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CURRICULUM IN E-LEARNING - TECHNOLOGY ENHANCED LEARNING

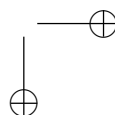
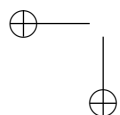
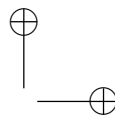
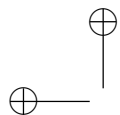
Development of a system to manage motor disorders in Parkinson's disease

Ph.D. Dissertation of:
Lucia Pepa

Advisor:
Prof. Luca Spalazzi

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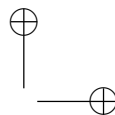
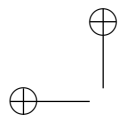
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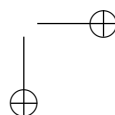
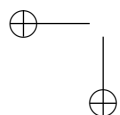
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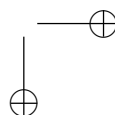
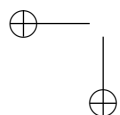
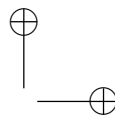
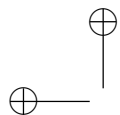
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a Tommaso Leo





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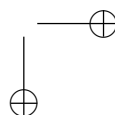
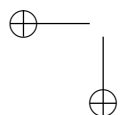
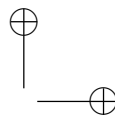
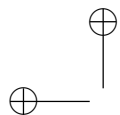
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Ancona, Gennaio 2016

Lucia Pepa



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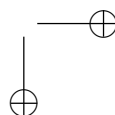
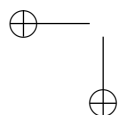
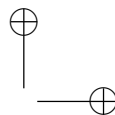
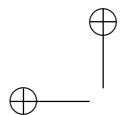
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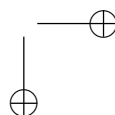
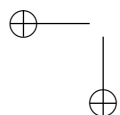
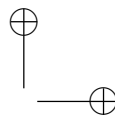
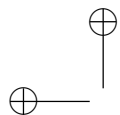
Ancona, Gennaio 2016

Lucia Pepa



Abstract

Increase in longevity caused an increase in age related diseases, with a high impact on elderly quality of life. Parkinson’s Disease (PD) is a neurodegenerative pathology associated with the advent of motor disorders. Among these, Freezing of Gait (FoG) is a common and highly distressing motor block that manifests as a transient inability to move forward despite the intention to walk. Two main problems are associated with FoG: lack of clinical knowledge and resistance to pharmacological treatment. Rehabilitation therapy can alleviate FoG, in fact evidences showed that the delivery of rhythmic stimuli (cues) helps patients to overcome the block. Given this background, the thesis aims to develop a system to manage FoG in order to face the above problems. Usability and acceptability requirements led the design process. The proposed system is composed of a mobile part and a server part. The first one consists of a smart-phone app able to monitor the gait, detect FoG episodes, provide cues, store collected information and send this data to the remote server. The server side part is composed of a database to store monitoring and clinical information about patients and a web application to allow an effective and accessible consultation of FoG monitoring data by clinicians, who can use this information to improve their knowledge and customize patients’ and pharmacological and rehabilitation therapies. Smartphone reliability in monitoring gait parameters was tested on healthy subjects, through comparison with stereophotogrammetry, which is the gold standard for gait analysis. The architecture was tested on 60 patients in FoG monitoring, reaching high scores of sensitivity, specificity, accuracy and precision. Usability and acceptability was also assessed through questionnaires, revealing patients’ attitude to use the system. The obtained results suggest the architecture potential to be applied in a daily living scenario, thus improving patients’ quality of life and clinical management of FoG.



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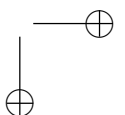
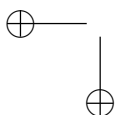
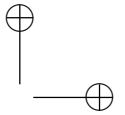
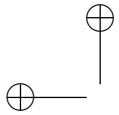
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Chapter 1

Introduction

Movement is an important aspect in our lives: it is the main way we interact with the world and with other people. We start learning motor skills since the time of our birth. In 1982, Richard Schmidt defined motor learning as a set of processes associated with practice or experience leading to permanent changes in skilled behavior [7]. Three key aspects arise from this definition. First, learning is a process, that is a set of underlying events, occurrences, or changes that happen when people practice and allowing them to become skilled at some task. Second, learning is a direct result of practice and experience. Third, it produces relatively permanent changes in skilled behavior. Even if ancient, this definition is still actual, since these three aspects (process, practice and experience, retention) are considered milestones, e.g., in Willingham’s (1998) [8] and Dayan and Cohen’s (2011) [9] definition.

Motor learning involves two stages [10, 11, 9]: an early, fast learning stage, characterized by rapid improvements observed during a single training session; and a later, slow learning stage, when further gains develop across several sessions of practice. The relative duration of fast and slow learning is highly task specific [9]. After the slow phase of learning automatism is reached. Researchers agree on the importance of a further intermediate stage between fast and slow learning [11, 10, 9], corresponding to the consolidation process of the motor routine. Progression from fast to slow motor skill learning is thought to rely on appropriate consolidation, defined as the progressive stabilization of a recently acquired memory [12]. Evidences reported delayed, off line (6-8 hours after the first training session), gains in performance without additional practice. This off line process is called "memory consolidation" [13, 10] and it begins as soon as some training has been done, thus after the brain has been exposed to sufficient relevant behavioral experience [10]. Sleep plays a critical role in this memory consolidation phase. Several studies demonstrated the correlation between off line learning and rapid eye movement sleep: delayed gains in performance on a motor sequence task are triggered after a period of sleep, but not following an equivalent period of daytime [14, 15].

In human beings, system for motor control and learning has three compo-

Chapter 1 Introduction

nents: sensory system (for example visual, auditory, somatosensory, haptic, systems), control system (central nervous system) and motor system (muscles, the actuators). Central nervous system areas mainly involved in motor control and learning tasks are motor cortex, cerebellum and basal ganglia. Unluckily, diseases or trauma can hit any of the three components of the sensory-motor system, thus leading to a loss of motor skills and motor learning ability and hence a reduction of quality of life.

This thesis deals with the effects of Parkinson’s disease (PD) and proposes a technological solution to face motor disorders rising from this pathology. PD is a neurodegenerative pathology affecting basal ganglia, which have a primary role in motor learning and in the execution of automatic movement [10, 16, 17]. Neuroimaging studies suggested that throughout the learning process there is a shift from cortical to subcortical neural activity (during the early stage attention is required, while with practice the motor task can be executed automatically, with little attention) and that both basal ganglia and cerebellum increase their role in later stage of learning, hence during automatization [18, 10, 16]. In particular, basal ganglia are mainly responsible for motor sequence learning, while cerebellum for motor adaptation tasks (learn to adapt to environmental perturbations) [10, 16]. Furthermore, the importance of basal ganglia in retention of learned motor skills was also documented [10, 19]. As a consequence, automatic movements are impaired in people with PD [20, 21], several motor symptoms manifest [22], and the question whether motor learning is impaired in people with PD raised [17, 16, 21].

Typical motor symptoms in PD are bradykinesia, akinesia, tremor, rigidity, postural instability, festination, freezing of gait [22]. These deficits generally lead to a loss of independence, immobility and high cost for health care systems. The advent of motor disorders joined with the possible impairment in motor learning poses difficulties in adopting effective strategies to recover motor function. Possible approaches are: pharmacological therapy, surgical treatment, and rehabilitation therapy. The standard drug therapy adopted to manage PD symptoms is levodopa. However, despite the advances in pharmacological and surgical treatments, some gait and balance deficit develop and cannot be adequately controlled. Therefore, rehabilitation therapy may offer an important contribution in patient management.

In general, positive effects of physical activity on the central nervous system are well documented in the literature [23, 24, 25]. Knowledge of motor learning is critical for optimal design of rehabilitation interventions. For this reason, many research groups addressed the question of motor learning in PD. The starting point seems to be that while the fast stage of learning (acquisition) is preserved, automaticity and retention are less efficient [26, 27, 16, 21]. The most interesting rehabilitation strategy found by researchers to enhance motor

learning and improving motor function is the use of augmented feedback, such as external rhythmic stimuli (cues). The mechanism underlying cueing effect in PD were often explained as activating brain networks involving cerebellum (which is in fact responsive to environmental perturbations, as explained above) instead of the standard network involving basal ganglia [28, 29]. Several studies demonstrated positive effects of cues on motor functions such as gait and hence contributed to increase the interest towards rhythmic cues as a rehabilitation tool [30, 31, 16, 32].

The use of cues to enhance gait was widely applied by clinicians to contrast a particularly impairing motor disorder: the Freezing of Gait (FoG). Among motor symptoms affecting people with PD, FoG is one of the most important predictive factor of disability, morbidity and mortality [33, 34, 35]. It is defined as a ‘brief, episodic absence or marked reduction of forward progression of the feet despite having the intention to walk’ [2]. It is very distressing and related to a high risk of falls [36]. FOG pathogenesis is largely unclear, because of its episodic, heterogeneous and erratic nature, that makes it difficult to be studied in a clinical setting. Moreover, both cognitive and affective factors have been acknowledged as possible determinants of FOG [37, 38]: a dual-task during gait frequently causes a FOG episode, but attention focused on gait is able to overcome it effectively. FOG may resist to or even worsen under dopaminergic medication [39], but it improves if external sensory cues are provided, mainly responding to auditory cues, like the metronome rhythm [40, 41].

The development of a portable assistive device capable to detect FOG, whenever it occurs during daily living, would help to monitor it and to correctly assess the efficacy of rehabilitation strategies aimed at relieving this symptom. Moreover if the system could also provide time-locked auditory cues it would be a quite appealing tool for enhancing patient’s activities and quality of life.

While approaching the design of any medical device, acceptability and usability requirements cannot be neglected. Technology acceptance is an essential requirement in fields like ambient assisted living, pervasive or ubiquitous health-care. Perceived usefulness and perceived ease of use (usability) are key factors for acceptability [42]. However when dealing with health related applications other aspects are also crucial, these include: miniaturization, embeddedness (integration in an everyday device), inconspicuousness (the technology should not label the user as ill and should not break user’s intimacy and privacy), networking (enabled wireless data exchange), context sensitivity (information about the environment) [43, 44]. A consumer device like the smartphone satisfies several of the above acceptability aspects and hence it is used as part of the architecture built to manage FoG. Apart from the embeddedness, inconspicuousness, networking capabilities and context sensitivity that are clearly satisfied; the wide spreading of smartphones in society and health related ap-

Chapter 1 Introduction

plications [45, 46] suggests a high perceived usefulness and perceived ease of use. Furthermore smartphone apps can be made as user friendly as needed.

1.1 Objective

This thesis proposes a technological solution to face problems caused by motor disorders rising from Parkinson’s disease. Hence, the objective is the development of a system with the following main functions:

- Management of motor disorders, in particular the FoG;
- Maintenance or re-learning of motor competences.

The word "management" stands for detection, storage and data presentation. First of all, the system should be able to detect abnormal gait episodes, such as FoG. Then, it has to store data collected during gait monitoring (they are data concerning both gait parameters and detected FoG episodes). Finally, the system should provide an easy and intuitive way to allow clinicians to consult monitoring data, thus increasing their knowledge about FoG and verifying the effectiveness of prescribed therapies. The absence of these two last functions would make almost useless the FoG detection system (why collecting data, if they cannot be used?).

For what concerns motor skills maintenance or re-learning, the system should help the patient to avoid FoG or at least overcome it. To this purpose, the cueing strategy was adopted in this thesis, given the strong evidences of its benefits [30, 31, 16, 32, 40, 41].

1.2 Thesis organization

In order to reach the aim described in the previous section the work of this thesis went through several phases, that reflect the general organization of this book.

Firstly, an extensive literature review about addressed topics was conducted and it is described in Chapter 2. In details, section 2.1 presents FoG definition and describes FoG characteristics. Works reporting the most important disclosures about FoG are discussed: whenever someone wants to solve a problem, he must firstly knows the problem. In section 2.2, the use of sensory cueing as a rehabilitation tool is discussed: what are cues? Why are they helpful? How can they be employed to enhance motor learning? From the analysis of FoG characteristics, the most discriminatory and significant gait parameters related to FoG can be found. Since the smartphone will be used to carry out FoG management, the methods proposed in the literature to estimate these

1.3 Thesis contribution

gait parameters using wearable sensors should be investigated (Section 2.4). Finally, previous works that developed FoG detection systems (Section 2.3) or architectures for clinical data management (collection, transmission, access) (Section 2.5) are described.

Chapter 3 describes in details the developed architecture 3.1 and its components:

- The smartphone application 3.2 for FoG monitoring and rhythmic cues delivery, with particular attention on the features used to detect FoG (Section 3.3) and on classification methods adopted (Section 3.4).
- The database (Section 3.5.1) designed to store monitoring data.
- The web application (Section 3.5.2) to access clinical and monitoring data.

Chapter 4 explains experimental protocols designed to assess the developed architecture on both healthy subjects, in Section 4.1, and patients with PD, in Section 4.2. Tests on healthy subjects are necessary to verify the reliability of a smartphone in gait monitoring, while test on patients with PD have the primary aim to evaluate smartphone reliability in FoG detection and user’s acceptance towards the system. Results are presented in Section 4.3 and discussed in Section 4.4.

In chapter 5 the most important contributions and findings of this work are highlighted and overall conclusions are drawn.

1.3 Thesis contribution

A system able to address the needs explained in this introduction is expected to bring several positive outcomes from a scientific, social and economic point of view:

- *Scientific impact*

The work carried out in this thesis opens new application scenarios for technological consumer devices like mobile phones. Novel algorithms for FoG detection are proposed and tested on a wide number of subject. Finally, clinical knowledge about FoG can be improved with the help of this monitoring system.

In particular, three main contributions to the scientific literature related to FoG management were produced:

- Adopted technologies: they are popular and easy to use, enabling a daily living usage. To the best of the knowledge collected during

Chapter 1 Introduction

the years of study, early published works were the first evidences of real time FoG detection using only a smartphone for both sensing and processing function [47, 48, 49].

- Classification algorithm: Fuzzy Logic applied to FoG detection. Works published for the 10th IEEE/ASME International Conference on Mechatronic and Embedded Systems and Applications [50] and for the 2nd IEEE World Forum on Internet of Things [51] are a novel contribution for the literature, applying for the first time Fuzzy Logic to FoG detection.

- *Social impact*

The development of a system for FoG management suitable for at home applications will provide positive outcomes from a social point of view.

- The use of rhythmic sensory cueing to reduce or avoid FoG episodes will improve motor function (in particular gait) thus enhancing mobility, independence, active aging and social participation.
- By the use of the web platform, as explained in the work presented during the 2nd IEEE World Forum on Internet of Things [51], clinicians can easily access FoG monitoring data, thus improving their knowledge about the phenomenon and assign customized rehabilitation and pharmacological therapies to patients, increasing their effectiveness.

- *Economic impact*

The improvement in gait function associated with sensory cueing would cause a reduction in falls, which are strongly related to FoG [36], decreasing health-care costs.

1.4 Publication list

The result of this thesis are contained in the following papers.

International journals:

- L. Pepa, M. Capecci, F. Verdini, M. Ceravolo, and T. Leo, “An architecture for reducing the freezing of gait during the daily life of patients with Parkinson’s disease,” *Gait and Posture*, vol. 40, no. Supplement 1, p. S2, 2014.
- L. Ciabattini, A. Freddi, S. Longhi, A. Monteriù, L. Pepa and M. Prist, “An Open and Modular Hardware Node for Wireless Sensor and Body Area Networks”, *Journal of Sensors*.

1.4 Publication list

International conferences:

- L. Pepa, M. Capecci, F. Verdini, M. G. Ceravolo and L. Spalazzi, “An Architecture to Manage Motor Disorders in Parkinson’s Disease”, IEEE World Forum on Internet of Things, 14-16 Dec, 2015, Milan, Italy.
- L. Pepa, G. Marangoni, M. Di Nicola, L. Ciabattoni, F. Verdini, L. Spalazzi and S. Longhi, “Real Time Step Length Estimation on Smartphone”, in IEEE International Conference on Consumer Electronics (ICCE), Jan 2016, Las Vegas.
- L. Pepa, F. Verdini and L. Spalazzi, “Un’architettura per la gestione dei disturbi motori nella malattia di Parkinson”, XXVI Congresso ALASS, Ancona, Italia, Settembre 2015
- L. Pepa, F. Verdini and L. Spalazzi, “Experimental Evaluation of a Smartphone Based Step Length Estimation”, in: 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Milan, Italy, August 25-29, 2015
- L. Pepa, F. Verdini, M. Capecci, and M. Ceravolo, “Smartphone based freezing of gait detection for Parkinsonian patients,” in Consumer Electronics (ICCE), 2015 IEEE International Conference on, Jan 2015, pp. 212–215.
- L. Pepa, M. Rossini, L. Spalazzi, and F. Verdini “Step length estimation for freezing of gait monitoring in Parkinson’s disease” Workshop on Mobile Networks for Biometric Data Analysis (mBiDA), 2014
- L. Pepa, F. Verdini, M. Capecci, F. Maracci, M. G. Ceravolo, and T. Leo, “Monitoring freezing of gait with a smartphone,” 1th Clinical Movement Analysis World Conference, SIAMOC 2014
- L. Pepa, L. Ciabattoni, F. Verdini, M. Capecci, and M. Ceravolo, “Smartphone based fuzzy logic freezing of gait detection in Parkinson’s disease,” in Mechatronic and Embedded Systems and Applications (MESA), 2014 IEEE/ASME 10th International Conference on, Sept 2014, pp. 1–6.

National conferences:

- M. Capecci, L. Pepa, F. Verdini, E. Andrenelli, T. Leo, M. G. Ceravolo “Predicting the Freezing of Gait in Parkinson’s Disease with a smartphone: comparison between two algorithms for detecting FOG”, III Congresso Nazionale LIMPE/DISMOV-SIN, November 2014

Book chapters:

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- M. Prist, L. Ciabattani, A. Moneriù, L. Pepa, A. Freddi and S. Longhi, “An Open Modular Node for Wireless Body Area Networks”, 6th Italian Forum on Ambient Assisted Living, Lecco, Italy, May 19-22, 2015.
- L. Pepa, F. Verdini, M. Capecci, F. Maracci, M. Ceravolo, and T. Leo, “Predicting freezing of gait in Parkinson’s disease with a smartphone: Comparison between two algorithms,” in Ambient Assisted Living, B. Andò, P. Siciliano, V. Marletta, and A. Moneriù, Eds. Springer International Publishing, 2015, pp. 61–69
- L. Pepa, M. Rossini, L. Spalazzi, and F. Verdini “Step length estimation for freezing of gait monitoring in Parkinsonian patients” Workshop on Mobile Networks for Biometric Data Analysis (mBiDA), 2014
- L. Pepa, F. Verdini, M. Capecci, M. Ceravolo, and T. Leo, “Can the current mobile technology help for medical assistance? the case of freezing of gait in Parkinson disease,” in Ambient Assisted Living, S. Longhi, P. Siciliano, M. Germani, and A. Moneriu, Eds. Springer nternational Publishing, 2014, pp. 177–185.

Chapter 2

State of the art

Parkinson’s Disease (PD) is a neurodegenerative disorder of the central nervous system, in particular the basal ganglia, hence it affects motor and speech skills [52]. The primary abnormality in PD in a biochemical perspective is a dopamine deficiency due to degeneration of neurons [53]. This complex neurological degeneration of basal ganglia in PD particularly causes a severe difficulty in motor planning, action and execution of non-attention demanding tasks (automaticity) [54, 55].

PD is among the most common neurodegenerative disorders [56]. According to the Italian national statistic institute (ISTAT), PD is the second most lethal neurodegenerative disorder in Italy, as Fig. 2.1 shows. Incidence and prevalence of PD are rather high among elderly people, the rate of affected individuals being around 1.5% in people aged 65 years and beyond [57].

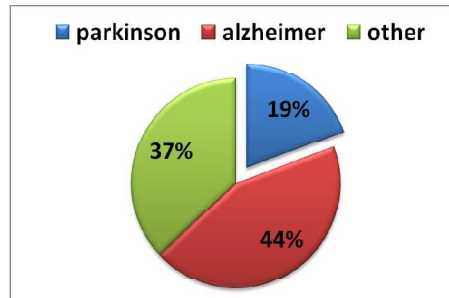


Figure 2.1:

Causes of death among patients with neurodegenerative diseases.

PD is expected to impose an increasing social and economic burden on the community due to the progressive disability and the complications related to gait and balance impairments. Typical motor disorder of PD are bradykinesia (i.e. slowness of movement), tremor, rigidity, flexed posture, postural instability, festination and Freezing of Gait (FoG) [22]. Although gait disorders are quite a distinctive feature across all disease stages, Freezing of Gait (FoG) may

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be regarded as the most frequent and disabling condition, involving up to 70% PD people after 10 years of clinical onset [35]. FoG highly impairs mobility, causes falls [58, 59] and reduces quality of life [60]. The pathogenesis of FoG is not understood and empirical treatments are of poor efficacy. For these reasons, FoG is an important clinical problem. To overcome this drug-resistance, clinicians found alternative approaches, such as the use of rhythmic cues [61].

The state of the art about FoG pathogenesis and characteristics is exposed in paragraph 2.1; the use of rhythmic cues as a rehabilitation tool is presented in paragraph 2.2; finally, technological solutions adopted to monitor FoG are discussed in paragraph 2.3.

2.1 Freezing of gait

Freezing of Gait (FoG) is one of the most disturbing and least understood symptom in PD. According to Giladi and Nieuwboer [62], FoG is defined as:

“ An episodic inability (lasting seconds) to generate effective stepping in the absence of any known cause other than parkinsonism or high-level gait disorders. It is most commonly experienced during turning and step initiation but also when faced with spatial constraint, stress and distraction. Focused attention and external stimuli (cues) can overcome the episode. ”

This definition contains the most important characteristics of FoG. First of all, it is episodic hence its occurrence is random and not systematic [63, 64]. A widely accepted evidence concerns the difficulties of observing FoG in a clinical environment [65]. It often happens that patients reporting several and recurring FoG episodes during their daily activities do not manifest FoG at all during their periodic clinical examination. This is one of the reasons why clinicians poorly know and understand FoG: they cannot observe and study this motor symptom.

Secondly, the definition says that FoG manifests as a sudden and transient inability to walk (see Figure 2.3 for a graphical explanation of this walking block), most subjects report the subjective feeling of their feet glued to the ground. Hence it is a motor block with a high impact on patient’s quality of life. FOG has been associated with increased risk of falls and poor quality of life [36]; it leads people with PD to limit their community ambulation, thus reducing their activity levels and exercise capacity [66].

Another important clinical feature of FoG is its heterogeneity: several kinds of FoG have been observed by clinicians [63, 64]. Such heterogeneity concerns both the situations that elicit FoG and the leg movements that can be associated with a FoG episode. FoG is mainly triggered by gait initiation, turning, the presence of an obstacle or a narrow place. Furthermore cognitive or emotional stress can also induce FoG. About leg movements, Schaafsma and colleagues

2.1 Freezing of gait

[65] distinguished three different FOG subtypes:

1. FOG associated with very small shuffling steps and with minimal forward movement (shuffling with small steps);
2. FOG with some leg trembling but no effective forward motion (trembling in place);
3. complete akinesia, i.e., no observable motion of the legs.

A recent review, based on an NIH sponsored gathering of experts, described FOG as a “mysterious phenomenon” [2] and proposed 5 directions for developing hypotheses on the pathophysiology of FOG, based on publications between January 1966 and April 2011. These 5 “hypotheses” attributed FOG to:

1. abnormal gait pattern generation;
2. a problem with central drive and automaticity of movement;
3. abnormal coupling of posture with gait;
4. perceptual malfunction;
5. frontal executive dysfunction.

With the purpose of increasing their knowledge, researchers extensively studied FoG in laboratory setting using measurement instruments to quantitatively assess FoG features. The most used variables to evaluate FoG were:

- cinematic variables: body segment motion, absolute and relative angular excursions. They were measured mainly through stereophotogrammetry.
- dynamic variables: ground reaction forces, centre of pressure ¹ trajectory, joint moments. They were measured by means of force platforms and pressure insoles.
- myodynamic variables: muscular electrical activity, muscle activation timing ² during motor gestures. Surface electromyography was used to measure these variables.

In this line of research, some works particularly contributed to enlighten important FoG characteristics that have been used by other researchers to improve clinical knowledge or developing autonomous FoG monitoring systems.

¹It is the application point of the ground reaction force. Furthermore it is the ground projection of the body centre of mass.

²It is the evaluation of ON and OFF periods of muscles during a motor gesture. The discrimination between active (ON) or inactive (OFF) muscle is threshold based.

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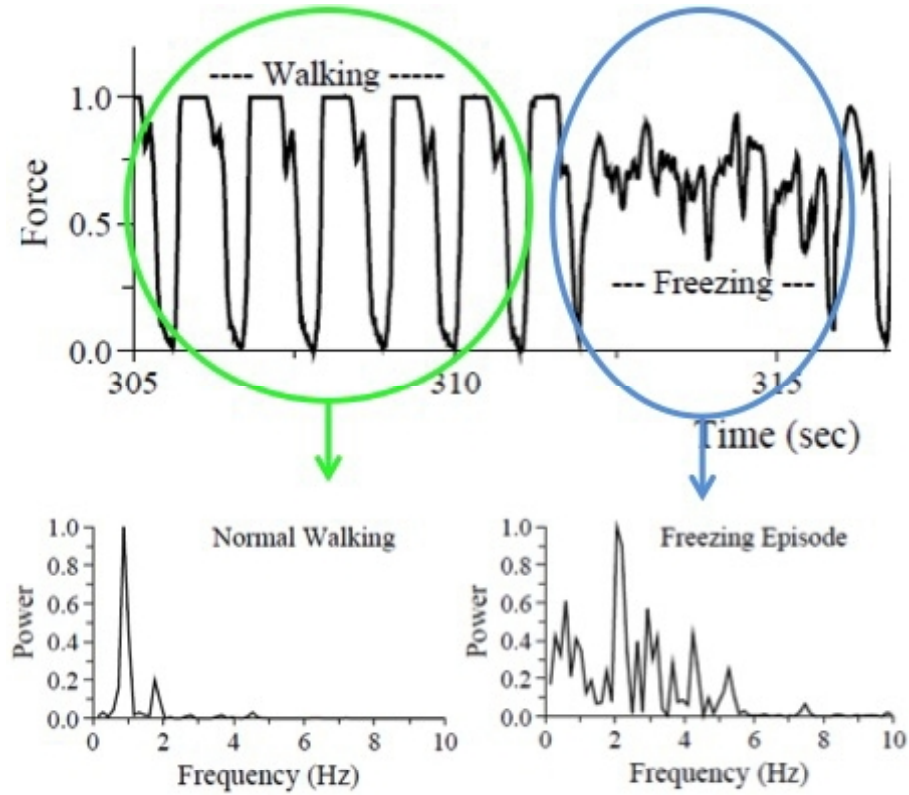


Figure 2.2: Time series spectral analysis of force signal during normal walking (green) and during a FoG (blue). The tidy stripe spectrum of normal walking is lost. Furthermore the power content is shifted to higher frequencies. Fonte: Hausdorff et al. [1]

In 2003 Hausdorff et al. [1] characterized lower limbs movements using insole pressures in order to gain insight about underlying FoG mechanisms. This is an important milestone in FoG research since it is one of the first works that proved FoG is not an akinetic phenomenon and tried to quantitatively describe movement pattern of lower limbs during FoG. Using spectral analysis they found a shift of power content from a low frequency band (0-3 Hz) to higher band (3-6 Hz) ³, as shown in Figure 2.2.

Furthermore using fractal analysis methods authors could state that FoG is not a frozen akinetic state, nor a random attempt at overcoming motor block. Instead, the forces under the feet oscillate in a fairly organized pattern. However, in contrast to walking and resting leg tremor, the spectrum was

³This finding will be used later by Moore et al. [67] to define a freezing index, which will be a successful and fundamental feature for automatic FoG detection systems, as explained in section 2.3.

2.1 Freezing of gait

broadband and more complex. This complex movement pattern may reflect the activation of multiple networks during FoG.

Once ascertained that FoG is not an akinetic phenomenon, also Jacobs et al. [68] tried to explain underlying mechanisms of movements observed during FoG. To this purpose authors searched a correlation between knee trembling during FoG and anticipatory postural adjustments. Anticipatory postural adjustments⁴ of people with FoG with respect to controls were examined using two force platforms (one under each foot) and three electromyographic sensors (bilateral medial gastrocnemius, anterior tibialis and tensor fascia latae). They observed a single adjustment followed by a step in controls and multiple adjustments coexistent with the knee trembling commonly observed during FoG as well as delayed, inadequate or no stepping in people with PD. These multiple adjustments had the characteristic frequency of 3-6 Hz; furthermore they were not delayed in onset and were of similar or larger amplitude than the single APAs exhibited by the control subjects. These findings enlightened a relation among anticipatory postural adjustments and FoG trembling. The authors hypothesized a possible explanation of FoG movements as an inability to couple a normal anticipatory postural adjustment to the stepping motor pattern.

Another contribution to explain FoG underlying mechanisms was produced by Nieuwboer et al [69]. Author’s aim was to test the hypothesis that people with PD have disturbed coordination of the gastrocnemius and anterior tibialis muscles prior to FoG, affecting both the timing and the magnitude of electromyographic activity. By the use of two electromyographic sensors placed on anterior tibialis and gastrocnemius, they analyzed and compared temporal pattern and amplitude of lower limbs muscular activation of FoG, normal walking and voluntary stop. Several differences were founded in FoG with respect to walking and stop, concerning both amplitude and timing of muscular activation. In particular, a premature timing of anterior tibialis and gastrocnemius activity occurred before FoG, which was interpreted as a disturbance of central gait cycle timing. However, the observed changes contribute to insufficient forward progression, deceleration and eventually a breakdown of movement.

The same protocol (comparing FoG with normal walking and voluntary stop) was used to investigate spatiotemporal parameters of gait [70, 71] variations before and during a FoG. Six stereophotogrammetric cameras were employed to analyze the gait of ten patients with PD. The following observations came up from the trials:

- reduced angular excursions of joints (of about 31 – 62%) in sagittal plane;
- progressive decrease in stride length;

⁴They were elicited by backward translation of a movable platform

Chapter 2 State of the art

- decreased gait speed;
- excessively increased step cadence (with the square of gait speed);
- increased double support phase.

Authors interpreted increased double support phase as a compensatory strategy for postural instability, while for what concerns the increase in step cadence they suggested a disorder of gait rhythmic control. Hence FoG seemed to be caused by a combination of an increasing inability to generate stride length superimposed on a dyscontrol in the cadence of walking.

In summary, from the analysis of the quoted studies the most important characteristics of FoG emerged (Figure 2.3) and they can be classified in two subgroups:

1. Time-domain characterization:
 - progressive reduction of step length joined to an increased in step cadence and a decrease in gait speed;
 - reduced joint excursion of hip, knee and ankle;
 - disordered temporal control of gait cycle.
2. Frequency-domain characterization:
 - high frequency (3-6 Hz) lower limbs trembling.

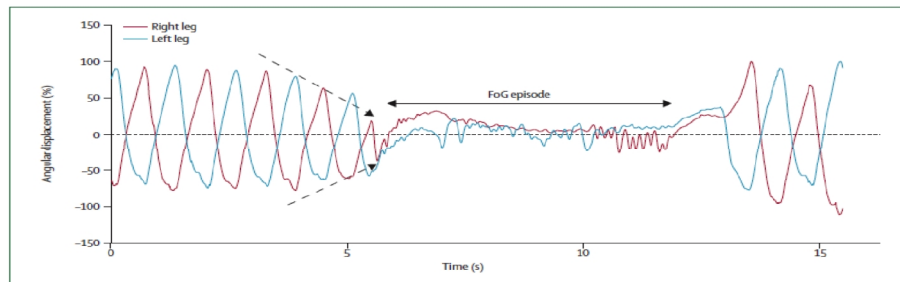


Figure 2.3: Angular displacement of right (red line) and left (blue line) leg during a FoG episode: the standard periodic oscillatory walking trend is completely interrupted. Figure from Nutt et al. [2].

Scientific implications of these findings are important. First of all, hypothesis concerning FoG pathogenesis can be formulated. Furthermore, researchers own measurable parameters (step length, step cadence, gait speed, gait variability, frequency content) that can be used to quantitatively assess FoG. These variables can be employed to develop autonomous monitoring system, that could be useful in a daily living context to gain knowledge about FoG (given its episodic

2.2 Cues

nature, FoG manifests much more during daily living rather than during clinical examinations).

Another critical problem of FoG is its effective management, which is considered a challenge for clinicians given its limited responsiveness to both drug treatment and functional neurosurgery [2, 72]. A promising approach is rehabilitation therapy, in particular the cueing strategy (as indicated in FoG definition) can alleviate or overcome FoG. The use of cues as a rehabilitation tool in PD will be explained in detail in the next session (2.2).

The above described background stimulate researchers to find solution to help both patients (by avoiding or limiting FoG episodes during daily living) and clinicians (by improving their knowledge about FoG). The state of art concerning this research question is described in paragraph 2.3.

2.2 Cues

The usefulness of sensory cueing in improving gait performance and in particular in alleviating FoG has ancient origins. The effectiveness of utilizing sensory systems - for example, vision - to facilitate locomotor activity was first described by Martin [73] over 25 years ago. In a later study, Forssberg et al. [74] reported beneficial effects of visual guidance on gait movements in patients with PD. In 1992 Richards et al. [75] compared the effects of visual and auditory cues on gait patterns in patients with PD under on and off levodopa. In that study patients walked faster with both cues. Auditory cues, however, led to increases in both stride length and cadence, while visual cues (floor markers) caused a longer stride length but slower cadence. A great number of studies have continued to provide evidences of cue effectiveness until now [76, 77].

Throughout the years researchers provided definition of the term “cueing”. According to Cools et al. [78] (1993), cues are ‘contextual or spatial stimuli which are associated with behavior to be executed, through past experience’. Horstink et al. [79] distinguished between cues and stimuli, stating that ‘cues give information on how an action should be carried out and are hence more specific than simple stimuli’. On the basis of these observations a more recent definition of cue particularly suitable for the case of PD was provided and used in later works [31, 29, 30]. According to this definition, cueing is operationally defined as ‘applying temporal (rhythmical) or spatial stimuli associated with the initiation and ongoing facilitation of motor activity (gait)’ [80].

Rhythmic cues can be of different nature: visual (e. g. colored lines on the floor), auditory (e. g. walking at the rhythm of music or metronome) or somatosensory (e. g. walking on a treadmill), but in the literature there’s good agreement that auditory cues are the most efficient in enhancing gait execution [30, 81, 75, 76].

Chapter 2 State of the art

In the introduction, motor learning was defined as a set of processes associated with practice or experience [7]. Areas of central nervous system mainly involved in this process are motor cortex, basal ganglia and cerebellum [10]. PD affects basal ganglia, hence the motor learning process is impaired in people with PD, in particular during the later stages of pathology (automaticity and retention) [18, 55, 10, 16]. Furthermore, not only motor learning of new skills is threaten in PD but also previously learned skills are threaten, for the same reason of basal ganglia involvement in the automatic execution of learned movements [16].

However, the role of rehabilitation in preserving motor skills and enhancing motor learning has been addressed for years [82]. In fact, the central nervous system (in particular the basal ganglia in this case) is capable of neuroplasticity and physical activity particularly stimulates this process [83, 84]. A number of studies supported this thesis providing evidences about the ability of motor learning in people with PD [21], as well as improvements in motor function as a result of training [16, 31]. In particular, external rhythmical cues revealed a promising rehabilitation tool [30].

These evidences encourage the development of technological systems to support patient’s training and rehabilitation program. The use of technology for the rehabilitation therapy can bring several advantages: automatization, at-home execution and supervision. Thus a technological system able to assist and guide the patient in a daily rehabilitation program at his home can improve and enhance benefit of rehabilitation therapy.

The EU-funded research project CuPiD (closed-loop system for personalized and at-home rehabilitation of people with Parkinson’s disease) [85] is an example of this research field. The system proposed for the project is a wearable architecture composed of three inertial measurement units and a smartphone [3], as shown in Fig. 2.4: two sensors are place on shoes and one is mounted on the trunk. The smartphone acts as a portable processing function. The CuPiD system has two functions (corresponding to two smartphone applications) [86]:

- the audiobiofeedback (ABF-gait) app, that it monitors some important gait features (cadence, stride length, symmetry and gait speed) and on the basis of their trend it feeds back instructions to the patient in order to improve his gait.
- the instrumented cueing app for FoG training (FoG-cue app) with a FoG detection option, an exercise menu and an intelligent cueing option.

After six weeks of training with CuPiD, twenty patients improved significantly on single and dual task gait speed with respect to controls.

Lopez et al. [87] proposed Listenmee, an intelligent glasses system with a portable auditory device, that generates auditory rhythmic cues matching

2.2 Cues

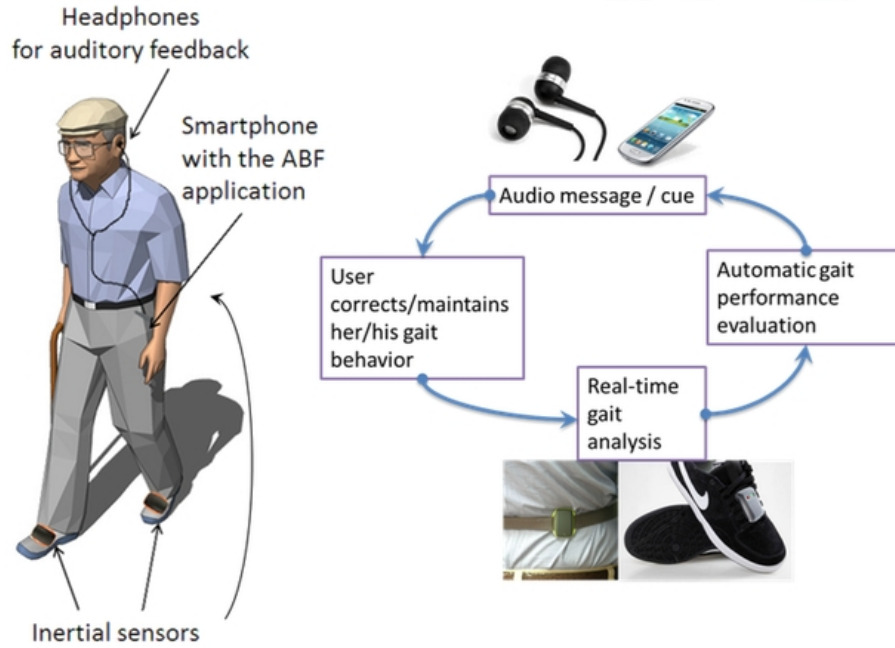


Figure 2.4: CuPiD architecture. Fonte: Casamassima et al. [3].

the patient’s step frequency to improve walking in PD patients. Patients can select the sounds manually, including the desired cueing rate, using the Listenmeee smartphone app. Listenmeee was tested in a gait analysis laboratory and results revealed significant improvements in step cadence, stride length and walking speed.

Another system to support gait training through rhythmic auditory cues was proposed by Mazilu et al. [4]. Their system is composed of two ankle-mounted inertial measurements units and a smartphone as processing unit, see Fig. 2.5. The software consists of an Android application supporting the exercises and the assistive cueing, all based on the FoG-detection module that analyzes in real-time data received from the sensors. The rehabilitation module supports three types of exercises: gait initiation, turns and response inhibition.

Recently, Ellis et al. [88] validated a smartphone application able to quantify gait variability and provide rhythmic auditory cueing during walking. The smartphone performance was compared with heel-mounted footswitch sensors (to capture step times) and an instrumented pressure sensor mat (to capture step lengths).

However, even if rehabilitation, meant as cues delivery during supervised walking exercises, was effective in a laboratory setting, it did not always succeed at providing sustained functional benefits [41, 82, 30, 81]. Probably due

Chapter 2 State of the art

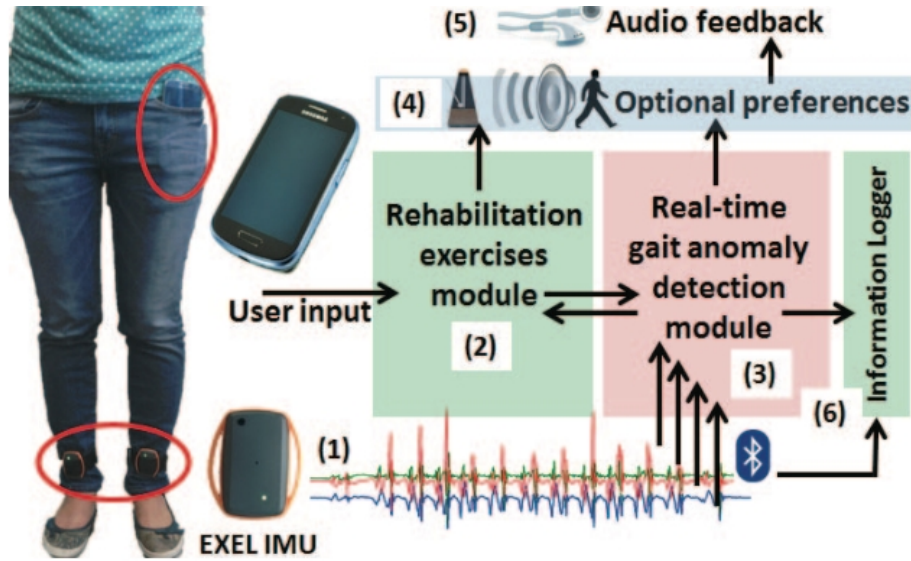


Figure 2.5: The GaitAssist system with its components: (1) sensors, (2) Rehabilitation exercises module, (3) FoG-detection module, (4) Preferences, (5) Feedback, and (6) Logging modules. Fonte: Mazilu et al. [4].

to the disease related impairment in motor learning mechanisms, particularly concerning the retention phase. In fact, while there are several evidences for motor improvements immediately after the intervention, results about the retention of motor benefits at the follow up (for example after three months) are absent or rather inconsistent [30, 31].

Many researchers have therefore advocated a model of cue delivery “as needed” [5, 89]. From a cognitive point of view such a device would implement a behavioural approach to re-learn ambulation.

In this thesis, rhythmic auditory cues were selected as the rehabilitation and feedback tool for the patient, given the evidences of their better effectiveness [30, 81, 75, 76].

2.3 Freezing of gait detection

In the last decade several systems have been proposed in the literature with the aim of detecting FoG episodes. The objectives of research were to monitor the disorder in order to improve clinical knowledge, to quantitatively assess FoG or to provide rhythmic cues to help the user to overcome possible FoG. Computerized methods to detect FoG can be grouped in five categories: (a) methods that analyze electromyography signals [90], (b) methods based on

2.3 Freezing of gait detection

3D motion analysis systems and goniometers [91], (c) methods based on foot pressure analysis [92, 93], (d) methods using electroencephalography [94], and (e) methods analyzing motion signals (accelerometers and gyroscopes) [95, 5, 96]. In this thesis the focus is on motion signals methods since inertial sensors embedded in a smartphone are used as sensing units.

Once selected the type of sensor used to detect FoG, the concerning literature can be discussed in relation to the hardware and the software of the built architecture. This separation allows to discuss the main contributions produced by this work with respect to the literature.

2.3.1 Hardware

The hardware mainly influences architecture usability, acceptability and cost. To this purpose, it is useful to distinguish three groups of systems:

1. body sensor network communicating with a computational unit, that must be near the user [97, 98];
2. body sensor network communicating with a wearable computational unit, like a smartphone, enabling online data processing [5, 89];
3. a single wearable mobile device performing both sensing and processing functions in real-time [50, 99].

Generally, systems belonging to the first group are not suitable for real time application in a daily living scenario [98, 67, 100, 101]. In fact they are applied only offline [67, 98, 101] or on simulation [100] and none of them implements a cueing delivery function.

For example, Moore et al. [97] built an architecture composed of seven inertial measurement units, three for each leg (mid-foot, shank, thigh) and one on the lower back. The sensors acquired triaxial linear acceleration and transmitted wirelessly to a computer for processing. The system of Tripoliti et al. [98] comprises six accelerometers (ankles, wrists, chest and waist) and two gyroscopes (chest and waist), that transmit data to a computer using Bluetooth.

Mancini et al. [64] proposed a system to quantify FoG for clinical practice by using body-worn accelerometers. It is composed of three inertial measurement units (equipped with tri-axial accelerometer and gyroscope) and a portable data receiver to transmit data wirelessly to a computer.

Some systems require a lower number of sensors, like one [102] or two wearable sensors [100, 103, 101], but actually they are not able to perform real-time FoG detection.

Only the architecture of Bachlin et al. [5] can be applied for online FoG detection and it is in fact at the boundary between the first and the second group.

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Three sensors attached to the body (shank, thigh and belt) transmit their data to a wearable computer through wireless Bluetooth link. The wearable assistant is equipped with earphones in order to produce rhythmic auditory cues whenever a FOG episode is detected. However, the entire architecture is too obtrusive and difficult to use (Figure 2.6).

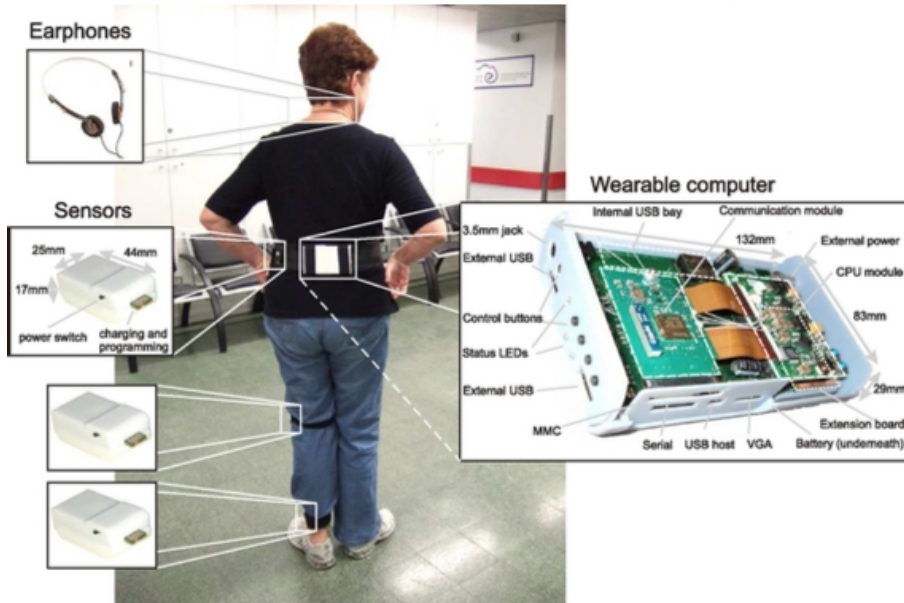


Figure 2.6: FoG detection and feedback assistant of Bachlin et al. [5] worn by a patient. Sensors are attached to the shank (just above the ankle) and the thigh (just above the knee) using an elasticized strap and Velcro. A third sensor is attached to the lower back to the same belt that the wearable computer is attached to. Fonte: Bachlin et al. [5].

The above examples show how development of medical products is often guided by medical necessity, technical feasibility, and economic interest, disregarding aspects of humans’ technology acceptance as well as the understanding of usage motives and barriers [44]. Since the major part of these systems requires additional and unknown technology to be worn by the patient, they scarcely satisfy usability and acceptability requirements. Instead, acceptability and usability issues must be taken into account, being critical features in the human interaction process.

According to [104], usability is “the extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specified context of use”. Technology acceptance is a quality attribute referring how users come to accept and use a technology taking into

2.3 Freezing of gait detection

account social implications as well as personal satisfaction and effort [105]. For a wider acceptance of healthcare monitoring systems, there is the need to consider important aspects:

- medical monitoring can generate in patients the perception of breaking their privacy;
- medical technology often refers to ‘taboo related’ areas, associated with disease and illness.

In this scenario, information and communication technology does not elicit oppressive or embarrassing feelings because of their popularity [44]. In particular smartphones offer a customizable user interface to increment perceived ease of use and inertial sensors to collect motion data.

In fact in the last years smartphones and other mobile devices gained increasing importance in healthcare applications [45]. Also in the field of interest for this thesis researchers studied the potential and the reliability of the smartphone to carry out FoG detection.

Initially, the smartphone was mainly used as a gateway between sensors and a computing and storing unit [89, 106, 107], as in the systems belonging to group two. Instead, recently, there are some studies that use only a smartphone to carry out FoG detection [50, 99], a great part of which is the result of this thesis.

Architectures belonging to group two allow real-time processing and are more suitable to be applied at home, but however a depth analysis of architecture usability and acceptability was not carried out.

An interesting implementation was provided by Jovanov et al. [96], who developed an automatic real-time system for FoG detection and acoustic cues delivery when FoG manifests. They used a sensor board placed at the knee and a wireless headset.

The REMARK (Personal Health Device for Remote and Autonomous Management of Parkinson’s Disease) project [108] aims to develop a Personal Health System with detection, response and treatment capabilities for the assessment and possible management of patients with PD. Their architecture is composed of a Body Area Network (immediate level) and an intelligent level for processing and analysing data [109]. The immediate level is composed of two inertial measurement units, a smartphone and some actuators [106, 109]. The sensing units are placed on the waist and on the wrist: the first identifies parameters related to posture and gait while the latter detects symptoms of tremor and dyskinesia. Possible actuators are an injection pump for drug delivery, an auditory cueing system and a Functional Electrical Stimulation System (acting as a haptic cueing system). The smartphone is a gateway between the immediate and the intelligent level.

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Mazilu et al. [89] propose a wearable assistant, composed of a smartphone as wearable computer and wearable accelerometers (hip, knee, ankle), for online detecting of FOG. When FOG is detected, the assistant provides rhythmic auditory cueing or vibrotactile feedback. Recently the same group of study [110] proposed an advancement of the system, called GaitAssist. It is composed of two ankle mounted inertial sensors that communicate data via Bluetooth to an Android smartphone. GaitAssist can provide the following functions: FoG detection, rhythmic auditory feedback and support for three kinds of training and rehabilitation exercises. This architecture was developed for the CuPiD project, hence it is the same used by Casamassima et al. [3] and Ginis et al. [86] for at home rehabilitation and training purpose.

The system proposed by Lorenzi et al. [107] is composed of inertial sensors (accelerometers and gyroscopes), a station for real time processing (smartphone/PC/tablet). They proposed two solutions: one with the sensor embedded in the headset and the other with two sensors on the shins.

Also this kind of systems requires the placement of multiple sensors on user body, possibly causing discomfort, hard wearability or embarrassment.

Finally, for what concerns the third group of systems, this work of thesis gave important contributions about the question of gait monitoring in PD and FoG detection with only a smartphone [47, 48, 50, 111, 51]. Recently, also Kim et al. [99] tested the reliability of the smartphone in an ambulatory setting with fifteen patients. They placed the smartphone in different positions: chest, waist, pocket and ankle.

The above discussion highlighted the lack of an extensive assessment of the smartphone reliability in real-time FoG detection. Furthermore, acceptability and usability, two essential requirements for assistive devices, are neglected or never assessed. This thesis addresses both needs by evaluating the smartphone reliability in a laboratory setting on a wide group of patients with PD and by submitting dedicated questionnaires on acceptability and usability to patients.

2.3.2 Software

The software of FoG detection systems includes two important steps that are shared by all proposed systems: features extraction and classification.

The features selected to detect FoG are inspired by studies discussed in Section 2.1, that reported the most important characteristics of FoG. This studies highlighted two characterizations, in frequency and time domain, suggesting suitable monitoring parameters to researchers. In fact, in the literature, FoG detection systems can be found using frequency features [112, 67, 5], time features [98, 102, 107], or both [89, 101, 113].

The first attempt to discriminate FoG and normal gait from body worn

2.3 Freezing of gait detection

sensors was made by Han et al. [112] using frequency characteristics.

Another milestone in FoG detection is certainly the work of Moore et al. [67], who defined an important frequency parameter, the Freeze Index (FI), using power spectrum analysis of vertical linear acceleration of the shank. This FI is defined as the ratio between the power in the “freeze” band (3-8 Hz) and the power in the “locomotor” band (0.5-3 Hz). Bachlin et al. [5] improved the Moore’s algorithm using a reduced window size to detect shorten FoG and a second parameter to avoid false positives during standing. This last parameter is the integral of the power spectrum in the band 0.3-8 Hz (“freeze” and “locomotor” band). Frequency features introduced in these two works are already used for FoG detection [113, 99, 110]. A further improvement of the FI was proposed by Chang et al. [100] who tried to achieve real time detection by adopting the generalized spectrogram with asymmetric windows and the asymmetric smooth filter to compute FI.

For what concerns time domain, the most used features are:

- entropy [89, 98, 113];
- spatial-temporal parameters of gait: stride length, frequency [114, 102], and duration [101], swing phase, single, and double support phases [114];
- other features, such as the angle between vertical axis and shin [107] and the change of shank transversal orientation [101].

For what concerns classification techniques, the major part of existing works uses threshold-based methods [67, 96, 5, 64, 102]. Other systems combines thresholds application with binary decision rules [115, 101]. Machine Learning techniques were also investigated. Some examples include Support Vector Machines [113, 110], Neural Networks [103, 107] or comparison of different classifiers [98, 89, 99].

In this thesis, Fuzzy Logic is used for the first time to detect FoG. Fuzzy Logic has the advantages of interpretability and the possibility to exploit a priori knowledge about a phenomenon. In fact, clinicians’ expertise about relationships between gait parameters and FoG occurrences can be translated in the form of *if...then* rules and hence used for FoG detection.

Tables 2.1, 2.2, 2.3 provide a comprehensive overview about state of art in FoG detection system. Works are listed in chronological order. In particular, the table summarizes the following aspects, which were discussed and highlighted in this section:

- the hardware used (column 2);
- extracted feature and their domain (columns 4 and 3 respectively);
- adopted classification method (column 5);

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- cues delivery function (column 6);
- real-time processing (column 7);
- patients with PD enrolled for testing (column 8) ⁵;
- acceptability and usability assessment (column 9).

Some observations can be done from the table. First of all, there is only a very recent work adopting only a smartphone [99]. Only few systems provide cueing function, real-time processing, and were tested on a quite high number of patients. Finally, none of them used Fuzzy Logic as classification method and none of them assessed acceptability and usability of their architecture.

2.4 Spatial-temporal parameters of gait

In Section 2.1 the relation between FoG and the gait parameter alteration was introduced. This relationship suggests the potential of spatio-temporal or frequency parameters of gait as significant FoG detectors. In fact, in the previous Section the state of the art about the hardware and the software of FoG detection systems was discussed and it was showed how frequency or time domain information can be successfully used to detect FoG. However, while the extraction of frequency domain features is a direct process that takes place on the acceleration signal, some of the most important and used time domain features include spatio-temporal parameters of gait, that can only be estimated from the acceleration signal.

In particular, step length (SL) and step cadence were selected to be included in the algorithm proposed in this thesis. In order to use these parameters in the FoG detection system the question of smartphone reliability in SL and step cadence estimation had to be addressed. As a starting point, the state of the art in SL and step cadence estimation through smartphone’s embedded sensors and through wearable inertial sensors was studied.

2.4.1 Step cadence

Walking cadence ("the beat, time, or measure of rhythmical motion or activity" [117]) has broad utility for applications that support fitness, rehabilitation, gaming or navigation. Hence, several cadence detection methods were proposed in the literature. Two main methods to estimate step cadence from wearable inertial sensors can be distinguished [118]:

⁵Number 0 means that the system was tested only on healthy subjects simulating FoG. Instead, "n. t." (which stands for "not tested") means that the system is only presented and no experimental result is given

2.4 Spatial-temporal parameters of gait

Table 2.1: Works investigating the development of a system for automatic FoG detection (Part 1).

Work	Hardware	Domain	Features	Classif.	Cue	Real-time	PD	A/U
Han et al [112]	2 U-AMS	Frequency	Power of wavelet decomposition level	Threshold			2	
Moore et al [67]	1 IMU	Frequency	Freeze index, Power	Threshold			11	
Jovanov et al [96]	1 sensor board + wireless headset	Frequency	Freeze index	Threshold	X	?	1	
Bachlin et al [5]	3 accelerometers + tiny computer	Frequency	Freeze index, Power	Threshold	X	X	10	
D.-Jovicic et al [103]	6 IMU	Time	Energy	Neural Networks, binary rules			4	
Stamatakis et al [114]	4 accelerometers	Time	gait velocity, step time and frequency, stride time and frequency, stride length, swing phase, single and double support phase	Threshold			1	
Zhao et al [115]	MiMed-Pants (5 accelerometers, trans-cables, transmitting unit) + PC	Time, Frequency	time domain: foot shaking duration, activity peaks main: freeze index	Threshold, binary rules	X		8	

Table 2.2: Works investigating the development of a system for automatic FoG detection (Part 2).

Work	Hardware	Domain	Features	Classif.	Cue	Real-time	PD	A/U
Mazilu et al [89]	3 sensors + smartphone	Time, Frequency	time domain: mean, var, std, entropy Frequency domain: energy, freeze index, power	Machine Learning	X		10	
Mancini et al [64]	3 IMU + portable data receiver	Frequency	Freeze index				21	
Tripoliti et al [98]	6 accelerometers + 2 gyroscopes	Time	Entropy	Machine Learning			16	
Moore et al [97]	7 IMU + PC	Frequency	Freeze index				25	
Coste et al [102]	1 IMU	Time	Stride length, cadence				4	
Djurić-Jović et al [101]	2 IMU	Time, Frequency	Time: stride duration, shank displacement, change of transversal orientation. Frequency: dominant range of power spectrum	Threshold, binary rules			12	

2.4 Spatial-temporal parameters of gait

Table 2.3: Works investigating the development of a system for automatic FoG detection (Part 3).

Work	Hardware	Domain	Features	Classif.	Cue	Real-time	PD	A/U
CuPiD [110, 3, 86]	2 IMU + smartphone	Frequency	total power, freeze power, loco power, freeze index	Support Vector Machine	X	X	18	
Chang et al [100]	2 IMU	Frequency	Freeze index with generalized spectrogram	Threshold			0	
Sijobert et al [116]	2 IMU	Time	Stride length, cadence	Threshold			7	
Kim et al [99]	smartphone	Time, Frequency	time domain: mean, var, std, RMS, IQR, kurtosis, entropy domain: energy, freeze index, power, Freeze and Loco band power, DC power	Machine Learning			15	
Lorenzi et al [107]	1 IMU on headset or 2 IMU on shins + PC/smartphone/tablet	Time	vertical acceleration, angle between vertical axis and shin, angular velocity	Neural Network, threshold	X		n.t.	
REMPARK [113, 106, 109]	2 IMU + smartphone/tablet + headset + Functional Electrical Stimulation device.	Time, Frequency	Freq: FFT, mean and std of amplitude in Freeze and Loco band, peak amplitude and frequency in Freeze and loco band, freeze index. Time: entropy	Support Vector Machine	X	X	20	

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1. Time domain: by analyzing the acceleration shape and detecting heel strikes ⁶ of each foot. The time domain method often relies on particular filtering of raw signal, peak detection and thresholds application, in order to detect the actual time instant of foot contact [119, 120, 121]. Moe-Nilssen et al. [122] proposed a cadence estimation by an unbiased autocorrelation procedure of the acceleration shape.
2. Frequency domain: by identifying the major frequency components of the signal during a given window of time [123]. Frequency based method is very straightforward, since it requires the identification of the fundamental (first) harmonic in the power spectrum [123], and it is suitable for real-time cadence estimation on mobile devices [124].

Both the discussed approaches have pros and cons. The time domain method does not require the computation of the power spectrum, but its performance is dependent on signal shape, amplitude, and sensor placement, furthermore, it often requires user specific thresholds [125]. On the other hand, the frequency domain method needs the acquisition of a data window with appropriate length and it does not provide the exact time instant of heel strike. Hence, the choice of a method or the other is application dependent.

2.4.2 Step length

Recently, inertial sensors, given their low cost, miniaturization, and wearability, were widely applied for gait analysis in both healthy [126] and pathological [127] subjects. In particular, a number of works proposed a single sensor placed on the lower trunk to estimate SL, in order to increase the acceptability of the system [6, 128, 88].

However, since inertial sensors do not provide direct measurement of gait parameters such as SL, estimation methods must be introduced. Existing approaches were classified in two categories, in order to enhance clarity in the following literature review: direct approach, that estimates SL from double integration of acceleration along the progression direction, and indirect approach. Among indirect approach, model-based and empirical ones could be further distinguished.

Some critical issues concerning direct approach comprise the compensation of integration drift error and the determination of an initial condition for velocity. Kose et al. [128] proposed a novel method based on the combination of a Kalman filter and an optimally filtered direct and reverse integration to solve the above mentioned problems. Also Bugane et al. [129] estimated SL from

⁶Heel strike: time instant when the foot hits the ground.

2.4 Spatial-temporal parameters of gait

double integration of antero-posterior acceleration, relying on the assumption that speed at foot contact was zero.

Among model-based approaches, the inverted pendulum model of human gait introduced by Zijlstra et al. [6] highlights a relationship between vertical change of body center of mass and SL, described by the following equation:

$$sl = 2\sqrt{2lh - h^2} \quad (2.1)$$

where l is the length of subject’s leg, while h is the difference between maximum and minimum height reached by body center of mass during gait cycle. The model is shown in Figure

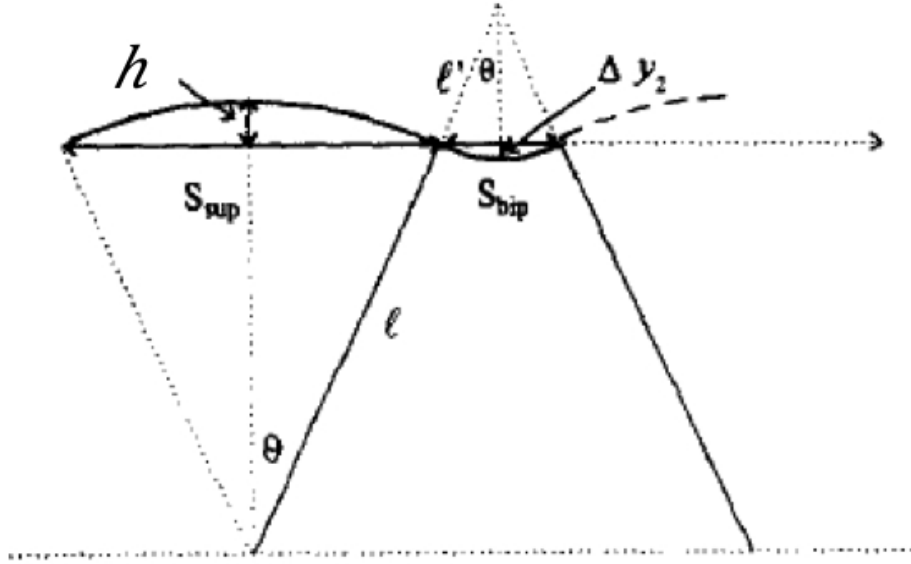


Figure 2.7: The inverted pendulum model of Zijlstra and Hof [6].

Since this relationship underestimates the actual SL, authors proposed the introduction of a correction factor set to 1.25 [130]. Gonzalez et al. [131] improved this model separating swing phase (modeled as in [6]), from the double stance phase modeled by another pendulum of unknown radius. The contribution of the second pendulum is set as a quantity proportional to foot length. Recently Zijlstra et al. [132] updated their method by introducing an individual correction factor and compared it with Gonzalez’s method [131]. The paper showed that all the proposed variations of the inverted pendulum model gave equally, highly reliable estimate of SL from lower-back accelerations. Lan et al. [133] used a smartphone for indoor location tracking and they estimated SL through the Pythagorean Theorem, which an exemplification of the inverted

Chapter 2 State of the art

pendulum model. However their approach could not take into account the underestimation introduced by equation (1). A richer model of human walking is proposed by Hu et al. [134], but it was used to estimate gait speed. Their model adds to the inverted pendulum model information about rolling-foot and waist rotation during gait.

For what concerns empirical approaches, researchers found several relations between SL and gait variables. For example Shin and Park [135] proposed a SL estimation based on a linear combination of walking frequency and acceleration variance. Also Sun et al. [136] introduced a mathematical relationship involving step frequency and acceleration variance. Furthermore, Ladetto [137] found an empirical linear relation between SL and step frequency, while Kim et al. [138] related the stride with acceleration magnitude and step period. Weinberg [139] expressed walking distance as a function of step frequency and the difference maximum and minimum values of vertical acceleration during a stride. A comparison of several SL estimators (both model-based and empirical) was provided by Alvarez et al. [140]. Empirical approaches have the advantage of being less computationally demanding, in fact they did not include double integration, but on the other hand they need a long and complex calibration to find optimal value for parameters appearing in their formula. Furthermore empirical methods are more suitable to estimate a mean value for SL or walking distance instead of the length of each step. For this reasons we chose the inverted pendulum model.

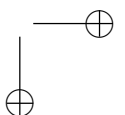
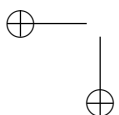
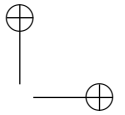
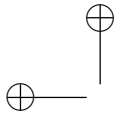
A possible limitation of the systems described above is the usage of inertial measurement units attached to the subject and processing units nearby to analyse data. This kind of architecture is not suitable in a daily living situation, since typical users lack the technical expertise for precise sensor usage and placement. Furthermore, from a social point of view users may not feel comfortable with sensors or other devices on his body. For this reason, in the literature there are some works using every-day technology like mobile phones to estimate SL in real-time for indoor localization [141, 142, 143], but they differ from our contribution for the SL estimation method adopted, the exiguous number of subjects, the experimental and evaluation methodologies. Ferrari et al. [144] used a smartphone as a real-time processing unit to monitor the gait of Parkinsonian patients, but the sensing part is composed of two sensors on the shoes. Sejdic et al. [145] developed an Android based gait monitoring device, but their system is composed of multiple sensors. Juen et al. [146] performed a wide and detailed experimentation on the use of mobile phones to monitor the gait, but their focus was mainly on gait speed. In another work [147] they estimated stride length through a linear regression model using eight spatiotemporal parameters and four demographic parameters. For this reasons, the inverted pendulum model was chosen in this work.

2.5 Telemedicine systems

Continuous technological advancements in wearable sensors, wireless communication and Internet connection enable development of systems for remote health monitoring with the potential to improve healthcare and the quality of life for elderly and chronic patients. A number of wireless body area networks have been proposed to monitor the body function for sporting, health, entertainment and emergency applications. These systems are generally three-tiers architectures composed of wearable sensors that communicate (preferably wirelessly) with a personal server and subsequently through the Internet with a remote medical database server [148, 149, 92, 150, 151].

The system architecture presented by Otto et al. [148] performs real-time analysis of sensor’s data, provides real-time feedback to the user, and forwards the user’s information to a telemedicine server. Kanthoc [150] proposed a system architecture for the monitoring of physiological parameters. The system is composed of a body sensor unit with Bluetooth connection, a gateway to forward data to a remote clinical server. Jamthe et al. [92] propose a solution for continuous monitoring of Parkinson patients in their home environment, embedding wireless sensors in patient’s vicinity. Sensors motes are placed in patient’s room and also shoes to monitor him from early fall detection and freezing of gait events. Data collected must be sent to a base station located in patient’s home.

The MEDiSN project [152] utilizes a wireless sensor network composed of a network gateway, physiological monitors and relay points, to monitor health status and transmit physiological data of patients. The physiological monitors are sensor devices which collect, encrypt and sign patients’ physiological data before transmitting them to a network of relay points that eventually forwards the data to the network gateway. The data received by the network gateway is stored persistently at a backend server, where clients can use a graphical user interface to access the data through different queries. The MASN project [153] has a similar architecture.



Chapter 3

Materials and Methods

This chapter contains the description of the developed system for FoG management. In particular, Section 3.1 provides an overview of the overall architecture; Section 3.2 describes in details the mobile application used to monitor gait during daily living; Section 3.3 introduces the parameters extracted from signals in order to detect FoG; Section 3.4 explains the FoG detection algorithm; and finally Section 3.5 describes the server side part of the architecture, which includes the database used for information storage and the web application.

3.1 The architecture

The proposed architecture is composed of a smartphone app, a database (DB) and a web app. In Figure 3.1 there is a graphical overview of the architecture and in Figure 3.2 there is the component diagram of the architecture.

In details, the smartphone application uses onboard inertial sensors to acquire motion data, the audio player to provide the auditory cues and a local sqlite database to store collected information about FoG. On the server side there is a database that is queried by a web application with dedicated areas for clinicians and patients.

3.2 Mobile app

The component diagram of the app is shown in Figure 3.2 to give an overview of the main app components and their relations. The smartphone app performs the following actions:

- monitoring gait parameters;
- detecting FoG;
- providing rhythmic acoustic stimuli in response to a FoG;
- saving gait parameters trend and FoG episodes in a local DB;

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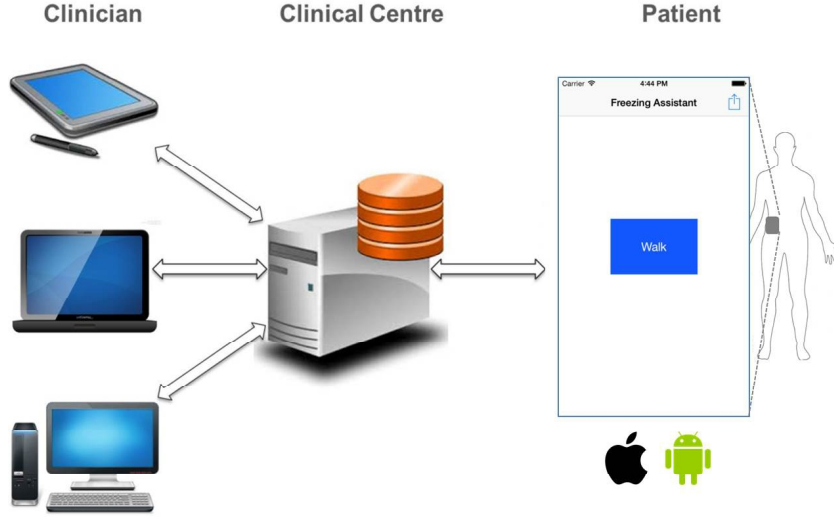


Figure 3.1: Architecture components: smartphone app, DB at the clinical center, clients interacting with DB through the web app.

- periodically uploading to the central DB all the information stored in the local DB.

In Fig. 3.2 there is also a component for fall detection, which is not discussed since it is at a too much early development stage, but it will be a future work.

The smartphone application was developed for the two main platforms iOS and Android, in order to guarantee the portability of the system. The smartphone is placed at user’s hip through an elastic belt and a socket. The socket should fit perfectly the smartphone, in order to hold it in vertical position (Figure 3.3). In fact for the processing purpose the alignment of accelerometer axis is critical only for the vertical one, but visual inspection of the right position for the socket is sufficient to maintain algorithm reliability.

The smartphone app collects and processes data from the available accelerometer. Figure 3.4 shows the general flow chart of the processing method. The application acquires vertical acceleration data at a frequency of 100 Hz and then it performs features extraction for FOG detection. In particular, firstly the application applies a sliding window (Hamming window) of 256 samples on acceleration data; the window shift is 40 samples. On each window the FFT and the power spectrum are computed. Finally, features used by the detection algorithm are extracted: the Freeze Index (FI) [67], the Energy (EN) [5], the Energy Derivative Ratio (EDR), the Step Cadence (SC) and the Step Length (SL). A detailed description of extracted features is given in the next Subsections. Computed features are sent in input to the FoG detection algorithm

3.2 Mobile app

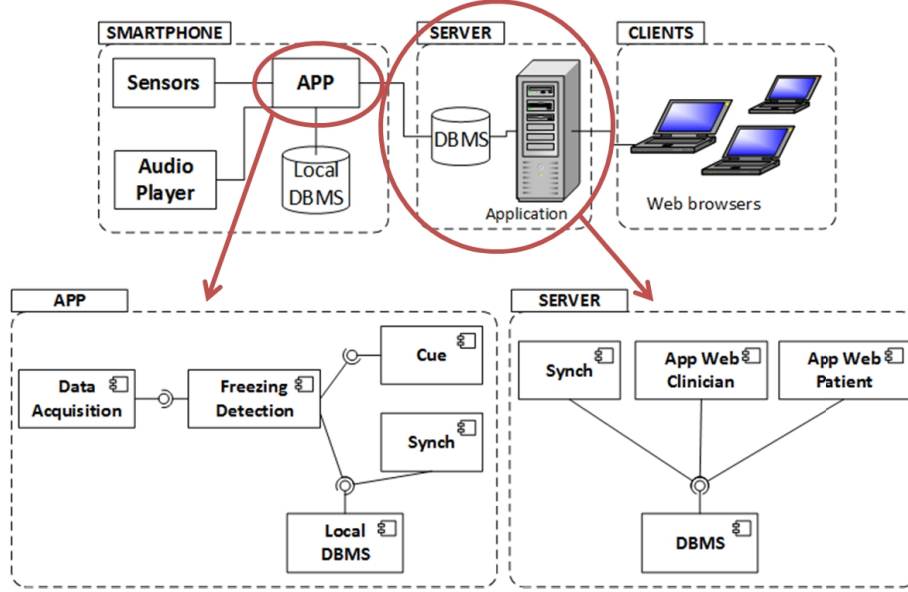


Figure 3.2: Component diagram of the architecture.

in order to decide whether a FoG is happening. Three classification algorithms were developed and tested during this work: a linear classifier, a Crisp Logic classifier and a Fuzzy Logic classifier. When the outcome of the classification process is positive (hence a FoG is detected), the app gives a rhythmic acoustic feedback to help the patient to resume walking. The feedback can be customized according to user’s preferences in order to be more effective.

In order to keep constant and reliable the data acquisition process, data acquisition and processing are performed in two parallel threads.

All the informations collected by the smartphone app (features calculated, FOG events detected and threshold values) are stored through an sqlite database internal to the smartphone and used later for statistical analysis. The Entity-Relationship model and the Relational model of this database are shown in Figure 3.5(a) and 3.5(b) respectively. During daily living usage the application transfers all these data to a server at the clinical centre periodically.

The user interface of the application was designed extremely intuitive and simple, in order to satisfy usability requirements. When the app is launched the patient can start the algorithm just pressing a button, as shown in Figure 3.3. After the FoG detection algorithm has been started the application disables all the buttons on the screen: in this way the user can wear the smartphone without the danger to accidentally activate or dis-activate application functions.

Chapter 3 Materials and Methods

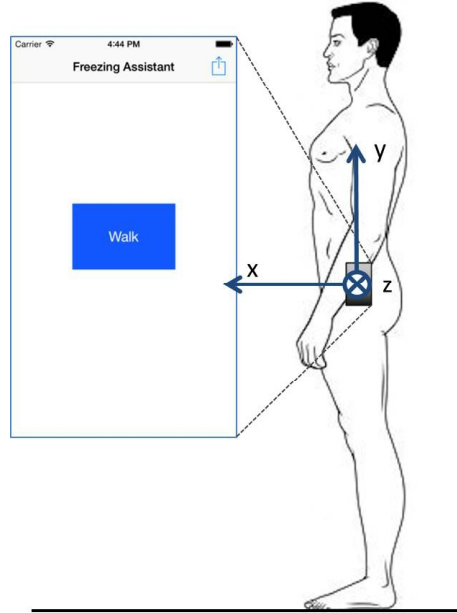


Figure 3.3: Smartphone placement and graphic user interface of the smartphone app for FoG management.

Before using the application, some settings must be carried out. The settings page is protected by password in order to avoid patients' accidental modifications of the settings, that would deteriorate the performance. In fact the user must not access the setting procedure, which is performed by clinicians in ambulatory during the periodical examinations.

Figure 3.6(a) illustrates the user interface to set up the following parameters: leg length (in meters), that is used for SL estimation; FI threshold and EN threshold, which are customized for each patient in order to adapt to patients' characteristics.

FI and EN thresholds are set through a calibration process that can be started and stopped using the corresponding buttons ("Start" and "Stop"). Before starting the process only the "Start" button is active, as indicated by the red background color. Instead, after starting, the "Start" button becomes inactive and the "Stop" button is available (Figure 3.6(b)). The calibration process requires a period of at least twenty seconds of standing posture while wearing the smartphone. At the end of the process, after pressing the "Stop" button, the application will display the threshold values just set. If something goes wrong or the elapsed time is too short, a message will suggest to repeat the

3.2 Mobile app

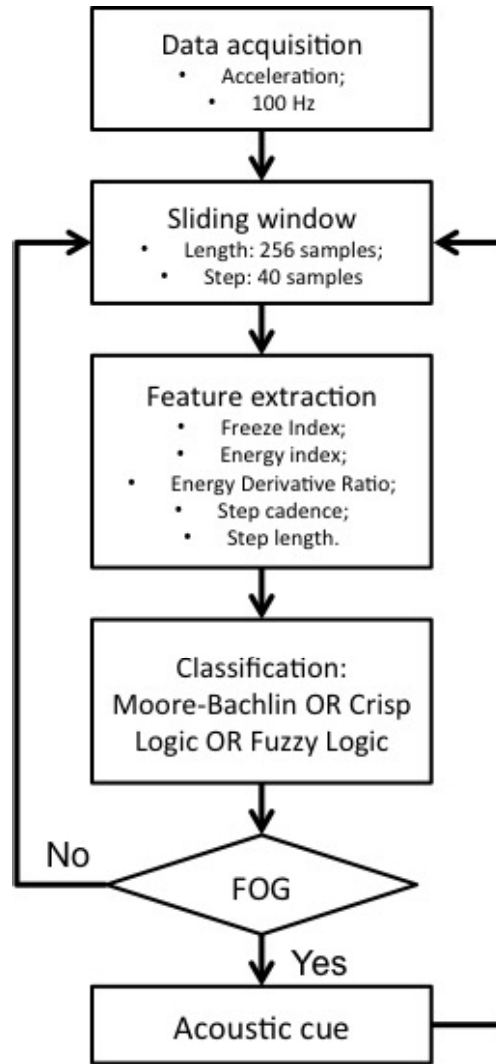


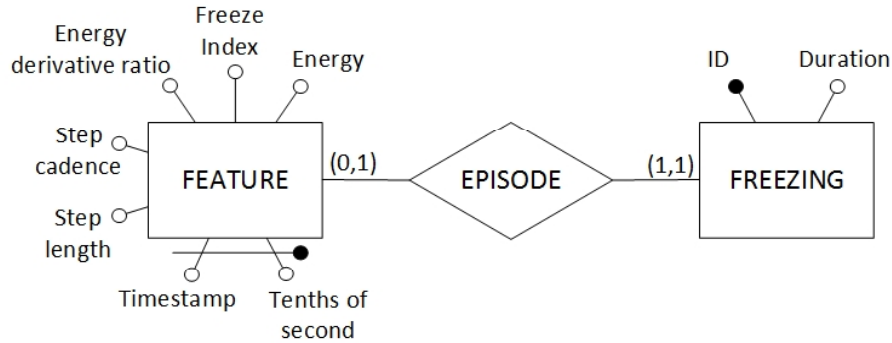
Figure 3.4: Algorithm flowchart of the smartphone application

calibration process.

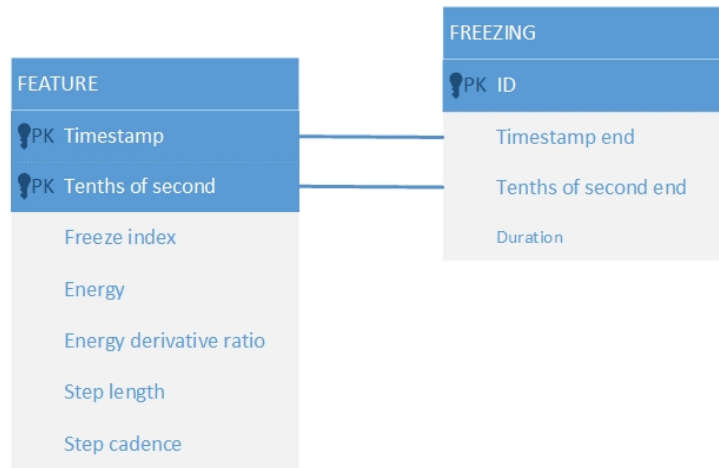
The button "STD" at the top right corner of the settings user interface offers the possibility to set standard values [67, 5] for FI and EN thresholds (Figure 3.6(c)).

Once the setting procedure is completed, the patient can use the application during his/her daily activities without any worries. The app usage is extremely intuitive and simple since the application functioning is almost entirely autonomous, the user had only to press the "Walk" button in the main

Chapter 3 Materials and Methods



(a)



(b)

Figure 3.5: Entity-Relationship (a) and Relational (b) models of the sqlite database on the smartphone.

view (see Fig. 3.3). This action will disable all the buttons of the user interface thus avoiding accidental pressings.

3.3 Extracted features

A FoG detection algorithm includes at least two steps: feature extraction (computation of significant parameter from acquired data) and classification (deciding if a tuple of features computed at a certain time instant belongs to a FoG or not FoG situation). As explained in Section 2.1, there are essentially two types of FoG characterization: in time and frequency domain. In this thesis, parameters were chosen from the frequency domain as well as from the time

3.3 Extracted features

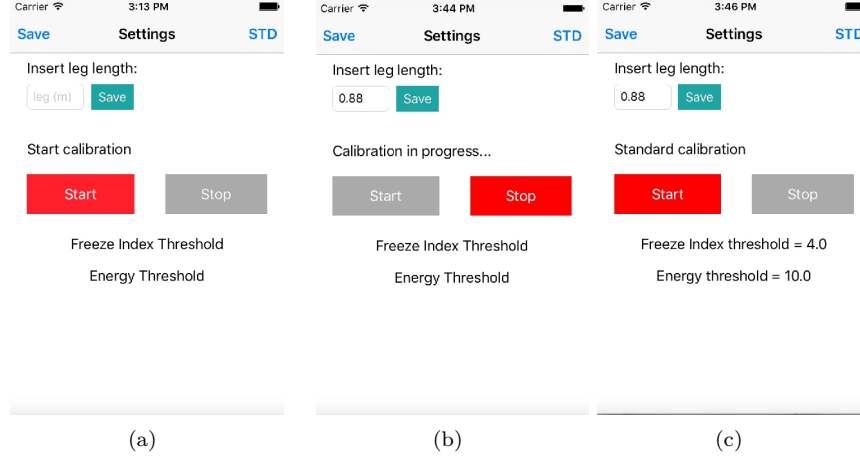


Figure 3.6: (a) Smartphone graphic user interface for settings: it allows to specify leg length and to start and stop the calibration process aimed at setting FI and EN thresholds. (b) Settings user interface during the calibration process: the "Stop" button is the only active. (c) Standard calibration option ("STD" button), which allows the setting of standard threshold values.

domain. Hence, the component "Freezing detection" in Figure 3.2 can be exploded in three components (see Fig. 3.7), two aimed at time and frequency domain features extraction and one responsible of classification.

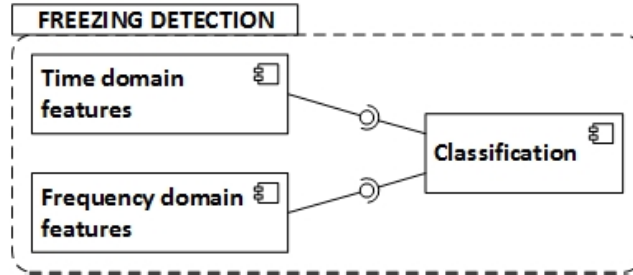


Figure 3.7: Component diagram of the FoG detection software

The smartphone app computes five features from acceleration signal: three frequency domain features and two time domain features. Frequency domain features are FI, EN, and EDR, while time domain features are SC and SL. The processing method used to compute their values is explained in the following paragraphs.

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3.3.1 Freeze Index

The Freeze Index (FI) was defined by Moore et al. [67] on the vertical acceleration signal of the shank. The Fast Fourier Transform (FFT) is applied on acquired data, and then the power spectrum is obtained. FI is finally computed as the ratio between the integral of power spectrum in the band 3–8 ("freeze band") Hz and in the band 0.5–3 Hz ("loco band"):

$$FI(t) = \frac{\int_3^8 \|X(t, f)\|^2 df}{\int_{0.5}^3 \|X(t, f)\|^2 df} = \frac{E_{3-8Hz}}{E_{0.5-3Hz}} \quad (3.1)$$

where $X(f)$ is the FFT of the acceleration signal and t is the current time instant, that is the time instant associated with the last sample in the current window. Since the application runs in real time, the power spectrum X is a function of the time (every window has its own power spectrum) in addition to frequency.

Later, FI computation was extended also to the other acceleration components (antero-posterior and medio-lateral) and to other sensor placements (acceleration signal acquired from the ankle [110, 5], knee [5], thigh [97], hip [89, 50] or trunk [5, 97]).

3.3.2 Energy

The Energy (EN) was introduced by Bachlin et al. [5] in order to reduce the number of false positive when applying the FI for FoG detection. The EN computation follows the FFT of the acceleration signal, as for the FI. Then, once computed the power spectrum of the Fourier Transform, EN is defined as the sum of the integral of the power spectrum (e.g. energy) in the freeze band (3–8 Hz) with the integral of the power spectrum in the loco band (0.5–3 Hz). In formula:

$$EN(t) = \int_{0.5}^8 \|X(t, f)\|^2 df \quad (3.2)$$

where the notation is the same as in Equation (3.1).

3.3.3 Energy Derivative Ratio

The Energy Derivative Ratio (EDR) is a novel feature introduced in this work, when performing elaboration on acceleration data acquired from real patients it was observed that this features could reduce the number of false negatives [50]. The EDR is defined as the ratio of the derivatives of the energy in the

3.3 Extracted features

freeze and loco band:

$$EDR(t) = \frac{\frac{d}{dt} \int_3^8 \|X(t, f)\|^2 df}{\frac{d}{dt} \int_0^{.5} \|X(t, f)\|^2 df} = \frac{\partial E_{3-8Hz}}{\partial E_{0.5-3Hz}} \quad (3.3)$$

Also in this case the notation is the same than in Equation (3.1).

3.3.4 Step Cadence

The Step Cadence (SC) can be estimated in both frequency domain or time domain from the acceleration signal.

SC is the step frequency and hence in the frequency domain it can be calculated as the second harmonic in the power spectrum (continuous component excluded), in fact it is exactly two times the stride frequency¹. Auvinet et al. [123] confirmed that the first power spectrum harmonic concerns stride frequency, while step frequency is the second power spectrum harmonic.

For what concerns the time domain, SC can be estimated by computing the inverse of the step period²:

$$SC = \frac{1}{HS_i - HS_c} \quad (3.4)$$

In the above equation HS_i is the HS time instant of the ipsilateral foot and HS_c is the HS time instant of the contralateral foot in the previous step.

Obviously the two domains contain the same information and hence the two methods are equivalent. However the one that implies less computational effort should be implemented. In the Crisp Logic algorithm the frequency domain method is implemented, since is less computationally demanding (the power spectrum is already required for FI and EN). Instead, in the Fuzzy Logic algorithm the time domain method is more convenient since there is the need to identify heel strike (HS) in order to estimate SL, as it will be explained in the following.

In the literature, several methods were proposed to identify HS from acceleration shape [121, 119, 120, 128, 135]. Some works investigated the detection of gait events also on pathological subjects [154, 155, 156]. Trojaniello et al. [157] compared the performance of five gait events detection methods for the estimation of gait temporal parameters. In this work, three HS detection methods were selected and compared: the method proposed by Zijlstra et al. [121]

¹In gait analysis the term stride stands for the entire gait cycle: the cycle starting from an heel strike and ending with the next heel strike of the ipsilateral foot. Instead, the term step stands for half a gait cycle: from an heel strike to the next heel strike of the contralateral foot

²time between two consecutive heel strikes, hence the heel strike of the ipsilateral and contralateral foot

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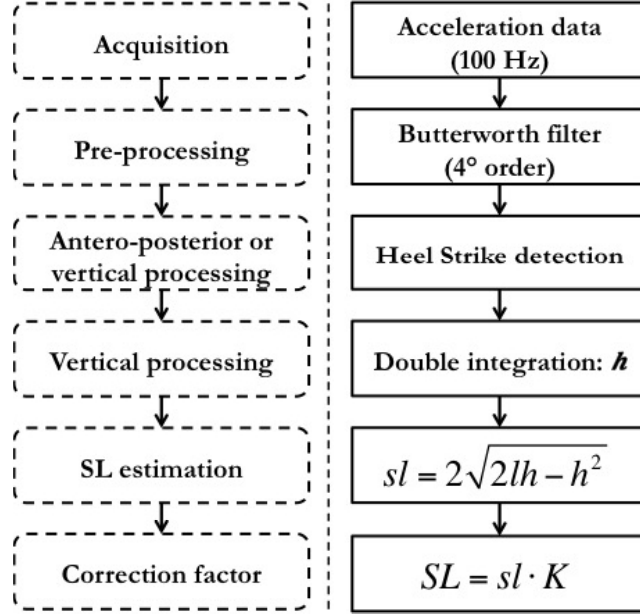


Figure 3.8: Flowchart of the SL estimation process.

(M1), the one proposed by Gonzalez et al. (M2) [119] and the one proposed by McCamley et al. (M3) [120].

In M1, AP acceleration is firstly low pass filtered at 2 Hz (zero lag Butterworth filter, 4th order) and in this signal zero-crossing time instant from positive to negative is identified. Finally the last antero-posterior peak in the 20 Hz filtered signal before zero-crossing is selected as HS [121].

According to M2, AP acceleration must be filtered through an 11th order FIR filter with 2 Hz cut off frequency, which introduces a five-sample delay. In the output signal of the FIR filter, authors search zero-crossing from positive to negative and each time one is found they compute the integral of the same signal between that zero-crossing and the previous zero-crossing from negative to positive. If this area is above a threshold the HS search is started in the same time interval used to calculate the area, otherwise it is considered a false positive. Whenever an area is not discharged, HS is chosen among peaks in the selected interval as the one that satisfies 3 heuristic rules [119].

While methods M1 and M2 search HS in the AP direction, M3 locates HS in the VT one. In particular authors integrate and then differentiate VT acceleration using a Gaussian continuous wavelet transform and they take the minima of the resulting smoothed signal as HSs [120].

The reliability of the three HS detection methods implemented on the smartphone was compared in a laboratory setting on healthy subjects (Section 4.1).

3.3.5 Step length

As explained in Section 2.4, several SL estimation methods were proposed in the literature, but in the proposed system the inverted pendulum model was chosen because it provides a good trade off between computational effort and calibration complexity. Moreover it is a suitable model for the smartphone placement (lower back).

In Figure 3.8 there is the flowchart of the SL estimation process. The first step is data acquisition, which is performed at a frequency of 100 Hz, as anticipated in Section 3.2. Then a 4th order, zero lag, low pass Butterworth filter with cut off frequency of 20 Hz is used to filter raw data, in order to delete noise and preserve frequency band significant for gait [121]. There was not the need to delete continuous component because user acceleration (without gravity) was already retrieved from the smartphone internal sensor.

The third essential step is HS detection: in fact many of the SL estimation methods described in Section 2.4, included the Zijlstra’s method chosen in this thesis, share the identification of HS as the first step. The previous subsection introduced the three HS detection methods that were investigated and compared on healthy subjects. However, only one of them must be implemented in the FoG management smartphone application. The method proposed by Zijlstra et al. [121] was chosen since it offers a good tradeoff between SC and SL estimation errors and computational effort, as it will be discussed in Subsection 4.1.4.

Once HS time instants are known, the vertical change of body centre of mass during a step can be computed from double integration of vertical acceleration between two consecutive HSs. The hypothesis of zero velocity at HS time instant provides initial condition for the first definite integral and keeps out integration drift error.

Then, according to inverted pendulum model, an estimation of SL can be obtained from vertical change of body centre of mass during a step (h) [6]:

$$sl = 2\sqrt{2lh - h^2} \quad (3.5)$$

The value of SL obtained from the above equation underestimates the actual SL, for this reason it must be multiplied for a correction factor K , that the literature suggests to set at 1.25 [130].

3.4 FoG Detection algorithm

Several FoG detection algorithm were developed and tested during these years, in order to find the best performing one. In the next Subsections they will be described in details.

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3.4.1 Moore-Bachlin algorithm

This algorithm was introduced in the literature by the works of Moore et al. [67] and Bachlin et al. [5]. It uses FI and EN: in particular, a FoG episode is detected when both FI and EN exceed their respective threshold:

$$mb \equiv (FI(i) > FI_{th}) \wedge (EN(i) > EN_{th}) \quad (3.6)$$

Where $FI(i)$ and $EN(i)$ are FI and EI values of the current window, FI_{th} and EN_{th} are FI and EN threshold values

In the literature FI threshold is set as universal for all subjects, while in this thesis FI and EN thresholds are user specific and they are computed as mean plus one standard deviation of parameters acquired in a 20 sec period of standing posture.

In Section 3.2 the graphic user interface made available by the application to led the thresholds setting was introduced (Figure 3.6).

3.4.2 Crisp Logic algorithm

This algorithm tries to overcome some limitations of the Moore-Bachlin algorithm. To this purpose, it adds the information of an important temporal parameter of gait (SC) in order to benefit from time domain FoG characterization (Section 2.1). A set of sentences was defined in order to handle start and end of FoG episodes. This algorithm was called "Crisp Logic" since its detection rules are threshold based or they rely on binary³ mathematical operators. Features used by this algorithm are FI, EN and SC. The concepts of SC increase and variation are used in this algorithm, because they are related to FoG start [71, 70], as explained in Section 2.1. For this reason, before defining sentences used to detect start a FOG episode start and stop, sentences used to identify SC increase and variation muse be introduced. In details, the algorithm considers a SC variation and increase according to the following sentences respectively:

$$a \equiv (SC(i) \neq SC(i-1)) \wedge (SC(i-1) \neq SC(i-2)) \quad (3.7)$$

$$b \equiv (SC(i) \geq SC(i-1)) \wedge (SC(i-1) > SC(i-2)) \quad (3.8)$$

where $SC(i)$, $SC(i-1)$, $SC(i-2)$, are the SC values in the last three windows. When condition (3.7) or (3.8) becomes true, the application detects a SC variation or increasing respectively.

Given the above definitions, the algorithm detects a FoG when FI and EI exceed their respective thresholds or when SC is varying or increasing. In

³that can be only true or false and the boundary between this two values is crisp.

3.4 FoG Detection algorithm

formula, the following sentence is used to detect a FoG:

$$mb \vee (a \vee b) \quad (3.9)$$

Where mb is the binary rule expressed in Equation 3.6 and finally a and b are the binary rules reported in Equations (3.7) and (3.8).

3.4.3 Fuzzy Logic algorithm

The impossibility to handle uncertainty is one of the most important limitation of logic based knowledge representation [158]. For this reason, the FoG detection agent was provided with more intelligence and hence with the possibility to handle uncertainty. In particular fuzzy logic was selected as a suitable knowledge representation. This choice was made for two main reasons. Firstly, fuzzy logic has the important advantage of an intuitive knowledge representation in the form of linguistic *if...then* rules expressed in a natural language, that enable an easy translation of clinical knowledge about the phenomenon into the inference system. A crisp value can be only above or under a certain threshold, while a fuzzy value can be "low", "medium", "high", or even "quite high", "quite low", thus being nearer to the natural language of people. Thus, using fuzzy logic, the FoG detection algorithm can be provided with the same knowledge of clinicians, because it uses the same language. However, like crisp variables need the assignment of a threshold, fuzzy variables need appropriate fuzzy sets identifying the domain zones related to linguistic terms. Secondly, probability, which is another important approach to uncertain reasoning, was already tested in previous works [98, 89].

Fuzzy rule-based systems have been successfully employed for system modeling in many areas. Depending on the intended application, fuzzy modeling research field can be divided into different approaches. The first is the linguistic fuzzy modeling where good human interpretability of the underlying fuzzy model is paramount for tasks such as knowledge mining and data analysis. This is usually achieved by adopting the Mamdani rule structure for knowledge representation. The other is the precise fuzzy modeling where Takagi-Sugeno and Tsukamoto fuzzy rule structures are generally used in the learned fuzzy model to achieve high output accuracies for function approximation and regression-centric applications. The approach considered for the FOG detection algorithm is the linguistic fuzzy modeling with Mamdani rule structure, in order to give the best interpretability to the rules.

The membership functions of the variables involved in the fuzzy system consist of triangular asymmetric and trapezoidal functions. The trapezoidal fuzzy set A in the universe of discourse U (the real line $\mathbf{R}$) with the membership function μ_A is parameterized by four real scalar parameters: (a, b, c, d) with

Chapter 3 Materials and Methods

$a < b \leq c < d$. This representation can be interpreted as a mathematical membership function as follows:

$$\mu_A(x) = \begin{cases} 0, & x < a \\ \frac{x-a}{b-a}, & a < x < b \\ 1, & b < x < c \\ \frac{d-x}{d-c}, & c < x < d \\ 0, & x > d \end{cases} \quad (3.10)$$

When $b = c$, the triangular function can be considered as a particular case of the trapezoidal one.

Let A and B be two fuzzy sets in the universe of the discourse U and let the membership functions of the fuzzy sets A and B be μ_A and μ_B , respectively. The intersection between the fuzzy sets A and B is defined as follows:

$$\mu_{A \cap B}(x) = \min \{ \mu_A(x), \mu_B(x) \}, \quad \forall x \in U \quad (3.11)$$

The union between the fuzzy sets A and B is defined as follows:

$$\mu_{A \cup B}(x) = \max \{ \mu_A(x), \mu_B(x) \}, \quad \forall x \in U \quad (3.12)$$

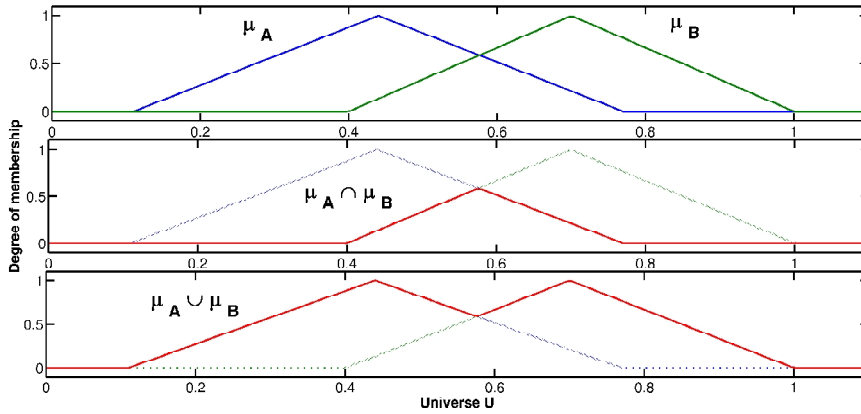


Figure 3.9: Sample of two fuzzy sets (fig. a) and their intersection (fig b.) and union (fig c.).

Two fuzzy inference systems were designed:

- the first system takes in input FI, EN, EDR and SC (because SL computation was not already included in the smartphone app);

3.4 FoG Detection algorithm

- the second systems takes in input FI, EN, EDR, SL and SC.

FI and EN are normalized over their respective threshold before enter the FIS. SL is normalized over the leg length.

Offline fuzzy inference system

The first fuzzy inference system was implemented offline in Matlab, with the aim of improving the smartphone performance in FoG detection. This optimization was conducted on data collected during the experimental session planned to test the Crisp Logic algorithm, as will be explained in Section 4.2.3.

Due to the episodic, heterogeneous and erratic nature of FoG it can happen, with the use of Moore-Bachlin and Crisp Logic algorithm, the occurrence of a false negative when a window is classified as non-FOG despite the patient manifests the symptom in that time instant. An accurate analysis was performed on the acquired data, comparing them to the FoG episodes occurred during video recording. In particular, Fig. 3.10 shows a sample of freezing occurrence hard to identify considering only "Freeze Index", "Energy" and "Step Cadence", which were the Crisp Logic algorithm features.

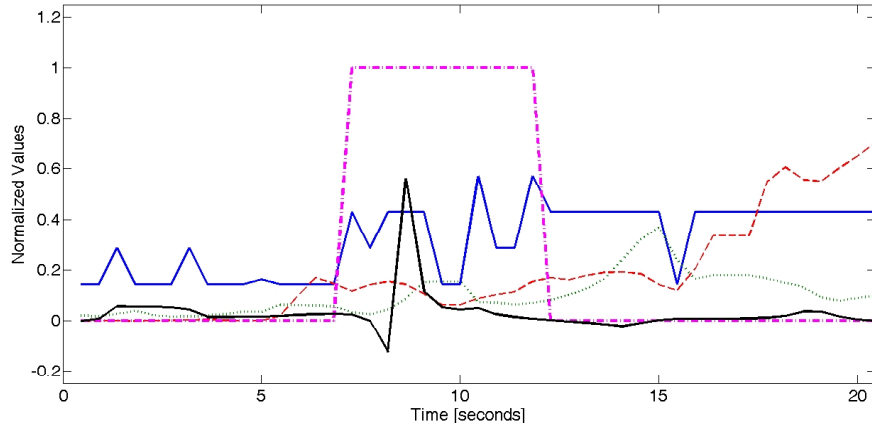


Figure 3.10:

Freezing of Gait occurrence A (purple dotted line) and related variables. Cadency (blue continuous line), Freeze Index (red dashed line), energy sum (green dashed line) and energy derivative ratio (black continuous line).

The analysis of such occurrences let us consider the introduction of the new variable "Energy Derivative Ratio" defined in Section 3.3 that, combined with the step cadence information, could overcome some false negative episodes.

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Table 3.1:

Considered fuzzy sets for the input variables: linguistic terms and their corresponding trapezoidal fuzzy sets.

Input variables	Linguistic terms	Fuzzy sets (a, b, c, d)
Freeze Index	Low	0 , 0 , 0.25 , 0.5
	Medium	0.3 , 0.5 , 0.7 , 0.9
	High	0.75 , 1.0 , 1.25 , 1.5
	Very High	1.25 , 1.5 , $+inf$, $+inf$
Energy	Low	0 , 0 , 0.3 , 0.5
	Medium	0.3 , 0.5 , 0.7 , 0.9
	High	0.7 , 0.9 , $+inf$, $+inf$
Step Cadence	Zero	0 , 0 , 0.25 , 0.5
	Low	0.25 , 0.5 , 0.75 , 1
	Medium	0.75 , 1 , 1.75 , 2.25
	High	1.75 , 2 , $+inf$, $+inf$
Energy	Negative Big	$-inf$, $-inf$, -0.5 , -0.2
Derivative	Negative Small	-0.5 , -0.2 , -0.1 , 0
Ratio	Zero	-0.05 , -0.01 , 0.01 , 0.05
	Positive Small	0 , 0.1 , 0.2 , 0.5
	Positive Big	0.2 , 0.5 , $+inf$, $+inf$

Fuzzy sets designed for this system are shown in Table 3.1, and Fig. 3.11 shows a graphical example about the feature EDR. FI and EN input variables are normalized over their respective thresholds.

Fig. 3.12 shows another FoG occurrence clearly identifiable considering: only an "high" value of the Freeze Index (seconds 21 – 26), an "high" value of the Energy coupled with a "high" step cadence variation in the middle of the window and, at the end of this freezing episode, a "medium" step cadence variation together with a "high" energy derivative ratio and a "medium" energy.

A sample of the fuzzy rule base consequently obtained is shown in Table 3.2.

The output of the offline fuzzy inference system engine is the $FOG_{likelihood}$ and fuzzy sets are: (L) Low, (M) Medium, (H) High, (VH) Very High. The output membership functions are shown in Fig. 3.13 and their values are reported in Table 3.3.

The Max-Min fuzzy inference algorithm is considered. The fuzzy logic controller uses the following equation in the defuzzification phase:

$$mCoA = \frac{\int f(x) \cdot x dx}{\int f(x) dx} \quad (3.13)$$

3.4 FoG Detection algorithm

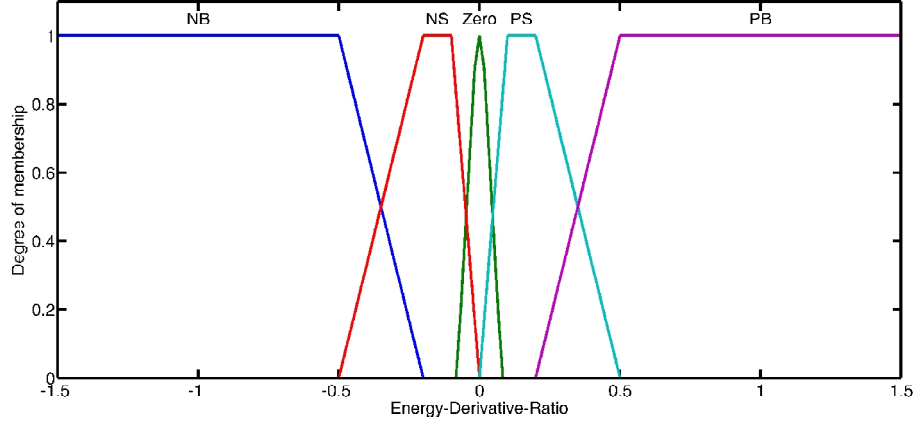


Figure 3.11:
Fuzzy sets for the input variable *EnergyDerivativeRatio*.

where mCoA is the modified center of area and $f(x)$ the output of the inference process. The interval of integration is between the minimum membership function value and the maximum membership function value. Note that this interval might extend beyond the range of the output variable.

After the defuzzification process $FOG_{likelihood}$ is obtained and a FoG occurrence is determined when the $FOG_{likelihood}$ has a value greater than 0.5.

Online fuzzy inference system

For what concerns the second fuzzy inference system, it was implemented on the smartphone for online usage. Since CPU and RAM management is a critical issue when performing real time processing tasks on a mobile device, the system was designed as a cascade of two subsystems (as shown in Fig. 3.14), thus reducing its computational weight.

Frequency parameters (FI, EN and EDR) are sent as input to the first engine, which produces a first FOG likelihood in output. This FoG likelihood becomes the input of the second engine together with SC and SL. Values chosen for the fuzzy sets are reported in Table 3.4 and a graphical sample is shown in Fig. 3.15. FI and EN values are normalized over their respective thresholds and SL is normalized over leg length.

Both the partial output FOG_f and the overall output $FOG_{likelihood}$ have the same fuzzy sets described previously (Fig. 3.13 and Table 3.3).

The entire set of fuzzy rules for the frequency engine and the time engine is reported in Table 3.5 and 3.6 respectively.

Also this fuzzy inference system uses the Max-Min fuzzy inference algorithm.

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Table 3.2:

FIS sample. The last column, the fuzzy inference system output, is the likelihood to have a FOG event.

FI	EN	SC	EDR	FOG
VH	H	-	-	VH
H	H	-	-	H
H	M	-	NS	H
H	H	-	NB	VH
H	-	H	-	VH
M	L	-	PB	H
M	L	-	NB	VH
M	H	Z	-	L
L	H	Z	-	L

Table 3.3:

Considered fuzzy sets for output variables: linguistic terms and their corresponding trapezoidal fuzzy sets.

Output variables	Linguistic terms	Fuzzy sets (a, b, c, d)
FOG	Low	0 , 0 , 0.1 , 0.2
	Medium	0.1 , 0.2 , 0.4 , 0.5
	High	0.4 , 0.5 , 0.7 , 0.8
	Very High	0.7 , 0.8 , 1 , 1

3.4 FoG Detection algorithm

Table 3.4:

Considered fuzzy sets for the input variables: linguistic terms and their corresponding trapezoidal fuzzy sets.

Input variables	Linguistic terms	Fuzzy sets (a, b, c, d)
Freeze	Low	0 , 0 , 0.25 , 0.5
Index	Medium	0.3 , 0.5 , 0.7 , 0.9
	High	0.75 , 1.0 , 1.25 , 1.5
	Very High	1.25 , 1.5 , $+inf$, $+inf$
Energy	Low	0 , 0 , 0.3 , 0.5
	Medium	0.3 , 0.5 , 0.7 , 0.9
	High	0.7 , 0.9 , $+inf$, $+inf$
Energy	Negative Big	$-inf$, $-inf$, -0.5 , -0.2
Derivative	Negative Small	-0.5 , -0.2 , -0.1 , 0
Ratio	Zero	-0.05 , -0.01 , 0.01 , 0.05
	Positive Small	0 , 0.1 , 0.2 , 0.5
	Positive Big	0.2 , 0.5 , $+inf$, $+inf$
Step	Low	0 , 0 , 0.7 , 0.9
Cadence	Medium	0.8 , 1 , 1.7 , 1.9
	High	1.8 , 2 , $+inf$, $+inf$
Step	Low	0 , 0 , 0.7 , 0.9
Length	Medium	0.8 , 1 , 1.7 , 1.9
	High	1.8 , 2 , $+inf$, $+inf$

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Table 3.5: Frequency engine. The last column, the fuzzy inference system output, is the likelihood to have a FoG event, according to frequency parameter.

EDR	FI	EN	FOG_f
NB	L	-	H
NB	M	-	VH
NB	H	-	VH
NS	L	-	L
NS	M	L	L
NS	M	M	M
NS	M	H	M
NS	H	L	M
NS	H	M	H
NS	H	H	H
Z	L	-	L
Z	M	L	L
Z	M	M	L
Z	M	H	M
Z	H	L	M
Z	H	M	H
Z	H	H	H
PS	L	-	L
PS	M	L	L
PS	M	M	M
PS	M	H	M
PS	H	L	M
PS	H	M	H
PS	H	H	H
PB	L	-	H
PB	M	-	VH
PB	H	-	VH
-	VH	-	VH

3.4 FoG Detection algorithm

Table 3.6: Time engine. The last column, the fuzzy inference system output, is the likelihood to have a FoG event.

FOG_f	SC	SL	$FOG_{likelihood}$
L	L	L	M
L	L	H	M
L	M	-	L
L	-	M	L
L	H	L	H
L	H	H	M
M	L	L	H
M	L	H	H
M	L	-	L
M	-	M	L
M	H	L	VH
M	H	H	M
H	L	L	H
H	L	M	M
H	M	L	H
H	M	M	M
H	H	-	VH
H	-	H	VH
VH	L	M	H
VH	L	H	VH
VH	M	M	M
VH	M	H	H
VH	H	-	VH
VH	-	L	VH

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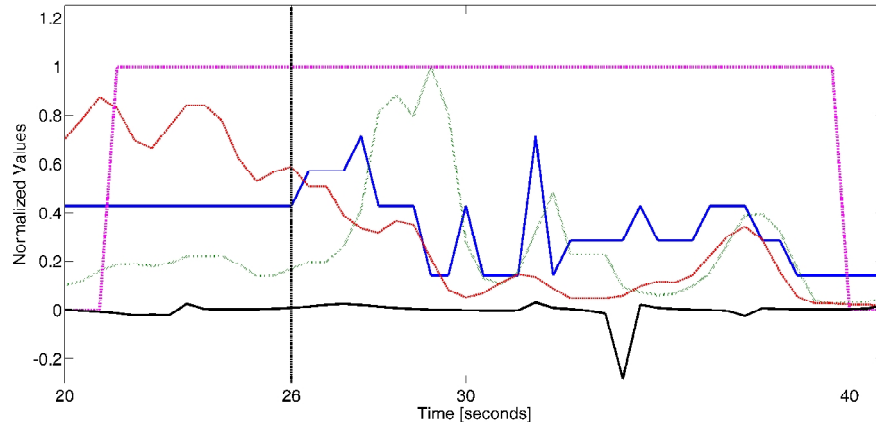


Figure 3.12:

Freezing of Gait occurrence B (purple dotted line) and related variables. Step Cadence (blue continuous line), Freeze Index (red dashed line), energy sum (green dashed line) and energy derivative ratio (black continuous line).

For what concerns the defuzzification process, it is the same introduced in the previous paragraph for the offline system, hence it uses the modified center of area to calculate the output of the inference process ($FOG_{likelihood}$).

After the defuzzification process a FoG occurrence is determined when the $FOG_{likelihood}$ has a value greater than 0.6.

The second Fuzzy Inference system was implemented on the smartphone (iOS and Android operative systems) using the fuzzy logic library developed in C++ and Java programming languages by Juan Rada-Vilela [159].

3.5 Server

Data collected by the smartphone app during FoG monitoring are sent to a server where they are stored in a database and managed by a web application in order to retrieve and present useful information.

3.5.1 Database

The database at the clinical server stores the following information: web app users' personal details, patients' monitoring data from the smartphone app, pharmacological and rehabilitation therapies assigned by clinicians to patients. The entity-relationship model of the DB is shown in Figure 3.18. MySQL was used to create and manage the DB.

3.5 Server

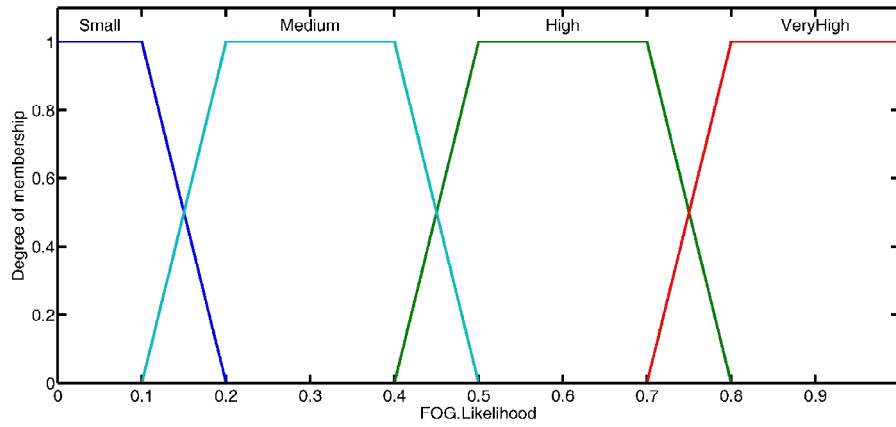


Figure 3.13:
Fuzzy sets for the output variable $FOG_{likelihood}$.

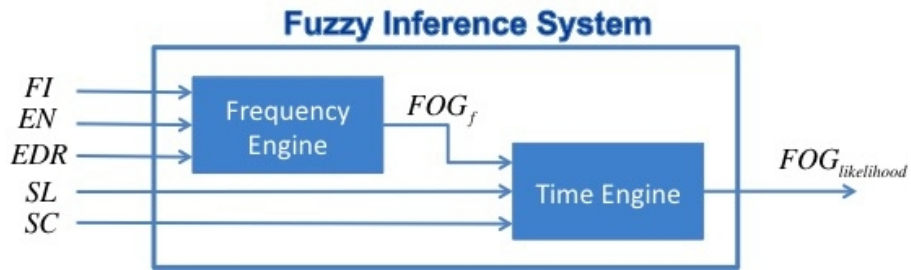


Figure 3.14:
Fuzzy inference system implemented on the smartphone.

3.5.2 Web app

Web app users can be the primary (or administrator), clinicians or patients and each of them has dedicated areas protected by authentication. The web app allows users to communicate with the central DB and to consult information of interest through dedicated graphic interfaces.

On the basis of the user logged in, the web app allows the following functions:

- Clinician:
 - FoG monitoring data consultation, with the possibility filter the search for date, time or parameter values;
 - pharmacological and rehabilitation therapy assignment to their patients.
- The Primary has the same functions of the clinicians and in addition:

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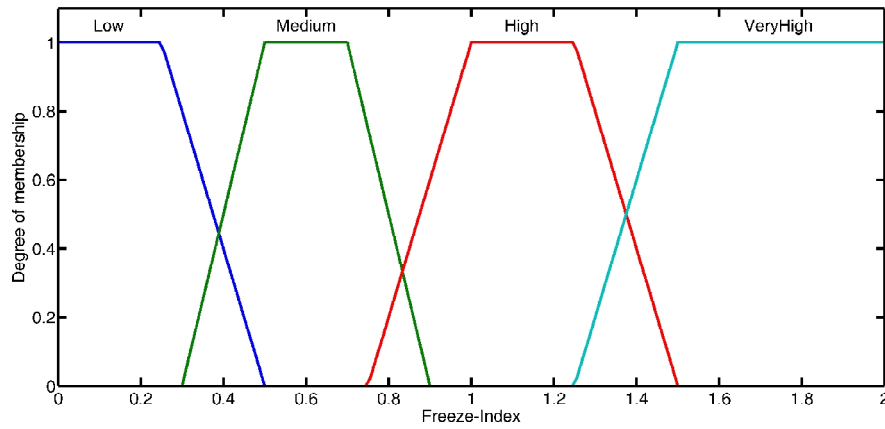


Figure 3.15: Fuzzy sets for the input variable *FreezeIndex*. The x-axis is the ratio between the actual *FreezeIndex* computed and the threshold.

- users management: to insert, delete, and modify web app users;
 - drugs management: to insert, delete, and modify the drugs that can be used to define pharmacological therapies;
 - motor exercises management: to insert, delete, and modify the motor exercises that can be used to define at home rehabilitation therapies.
- Patient:
 - visualize rehabilitation and pharmacological therapy assigned to him;
 - manually loading FoG monitoring data.

An overview of users and their functions is given by the use case diagram in Figure 3.16.

More in details, clinician’s area offers the consultation of FoG monitoring data, for example requesting the number of FoG episodes in a given time interval or parameters trend during a FoG. In particular the search can be filtered by time interval, FoG duration, parameter values (equal, grater or less than a specified value or comprise to specified values). Furthermore the app can display search results in dedicated graphic plots.

Each clinician is allowed to consult only data of her/his own patients, while the primary can see the information of all the patients followed by the clinic.

Figure 3.17 shows some screenshots about the function of FoG monitoring data consultation in clinicians area.

3.5 Server

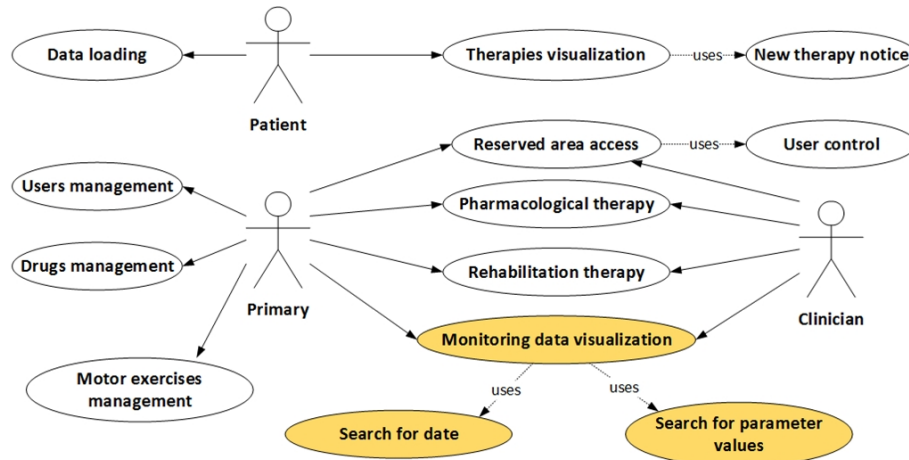


Figure 3.16: Use case diagram of the web app.

Another important function of the clinician’s area is the possibility to remotely update patients’ pharmacological and rehabilitation therapies. In this way, if the clinician perceives important changes in the health status of her/his patients, she/he can change their therapies without the need to wait for the next medical examination.

Patient’s area allows her/him to see the actual pharmacological and rehabilitation therapy. A message alerts the patient as soon as a change involving any therapy has happened. The message appears after each login until the patient visualizes the changes. Furthermore, in the patient reserved area, there is also the possibility to manually upload FoG monitoring data. The smartphone application automatically sent these data, but however, for users that feel really confident with technology, this function allows the uploading even if the smartphone has some problem of Internet connection.

Figure 3.17: Web app clinician area.

3.5 Server

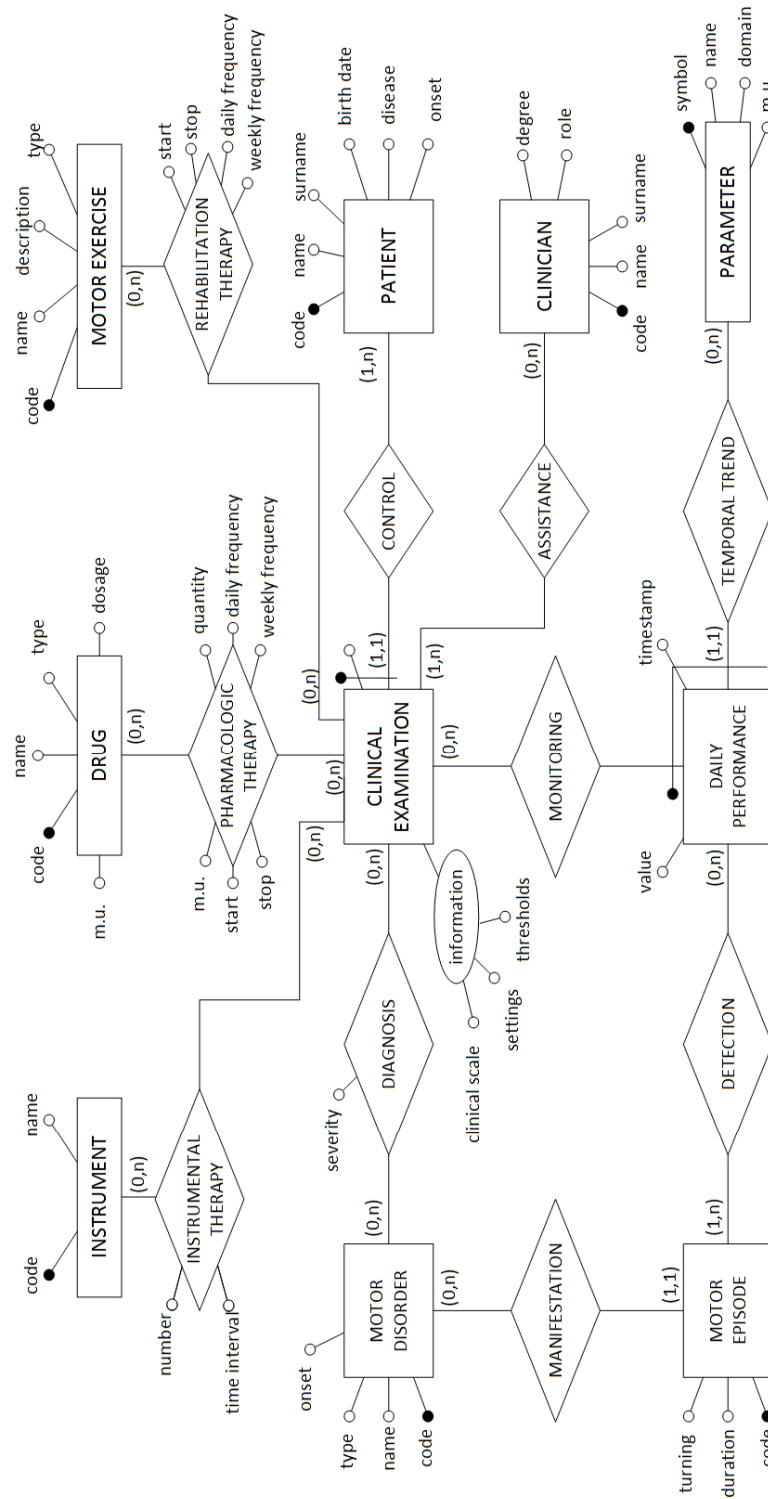
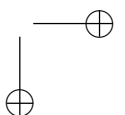
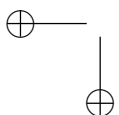
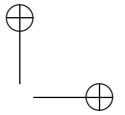
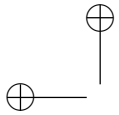


Figure 3.18:
Entity-relationship model of the database.



Chapter 4

Tests and Results

In this chapter experimental protocols used to evaluate the system and results will be presented. Tests on two categories of subjects must be carried out: on healthy and pathological ones.

First of all, since the proposed architecture uses the smartphone to estimate some important spatio-temporal parameters of gait (SC and SL), smartphone reliability assessed through comparison with stereophotogrammetry. In fact, whenever there is an estimation process for a parameter, it becomes necessary to validate the parameter estimate obtained from the proposed method against the parameter measure obtained with gold standard. This procedure is not necessary for frequency parameters (FI, EN, and EDR), since they were defined on the accelerometer signal ¹, hence the smartphone provides actually a measure of these parameters and not an estimate. Experimental set up, subjects, evaluation criteria and results of this phase are presented in Section 4.1.

Then, once verified smartphone reliability in gait analysis, its performance in FoG detection was evaluated on patients with PD. Experimental set up, subjects and evaluation criteria are explained in Section 4.2, while results are presented in Section 4.3.

4.1 Healthy subjects

Tests carried out on healthy subjects had the primary objective of assessing smartphone reliability in the estimation of spatio-temporal parameters of gait, in particular SL and HS (SC estimation is a direct consequence of HS detection). If the outcome was positive, these parameters would be used for FoG detection, given the strong relationship between time instants before and during a FoG and spatio-temporal parameters of gait [70], as discussed in Chapter 2, Section 2.1.

¹FI was defined by Moore et al. [67] on the vertical acceleration of the shank, but it was later extended to all sensor placement and axes [97]. EN was defined by Bachlin et al. [5] on the acceleration signal (all axes and placements). EDR was defined during this work [50]. Furthermore, these features lose significance for healthy subjects, since they were defined on patients with PD properly for FoG detection.

Chapter 4 Tests and Results

A first issue to take into account when approaching to the problem of gait analysis through a smartphone is that it may introduce inaccuracies in sensor placement. In fact, once attached to the human body, contact between the wide phone surface and body contours can cause a misalignment between accelerometer axes and the axes of a fixed reference frame (RF) (Fig. 4.5), identifying the actual movement directions (antero-posterior (AP), vertical (VT) and medio-lateral (ML)). The acceleration measured in the smartphone RF was corrected by expressing the vector in two RFs with the axes defined in order to be parallel to the actual AP, VT and ML directions.

As explained in Section 3.3 of Chapter 3, the inverted pendulum model was adopted for SL estimation, since it is particularly suitable for our hardware configuration (a smartphone placed on the lower back). The estimation obtained with Equation (3.5) was corrected by a multiplication factor K , that was optimized for each subject through the least square method.

Heel strike (HS) detection is a critical issue for this approach, as a matter of fact several methods have been proposed in the literature to locate HS in the typical acceleration shape of the lumbar region during gait. Some of these methods were selected and compared: the method proposed by Zijlstra et al. [121] (M1), the one proposed by Gonzalez et al. (M2) [119] and the one proposed by McCamley et al. (M3) [120].

Hence two main objectives were addressed with this study:

1. using a smartphone to estimate SL through the inverted pendulum model applying different HS detection methods;
2. evaluate the effects of smartphone placement on system performance.

4.1.1 Experimental set up

The reliability of our system for SL computation was evaluated by comparison with a stereophotogrammetric system composed of six infrared cameras, which acquired the position of reflective markers in a fixed RF at 100 Hz sample frequency.

Eleven healthy subjects (8 males, 3 females), aged between 22 and 30 years, took part in the tests. Each subject performed 9 walking trials, 3 at their normal (preferred) speed, 3 at higher speed and 3 at lower speed. Subjects were only said to walk at 'normal', 'high' and 'low' velocity, leaving actual values chosen by each subject's habit. During each trial, subjects were asked to walk forth and back along a straight platform (about 10 meters) inside the visual field of infrared cameras. Nine reflective markers were placed on pelvis and feet. The pelvis was identified by three markers: two over the left and right anterior superior iliac spines and the third on the middle point between

4.1 Healthy subjects

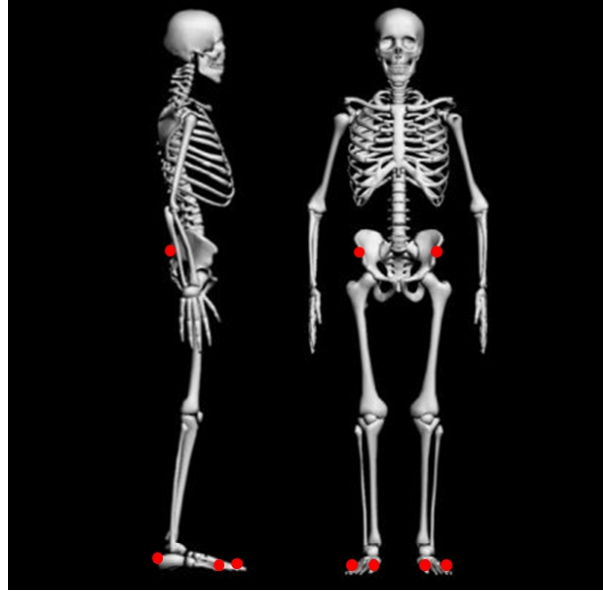


Figure 4.1: Markers' placement during tests.

the posterior superior iliac spines (in particular, this position coincides with the smartphone surface). Each foot was identified by three markers placed on: heel, first and fifth metatarsal head. Markers' position is shown in Fig. 4.1.

During trials simultaneous acceleration signal was acquired from the smartphone placed at subject's lower back. Each trial started with the execution of a jump, which was used as synchronizing event for smartphone data and stereophotogrammetric data. Fig. 4.2 shows VT position and VT acceleration signals of the marker placed over the smartphone surface during the jump. The acceleration trend was obtained by double differentiation of the position. The overlapping of the two shapes shows a correspondence between the sample of maximum height and a middle relative peak in the VT acceleration shape.

Furthermore, using the timestamp of smartphone's samples, the actual sample frequency could be inferred, because retrieving data from smartphone sensors could not happen at a perfectly correct and fixed rate, as in the gold standard. A resample of the signal with lowest sample frequency between smartphone and infrared cameras was made in order to reach the same length. In conclusion, by using the jump and resampling, alignment of stereophotogrammetric and smartphone signals in time was reached.

After each experimental session, the angle between magnetic north and walking platform was measured by the use of a digital compass. This data was used to align the north RF with the walking platform.

Figure 4.3 shows the Matlab graphic user interface developed in order to

Chapter 4 Tests and Results

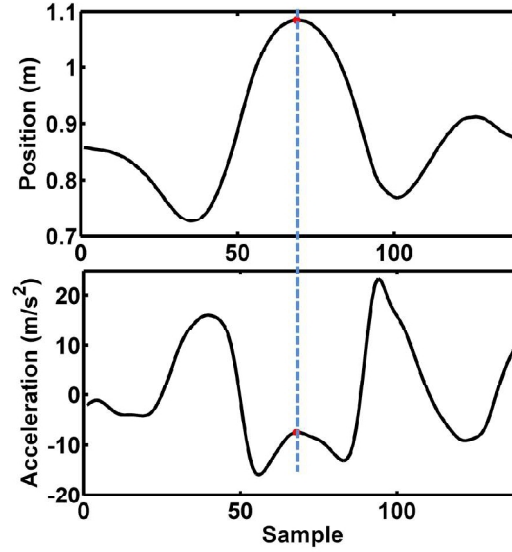


Figure 4.2: Position (top plot) and acceleration (bottom plot) signal of the VT coordinate of the marker placed on the middle point between the posterior superior iliac spines (and hence on smartphone surface) during a jump. The sample that reaches the maximum in height corresponds to the middle relative peak of the acceleration shape.

synchronize smartphone data with stereophotogrammetric data and to evaluate smartphone reliability in HS detection and SL estimation. The top plot of the interface shows the smartphone vertical acceleration data of an entire trial (starting with a jump, followed by forth and back inside the visual field of infrared cameras). By zooming in the jump segment the sample corresponding to the point of maximum height in the jump can be founded. Middle plots shows antero-posterior accelerations of forth and back steps recorded by the cameras: red dots indicate real HS time instants, obtained from the gold standard, while green dots correspond to the HS time instants estimated by the Zijlstra’s method (M1). Finally in the bottom plots there are estimation errors for forth and back steps.

Data acquisition

The component diagram of the smartphone application was firstly presented in Figure 3.2, then, in Figure 3.7, a zoom on the FoG detection component was made. Now the interest is on time domain feature estimation, hence the a further explosion on the component "Time domain features" is given in Fig. 4.4. It must be specified that this part of the software was implemented also

4.1 Healthy subjects

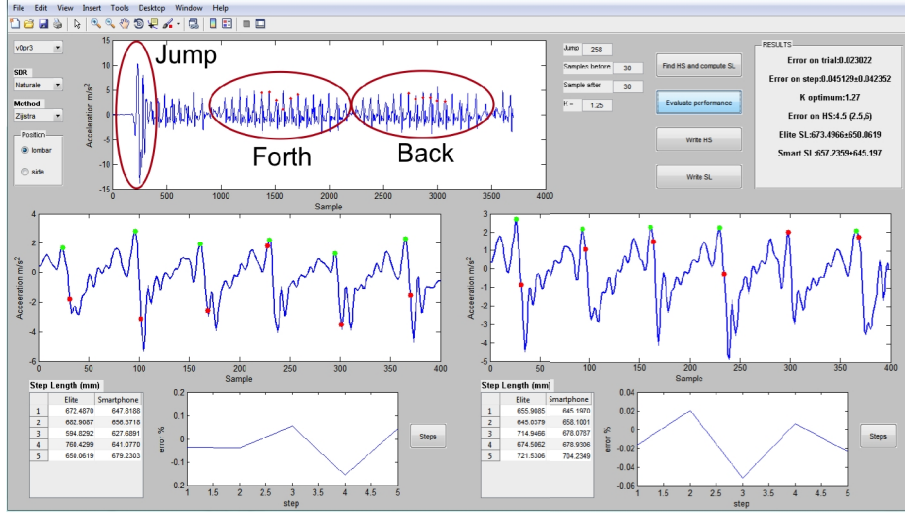


Figure 4.3: Matlab graphic user interface used to synchronize and elaborate smartphone data. The top plot of the interface shows the smartphone vertical acceleration data of an entire trial (starting with a jump, followed by forth and back inside the visual field of infrared cameras). Middle plots shows antero-posterior accelerations of forth and back steps recorded by the cameras: red dots indicate real HS time instants, obtained from the gold standard, while green dots correspond to the HS time instants estimated by the Zijlstra’s method (M1). Finally in the bottom plots there are estimation errors for forth and back steps.)

offline in Matlab in order to make possible a reliable data analysis. In fact there is the need of synchronization to compare single steps between smartphone and stereophotogrammetric system, but the two systems can be synchronized only offline. Furthermore the focus of this phase of study is the comparison of several HS detection methods and several RFs, while only one of them can run during online functioning.

For this reason, also the component "Data acquisition" of Figure 3.2 was slightly modified. In particular, during this experimental session, the smartphone app acquired data from onboard sensors at a sample frequency of 100 Hz and stores them in a text file. The application saved the following data: tri-axial acceleration in the smartphone RF (Fig. 4.5), rotation matrix of smartphone RF with respect to a north RF, rotation matrix of the smartphone RF with respect to a particular RF defined manually and finally the timestamp of each sample.

The north RF was defined in the following way: positive x pointed towards magnetic north and positive z had the same direction of gravity but with

Chapter 4 Tests and Results

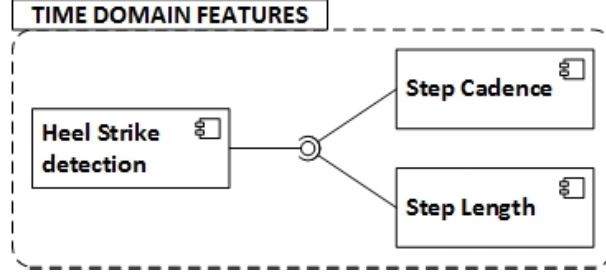


Figure 4.4: Component diagram of the SL estimation application.

opposite sign. For what concerns manual RF: positive y direction was inside a plane parallel to the floor and pointed toward the forward walking direction (like x -axis of laboratory RF in fig. 4.5), positive z was perpendicular to the floor and points upward.

North RF and manual RF was used to take into account possible errors in smartphone placement. In fact the smartphone is bigger than an inertial sensor and furthermore, while inertial sensors are attached to the body, an elastic belt is used to hold the smartphone in the right position. This two differences with respect to the use of inertial sensors can lead to a non-coincidence of accelerometer axes with AP, ML and VT axes of the subject. After launching, the application asked the user to calibrate the compass through a dedicated user interface, which suggested the user to move the smartphone in a certain way. This operation was essential to allow the smartphone to correctly identify magnetic north and hence compute the rotation matrix of smartphone with respect to north RF.

4.1.2 Evaluation

The first objective of this test was the evaluation of smartphone reliability in SL estimation through the inverted pendulum model applying three HS detection methods. Hence two aspects of the system were evaluated: the performance 'in time', that is the accuracy in HS detection, and the performance 'in space', hence the accuracy in SL estimation. Since three HS detection methods were tested, all the features used for assessing these two aspects were computed for each method.

The second objective was to evaluate the effects on performance of three different RFs defined in the smartphone, hence both the data analysis explained above were performed not only across different HS detection methods but also for each of the three RFs considered. In conclusion, each variable introduced to evaluate the performance was computed for nine scenarios, generated from the combination of HS detection methods and RFs considered.

4.1 Healthy subjects

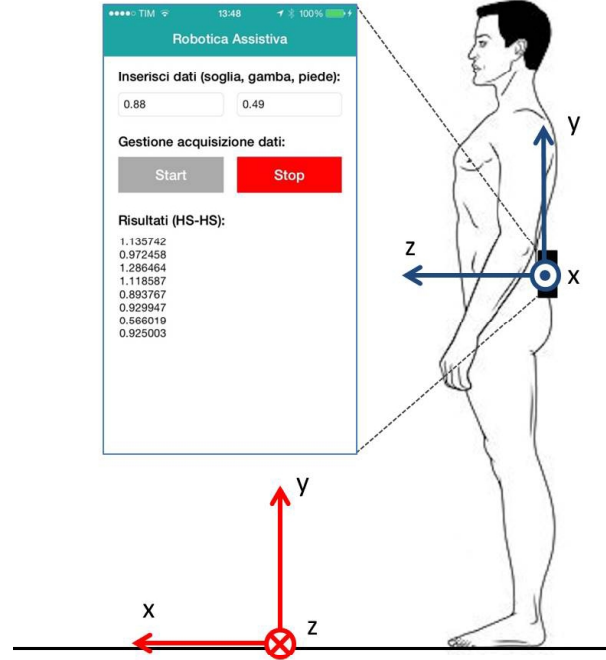


Figure 4.5: Smartphone placement and accelerometer reference frame (blue), laboratory reference frame (red)

The hypothesis of normal distribution for each subject’s SL and step cycle duration was tested prior to elaborate data, in order to verify the correctness of mean and standard deviation as statistical indicators for the overall performance. Subject’s steps were grouped by velocity and each group of steps was submitted to Lilliefors test to assess the validity of the hypothesis of normal distribution. The participant group was homogeneous; consisting of young, healthy individuals without reported injuries. Performance differences between subjects were assessed with an ANOVA test on inter-subject variability.

For what concerns the error in time, hence in HS detection, first of all the performance of the nine scenarios was evaluated through the sensitivity of step detection (a step is detected if both the HS delimiting it were detected): number of detected steps over total steps. Then the accuracy of HS detection was assessed by computing for each HS the difference in seconds between the real one and the estimated one. Real HSs were found by visually inspecting markers movement during trials, in particular the trajectory of markers on heel.

The evaluation of SL estimation was carried out by computing the estimation error on single steps and on distance covered during each trial. For what concerns single steps, estimation error was computed according to the next

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formula:

$$e_s = sl_g - sl_s \quad (4.1)$$

where sl_g is the gold standard SL and sl_s is the estimated SL, hence the measurement unit of e_s is *cm*. The dimensionless trial error was calculated in the following way:

$$e_t = \frac{\|distance_g - distance_s\|}{distance_g} \quad (4.2)$$

where $distance_g$ is the distance covered during the trial, obtained summing all the trial SLs measured by the gold standard, whereas $distance_s$ is the estimation of the distance covered during the trial, obtained with the cumulative sum of the estimated SLs for that trial.

4.1.3 Results

Table 4.1 reports subjects’ anthropometric data, number of steps and linear velocity (mean and standard deviation) for each subject at the three different paces.

A total of 974 steps were collected from all the trials: 387 for low velocity, 319 for normal velocity and 268 for high velocity.

Lilliefors test did not reject the hypothesis of normal distribution for subjects’ SLs and step cycles at the three velocities. The level of significance was set at 0.01. Hence mean and standard deviation of estimation errors were reported for both SL and HS.

ANOVA tests for inter-subject variability was applied to subjects’ errors in SL and HS detection across all the nine scenarios. It revealed that there are no statistically significant differences in performance among subjects, since the probability of the null hypotheses that all groups have the same mean was always higher than 0.98. As a consequence, estimated SL and HS confidence are averaged for the participant group.

In the following subsections results about smartphone reliability in HS detection and SL estimation are presented.

Heel Strike

The sensitivity of step detection is reported in Table 4.2, grouped by velocities. Each row describes the performance of a particular scenario. In details, M1, M2 and M3 indicate the three HS detection methods adopted (as explained in section 3.3), while the smartphone, north and manual RF are denoted by SM, NO and MA respectively.

4.1 Healthy subjects

Table 4.1: Subjects’ anthropometric data, steps and velocities ranges

Subj	Sex	BMI kg/m^2	Leg cm	Low velocity			Normal velocity			High velocity		
				Steps	Mean (m/s)	SD (m/s)	Steps	Mean (m/s)	SD (m/s)	Steps	Mean (m/s)	SD (m/s)
1	F	19.5	88.5	42	0.88	0.07	33	1.25	0.06	29	1.68	0.18
2	M	27.7	91.6	40	0.87	0.07	31	1.41	0.07	24	2.17	0.12
3	M	28.4	80.5	38	1.01	0.05	33	1.18	0.04	30	1.58	0.05
4	M	20.4	87.5	35	1.14	0.07	30	1.44	0.07	24	2.26	0.10
5	M	20.1	86.4	32	1.19	0.06	26	1.64	0.04	24	2.09	0.08
6	F	20.9	88.0	32	0.69	0.07	29	1.34	0.06	24	1.75	0.07
7	M	25.9	89.1	31	0.65	0.02	26	1.03	0.06	22	1.48	0.07
8	F	20.8	64.7	42	0.66	0.06	31	1.23	0.07	27	1.63	0.09
9	M	25.7	87.0	32	0.88	0.07	26	1.39	0.07	21	1.96	0.07
10	M	23.8	88.6	35	0.78	0.04	31	1.18	0.04	25	1.54	0.10
11	M	21.2	87.5	28	1.08	0.05	23	1.37	0.05	18	2.01	0.06

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Table 4.2: Sensitivity results

HS	RF	Low	Normal	High
M1	SM	98.97%	96.87%	98.88%
M1	NO	74.42%	85.27%	82.46%
M1	MA	80.88%	90.28%	66.04%
M2	SM	71.32%	71.16%	57.09%
M2	NO	51.16%	55.49%	51.49%
M2	MA	55.04%	63.95%	44.78%
M3	SM	93.28%	100%	100%
M3	NO	96.12%	100%	100%
M3	MA	96.12%	100%	100%

The other variable used to evaluate HS detection accuracy was the distance in seconds between the real HS and the estimated HS. Table 4.3 shows mean and standard deviation (named SD in the table) of HS detection errors for different velocities among the nine scenarios. For each scenario the mean and standard deviation of HS detection error are computed among all subjects’ steps at a certain velocity, detected using that HS detection method and RF. Furthermore in each row is reported the mean and standard deviation of all subjects’ step cycles (named SC in Table 4.3) at a certain velocity detected in the corresponding scenario; hence the reader can have an idea of the amount of error with respect to the step cycle duration.

Step Length

As explained in section 4.1.2, the quality of SL estimation was evaluated in two different ways: with the computation of the estimation error on single steps and on the entire trial.

Table 4.4 shows the performance of the system in SL estimation of single steps. Also in this table labels SM, NO and MA refer to the smartphone, north and manual RF respectively. Results are grouped by velocities and for each velocity mean and standard deviation of measured SLs (the first two columns ‘Mean’ and ‘SD’ for each group in Table 4.4), mean and standard deviation of the errors e_s (equation (4.1)) of all subjects’ steps at a given velocity (the last two columns ‘Error’ and ‘SD’ for each group in Table 4.4) are reported. It must be noticed that mean and standard deviation of measured SLs is different across the scenarios even for the same velocity, because the nine combinations

4.1 Healthy subjects

Table 4.3: Heel strike detection

		Low				Normal				High			
Meth	SDR	SC	SD	Error	SD	SC	SD	Error	SD	SC	SD	Error	SD
		(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)	(s)
M1	SM	0.72	0.12	0.009	0.052	0.61	0.08	0.010	0.053	0.48	0.05	0.014	0.045
M1	NO	0.72	0.11	0.008	0.050	0.60	0.07	0.005	0.031	0.49	0.05	0.011	0.041
M1	MA	0.72	0.11	0.009	0.048	0.60	0.06	0.007	0.040	0.48	0.05	0.010	0.040
M2	SM	0.73	0.11	0.010	0.059	0.61	0.13	0.011	0.049	0.49	0.07	0.015	0.039
M2	NO	0.75	0.16	0.008	0.043	0.63	0.16	0.007	0.029	0.49	0.06	0.010	0.032
M2	MA	0.75	0.13	0.007	0.047	0.62	0.12	0.006	0.026	0.48	0.06	0.011	0.036
M3	SM	0.71	0.09	0.003	0.026	0.61	0.06	0.002	0.023	0.48	0.04	−0.002	0.020
M3	NO	0.72	0.08	−0.003	0.029	0.61	0.07	−0.002	0.022	0.48	0.04	−0.002	0.022
M3	MA	0.72	0.08	−0.002	0.026	0.61	0.07	−0.002	0.021	0.48	0.04	−0.002	0.022

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of HS detection methods and RFs were able to recognize different steps and naturally only the steps detected by that particular scenario can be considered.

Figure 4.6 shows the estimation error on the entire trial, computed for each trial according to equation (4.2). Each graph is related to a gait speed. Inside each figure there are three groups of boxes related to the three HS detection methods implemented, and inside each group there are three boxes corresponding to the RFs used: red indicates smartphone RF (labelled SM in the legend), green stands for north RF (labelled NO) and blue is manual RF (labelled MA). For each box the bottom and top edge represents the 25th and 75th percentile of all the trial errors respectively, while the middle line indicates the median value. The stems above and under each box cover all the values of trial errors except for the ones considered outliers, which are plotted through a small red cross. Points that are higher than $q_3 + 1.5(q_3 - q_1)$ or lower than $q_3 - 1.5(q_3 - q_1)$ (where q_1 and q_3 are the 25th and 75th percentiles, respectively) are considered outliers.

In order to illustrate a possible effect of walking speed, Fig. 4.7 reported the cumulative probability of trial errors at different velocities. In particular, each graph in the figure is related to the trial errors of a certain HS detection method considering the smartphone RF and the three lines stand for the different walking speed (green for low, red for normal and blue for high speed). For conciseness only the smartphone RF is plotted, since from Fig. 4.6 it can be seen that except for M1 and high velocity there are not important differences across different RFs.

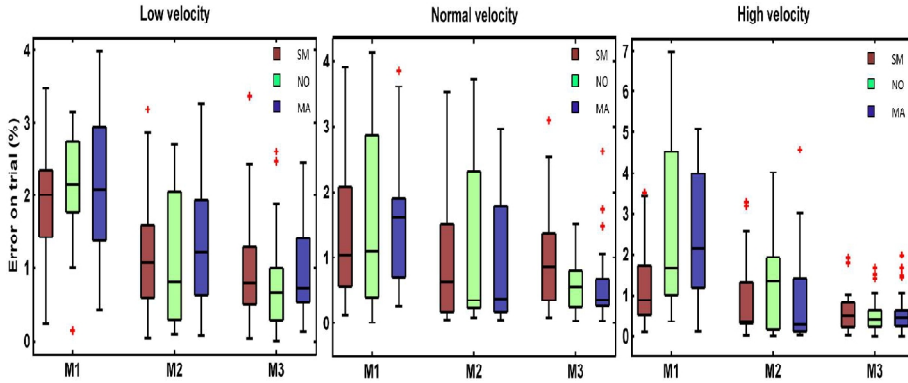


Figure 4.6: Trial error for low (left), normal (centre) and high (right) velocity. Inside each graph boxes are grouped by HS detection method and for each method results of the three RFs adopted are plotted: red for the smartphone RF (SM), green for north RF (NO) and blue for manual RF (MA). Outliers are plotted by small red crosses.

4.1 Healthy subjects

Table 4.4: Step Length Estimation

Meth	SDR	Low			Normal			High		
		SL (cm)	SD (cm)	Err (cm)	SL (cm)	SD (cm)	Err (cm)	SL (cm)	SD (cm)	Err (cm)
M1	SM	63.5	6.5	1.3	72.8	6.5	1.1	87.0	10.2	1.0
M1	NO	62.0	6.6	1.4	71.5	5.5	1.3	85.2	9.7	2.3
M1	MA	63.1	7.4	1.0	72.7	6.3	1.2	87.1	10.7	2.4
M2	SM	62.3	6.6	0.9	74.4	5.4	0.9	88.3	8.2	0.5
M2	NO	61.7	8.2	0.5	74.6	6.0	0.8	87.8	10.7	0.7
M2	MA	62.5	7.2	0.9	74.3	5.2	0.7	87.7	9.6	0.6
M3	SM	63.8	6.8	0.6	73.7	7.1	0.5	88.7	11.0	0.5
M3	NO	64.0	7.0	0.4	74.0	7.9	0.3	87.8	10.8	0.4
M3	MA	64.0	7.0	0.6	72.6	5.7	0.4	86.2	10.5	0.5

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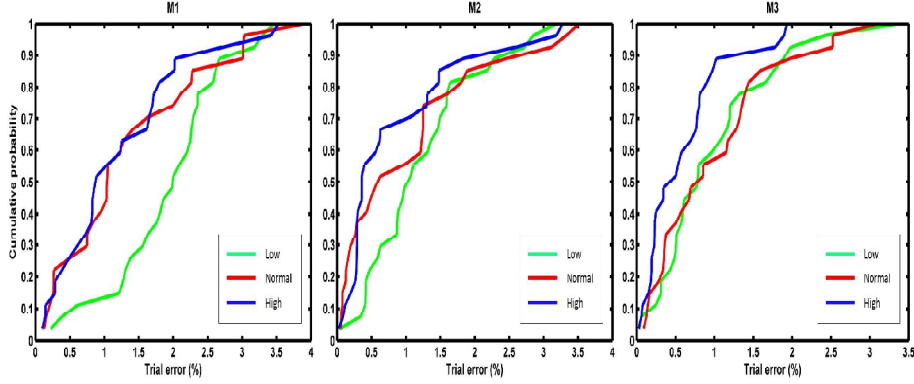


Figure 4.7: Effect of velocity on trial error considering the smartphone RF: green, red and blue lines indicate the error for low, normal and high velocity respectively. Each graph is related to one HS detection method.

4.1.4 Discussion

Tests on healthy subjects were conducted with two main objectives. The first one was the comparison of three HS detection methods in a smartphone based SL estimation. The second one was the evaluation of the effects of a possible misalignment of smartphone RF with AP, VT and ML directions. To this purpose, results obtained from smartphone RF were compared with those obtained using the acceleration vector expressed in two RFs defined properly to ensure the alignment of coordinate axes with actual AP, VT and ML directions. Hence each result of the study is affected by two factors: the HS detection method used, and the RF used for the smartphone. For clarity, in the following, the effects of this two factors on performance will be discussed separately.

For what concerns step detection, from Table 4.2 it can be noticed that independently from the RF considered M1 and M3 showed a better sensitivity than M2. Instead considering a single HS detection method, the use of a corrected RF (either the north one, NO, or the manual one, MA) worsens the sensitivity for M1 and M2, while it improves the sensitivity for M3. This difference can be explained by the acceleration components used for HS detection in the three methods: in fact while both M1 and M2 use the AP direction (M2 uses also the VT one in some condition) M3 uses only the VT component of the acceleration. The rotation matrices used to obtain acceleration vector in the north and manual RF were acquired from the smartphone, which computes them through an internal fusion algorithm (unknown) integrating information brought by onboard sensors (like the magnetometer to locate magnetic north). The above finding suggests that smartphone’s internal algorithm responsible for computing the rotation matrices can make some mistakes in correcting AP

4.1 Healthy subjects

direction (for example due to a transient lost of calibration of the compass or to an electromagnetic interference), while it is more robust and reliable for the VT component.

Results about HS detection confidence reported in Table 4.3 showed error ranges comparable to previous works in the literature using the same methods [121, 119, 120]. All the selected methods reached an acceptable performance with a mean error always under 0.02 s, however a slightly better performance was observed for M3, as in [120]. The more accurate HS detection of M3 results also in lower errors for SL estimation, as expressed in Table 4.4, highlighting the importance of HS location to obtain a more accurate SL estimation using the inverted pendulum model. A one way ANOVA showed that there are not statistically significant differences in HS detection error across different RF ($p > 0.94$).

For what concerns the error in SL estimation two indicators were used: the error on trial and on single step. Results about single step error revealed that M3 reached a slightly better performance, with a mean error under 1 cm and standard deviation under 6.2 cm. Kose et al. [128], who performed a step by step evaluation, obtained mean errors of 0.9 ± 1.7 cm for right steps and -0.8 ± 1.6 cm for left steps. However, they used a dedicated hardware and a different SL estimation method. Despite M1 and M2 reached similar performances in HS detection accuracy, M2 gave lower errors in SL estimation. The reason of the difference may be explained by the high gap in detected steps: the correction factor optimization for M2 was performed on less steps than M1, giving probably better results. On the other hand, all the methods gave low errors on the estimation of the distance covered: fig. 4.7 shows that the 90% of trial errors were under 3% for M1 and M2 and under 2.5% for M3. These ranges are comparable to other systems presented in the literature. For instance, Sayeed et al. [160] made a comparison of several SL estimators and for the inverted pendulum model they obtained a Root Mean Square Error of 0.072 m on a real SL of 0.64 m. Gonzalez et al. [131] reported an estimation of the distance covered ranging from 94.5% to 106.07%. Juen et al. [146], who used the smartphone, estimated walking distance in two different ways obtaining a mean error of 1.82% in one case and 18.78% in the other, for healthy subjects. Percentage errors reported by Kose et al. [128] on the traversed distance varied from -1.6% to 1.7% .

The obtained results for HS detection and SL estimation showed a slightly better performance of M3 with respect to M1 and M2. However, given the similar scores for step detection (Table 4.2) of M1 and M3 and the high standard deviations of obtained errors, an absolute preponderance of M3 on M1 cannot be stated. Furthermore, error ranges for all the compared methods are much lower than the SC variation and decreased observed by clinicians before a FoG

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[70]. Hence both M1 or M3 (from Table 4.2 M2 seems to lose many steps) can be applied to detect FoG.

4.2 Parkinsonian patients

Tests on patients with PD had three main objectives:

- evaluation of smartphone reliability in FoG detection;
- evaluation of the effectiveness of acoustic cues on patients’ gait;
- assessing acceptability and usability of the proposed architecture.

As explained in section 3.4, three FoG detection algorithms were developed, hence several experimental sessions were planned and executed in order to evaluate possible improvements after algorithm updates. For this reason this Section is organized as follows: in Subsection 4.2.1 evaluation metrics are explained, that are common throughout all the experimental sessions; in Subsection 4.2.2 the experimental set up for Moore-Bachlin algorithm evaluation session is presented and finally the experimental sessions planned to evaluated the Crisp and Fuzzy Logic algorithms are explained in Subsection 4.2.3.

4.2.1 Evaluation metrics

The smartphone app has the primary objective of detecting FoG episodes. Hence, it performs a binary classification problem: deciding whether a particular sample (a tuple with the values of FI, EN, EDR, SC and SL computed in a certain time instant) belongs to the FoG or not FoG class. The performance of the classification algorithm was evaluated by means of the following statistical measures: sensitivity, specificity, accuracy and precision. They were computed according the following formulas:

$$Se = \frac{tp}{tp + fn} \quad (4.3)$$

$$Sp = \frac{tn}{tn + fp} \quad (4.4)$$

$$Ac = \frac{tp + tn}{tp + fn + tn + fp} \quad (4.5)$$

$$Pr = \frac{tp}{tp + fp} \quad (4.6)$$

where true positives (tp) are the windows correctly classified as FoG, false negatives (fn) the windows classified as non-FoG despite the patient manifests

4.2 Parkinsonian patients

the symptom in that time instant, true negatives (tn) the windows correctly classified as non-FoG and false positives (fp) the windows wrongly classified as FoG despite its absence.

Furthermore, it is useful to calculate the number of FoG detected by the app over the total FoG episodes manifested by the patient². This evaluation parameter is important because it includes the information about the percentage of FoG episodes during which patients received acoustic feedback.

The second objective concerned the effectiveness of acoustic cues for improving patients’ gait and helping patients to resume walk when the manifest FoG. To this extent, in each session all the walking trials were executed twice, once without cues and once with cues. The order of execution (firstly without cues and then with cues or vice versa) was randomized in order to avoid results from being biased by some training effect. Variables used to evaluate cue effectiveness were: time of execution and percentage of time frozen (the percentage of time the patient was freezing with respect to the total duration of the trial). They were compared among trials with and without cues.

Finally acceptability and usability were also evaluated. They are two essential requirements when developing system for medical assistance or healthcare: in the next paragraph their definitions will be given and the evaluation method will be explained.

Acceptability and Usability

The system was built in order to respond to usability and acceptance criteria [105, 161]. Individual acceptance and use of information and communication technology has been widely studied in a job related contest and resulted in the Unified Theory of Acceptance and Use of Technology (UTAUT) [42, 105, 161]. Little attention has been paid to user acceptance of medical technology, while several studies [162, 163] showed that acceptability and usability barriers are the major obstacles to the approval and diffusion of medical assistive technology.

The term usability does not refer to an intrinsic characteristic of the instrument, as to the process of interaction between classes of users, product and purpose. Usability is a property that defines the effectiveness, efficiency and satisfaction with which specified users achieve specified goals in particular contexts using a certain technology [42, 105, 161].

For what concerns acceptability, on the basis of longitudinal field studies conducted across heterogeneous contexts, the following constructs appeared

²Even if this evaluation metric is a sensitivity metric, it is different from the definition of sensitivity provided by Equation (4.3). While the definition of Equation (4.3) takes into account the reliability in identifying the start, stop, and duration of any FoG (since it considers the single processing windows) episode, this definition is just a binary test of presence/absence of FoG, or in other words a hit rate of detected FoG episodes.

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to be significant and directly related with information technology acceptance [105]:

- performance expectancy (the degree to which an individual believes that using a particular system would improve his or her job performance);
- effort expectancy (the degree of simplicity);
- social influence (the degree to which an individual perceives that others believe he or she should use a particular system);
- facilitating conditions (the degree to which an individual believes that an organizational and technical infrastructure exists to support the use of a particular system).

Moreover, recently, Venkatesh et al [161] integrated hedonic motivation, price value, and habit into UTAUT in order to tailor it to the consumer technology use context.

Considering that, for a medical technology, a validated test for assessing the usability and acceptability does not exist, a questionnaire that reflected the general UTUAT principles was proposed.

During the first two sessions (Moore-Bachlin algorithm and Crisp Logic algorithm) three main aspects of acceptability were studied: non-invasiveness, nonobtrusiveness, and technical confidence. For what concerns invasiveness and obtrusiveness, they were evaluated by asking participants if they believed the system invasive or obtrusive. While technical confidence was assessed by letting the patients wear and start the smartphone before a trial.

Instead, during the Fuzzy Logic experimental session, acceptability and usability were measured by asking patients to answer YES or NO to the following questions, according to UTAUT suggestions [42, 105]:

1. Perceived Ease of Use
 - *Do you find the system easy to use?*
2. Intention to Use
 - *Assuming You will be given access to the system, would You use it?*
3. Perceived Usefulness
 - *Using the system during Your daily living would be possibly useful to improve walk?*
4. Price
 - *Do you expect it to be too expensive?*

4.2 Parkinsonian patients

5. Obtrusiveness

- *Do you think that it could be too much intrusive for your privacy?*

The interview was carried out by a physician who did not attend the experiment.

4.2.2 Moore-Bachlin algorithm

In recent years other research groups attempted to use a smartphone to detect FoG, but during initial study stages the use of a smartphone to carry out all the functions concerning FoG detection (data acquisition, processing and storage) was a novelty. For this reason, the author decided to plan an initial experimental session to assess if the smartphone could be able to provide a comparable performance in FoG detection with respect to standard systems used in the literature (wireless body sensor networks).

The smartphone app was tested on 22 patients (16 males and 6 females). Two kinds of tests were conducted. Patients taking part in the first test had to perform three exercises: a Time Up-and-Go test (TUG) [164], a TUG with dual-task [165] and a FoG-inducing path.

The TUG test asks the patient to stand up from a chair, walk straight for 5 meters, turn 180 degrees, walk back towards the chair and sit down. The TUG with dual task asks the patient to perform the just explained exercise while doing some mathematical operations aloud or carrying a tray with water glasses. The FoG-inducing path is a path defined in order to induce FoG in the patient. It starts and ends in sitting position, and it includes narrow passages, turns and stairs.

Each of these exercises was repeated three times. During the other test the patient walked freely around the clinic. All the trials were video recorded. Twelve patients took part in the first test and ten at the latter.

Among all the participants there were 2 patients affected by rest tremor: the effects of this disturbance on the algorithm performance can be assessed. Studies show that frequency bands of FoG and tremor are quite entirely overlapped [166], so a great loss of sensitivity can be expected in patients with rest tremor of distal arts. For this reason sensitivity results are both globally presented with respect to the whole sample and, separately, with reference to those with rest tremor.

4.2.3 Crisp Logic and Fuzzy Logic algorithms

The experimental set up was the same for both sessions related to the Crisp Logic and the Fuzzy Logic algorithm. Throughout the assessment protocol, the constant aim of the investigators was to obtain a sequence of videos depicting

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a wide range of FOG types and severities, in order to define the architecture reliability and the external validity of the study, that is to say the transferability of results to all daily living situations. Therefore, patients were assessed, in the morning and under the effect of their own chronic dopaminergic therapy, while they were performing different types of video-recorded TUG test, as described in the following. Patients performed three kinds of TUG tasks designed to provoke FOG on a standardized course of 5 meters:

- the standard TUG test modified (5 meters) by Shumway-Cook et al. [164],
- the Cognitive Dual Task TUG test as described by Hofheinz et al [165],
- the Manual Dual Task Timed Up and Go test, which was inspired to Lundin-Olsson [167] and Baker’s et al [40] experimental protocols.

Each patient was asked to repeated each type of TUG for three times.

Walking trials were recorded on a digital video camera from a consistent vantage point for later analysis, and each video showed a complete TUG trial starting and ending in the seated position. Simultaneous acceleration data was acquired from the trunk during the TUG trials described above. Synchronization of the video and accelerometer recordings was performed prior data collection by alignment of the video camera and data acquisition computer clocks.

A first session of tests was planned in order to evaluate the Crisp Logic algorithm and 20 patients were enrolled. Data collected during this first session were used to design the Fuzzy Logic algorithm which was finally implemented on the smartphone. After smartphone implementation, the online performance of this algorithm was tested on 19 patients.

4.3 Results

In this Section, obtained results of the three experimental sessions designed to test the developed algorithms are presented.

4.3.1 Moore-Bachlin algorithm

In the first experimental session 115 FOG events were observed by clinicians based on video recordings. The application correctly identified 92 of them.

Results concerning sensitivity, specificity, precision and accuracy are presented in Table 4.5. For each patient, in addition to Specificity (Sp), Accuracy (AC), Sensitivity (Se) and Precision (Pr) scores, the table indicates the number of FoG episodes actually manifested during trials (second column: FoG) and,

4.3 Results

among these, the ones detected by the smartphone (third column: detected FoG (dFoG)). The last row of the table shows global results: total observed FoG events, detected FoG, overall sensitivity, specificity, accuracy and precision computed as the mean over all the patients.

Table 4.5: Results of Moore-Bachlin algorithm: observed (FoG) and detected (dFoG) FoG episodes, Specificity (Sp), Accuracy (AC), Sensitivity (Se) and Precision (Pr) of FoG detection for each patient and over all the patients (last row)

Patient	FoG	dFoG	Tremor	Sp	Ac	Se	Pr
1	3	1	X	100%	53.64%	42.78%	100%
2	2	2		87.32%	86.73%	85.42%	63.26%
3	0	—		96.88%	96.88%	—	—
4	0	—		98.81%	98.81%	—	—
5	1	1		96.23%	98.21%	100%	68.53%
6	13	1	X	100%	32.47%	26.18%	100%
7	7	4		97.34%	89.76%	78.95%	80.55%
8	0	—		93.46%	93.46%	—	—
9	7	7		81.93%	79.94%	75.33%	64.39%
10	0	—		100%	100%	—	—
11	2	2		94.35%	82.16%	79.65%	76.84%
12	16	16		97.79%	91.22%	88.49%	59.92%
13	12	12		81.10%	90.60%	92.57%	67.96%
14	25	25		85.66%	87.64%	89.15%	71.23%
15	4	4		92.87%	92.57%	84.21%	24.26%
16	7	6		67.07%	68.93%	78.46%	31.78%
17	0	—		100%	100%	—	—
18	0	—		84.53%	84.53%	—	—
19	0	—		100%	100%	—	—
20	5	4		99.79%	95.61%	67.61%	97.96%
21	8	4		99.77%	88.62%	53.96%	98.68%
22	3	3		99.07%	95.87%	71.43%	90.91%
TOT	115	92		93.36%	86.16%	74.28%	73.08%

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Another aspect to evaluate was the effect of distal arts rest tremor on performance. In Table 4.5 patients affected by rest tremor are indicated with a cross ("X") and in fact these patients showed the lowest values of sensitivity.

Global obtained scores are: 74.28% for sensitivity, 93.36% for specificity, 73.08% of precision and 86.16% of accuracy.

An example of trial is shown in Fig. 4.8. Blue line is FI trend, red line is customized FI threshold and green line indicates FoG episodes.

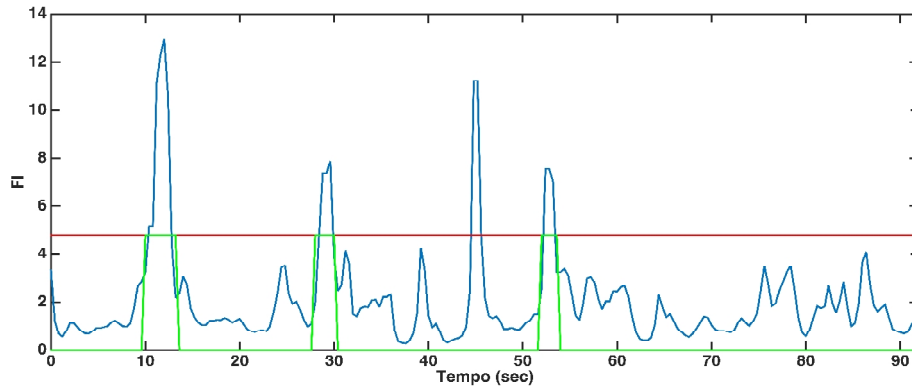


Figure 4.8: An example of trial with Moore-Bachlin algorithm working online. Blue line is FI trend, red line is customized FI threshold and green line indicates FoG episodes.

4.3.2 Crisp Logic algorithm

The Crisp Logic algorithm added SC information with respect to the Moore-Bachlin algorithm. Table 4.6 shows Sensitivity (Se) and Specificity (Sp) results for the Crisp Logic ("CL" in the table) algorithm compared with the Moore-Bachlin ("MB" in the table) algorithm. While Table 4.7 reports Precision ("Pr" in the table) and Accuracy ("Ac" in the table) scores.

The Crisp Logic algorithm worked online during trials, while the Moore-Bachlin algorithm was applied offline using the data stored in the internal sqlite database.

As expected, with the addition of a further FoG condition concerning step cadence the specificity of our system decreased from 84.72% to 76.24%, also precision and accuracy slightly decreased. However, sensibility significantly increased from 69.13% to 82.70%. Furthermore, the Crisp Logic algorithm was able to detect twelve FoG episodes more than Moore-Bachlin algorithm: it correctly recognised 110 episodes over the 122 observed in total, with respect to the 98 FoG episodes detected by Moore-Bachlin algorithm.

In fact, according to the work of Schaafsma et al. [65], clinicians observed

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Table 4.6: Sensitivity and specificity results for the Crisp Logic algorithm compared with Moore-Bachlin algorithm

Patient	FoG	FoG det.		Se		Sp	
		MB	CL	MB	CL	MB	CL
		(%)	(%)	(%)	(%)	(%)	(%)
1	2	2	2	81.25	93.75	98.94	92.62
2	14	12	13	63.31	78.00	58.21	53.36
3	3	3	3	81.11	83.33	98.46	88.96
4	2	2	2	40.00	66.67	96.52	84.01
5	9	8	9	46.37	69.54	98.36	95.46
6	2	2	2	88.52	100	38.79	33.36
7	11	8	11	64.86	85.38	90.57	82.56
8	8	8	8	57.35	68.76	94.95	81.57
9	14	13	13	95.64	96.51	41.39	36.41
10	0	—	—	—	—	85.64	82.55
11	0	—	—	—	—	99.51	80.53
12	6	4	4	77.92	87.92	91.42	76.36
13	10	3	4	46.11	58.13	83.90	83.70
14	1	1	1	71.11	77.64	44.42	42.99
15	11	8	9	52.15	76.63	95.62	89.22
16	11	8	8	76.79	92.14	90.40	85.63
17	0	—	—	—	—	97.47	76.87
18	2	2	2	87.50	89.80	98.35	78.04
19	2	2	2	70.00	100	92.37	88.21
20	14	12	14	75.26	81.71	99.10	92.34
TOT	122	98	107	69.13	82.70	84.72	76.24

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Table 4.7: Precision and Accuracy results for the Crisp Logic algorithm compared with Moore-Bachlin algorithm

Patient	FoG	FoG det.		Pr		Ac	
		MB	CL	MB	CL	MB	CL
		(%)	(%)	(%)	(%)	(%)	(%)
1	2	2	2	50.00	47.05	95.18	84.09
2	14	12	13	61.32	61.09	56.30	68.62
3	3	3	3	71.43	67.13	97.94	85.60
4	2	2	2	58.00	54.70	94.74	84.66
5	9	8	9	88.79	75.23	88.45	88.08
6	2	2	2	44.27	42.57	79.11	73.17
7	11	8	11	61.02	56.08	82.50	88.22
8	8	8	8	67.78	55.33	88.13	76.49
9	14	13	13	65.50	62.18	63.64	68.85
10	0	—	—	—	—	85.35	82.55
11	0	—	—	—	—	99.51	80.53
12	6	4	4	62.14	58.17	91.40	87.11
13	10	3	7	54.70	69.11	65.08	75.24
14	1	1	1	50.20	50.18	43.63	43.11
15	11	8	9	67.33	66.24	88.38	73.85
16	11	8	8	72.50	59.23	89.05	81.59
17	0	—	—	—	—	97.47	76.87
18	2	2	2	42.35	39.07	89.43	68.04
19	2	2	2	56.67	50.03	96.75	87.67
20	14	12	14	91.38	89.49	41.82	63.6
TOT	122	98	110	62.67	58.99	81.69	76.90

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that three kinds of legs motion can occur during FOG: (i) small shuffling steps with minimal forward movement (shuffling with small steps), (ii) legs trembling in band 3 to 8 Hz but no effective forward motion (trembling in place), and (iii) complete akinesia, i.e., no observed legs motion. The detection rule of the Moore-Bachlin algorithm, based on FI, is indicated for only one kind of FoG (legs trembling in band 3 to 8 Hz) and it seems difficult that it could be effective in the other cases. FoG episodes characterized by complete arrest of gait or by small, disturbed, and rapid steps could be detected in relation to step cadence information [62].

Fig. 4.9 reports temporal trends of cadence and FI during a TUG trial of patient 13, who presents an akinetic FOG. The red line represents in both graphs the real instants of FOG as assessed by clinicians from video recordings. Particularly, in Fig. 4.9(a) it takes value 1 during a FoG and 0 in the other time instants, while in Fig. 4.9(b) during a FOG the red line takes the value of the FI threshold. The blue line in Fig. 4.9(a) is cadence trend, while in Fig. 4.9(b) it represents FI variation. In Fig. 4.9(a) the green line takes value 1 when the algorithm finds an increase in cadence or a cadence variation. With the only information of FI the system would not detect anyone of the two FOG events, while cadence augment permits our algorithm to detect both the events and to give the acoustic feedback to the patient.

Algorithm performance could be improved by adding further information on gait, such as step length, which is another important parameter in FoG characterization. In fact in fig. 4.9(a) there is one false positive, due to a voluntary increment of speed and hence cadence. According to studies [62, 168] the period just before FOG is characterized by an increased step cadence, decreased stride length, and decreased angular excursion of leg joints. Hence with step length information a FOG event could be distinguished by a voluntary increment of gait speed, which generally causes an increase in both cadence and step length.

Another way to improve the performance is by increasing the intelligence of the detection algorithm and Fuzzy Logic seemed to be a suitable solution for this application. To this extent a Fuzzy Logic algorithm was developed, as explained in Paragraph 3.4.3, and tested offline on the same data collected in this experimental session.

Table 4.8 shows a comparison of the performances obtained with the use of the three algorithms on two patients with particular FoG occurrences. Table 4.9 shows a comparison of the performances obtained on the whole data set.

Results indicate that the evolution of this architecture is capable of identifying FOG episodes with a high sensitivity and specificity.

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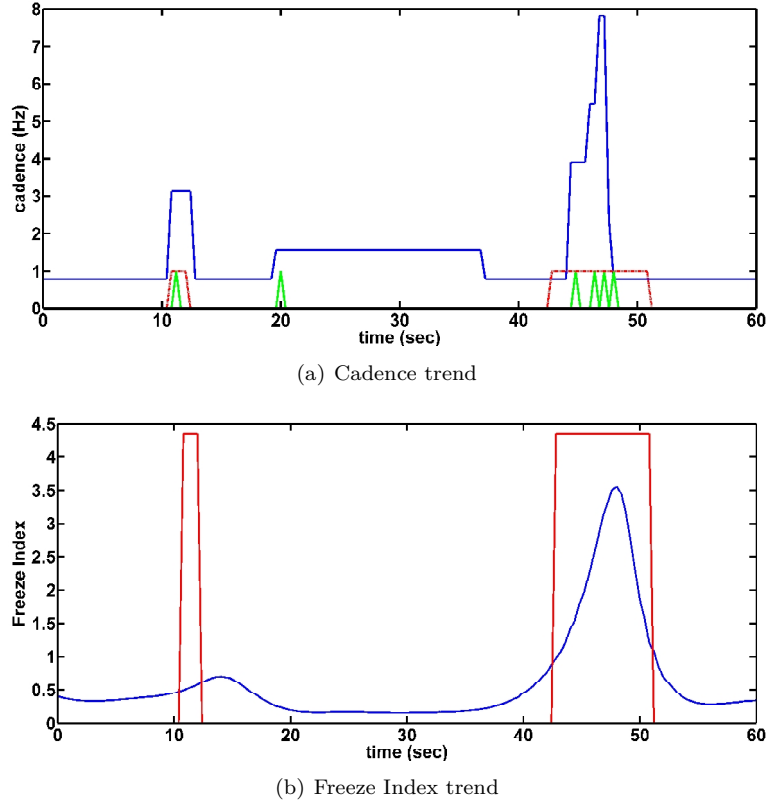


Figure 4.9: (a) Cadence trend during the first TUG trial of patient 14: the blue line is cadence as calculated by the application; the green line shows cadence variation or increase; the red line shows the time interval of FOG as assessed by video recordings. (b) FI trend during the first TUG trial of patient 14: the blue line is FI as calculated by the application; the red line shows the time interval of FOG as assessed by video recordings, during the FOG the red line take the value of FI threshold

4.3 Results

Table 4.8:

Algorithms performance comparison. Sensitivity and specificity results for two patients.

Patient Id.	Algorithm	Sensitivity	Specificity
4	MB	40.00%	96.52%
4	CL	66.67%	84.01%
4	FL	85.12%	98.75%
6	1	88.52%	38.79%
6	2	100%	33.36%
6	3	100%	74.26%

Table 4.9:

Algorithms performance comparison. Whole data set results for sensitivity and specificity.

Method	Sensitivity	Specificity
MB Algorithm	69.13%	84.72%
CL Algorithm	82.70%	76.24%
FL Algorithm	89.43%	97.16%

4.3.3 Fuzzy Logic algorithm

During the experimental session to evaluate the performance of Fuzzy Logic algorithm, a total of 180 FoG episodes were observed and the smartphone with the Fuzzy Logic algorithm running online detected 176 of them reaching a binary sensitivity of 97.78%.

Table 4.10 shows sensitivity, specificity, precision and accuracy scores for each patient, while the last row reports mean results. A sensitivity of 93.08%, a specificity of 90.98%, a precision of 71.23% and an accuracy of 85.47% were obtained over all the patients.

Figure 4.10 displays an example of the Fuzzy Logic algorithm working on-line during a trial of a patient enrolled in the study. The red line takes a value of 1 when there is a FoG, blue line is SL, green line is SC, black line is EDR, purple line is FI and yellow line is EN. The patient manifested a FoG lasting about six seconds. The start of the FoG is marked by an anomalous increase in SL and decrease in SC (a paradoxical situation) and a big spike in EDR. During the FoG there are abnormal and high oscillation in SL and SC and a high value of FI. The end of the FoG is characterized by a negative big variation of EDR, a medium FI, a low SC and high SL.

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Table 4.10: Observed (FoG) and detected (dFoG) FoG episodes. Sensitivity, specificity, precision and accuracy of FoG detection. The last row shows global results.

Patient	FoG	dFoG	Sensitivity	Specificity	Precision	Accuracy
1	4	4	100%	84.36%	57.65%	79.76
2	35	35	81.78%	86.88%	81.30%	86.00%
3	18	18	87.89%	94.94%	84.34%	92.71%
4	4	4	94.52%	84.78%	66.67%	77.67%
5	8	8	99.17%	97.72%	96.97%	97.83%
6	12	12	95.13%	97.21%	82.88%	95.58%
7	17	17	93.57%	81.80%	57.50%	69.61%
8	19	17	61.86%	91.50%	78.50%	86.17%
9	19	18	70.71%	84.57%	87.30%	77.65%
10	4	4	100%	89.17%	60.40%	87.50%
11	2	2	100%	94.17%	74.75%	92.54%
12	2	2	90.00%	96.50%	75.00%	94.83%
13	4	4	88.00%	93.83%	56.33%	74.27%
14	2	2	100%	86.33%	66.90%	87.06%
15	0	-	-	91.33%	—	81.00%
16	24	23	69.57%	92.67%	53.18%	82.85%
17	0		-	78.33%	—	71.61%
18	6	6	66.67%	95.89%	60.00%	95.09%
19	0		-	95.33%	-	94.12%
TOT	180	176	87.43%	90.38%	71.23	85.47%

4.3.4 Cue effectiveness

Results for cue effectiveness are reported in Table 4.11. Both time of execution and percentage of time frozen are grouped for trials type (TUG stands for the standard TUG test, CG for the TUG test with cognitive task and MA for TUG test with manual task), because different exercises have different cognitive and motor effects on the patient and hence they can affect in a different way cue effectiveness. The values reported in the table are the mean over the 3 trials of the same type. When percentage of time frozen is 0.0% means that in those

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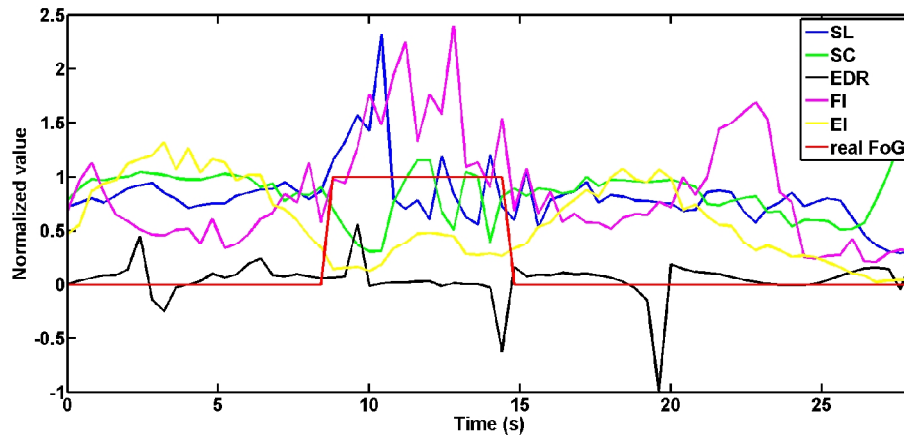


Figure 4.10: An example of the fuzzy logic algorithm working online.

trials the patient did not manifest FoG.

By observing the table, it can be noticed that the cueing therapy did not always cause a reduction of the execution time and the frozen time. Some patients manifested a worsen performance without cues than with cues. For example patients 2 and 3, which had also important gait impairment (from Table 4.10 it can be seen that they experienced many FoG episodes).

4.3.5 Acceptability and Usability

As previously discussed, during the first two sessions (Moore-Bachlin algorithm and Crisp Logic algorithm) three main aspects of acceptability and usability were assessed: non-invasiveness, nonobtrusiveness, and technical confidence. With respect to the invasiveness and obtrusiveness, none of the patients felt embarrassment or discomfort in wearing the smartphone. Regarding the technical confidence, the major part of the patients taking part in our experiment did not already own the technical expertise needed to manage a smartphone, mainly due to their age. However, all of them were apt to learn how to launch the app and moreover their background always includes a young relative much engaged with this kind of technology. Some patients expressed their strong desire in using the architecture at home due to the benefit found during the trials.

For what concerns the last experimental session, results about questionnaire answers are reported in Table 4.12. all patients requested to wear the architecture accepted. After ending the experiment, 17/19 (89%) patients affirmed that the system was easy to use, 16/19 (84%) thought that they could use it because it would be useful to improve gait (16/19 – 84%). The architecture

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cost was assumed to be acceptable for the majority (18/19 – 95%) and its obtrusiveness negligible (19/19-100%).

4.4 Discussion

Results presented in the previous Section about tests on people with PD are now discussed, in order to highlight the major findings.

Experimental tests on people with PD went through three main phases corresponding to the three developed algorithms. Results coming from these sessions are discussed separately in three dedicated Subsections, in order to enhance clarity.

4.4.1 Moore-Bachlin algorithm

The first experimental session was mainly planned in order to investigate the potential of the smartphone in FoG detection. Hence, an accredited algorithm of the literature, the Moore-Bachlin algorithm, was implemented on the smartphone and tested in real-time.

Obtained results reached a value of 93.36% of specificity, 74.28% of sensitivity, 86.16% of accuracy and 73.08% of precision. These scores indicate that the proposed architecture is capable of identifying FOG episodes with suitable sensibility and specificity, comparable to previous studies in the literature [5],[89],[67].

Moore et al. [97] obtained 84.3% of sensitivity and 78.4% of specificity when using a 7 sensors configuration. Sensitivity and specificity became 86.8% and 82.4% respectively for the hip sensor alone. Bachlin et al. [5] reported a mean sensitivity of 73.1% and specificity of 81.6%; these values increased to 88.6% and 92.4% respectively after an offline parameter optimization. Results in sensitivity and specificity obtained from Mazilu et al. [89] are divided for sensor placement and sensor axes. Therefore obtained results can be compared with their performance results for vertical axes of hip sensor, which are 83.68% of sensitivity and 98.26% of specificity. However in the latter work authors used a different classification algorithm. This comparison is promising given the novelty of the architecture, which were the first attempt to manage FOG using only a smartphone-like device [48].

Although these encouraging results, much work had to be done in order to improve system performance. In fact, it can be noticed that algorithm performance manifests some user-dependent characteristics. For some patients it worked exceptionally, but there are some other patients that experienced a lower performance. This large variability was found also in other studies [5],[89] and it was believed to be due to different walking style among subjects.

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However, this study suggests also a possible correlation of algorithm failure in presence of rest tremor. Rest tremor causes an increase in the customized threshold set before starting the trials, which results in a loss of performance. On the other hand, if a lower threshold were set, specificity would drop. Rest tremor can be interpreted as a disturbance, since its frequency content is exactly between 3 and 8 Hz [166], the same band used to compute the freeze index. To overcome this problem additional features were implemented in the algorithm, apt to discriminate FoG from tremor of distal arts, since it is clear that multidimensional approaches [89],[98] give better results.

Both the high score of performance results and the unobtrusiveness demonstrate the potential use of the architecture in monitoring, gait assistance during daily living and rehabilitation therapy.

4.4.2 Crisp Logic algorithm

Global results of the second experimental session (Moore-Bachlin algorithm: 69.13% sensitivity, 84.72% specificity, 62.67% precision, 81.79% accuracy. Crisp Logic algorithm: 82.70% sensitivity, 76.24% specificity, 58.99% precision, 76.90% accuracy) are in accordance with previous works in the literature [5, 49, 48], confirming the reliability of the smartphone in FoG monitoring.

The Crisp Logic algorithm adds to the Moore-Bächlin algorithm the computation of step cadence. This upgrade has been decided on the basis of studies [70, 169] relating FoG to the disruption of temporal, rather than spatial, characteristics of gait. Adding information about step cadence improved the algorithm sensitivity by about 13% reaching a value of 82.70%. In fact, step cadence information is essential to detect akinetic and shuffling subtypes of FoG [65], while it can happen that freeze index does not increase during akinetic or shuffling FoG.

However a slightly decrease in specificity was observed: from 84.72% to 76.24%. The addition of a further condition in logical disjunction (Equation (3.9)) caused an increase in false positives. In particular, during a turning step cadence may vary or increase even if the patient does not have FoG. For this reason, during this session, the reliability of the system in identifying FoG presence at the turning was also evaluated. To this purpose, all the turnings in which patients experienced and do not experienced FoG were counted. Than sensitivity of the system at the turning was computed as the turning FoGs detected by the system over the total number of turning FoGs. While specificity of the system at the turning was found as the number of turnings without FOG in which the system does not detect an episode over all the turnings without FOG. Obtained scores for sensitivity and specificity were: 80.63% and 85.87% for Moore-Bachlin algorithm, 95.00% and 82.33% for Crisp Logic algorithm.

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The higher sensitivity of this Crisp Logic algorithm with respect to Moore-Bachlin algorithm can be explained by the following reasons. While the freeze index is particularly suitable to detect trembling FoG, it can fail to detect akinetic and shuffling FoG. Instead, step cadence information is useful to detect these situations. In shuffling FoG there is actually a transition from the normal step cadence to a higher step cadence where condition b (Equation (3.8)) becomes true. In akinetic FoG step cadence changes randomly without the periodic contribution of walking, making condition a (Equation (3.7)) true.

This findings are consistent with results obtained by other works that improved the performance of frequency domain information with the addition of temporal information [102, 100, 95].

However, the heterogeneity and complexity of FoG phenomenon suggest the use of artificial intelligence techniques in order to improve performance. The development of the Fuzzy Logic algorithm, which was tested on the same data confirmed this hypothesis [50] reaching a sensitivity value of 89.43% and a specificity of 97.16% (Table 4.9). Fusing together the information of FI, EN, SC, and EDR the Fuzzy Logic algorithm, compared with the other two, show a greater capability to reduce false negatives and false positives, improving sensitivity by 20% and 7% and specificity by 13% and 21% with respect the first two algorithms (Table 4.9).

Outcomes from the usability and acceptability questionnaire showed that patients enrolled in the study were willing to test the system and, in most cases, they considered it useful, easy to employ, not expensive and not intrusive. Up to 80% of them affirmed that they could use it.

4.4.3 Fuzzy Logic algorithm

The smartphone app showed a high performance in real time FoG detection (mean sensitivity of 87.43%, mean specificity of 90.38%, mean precision of 71.23%, mean accuracy of 85.47%; FoG hit rate of 97.78%: 176 out of 180 FoG episodes were detected) with respect to previous works in the literature [5, 67, 97, 47, 48] which uses simple linear classifiers. Hence results confirmed previous findings concerning the use of a Fuzzy Logic based detection algorithm [50], where it was found that increasing the intelligence of the FoG detection algorithm will result in higher reliability.

The inter-subject performance variability almost disappeared in this session, as it can be seen from Table 4.10.

Obtained scores are also consistent with other works in the literature. Tripoliti et al. obtained a mean accuray of 89.00%, but however they used an architecture composed of six accelerometers and two gyroscopes. The system proposed by Mazilu et al. [4], that used two inertial measurement units on the ankles,

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achieved a FoG hit rate of 94.94% (169 out of 178 FoG episodes were detected) and a specificity 94%.

The higher performance results and the light computational effort demonstrate a great potential for the use of Fuzzy Logic algorithm coupled with the smartphone unobtrusive architecture in FoG monitoring during daily living.

4.4.4 Cue effectiveness

Cue effectiveness results reported in Table 4.11 revealed a general decrease in the execution time and percentage time frozen when the system provided rhythmic auditory feedback after FoG detection. However there are some exceptions. For example, patient 1 that was frozen for 2.9% of the TUG tests execution time when the cue feedback was available, with respect to a 0% of time frozen when the cue was not available. However the small amount of frozen time demonstrates the benefit of auditory cue to resume gait (in fact Table 4.10 shows a sensitivity of 100% for subject 1, indicating that the system immediately recognized FoG episodes and gave the feedback). Instead performance got worst in patients 2, 3, 8 and 12 when the system provided auditory cues after FoG detection.

A possible explanation of this difference in cue effectiveness may reside in the amount of gait impairment manifested by those patients. In fact, as it can be seen from the number of FoG reported in Table 4.10, patients 2, 3 and 8 performed trials with greater difficulties in gait with respect to the other patients. Hence it is possible that rhythmic auditory cues lose or decrease their effectiveness when they act on patients with important cognitive or motor difficulties.

Another possibility can be the need to customize the cues on the basis of patient characteristics. In fact the application uses the same acoustic stimulus for all the patients: a metronome ticking at 1 Hz frequency, but probably both cue frequency and melody should be adapted to patient’s step frequency and musical preferences (as it happens for ringtones) in order to be more effective.

4.4.5 Acceptability and Usability

Acceptability and usability investigations carried out during the three experimental sessions revealed a general willingness of patients to use the system during their daily living and proved the satisfaction of acceptability and usability requirements. In fact positive answers to the questionnaire were quite high (see Table 4.12).

However, many patients found difficulties when, during the first two sessions, they were asked to manually launch the application and wear the smartphone. Usually, the major problems were to unlock the smartphone and open the

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application, since they were not confident with the touch screen. Instead, they were able to immediately and easily understand the application functioning.

Hence, even if questionnaire answers highlight that patients believe the system is acceptable and usable, this generation of elderly does not often own the technical expertise to interact with smartphone touch screen. However, given the strong widespreading of smartphones, it can be expected that the next generation of elderly will certainly have the minimal technical expertise and confidence to open a smartphone app.

Table 4.11: Cue effectiveness results

Patient	Execution Time (s)						Frozen Time (%)					
	TUG		CG		MA		TUG		CG		MA	
	no cue	cue	no cue	cue	no cue	cue	no cue	cue	no cue	cue	no cue	cue
1	19.3	19.3	35.3	28.7	34.7	26.7	0.0	2.9	7.2	0.0	0.0	0.0
2	25.5	29.6	48.3	46.3	46.1	45.7	22.4	44.7	62.9	63.3	50.7	62.8
3	13.5	16.3	30.3	38.1	18.7	20.7	0.0	0.0	17.3	45.7	12.7	22.7
4	16.0	14.5	18.3	16.5	24.0	21.5	0.0	0.0	11.2	0.0	0.0	0.0
5	13.6	13.2	18.5	17.0	16.2	16.0	11.6	11.1	22.2	10.3	0.0	0.0
6	26.0	20.0	30.1	22.5	26.3	20.7	10.5	0.0	13.8	0.0	21.6	9.2
7	12.3	12.6	13.2	14.2	19.5	19.6	10.9	5.2	0.0	6.1	18.7	8.8
8	27.2	32.2	50.1	44.5	41.2	35.1	10.2	24.8	20.5	30.2	22.6	20.7
9	42.2	32.6	95.5	71.0	86.3	67.8	42.0	24.0	80.2	68.9	70.0	56.5
10	19.3	19.1	20.8	22.3	25.0	26.4	0.0	0.0	8.0	8.0	7.8	7.6
11	30.0	32.8	34.2	31.6	33.5	39.5	7.8	0.0	0.0	0.0	0.0	4.9
12	26.3	43.5	27.2	34.3	28.3	30.4	0.0	7.3	0.0	9.7	0.0	0.0
13	18.1	20.0	16.8	21.6	19.3	21.8	15.0	7.1	0.0	0.0	15.0	12.7
14	12.3	14.2	14.2	12.5	13.1	13.4	0.0	0.0	0.0	0.0	10.3	0.0
15	20.8	22.2	25.1	28.3	25.4	23.5	0.0	0.0	0.0	0.0	0.0	0.0
16	43.5	43.2	92.3	93.7	56.6	64.3	12.6	5.5	30.1	15.9	20.9	15.3
17	12.4	12.4	13.4	14.2	12.8	13.9	0.0	0.0	0.0	0.0	0.0	0.0
18	18.2	18.1	25.4	25.6	22.3	21.9	1.5	0.0	2.6	6.5	0.0	0.0
19	20.0	22.7	26.5	29.3	25.6	22.4	0.0	0.0	0.0	0.0	0.0	0.0

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Table 4.12: Acceptability and usability results of the Fuzzy Logic experimental session in response to the questionnaire introduced in Section 4.2.1.

Questionnaire item	Positive outcomes	Percentage score
Perceived Ease of Use	17/19	89.47%
Intention to Use	16/19	84.21%
Perceived Usefulness	16/19	84.21%
Price	18/19	94.74%
Obtrusiveness	19/19	100.0%

Chapter 5

Conclusion

The thesis objective was the development of a system to manage motor disorder in PD, in particular the FoG. It was designed according to usability and acceptability requirements, thus in a user centered way, taking into account user’s needs. The design and development processes lead to a system composed of three main components:

- Smartphone: to perform real time gait monitoring and FoG detection.
- Database: to store the information coming from smartphone monitoring, patient’s clinical history and followed therapies (pharmacological, rehabilitation, instrumental).
- Web application: to consult database information, in particular an easy and intuitive graphic interface allows the access to FoG monitoring data.

Before applying the smartphone to monitor the gait of people with PD and detect FoG, its reliability in monitoring important gait parameters was before assessed in a laboratory for movement analysis. Positive outcomes obtained from this phase allowed to use important gait parameters, such as SL and SC, in the FoG detection algorithm.

The development of a reliable FoG detection algorithm went through three main steps, that highlighted how performance improved by progressively increasing the intelligence and the complexity of the detection algorithm.

Firstly, a qualified algorithm (Moore-Bachlin algorithm) described in the literature [67, 5] was implemented and tested on the smartphone (sensitivity: 74.28%, specificity: 93.36%, accuracy: 86.16%, precision: 73.08%).

Secondly, a Crisp Logic algorithm was developed, adding SC information and defining a set of binary rule (propositions) that are applied to find the start and the stop of a FoG episode. (sensitivity: 82.70%, specificity: 76.24).

Finally, a Fuzzy Logic algorithm was developed. This algorithm uses five features extracted from acceleration signal: FI, EI, EDR, SC, SL. High scores were reached from experimental tests in laboratory setting (sensitivity: 87.43%, specificity: 90.38%, precision: 71.23%, accuracy: 85.47%).

Chapter 5 Conclusion

The Fuzzy Logic algorithm showed the best performance and reliability in FoG detection.

Cueing strategy revealed some positive outcomes in improving gait function, but the presence of some exceptions suggested that further investigations are needed.

Usability and acceptability were also evaluated on twenty subjects and results highlighted positive attitude towards the use of the system.

The work of thesis provided some important contribution to the literature:

- FoG management entirely accomplished on a smartphone:
 - smartphone sensors showed a reliability comparable to dedicated sensors used by other architectures in the literature;
 - acceptability and usability of the system were evaluated on patients with PD.
- Fuzzy Logic applied for the first to FoG detection revealed a successful performance;
- A novel frequency domain feature was defined and it proved to be significant in identifying FoG.

In conclusion, the developed architecture revealed itself reliable in gait monitoring and FoG detection both in healthy and pathological people. Patients generally appreciated the system and were apt to use it during their daily activities.

However this study has some limitations, which suggest future works. Firstly, given the high reliability reached in ambulatory setting and the high acceptability and usability, the system could be tested in real-life scenario at patient’s home. Furthermore, the motor learning potential of cues delivered by the smartphone was not always clear and effective. A possible explanation may be the need of customizing cueing modality according to patient preferences. Hence, the function of cues customization should be implemented on the smartphone.

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