step time (s)	0.53 ± 0.02	
	Stride time (s)	1.13 ± 0.05	
	Step length (m)	0.54 ± 0.05	**Error (treadmill)**
	Gait speed (km/h)	3.54 ± 0.02	1.14 %

Comparing the average values of the estimated gait speed with the values of the treadmill, it is verified that these values are very close, and consequently the associated **error** is considerably **low**. However, it is noted that for a lower speed, the error increases, due to the fact that the accuracy of the correct identification of the toe-off events is lower. Lastly, despite being a subjective comparison, **the estimated step time, stride time and step length are in accordance with the literature values,** if we consider these values a term of comparison standard for healthy and adult subjects.

6.3.4.2 **Offline** Detection of gait events and Estimation of gait parameters **on the ground**

When testing the offline proposed algorithm with healthy subjects on the ground, it was concluded that the algorithm is accurate since the **percentage of accuracy of toe-off detection was very high (98.33%).**

Table 6.17 shows the average values obtained for the gait parameters under analysis, for the group of healthy subjects. When comparing the estimated values with the literature values, it is verified that the percentage of error is low.

Table 6.17 - Gait parameters estimated and measured error (percentage mean ± SD error), for the healthy subjects (in offline, on the ground)

Gait Parameters Estimated	Estimated Value	Error (literature)
Step time (s)	0.52 ± 0.15	3.70 %
Stride time (s)	1.11 ± 0.02	3.60 %
Step length (m)	0.73 ± 0.12	7.59 %
Gait speed (km/h)	4.01 ± 0.26	5.64 %

The **accuracy of the toe-off detection** in the group of **PD patients** decreases to **87.02**%, as shown in Table 6.18. The fact that the accuracy is lower for this group of subjects is due to the acceleration **gait signal in the pathological subjects presents irregularities** with respect to the standard signal that was presented in **Figure 6.6**.

Since **the gait parameters estimation depends heavily on the correct identification of the toe-off** and given that, **the percentage of accuracy has decreased for the patients with PD**. Table 6.18 presents the values of gait parameters for the patient who presented the highest percentage of identification accuracy of toe-off (97.02%). Furthermore, these values are compared with another study described in the literature which evaluates some of these parameters in analysis. Although **the estimated values are close**, **they still show some discrepancy**. However, it should be noted that the values obtained in the literature study were based on data acquired by a gyroscope located in the ankle. Note that, data of the gyroscope are susceptible to less noise than the data of the accelerometer and these tests were performed with more PD subjects [108].

Table 6.18 - Gait parameters estimated and measured error (percentage mean error), for the PD patient (in offline, on the ground)

Gait Parameters Estimated	Estimated Value	Literature Study[108]	Error (literature)
Step time (s)	0.65	0.57	14.03 %
Stride time (s)	1.28	1.14	12.28 %
Step length (m)	0.53	-	-
Gait speed (km/h)	2.94	3.06	3.92 %

6.3.4.3 **Real-time** Detection of gait events **on the ground**

The performance of the real-time algorithm is demonstrated in Table 6.19, where it is possible to analyze the **percentage of accuracy** of correct identification of the toe-off event, the p**ercentage of delayed and advanced detection** and th**e delay and advance delay times**, for **healthy subjects** and **PD patients**. Note these results were compared with the signals from the FSR. In the group of the **healthy subjects**, **the percentage of accuracy was higher**, **when compared with the patients group**. The percentage of occurrences of delays and advances, as noted above, occurs due to c**hanges in cadence** and v**ery close local and global peaks**, especially in the pathological gait signal.

Table 6.19 - Algorithm performance in terms of accuracy, percentage of occurrence and duration of delays (delayed detection) and advances (earlier detection) for toe-off gait event (in real-time, on the ground) for the healthy subjects and PD patients.

Gait event	Subjects	Accuracy (%)	Delay (mean ± SD)		Advance	
			%	ms	%	ms
Toe-off (right and left)	Healthy	88.99	12.2	1.52 ± 0.08	2.72	2.1±0.17
	PD	73.13	19.1	2.55 ± 1.08	5.75	3.3±0.33

6.3.4.4 Further considerations

Although throughout this subsection only the percentage of accuracy for toe-off detection has been reported, all of the previously discriminated gait events are detected. It is possible to verify this detection in Figure 6.13.

It is verified that the implemented algorithm detects the **right/left heel strike (1st local maximum), right/left foo-flat (global maximum), right/left toe-off (local minimum), right/left mid-stance (2nd local maximum), right/left heel-off (global minimum)**, for the right and limb, respectively.

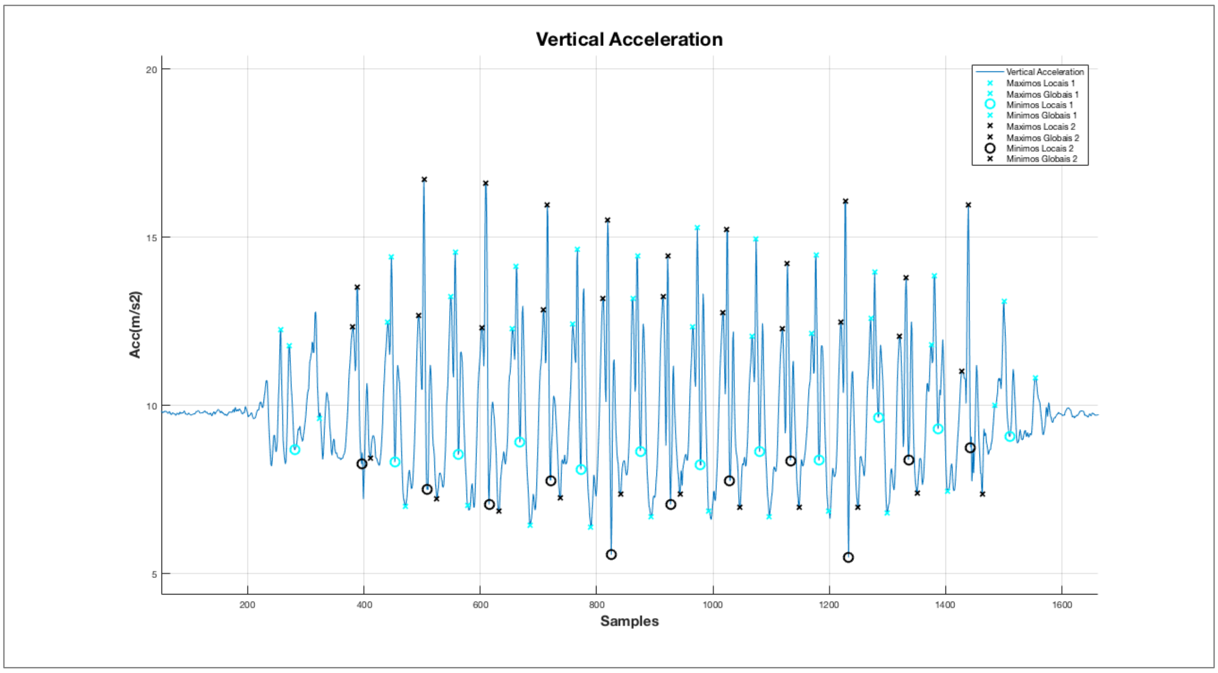


Figure 6.14 - Representation of gait events detection throughout the vertical acceleration (m/s^2).

Lastly, in order to prove the **adaptability of the developed algo**rithm, the toe-off detection is shown in Figure 6.14. Note that at the end of a third gait cycle, the **threshold calculation is adapted** based on the previous detected values, for each leg. In this figure, it is only represented the threshold for the toe-off detection, a local minimum: note that at the end of the third cycle, for instance, the threshold for the toe-off detection on the left leg (marked in

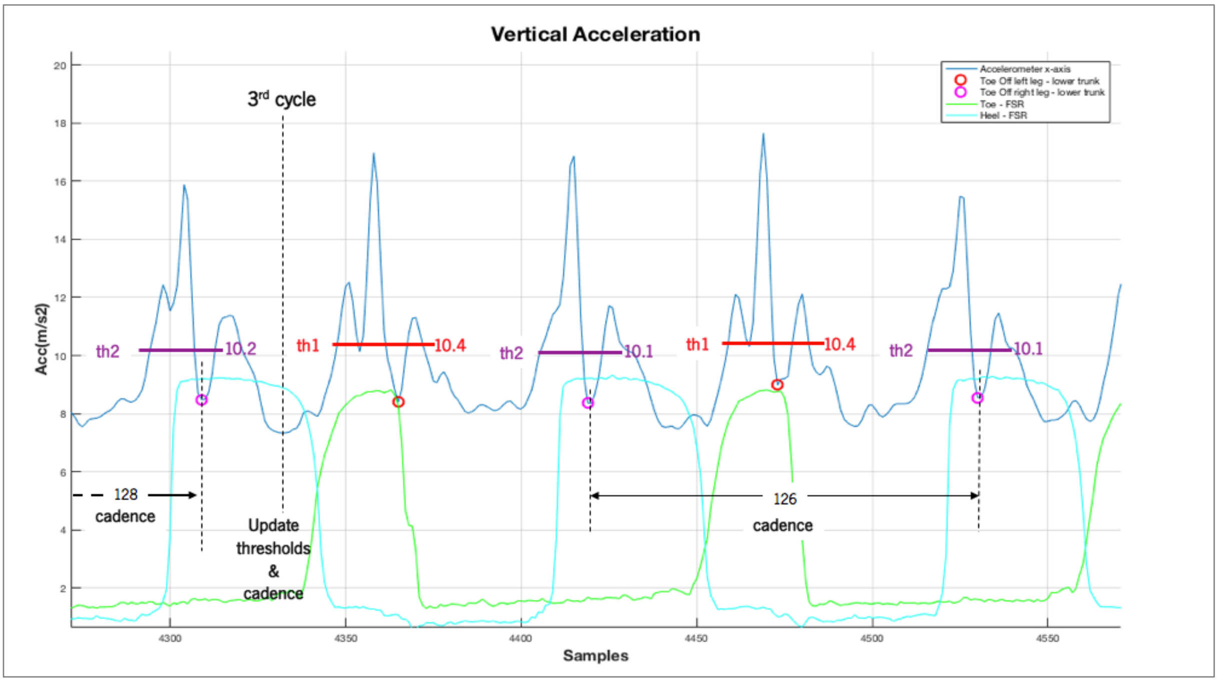


Figure 6.13 - Representation of gait events detection throughout the vertical acceleration (m/s^2) and FSRs output, in two steps of healthy subject (walking). It is pointed out the value of the adaptive thresholds (in this example for the toe-off detection for the right and left foot, a local minimum) and the value of the cadence (a specific defined range for each gait event).

purple) goes from 10.2 to 10.1 and remains with this value during the following three cycles. The same occurs for all thresholds of each detected event. Furthermore, the **calculation of the cadence for each event is adapted** according to the detection of the events during three gait cycles. This is why at the end of a third cycle this value is also adapted.

6.3.4 Conclusions to Future Considerations

This section described the development of a **real-time and offline adaptive tool for human gait detection and estimation of gait parameters**, from the **acquired vertical acceleration in the lower trunk**, was described. The proposed algorithm stands out from the existing approaches since it uses a robust FSM triggered by decision rules with **adaptive thresholds, cadence** and **only one-axis** from an IMU mounted in the waistband developed.

The validation of the adaptive system for detection and estimation of the gait events and parameters was accomplished in three conditions with different groups of subjects: **1 –offline on a treadmill; 2 - offline on the ground; and 3 –real-time on the ground.**

Considering the **offline detection and estimation of gait events and parameters in on a treadmill** with **healthy subjects**, the algorithm has shown **to be very accurate and time-effective**. **The same** was verified **in offline on the ground** with **healthy subjects**. However, in this last condition of test (on the ground), in the validation with **PD patients**, the **accuracy of the proposed tool of detection and estimation decreased**, since the vertical acceleration **signal in PD patients presents some irregularities** due to the motor gait symptoms present in this pathology. In fact, this signal differs from the one of healthy subjects and the algorithm should be designed for parkinsonian and not for healthy. To overcome this situation more tests should be performed with patients in order **to find a pattern that allows establishing more metrics for the rules of decision of the FSM**. Concerning the **real-time validation**, once again, **the accuracy and time-efficiency was higher for healthy subjects**.

It is also important to note that the accuracy of the detection of gait events is affected by the **high susceptibility to noise** when using the **acceleration signal** from the built-in accelerometer of the IMU. Consequently, any error in the detection of gait events, in particular toe-off, affects the estimation of gait parameters.

The validation of the proposed algorithm, with specific detection of the toe-off event and estimation of gait parameters, allowed us to proceed to the next step of construction and testing of the final system.

6.4 Final System Validation

The tests of detection of the best perceived frequency around the abdomen enable to determine the minimum frequency of perceived vibration with the developed system: above 160 Hz (up to 250 Hz). In this way, it was possible to identify the frequency of vibration that is used in the validation of the final system: it was chosen to provide a vibrotactile stimulus with a **frequency of 200 Hz**. In addition, although this test focused on determining the best perceived frequency, it was also discovered the **minimum interval - 250 ms** – during which the stimulus must be provided so that the feedback is perceived according to the frequency of vibration.

Then, an algorithm of gait events detection was implemented and validated. In order to develop a closed-loop solution that provides vibrotactile neurofeedback in accordance to the user movement, the stimuli should be provided when the **toe-off event is detected**. This particular event was chosen since this solution aims to overcome FOG. **Patients reported that during FOG they feel their feet glued to the ground**. Thus, it seems ideal **to provide feedback exactly in the event** that corresponds to the moment **when the foot finishes to be in contact with ground**. Note that the detection of this event is important for the feedback control strategy, since providing vibrotactile feedback **integrated** and **synchronized with gait transition allows to provide a vibrotactile pattern in a discrete time**. This way, the patients are able **to incorporate the feedback into their sensory system**, trying **to replace the missing and broken nervous message involved in the motor tasks**.

Moreover, the implementation of the toe-off detection algorithm permits **to estimate the gait parameters** which are important to accomplish a continuous evaluation of the patients, very useful for the clinicians.

All these steps followed allowed to reach the final validation of the developed waistband, as shown in Figure 6.15.

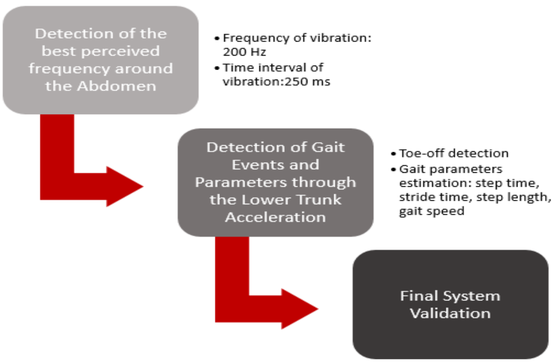


Figure 6.15 - All steps followed to the final system validation

6.4.1 System Overview

The e final system integrates most of the systems so far implemented for the previous tests. The system comprises a **Processing Unit**, an **Acquisition System**, a **Ground Truth System**, an **Actuation System**, a **Data Storage System** and a **Graphical Interface**, as is described in Figure 6.16.

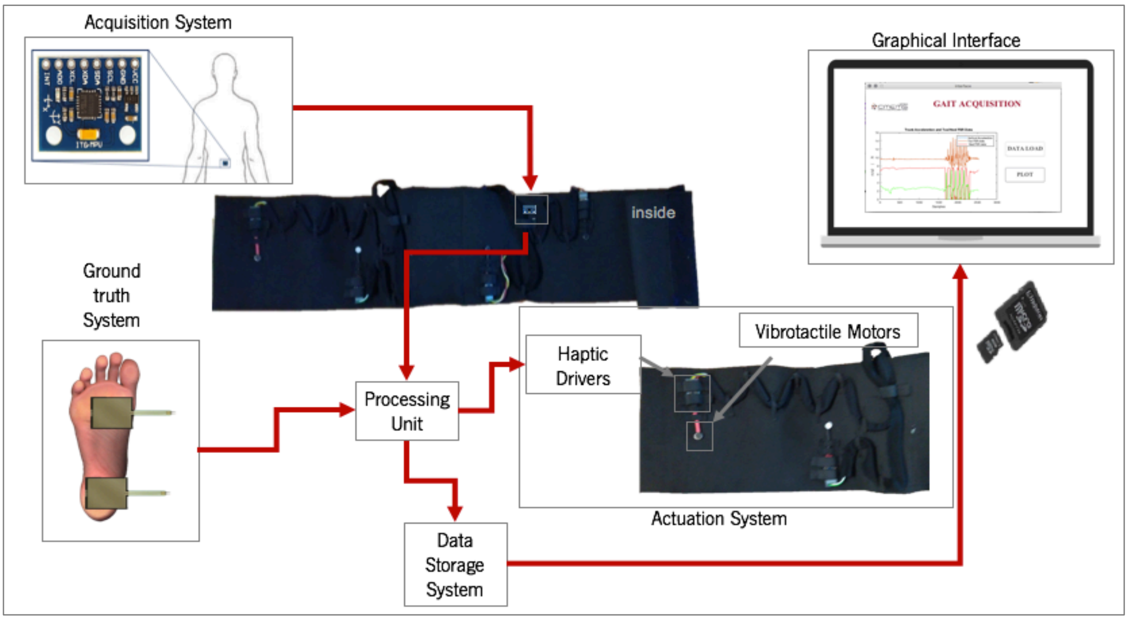


Figure 6.16 - Implemented system highlighting the Acquisition system, the Ground Truth System, the Processing Unit, the Actuation System, the Data Storage System and the Graphical Interfaces in MATLAB®.

The **system for sensory acquisition of gait**, implemented through an IMU, acquires the **vertical acceleration** of each user. Then, this information is sent to the processing unit, where **through a finite state machine (FSM) based on heuristic decision rules, the toe-off event of one of the legs is detected**. When this event is detected, a signal (PWM mode) is sent which **activates the haptic drivers** that **control the vibratory motors**. At this moment, **the vibratory motors provide the vibrotactile feedback at a frequency of 200 Hz for 250 ms**. This final solution enables the PD patients to incorporate the vibrotactile pattern provided and synchronized with their toe-off gait transition event into their physiological system. Note that, although the toe-offs of each leg are detected, the vibrotactile feedback is only provided in accordance with the leg that performed the first toe-off. The following Figure 6.17 is intended to show all this process, which explains the final system implemented, a waistband able to provide vibrotactile feedback to PD patients, helping them to overcome FOG.

Likewise, the **data storage system** allowed to **save the gait signal acquired** in each trial test from the acquisition system and the **ground truth system** (FSRs signals). Then this information storage was loaded and properly processed in a **MATLAB® interface.**

Figure 6.17 - Representation of the implemented system.

6.4.2 Methods & Validation

The validation of the this solution involved the same 6 healthy subjects (4 males and 2 females) which participated in the validation of the real-time gait detection algorithm on the ground. Thereby the morphological characteristics of these subjects are presented in the **Table 6.11**. Also, the validation of the proposed system, involves 2 PD patients (with the **same inclusion and exclusion criteria**), being their morphological characteristics pointed out in the follow Table 6.20.

Table 6.20 - Morphological characteristics (number, gender, mean ± SD age, mean ± SD weight and mean ± SD height) of the involved PD patients in the proposed validation

Number	**Gender**		**Age**	**Weight**	**Height**
	Female	Male			
2	1	1	74 ± 1.00 years old	69 ± 1.00kg	164.5 ± 9.5 cm

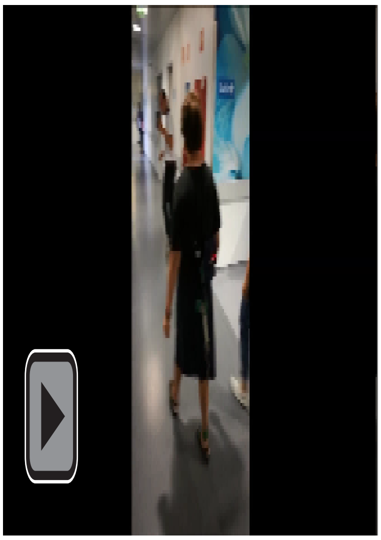


Figure 6.18 - Experimental test of validation of the final system with a PD patient.

The methodology followed consisted of **walking 20 m, three times, at a desired speed, freely and without obstacles**. In Figure 6.18 is presented an example of an experimental test accomplished in the Hospital of Braga with a PD patient. At the end of the experimental tests, the participants answered a **questionnaire** (Figure 6.19) in order to obtain an evaluation from the users about the use of the waistband.

Questions	Scores (1-Nothing, 2-Little, 3-Moderate, 4-High and 5-Very High)
Vibrotactile Feedback Perception (in general)	
Vibrotactile unit perception at navel	
Vibrotactile unit perception at right	
Vibrotactile unit perception at spine	
Vibrotactile unit perception at left	
Comfort	
Possible integration of the waistband with the vibrotactile feedback in their daily tasks	

Figure 6.19 - Self assessment questionnaires performed.

In addition, in the Figure 6.17 is showed the implemented MATLAB® interface, which allow to save the acquired gait data and the gait parameters estimated in an excel sheet.

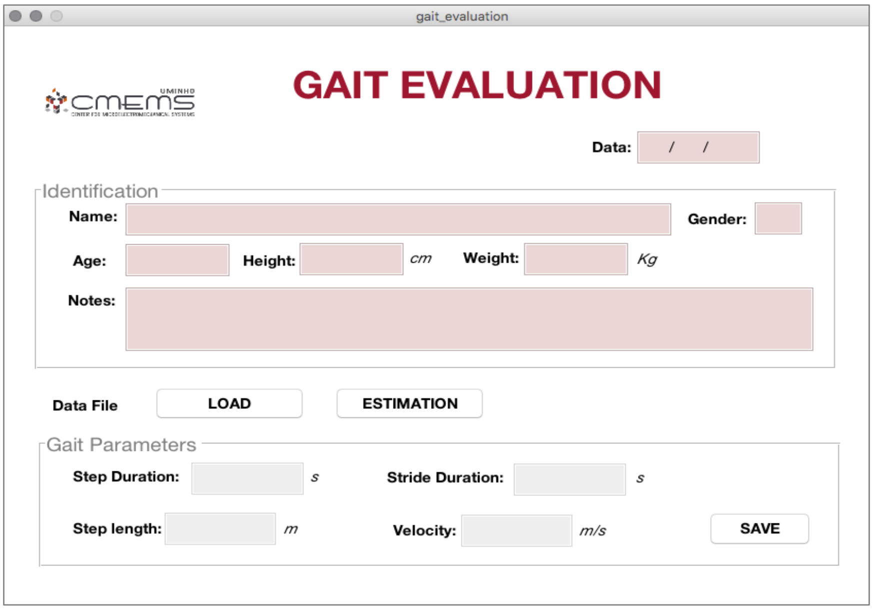


Figure 6.20 - Implemented MATLAB interface for display and save data from the performed experimental tests.

6.4.3 Results

The performance of the gait events detection algorithm is demonstrated in Table 6.21. It is possible to analyze the **percentage of accuracy** of correct identification of the toe-off event, the p**ercentage of delayed and advanced detection** and th**e delay and advance delay times**, for **healthy subjects** and **PD patients**. Note these results were compared with the signals from the FSR.

Table 6.21 . Algorithm performance in terms of accuracy, percentage of occurrence and duration of delays (delayed detection) and advances (earlier detection) for toe-off gait event (in real-time, on the ground) for the healthy subjects and PD patients

Gait event	**Subjects**	**Accuracy (%)**	**Delay (mean ± SD)**		**Advance (mean ± SD)**	
			%	ms	%	ms
Toe-off (right and left)	Healthy	87.55	13.33	2.01 ± 0.24	2.72	2.14 ± 1.17
	PD	75.23	18.14	1.32 ± 1.08	4.98	3.64 ± 1.23

A comparison among the group of PD patients with the healthy subjects, **the percentage of accuracy was higher for the healthy subjects**. The percentages of delay and advances are also justified through: changes in cadence and very close local peaks.

In Figure 6.21, the acquired acceleration signal, **highlighting the detected toe-off events**, and a signal describing **the exact moment in which the vibrotactile feedback was provided**. This feedback was provided **during 250 ms** (25 samples - 100 Hz sampling frequency), **when the toe-off event of one foot was detected**.

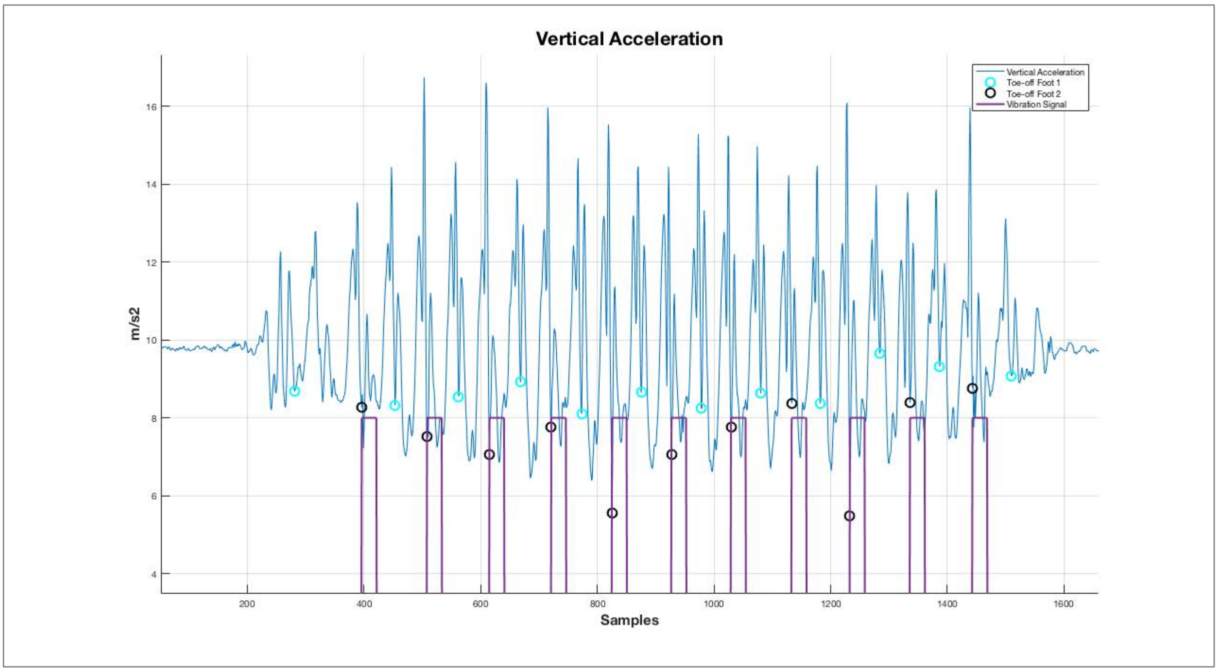


Figure 6.21 - Toe-off detection (cyan and black circle) through the lower trunk acceleration acquired in real-time (blue signal) and the moments when the vibrotactile feedback was provided (purple line)..

Table 6.22 presents the gait parameters estimated. As a comparison, the results obtained for healthy subjects are in agreement with the standard values of a normal gait, described in Table 6.15. However, for a continuous evaluation of the estimated gait parameters for PD patients, the tests should be repeated with the same patients to indicate if there has been any improvement. To do so, these results are stored in an excel sheet that allows evolutionary study the motor behavior of each patient. In the future, it will be efficient to implement a database to keep this ongoing evaluation.

Table 6.22 - Gait parameters estimated and measured error (percentage mean error), for the healthy subjects and PD patient

Gait Parameters Estimated	**Estimated Value (mean ± SD)**	
	Healthy subjects	PD patients
Step time (s)	0.63 ± 0.14	0.73 ± 0.15
Stride time (s)	1.12 ± 0.13	1.31 ± 0.12
Step length (m)	0.81 ± 0.14	0.75 ± 0.03
Gait speed (km/h)	4.15 ± 0.30	3.01 ± 0.06

Finally, with regard to the questionnaires carried out at the end of each experiment, they allowed a subjective analysis of whether the participants perceived correctly and effectively the feedback provided. Table 6.23 shows the obtained results with the questionnaires for healthy subjects and patients with PD.

By analyzing Table 6.23, it is verified that, in general, **all the healthy subjects evaluated the vibrotactile feedback perception with high scores**. However, it is necessary to take into account that the provided feedback is directly related to the accuracy of the identification of the toe-off event and, being this percentage smaller for the **patients group**, **it was expected that the vibrotactile perception was evaluated with a less value**. Another important factor is that the tests were only validated with two PD patients. For a better analysis, the system should be validated with a greater number of subjects. This thesis provided for a preliminary evaluation and a first case study.

Table 6.23 - Scores of the self-assessment questionnaires (mean ± SD)

Questions	**Scores (1-Nothing, 2-Little, 3-Moderate, 4-High and 5-Very High)**	
	Healthy subjects	PD patients
Vibrotactile Feedback Perception (in general)	4.25 ± 0.25	3.00 ± 1.00
Vibrotactile unit perception at navel	4.00 ± 0.00	3.00 ± 1.00
Vibrotactile unit perception at right	4.75 ± 0.25	3.00 ± 1.00
Vibrotactile unit perception at spine	3.75 ± 0.48	2.50 ± 0.50
Vibrotactile unit perception at left	3.25 ± 0.63	3.00 ± 1.00
Comfort	5.00 ± 0.00	5.00 ± 0.00
Possible integration of the waistband with the vibrotactile feedback in their daily tasks	5.00 ± 0.00	5.00 ± 0.00

Even though, it is important to highlight that **all participants show a high degree of acceptability in using the waistband in their daily tasks**. In fact, specially, in the experimental tests in the hospital with the PD patients and their families, they have shown interest in the **system**, asking interesting questions.

6.3.4 Conclusions to Future Considerations

The developed system, a waistband capable of providing vibrotactile feedback according to the gait of the users has been validated.

The **vibrotactile feedback is provided synchronously with the gait event transition detection**, ensuring that **the system works in harmony with the motor system of each user**. Therefore, the loop between the acquired gait and the vibrotactile feedback was closed, making this system a **Neurofeedback System using Vibrotactile Cues**.

However, it is important to note that the algorithm of toe-off detection must be improved, in order to study new metrics for more robust FSM working with parkinsonians. Thereby, more experimental tests should be carried out.

Nonetheless, **all users showed a high degree of acceptability in introducing this device in their daily lives**. For the moment, the users were able to walk normally while the vibrotactile feedback through the developed waistband. This conclusion is very important since it demonstrates that the developed device was focused on the **autonomy of each user**, **addressing the concept of multitasking without requiring too much cognitive burden.** However, more complex test have to be performed, specially considering the FOG occurrence.

6.5 Relevant Considerations

This chapter presented all the validations accomplished in the development of the proposed system.

Firstly, it was detected the **best frequency perceived around the abdomen**, concluding that this **should be at least 160 Hz**. Also in these experimental tests, the t**ime interval during which the vibrotactile feedback should be provided** was identified, **to be around 250 ms**. In fact, to carry out these tests, a temporal, spatial and spatiotemporal context was taken into account.

Next, **a real-time gait detection algorithm was validated through the vertical acceleration data in the lower trunk.** It was verified that the **algorithm is accurate and time-**

effective for healthy subjects, but should **be tested with more patients with PD**, in order to identify a new pattern among this group of subjects, to make the algorithm more robust. In addition, from this the gait events identification, in particular the toe-off, the gait parameters were estimated. Thus, the **step time, stride time, step length and velocity are estimated based on the inverted pendulum method**. This **estimator proved to be efficient for healthy subjects and parkinsonians**, however it strongly depends on correct gait detection.

Lastly, after detecting the best perceived frequency and implementing a real-time gait detection algorithm, it was possible to integrate these two components and test the final system: **a system able to provide time-discrete vibrotactile feedback according to the user's gait, in particular, at the moment of toe-off**. The system showed to be **synchronized** and all the users demonstrated a **positive opinion in the integration** of this device into their locomotion.

In conclusion, a set of steps were followed to validate the final system with healthy subjects and patients with PD. This system provides vibrotactile feedback harmonized with the gait of each person and also allows to collect all the relevant data to estimate and evaluate continuously the gait parameters, aiming to improve the performance of pathological gait.

CHAPTER 7 – CONCLUSIONS AND FUTURE WORK

PD is the second most common disease worldwide. It is characterized for being **a long-term degenerative disorder of CNS** for which there is still no cure, affecting the nigrostriatal system with motor and non-motor symptoms. One of the most debilitating motor symptoms in patients with PD are the freezing episodes, known as **FOG**. FOG corresponds to a **brief**, **episodic absence or marked reduction of forward progression of the feet despite the intention to walk**, which may lead **to falls** and **a loss of independence**.

Pharmacological approaches are always followed to help PD patients to improve their motor symptoms. However, there have been no significant scientific advances in the discovery of new methods in pharmacological scope. In addition, these methods d**o not alter the course of PD symptom**, **not preventing FOG** and, over time, patients may suffer from **medication habituation phenomenon**. **Non-pharmacological methods** are a **non-invasive** and **efficient solution** for helping PD patients to **improve motor symptoms** and **overcome FOG**. Among the various non-pharmacological methods, it was verified that patients can outstrip FOG when are using **Neurofeedback Systems** providing through **external cues**. Advantageously, the **Vibrotactile Neurofeedback Systems** can be implemented in **any environment** and are **easily accepted** by patients when compared with the other Neurofeedback Systems. However, the **current Vibrotactile Neurofeedback Systems** do not consider a number of factors such as **ergonomics**, **robustness**, **are not patient centered** and, consequently, **not easily accepted**.

In this thesis, it was developed a **Non-pharmacological System** based on **Vibrotactile Neurofeedback** with the main goal of **helping PD patients to overcome FOG**.

For the development of this system it was imperative to answer a set of questions that were answered after a critical study on the literature.

Thus, firstly, it was identified the **frequency range vibration that humans can discriminate**. It was concluded that, besides taking into account the perception at the skin level, it is also necessary to consider the perception at the level of the cerebral cortex. In this way, it was founded that, in general, the **human being is able to perceive a frequency range of 80 to 250 Hz**.

It was verified that the **lower trunk**, besides perceiving with high sensitivity the vibrotactile stimuli, it is ideal for the implementation of **wearable systems**, allowing the users to have greater **freedom of movement**, to perform **multitasking** and **to integrate the system** in their daily life. It is also concluded that it is important to **stimulate the navel and the spine** because these are zones that humans use **naturally as anatomical reference**s. In this way, it was decided to use **4 vibrotactile units** located in the **navel, right side, column** and **left side**, in order to consider the **anatomical reference zones** without **requiring too much cognitive effort**.

The **CNS is responsible for commanding and controlling motor tasks in humans**. In turn, **motor tasks are subconsciously subdivided**, since for each subtask muscle activity is different. Thus, the CNS, which has the function of controlling these subtasks, commands each action sequentially by **sending the nervous commands in the transitions of each sub task**.

Given that **during the freezing episodes** there is **a failure to route the nerve message** during the walking action, it is important **to detect the transition between each of the phases of the gait cycle**, so that **the stimulus can be provided in these transitions**. Thus, the **stimulus provided is incorporated into the physiological system of each patient, making possible to replace the failure in the nerve message** during a FOG episode. Finally, since the CNS processes the information in a time-discrete manner and in order to avoid the phenomenon of adaptation, it is important **to provide time-discrete feedback**.

Taking all of this into account, a **wearable system – a waistband -** was developed to provide vibrotactile feedback synchronized with the gait transition of each patient. For this purpose, all necessary hardware and software components were identified and implemented. Thereby, the developed device is composed of a **Gait Acquisition System (IMU), a Processing Unit (Arduino), an Actuation System (Haptic Drivers and Vibratory ERM motors), a Wireless Communication System (Bluetooth Module)** and a **Data Storage System (Micro SD card and respective module)**. In addition, **Graphical Interfaces** have also been developed in **Android** and in **MATLAB**.

Subsequently, a set of experimental tests were carried out until the validation of the final system developed.

First of all, experimental tests were performed with healthy subjects and PD patients **to detect the best perceived frequency around the abdomen**. These experimental tests also allowed us **to identify the minimum interval of vibration perception**. It was concluded that the vibrotactile feedback should be provided at **a frequency of at least 160 Hz** and for a **time interval of 250 ms**.

Then, an al**gorithm for detecting the gait events through the vertical acceleration acquired in the lower trunk** was validated using a **finite state machine based on heuristic decision rules delineated for healthy subjects**. This algorithm was implemented offline (on a treadmill and on the ground) and in real time (on the ground) and its validation first healthy subjects and then PD patients.

It was verified that **the algorithm is accurate in segmenting the gait in offline and in real time for healthy subjects**. However, the accuracy of this algorithm decreases when it is implemented for patients with PD. In this way, it is concluded that it will be necessary **to perform more experimental tests with PD patients** in order to find a pattern that allows to establish more metrics that can be applied in the heuristic decision rules of the state machine. Still in this experimental phase, based on the results of gait segmented by the developed algorithm, another procedure was validated for estimating some predefined gait parameters: s**tep time, stride time, step length** and **gait speed.** It was observed that **this algorithm is efficient in the calculation of these gait parameters**, but that **it depends heavily on the correct identification of gait events**.

It is noteworthy that it was essential **to detect the toe-off gait event transition** because this **was the event chosen to provide the vibrotactile feedback in the final system validation**. This event was chosen since this solution aims to overcome FOG. Patients reported that during FOG they feel their feet glued to the ground. Thus, it seems ideal to provide feedback exactly in the event that corresponds to the moment when the foot finishes to be in contact with ground.

Lastly, after detecting the best perceived frequency and implementing a real-time gait detection algorithm, these two evaluated components were integrated and the final system was tested. In this final system, the **Gait Acquisition System** acquires the **vertical acceleration** of each user. Then, this information is processed in the **Processing Unit** where **the toe-off event is detected**. When this event is detected, a signal is sent for the **Actuation System** and **the vibrotactile feedback is provided at a frequency of 200 Hz for 250 ms**. The **Data Storage System save the gait signal acquired** in each trial test and then this information can be loaded and properly processed in a **Graphical Interface.**

After validating the System with healthy and PD patients, it was concluded that **this system is able to provide time-discrete vibrotactile feedback according to each user's gait, in particular, at the moment of toe-of**f. The system showed to be synchronized and all the users were interested in **integrating this device into their daily life**.

As a final shot, the work herein presented enables to answer the **RQ**s outlined in **Chapter 1**:

- ***RQ 1****: What are the symptoms associated with FOG episodes and how it manifests in PD patients? Which is the best approach to help PD patients improve motor symptoms?*

FOG can be defined as a **temporary, sudden** and **involuntary disability to ongoing motor movement** and patients use a unique feeling to describe them: **the sensation of having the feet glued to the ground**. These episodes **can occur at any time** and can be manifested by three ways: **leg trembling, shuffling** and **complete akinesia**. At the present moment, the best approach to helping patients improve motor symptoms is through **Non-pharmacological Method**s.

- ***RQ 2:*** *Which are the non-pharmacological methods with greater potential to help PD patients to overcome FOG? Which kind of stimulus can overcome FOG episodes? Which feedback should be provided to patients?*

When using **external cues** through **Neurofeedback Systems**, the patients present less difficulties to overcome FOG. Neurofeedback systems using **vibrotactile sensory cues** can be used in any environment, are easily perceived by patients and are highly accepted.

- ***RQ 3:*** *What is the frequency range of vibration perceived by the mechanoreceptors of the skin in the human body? Where is the ideal location of the delineated system to provide vibrotactile feedback in human body? How many vibrotactile units are needed to provide the required stimulation and were should be place?*

The **frequency range of vibration** perceived by humans is **80 to 250 H**z. The **lower trunk is ideal for providing vibrotactile feedback** since, in addition to present high sensitivity to discriminate vibrotactile information, it fulfills a set of requirements that allows to implement a **wearable** and **cognitively light system**. It was used **four vibrotactile units**, placed at the **navel**, **right side, spine** and **left sid**e. This arrangement is justified by the fact that humans use the navel and the spine **as anatomical reference areas**.

- ***RQ 4:*** *How will it be possible to integrate the feedback provided in each patients' motor sensory system? How important is the detection of gait events for the feedback strategy to adopt? Should this strategy be continuous or discrete time driven?*

Since in FOG episodes, during gait cycle, **the routing of the nerve messages in the patients' motor sensory system is compromised**, it is important **to replace this failure**. Since it is the CNS which controls the nervous system and **it acts on the transitions of each motor subtask**, it is important **to provide feedback at these crucial moments** so that it can b**e integrated into the normal physiological system of each patient**. In order **to avoid the phenomenon of adaptation** and given that the CNS controls the motor system in discrete-time, feedback should also be provided in **discrete-tim**e.

- ***RQ 5:*** *Which are the electronic components required to provide the appropriate vibrotactile feedback? Which are the control mechanisms necessary to control the vibrotactile motors? Which are the sensors with greater potential to acquire the gait signal and be integrated in the developed system?*

Haptic drivers and **vibratory motors, ERM**, are ideal to be implemented in the actuation system for providing vibrotactile feedback. The haptic drivers control the motors through the **PWM mode**, since these motors work with **DC voltage**. **IMUs** present gr**eat potential to be built into wearable system**s and allow **to monitor the entire gait cycle**.

- ***RQ 6:*** *What is the frequency of vibration that should be provided in the vibrotactile feedback? How long should the vibrotactile stimulus be given? How to obtain a robust algorithm for gait event detection through the acceleration in lower trunk? How to incorporate this algorithm with the control system of the vibrotactile units in a synchronized way?*

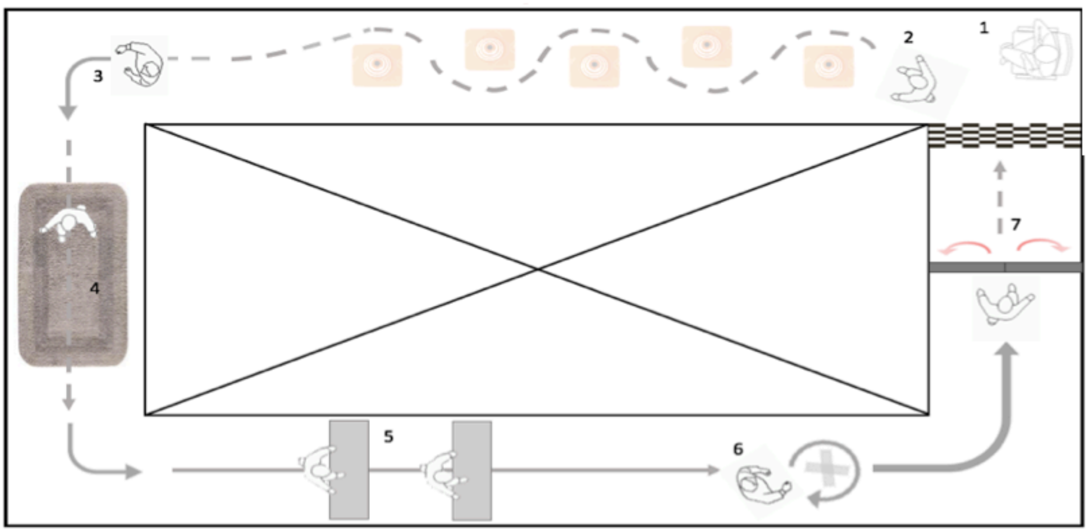
It has been concluded that the vibrotactile feedback should be provided at a frequency of **at least 160 Hz** and for a range of **250 ms** in order to be correctly perceived around the abdomen. In order to integrate the gait acquisition system in the developed system, the **vertical acceleration signal acquired in the lower trunk is used**. Gait segmentation is performed algorithmically **through a finite state machine**. The integration and synchronization of the sensory information acquired with the actuation system is possible through the **detection of the toe-off transition event gait**. At this moment, **the vibrotactile feedback is provided**. In this way, the provided vibrotactile feedback is synchronized with the gait event transition for each user.

Hereupon, it is concluded that the delineated goals and RQs raised in the introduction of this thesis were addressed (**Chapter 1**). It was developed and validated a Functional Feedback Vibrotactile System for Patients with Parkinson’s Disease: Freezing of Gait.

7.1 Future Work

For future work, it is imperative to perform more experimental tests with PD patients in order **to study the parkinsonian signal gait more and more, to the point of detecting FOG events**. In fact, as a future challenge, the goal is to detect FOG through **machine learning algorithms**. In this way, the vibrotactile feedback will have to follow a **predictive approach of the patients' motor behavior**.

In future experimental tests, it will be mandatory **to include presence of FOG** in the patients’ motor symptoms **as an inclusion criteria** and the developed system will be evaluated in a **multitasking contex**t. In fact, an **experimental protocol has already been developed** and a **total of 14 patients suffering from FOG episodes have been assembled**. This experimental



Motor tasks	Cognitive tasks
1 – Gait initiation	-
2 – Circumvent objects	Describe someone
3 – Turning a corner	-
4 – Passing through a carpet	Carry a glass of water
5- Passing through obstacles	Ask what ate/dined
6 – Turning around	-
7 – Crossing a gate	-

Figure 7.1 - Course and tasks that should be made by the PD patients, considering the 2CA corridor plant in Hospital of Braga.

protocol will consist of executing a pre-defined course with several situations that trigger FOG: **circumvent objects, turning a corner, passing through a carpet and obstacles, turning around, crossing gates and cognitive tasks**. Figure 7.1 aims to show how this course will be constituted. This validation will be performed at the Hospital de Braga, with collaboration from the Clinical Academic Center of Braga.

In order to store the information acquired for all patients it will be necessary **to implement a database** easily accessed through a **graphical interface**.

Also as a great future challenge, it is intended **to integrate other multimodal sensory systems such as auditory cues or augmented reality using smart glasse**s. In fact, in this dissertation, an algorithm for gait detection through an embedded IMU in a smart glass (ORA-2, Optinvent®) has already been accomplished and validated. The results were very positive and the accuracy of the algorithm in detecting gait events was high. However, it will be necessary to further study how this system should be integrated with the developed waistband.

Lastly, aiming t**o adopt a strategy of scientific and commercial dissemination through hospitals and clinical centers**, the **robustness** and **ergonomic will be improved**.

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