Characterization of Parkinson's Disease by quantifying gait analysis

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To my dear Javier for his inconditional support, love, and patience.
To my parents and bro for their support in this process.

Acknowledgments

Abstract

Parkinson's disease (PD) is the second most common neurodegenerative disorder that affects about 1% of the population over the age of 60. the motor system is affected by a set of motor symptoms, namely tremor, rigidity, and bradykinesia, which are usually evaluated by different clinical test and scales that depend on physician expertise. This work proposes an objective characterization of PD gait patterns by approximating the dynamic of the leg as a single grounded pendulum adding to spring and damper element. Characterization of the gait patterns was carried out with an experimental group of healthy subjects and Parkinson patients with different stages of the disease. This characterization was carried out by an approach that consisted of a simple method that estimates the force generated by the gait during the single support from the gait data describing the motion pattern for different stages of the disease compared with the control group. It was observed a decrease in the estimated force while the disease progress.

Keywords: Parkinson's disease, gait patterns, gait cycle

Resumen

La enfermedad de Parkinson (EP) es el segundo trastorno neurodegenerativo más común que afecta aproximadamente al 1% de la población mayor de 60 años. El sistema motor se ve afectado por un conjunto de síntomas motores, a saber, temblor, rigidez y bradicinesia, que son usualmente evaluados a partir de diferentes evaluaciones clínicas y escalas que dependen de la experiencia del examinador. Este trabajo propone una caracterización objetiva de los patrones de la marcha de la EP al aproximar la dinámica de la pierna a un único péndulo adicionado con un elemento de resorte y amortiguador. La caracterización de los patrones de marcha se llevó a cabo con un grupo experimental de sujetos sanos y de pacientes con Parkinson en diferentes estadios de la enfermedad. El enfoque consistió en un método simple que estima la fuerza generada por la marcha durante la fase de soporte en cada ciclo de la marcha, el cual puede describir el patrón de movimiento en diferentes estadios de la enfermedad en comparación con el grupo control. Observando una disminución en la fuerza estimada a medida que avanza la enfermedad.

Palabras clave: Enfermedad de parkinson, Patrones de marcha, ciclo de marcha

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1. Introduction

1.1. Parkinson's Disease

Parkinson's disease (PD), the second most common neurodegenerative disorder after Alzheimer's disease [15, 7, 29], was initially described by James Parkinson in 1817 and classified in 1967 after a study carried out on 856 PD patients during the period 1949 to 1964 [32], it described its cardinal motor manifestations which generally show an asymmetric onset and progression [22].

Anatomopathological basis of Parkinson's disease are commonly described as the progressive loss of dopaminergic neurons in the substantia nigra of the mesencephalon as well as the formation of intra-cellular inclusions called Lewy bodies [50, 38]. In 2003, Braak et al. [3] introduced a six-stage scale obtained by performing a brain autopsy that characterizes the disease progression process. (see Table **1-1**).

Furthermore, reported data about PD epidemiology estimate that this disease occurs in about 1% of the population over the age of 60 and its prevalence increases with age [31]. The annual incidence per 100,000 inhabitants ranges from less than 10 to more than 20. However, incidence studies may be affected by under-diagnosing of PD, especially among the most elderly [74] as it is not common to diagnose PD before 40 years, reaching a prevalence 4 or 5 people in every 100,000 aged 30-39 $\%$ [75].

1.1.1. Clinical features

Although Parkinson's disease is considered a motor syndrome, there are also non-motor alterations usually correlated with advanced age and disease severity affecting daily living activities [51]. Non-motor impairments, such as olfactory problems, constipation, depression, and rapid eye movement disorder, can occur in early stages though.

Regarding the motor system, which is the focus of this paper, manifestations involve disturbances causing some abnormal rigidity, tremor, bradykinesia and loss of postural reflexes (cardinal motor symptoms will be addressed later) [82, 39, 15]. Even though several attempts have been made to classify PD into a set of subtypes [68, 62, 61], due to its clinical heterogeneity, there is not a generalized consensus [42]. Nevertheless, patients' most salient

Table 1-1.: Braak staging

Braak staging	Structures affected	Dysfunction
Stage 1	Olfactory bulb, anterior olfactory nucleus	Olfactory
Stage 2	The raphe nuclei, gigantocellular reticular nucleus of the medulla oblongata	Sleep homoeostasis, visual hallucinations and sleep behavioural disorder (RBD),central autonomic control
Stage 3	Substantia nigra and Lewy body lesions begin to form in the pars compacta, basal nucleus of Meynert, a cluster of acetylcholine-rich neurons in the basal forebrain.	Tremor, rigidity, and bradykinesia
Stage 4	Severe dopaminergic cell destruction in the pars compacta, mesocortex and allocortex	Progression of symptoms stages 3
Stage 5	Neocortex, temporal, parietal, and frontal lobes, dorsal motor nucleus of the vagus nerve, the gigantocellular reticular nucleus, and the locus ceruleus	Neuropsychiatric symptoms such as depression, cognitive impairment, and visual hallucinations.
Stage 6	Fully invaded the neocortex, affecting the motor and sensory areas in the brain	Progression of symptoms stage 5

Braak staging describes the sequence and distribution of pathological changes in Parkinson's disease and the progression of motor and not motor symptoms. Adapted from [6].

features allow us to categorize them into 3 phenotypes; the Tremor predominance with a relative absence of other symptoms; the rigid-akinetic phenotype which would include the Non-tremor predominance; and the Mixed or indeterminate clinical one for those presenting instability and upset walking [70].

Likewise, the motor system alterations cause several effects on the gait of patients with Parkinson's disease. For this reason, it has studied three principal components implicated on the gait performance: gait initiation, balance, and locomotion which are assessed by different clinical tests used by clinicians, some of them are described in section 1.1.3. Namely, gait initiation in terms of kinematic gait analysis refers to the phase between the motionless standing and the steady state locomotion[4], that implies the movement of the COP behind the COM causing the COM to move forward.[57]. Martin et al [49] suggest that COM–COP

distance during gait initiation provides a useful tool for identifying subtle difficulties with movement performance in PD patients. On the other hand, balance corresponds to the coordinate action to maintain the control of the center of mass over the base of support in order to retain stability [65, 79]. And the locomotion corresponds to the action to move the body forward. which is examined by gait analysis systems that provide an examination of the normal and pathological gait patterns. In the case of individuals with PD, they experience deterioration in balance and postural control as well as a progressive reduction in the speed and amplitude of movements during the locomotion [53], that it causes a higher fall risk.

Besides, gait alterations in PD can be divided into two types: [31, 26] episodic and continuous. The former involves intermittent alterations apparently occurring randomly that may include manifestations such as festination, start hesitation, and freezing of gait while the latter refers to the pattern alterations of the more or less consistent gait, persisting and being evident all the time.

Rigidity

Rigidity refers to a form of muscle-tone increase [81]. that is velocity-independent during passive movement of a limb. Its examination relies on the examiner's expertise and perception of the patient's resistance to imposed movements [60]. Moreover, it is used as a diagnostic criterion as well as to evaluate the efficacy of therapeutic interventions [81]. A descriptive study of idiopathic Parkinson's disease found out that 83.6% of the patients are affected by rigidity [55]. Specifically, it focused on the measurement of one element [60], examining muscle EMG responses without including joint torque resistance to imposed movement.

Bradykinesia

Bradykinesia is the result of a disruption in normal motor cortex activity mediated by reduced dopaminergic function. Its initial manifestation is often slowness in performing activities of daily living and reaction time deficit. Other manifestations of bradykinesia also include loss of facial expression and reduced arm swing while walking; this cardinal PD feature appears to correlate best with the degree of dopamine deficiency [76]. Analysis of electromyographic recordings showed that patients with bradykinesia are unable to energize the appropriate muscles to provide enough force for initiating and maintaining large fast movements [28].

Tremor

Tremors are divided into rest and action (postural and kinetic); the rest one is considered a typical cardinal symptom in Parkinson's disease, almost always prominent in the distal part of an extremity and occuring at a frequency of 4 to 6 Hz. However, characteristically, rest

tremors disappear with action and during sleep with variable occurrence among patients and during the course of the disease. Action tremors associated with Parkinson's disease correlate directly with motor disability and contribute to weakness and bradykinesia [35].

Postural instability

Postural instability is a clinical hallmark in Parkinson's disease that usually develops at Hoehn and Yahr stage III being relatively rare in early-stage PD, and yet, the most common cause of falls contributing to the risk of hip fractures [14]. In order to understand the features of postural instability, it is necessary to clarify the factors present in normal postural responses which are frequently passive and active [2]:

- Passive factors relate to the Visco-elastic properties of stretched muscles, tendons and ligaments that contribute to the postural stability in small perturbation.

- Active ones refer to the muscular forces having importance in the automatic and voluntary responses during the displacement of the center of gravity.

Additionally, the rigidity and intrinsic muscle stiffness which occur in PD may superimpose upon the bradykinesia and cause a biomechanical delay of voluntary compensatory responses [2].

Non-motor symptoms

Non-motor symptoms include cognitive, sensory and autonomic dysfunction. This table **1-2** includes some typical dysfunctions and its factors occurrence in PD patients.

1.1.2.   Diagnosis criteria

Taking into account the progression of the illness, PD has been classically considered and studied as a motor disorder [15, 16] whose diagnosis is primarily based on the presence of a combination of associated cardinal-motor issues (bradykinesia, tremor and rigidity), exclusionary symptoms and response to levodopa [59, 34, 25].
In addition, the diagnosis criteria follow specific steps developed by UK Parkinson's Disease Society Brain Bank [33] (See Table **1-3**. while the examination is developed bearing in mind a set of rating scales mentioned below.

1.1.3.   Evaluation of motor impairment in PD

A number of rating scales are used for the evaluation of motor impairment in patients with PD. Two main of these measure the progression of the disease: the oldest scale published in 1967: *Hoelh and Yarh Scale* and the Modified Unified Parkinson's Disease Rating Scale

Table **1-2**.: Non-motor features in Parkinson's disease

Features	Dysfunction
Autonomic	orthostatic hypotension, sweating dysfunction, sphincter dysfunction and erectile dysfunction. 47 % (42/89) of PD patients
Neuropsychiatric	cognitive decline (84 %), depression (58 %), apathy (54 %), anxiety (49 %) and hallucinations (44 %)
Sleep	excessive daytime sleepiness, sleep attacks, Insomnia (.50 % prevalence),
Sensory	olfactory dysfunction (10 % increased risk for the disease), pain, paresthesia, akathisia, oral pain and genital pain

Based on: Jankovic, J. (2008). Parkinson's disease: clinical features and diagnosis. Journal of neurology, neurosurgery & psychiatry, 79(4), 368-376.

(2008) in which motor and non-motor symptoms are examined. Complementary scales, also used for the assessment of specific disturbances in postural, balance, arm-and-hand function and walking skills, are going to be described next:

Hoelh and Yarh Scale Depending on motor deterioration, this scale assesses the severity of overall Parkinsonism dysfunction based on bilateral motor involvement, the compromise of gait, and balance [83], classifying it by stages. At first, 5 of them were included although stages 1.5 and 2.5 were subsequently added taking into account the intermediate course of this illness [27]. The description of the current scale encompasses:

- Stage 1.0: Unilateral involvement with minimal only.

- Stage 1.5: Unilateral and axial involvement.

- Stage 2.0: Bilateral involvement without impairment of balance.

- Stage 2.5: Mild bilateral disease with recovery on pull test

- Stage 3.0: Mild to moderate bilateral disease; some postural instability; Physically independent

- Stage 4.0: Severe disability; still able to walk or stand unassisted.

- Stage 5.0: Wheelchair bound or bedridden unless aided.

Table 1-3.: UK Parkinson's Disease Society Brain Bank Diagnostic Criteria

STEP 1. Diagnosis of Parkinsonian syndrome
Bradykinesia
And at least one of the following:
a. Muscular rigidity
b. Rest tremor
c. Postural instability
STEP 2. Exclusion criteria for Parkinson's disease
History of repeated strokes, head injury, encephalitis
Sustained remission.
Strictly unilateral features after three years.
Supranuclear gaze palsy.
Cerebellar signs.
Early severe autonomic involvement.
Early severe dementia with disturbances of memory, language and praxis.
Babinski sign.
Presence of a cerebral tumour or communicating hydrocephalus on CT scan.
Negative response to large doses of levodopa (if malabsorption excluded).
MPTP exposure.
STEP 3. Supportive prospective positive criteria for Parkinson's disease. Three or more required for diagnosis of definite Parkinson's disease
Unilateral onset.
Rest tremor present.
Progressive disorder.
Persistent asymmetry affecting the side of onset most.
Excellent response (70–100 %) to levodopa.
Severe levodopa-induced chorea.
Levodopa response for 5 years or more.
Clinical course of 10 years or more

From: Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathicParkinson's disease. A clinico-pathological study of 100 cases. JNNP 1992;55:181-184

Unified Parkinson's Disease Rating Scale (UPDRS)   Unified Parkinson's Disease Rating Scale is a classification system designed for longitudinal follow up of the course of the disease, it was developed in 1984 and published in 1987. In 2008, a modified revised version consisting of 65 items (compared with the 55 of the original) was published by the Movement Disorder

Society (MDS); the MDS-UPDRS is grouped in 4 parts:

- I. Mentation, behaviour and mood: It includes the examination of "non-motor experiences of daily living"states of mind involving depression, motivation, sleep disturbance and cognitive impairment among others.

- I. Activities of daily living: It refers to the çoncerns of daily living motor experiences": examining factors such as speech, activities of daily living, tremor and falls

- III. Motor examination (mUPDRS): It comprehends the motor examination that assesses speech, facies, tremor in resting, intentional tremor, rigidity, rapid movements of the fingers, rapid hand movements, alternating and leg movements, getting up from a chair, posture, stability of posture, starting walking and bradykinesia.

- IV. Complications of therapy: This comprises motor complications as Functional impact of dyskinesias, Painful OFF-state, dystonia and others.

Other Rating Scales Other rating scales have been designed for exhaustive examination of the symptoms in Parkinson's disease. For example, people who experience disturbances in balance and posture can be assessed using rating scales like Tinetti Balance and Gait Assessment Tool (1987), Brunel Balance Assessment (2002), Timed Up and Go Test (1989) etc. while Fugl-Meyer Motor Assessment Scale, Finger-Tapping Test, Jebsen and Taylor test, and many other complementary scales [56], for assessing arm-and-hand function. Walking assessment commonly occurs making use of different tests like Six-Minute Walk Test and Functional Ambulation Category.

1.1.4.   Treatment and Prognosis

Once the patient is diagnosed with Parkinson's disease, experts plan the treatment in combination with different therapeutic sources (physical and pharmacological) in order to control the symptoms and in the later case, advise a surgery.

Therapeutic intervention: Therapeutic interventions have been developed to support the pharmacological and neurosurgical treatment on the patient with Parkinson's disease. For this reason, multidisciplinary teams in rehabilitation services work to maximize functional ability and minimize secondary complications in the case, for instance, of levodopa administration in long-term usage precipitating motor complications which can impact on the patient's quality of life even at an early stage of the disease [18]. Consequently, occupational therapists aim to maintain their patients' usual level of self-care, work and leisure activity for as long as possible [18] while physiotherapists focus on transfers, posture, upper limb

function, balance (and falls), gait, physical capacity and (in)activity [71], besides speech-language therapists, who can help people with PD maintain as many communication skills as possible through behavioral treatment techniques, instrumental aids and others.

Pharmacological treatment: Medication should be initiated when patients experience functional impairment or social embarrassment because of their symptoms [13]. All motor-symptom treatments include indicated Levodopa-PDDI even though it can produce adverse effects like orthostatic hypotension, dyskinesia and nausea. In the same way, dopamine agonists with an efficacy level of 2 (Efficacy scored from 1: most effective to 5: least effective) and similar adverse effects are also prescribed. Regarding early mild symptoms and motor fluctuations, MAOBIs (monoamine oxidase type B inhibitors) and COMTIs (catechol-Omethyltransferase inhibitors) are indicated -despite the fact they produce an exacerbation of levodopa and other adverse effects- as well as $\beta-$Blocker for specific symptoms like tremor.

Surgical procedures: Surgical procedures in patients with Parkinson's disease are indicated: when the pharmacological treatment has destabilized responses to alleviate the symptoms, as soon as higher doses of medications are required [77].; and for subjects in advanced stages. An example of these is Deep brain stimulation (DBS); a reversible procedure whose effect is based on electrical modulation of the nervous system, reducing tremor, rigidity, and improving the slowing of movement. Other available procedures that reduce contralateral parkinsonian symptoms effectively are pallidotomy and thalamotomy in spite of the fact that bilateral lesion procedures are associated with significant side effects like speech and cognitive disorders [37].

Prognosis

Prognosis is highly variable although in general terms, advanced age at the time of diagnosis and presentation as a rigid-akinetic form, would be predictive factors of a faster progression while the tremor start form has a better prognosis [64, 69]. Similarly, a biomarker closely associated with motor progression on the rate of nigrostriatal degeneration in PD [45] was studied over time by evaluating changes in extrapyramidal signs [47] and based on a larger cohort, revealing gait disturbance is an independent prognostic factor [41].

For this reason, knowledge of the features that predict the rate of progression would allow clinicians to carry planning and development of specific treatments out according to the disease progression. Even so, current rating scales are not sufficient since they are fully dependent on physicians' expertise. Thus, alternative approaches as the gait analysis which describes the ability to walk differentiating normal and pathological gait during a gait cycle [9], are available.

1.2. Gait analysis

Gait analysis is the systematic examination of walking, or moving the body forward [58]. This task requires a series of complex interactions between neuromuscular, musculoskeletal and osteoarticular systems [12]. An advantage of the gait analysis is that it permits to evaluate and identify the mechanisms of the normal and pathological gait during a gait cycle [9].

1.2.1. Gait cycle

The gait cycle is a repetitive pattern of motion of the lower limbs involving steps and strides. It is divided into two main phases [72] (See Figure **1-1**): single stance phase and double stance or swing phase. The former is the period of time between the first and the last contact of two consecutive supports of the same foot, in which one leg is on the ground (time of single support) and the other is swinging (correspond to 70-80 % of the gait cycle); whereas the latter spans the interval in which both feet are touching the ground (double support time about 20 - 30 %) [58].
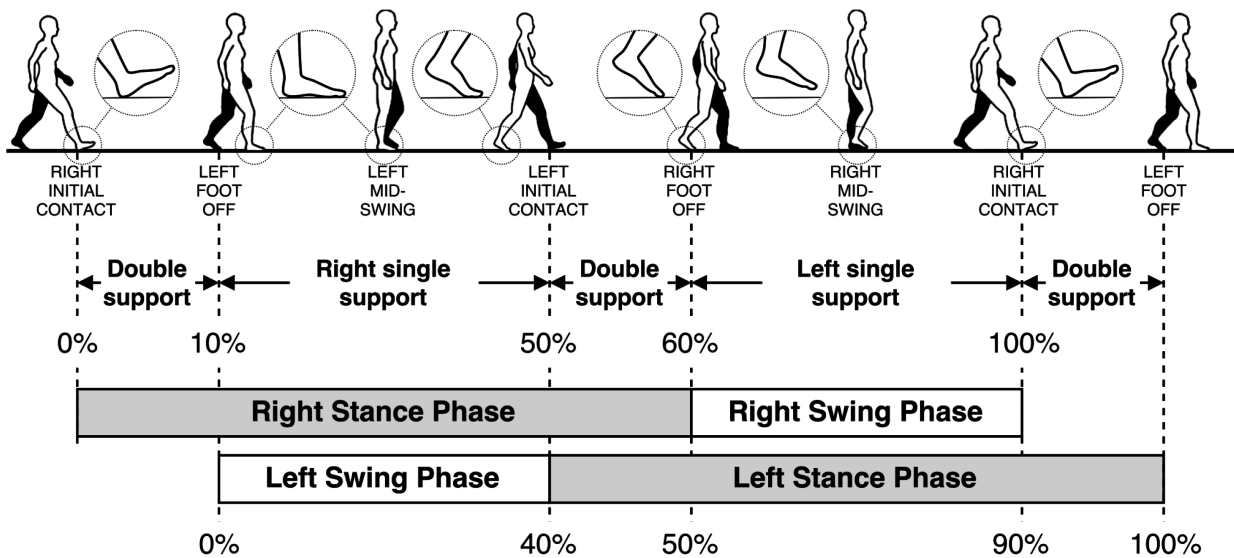
Figure 1-1.: Human Gait cycle
Ilustration From Tunca, C. et al. (2017)

Other classifications of gait cycle describe the transitions of the lower limbs during the advancement in more detail. One of them does it into 6 phases mentioned in the panel A of Table **1-4**, being centered in the different contact between foot and ground. The other classification is presented in panel B of Table **1-4** in which the stance and swing are subdivided into more specific movements.

Table 1-4.: Complementary classification of gait cycle

A	B
Heel Strike	Initial Contact
Foot Flat	Loading Response
Mid-Stance	Midstance
Heel-Off	Terminal Stance
Toe-Off	Pre swing
Mid-Swing	Initial Swing
	Mid Swing
	Late Swing

Spatiotemporal features

Studies of spatiotemporal characteristics provide objective information on three main features of the gait which are: stride length, cadence, and velocity [78].

- Stride length is the distance between two successive support points of the same foot on the ground. In other words, the distance between two steps.

- Cadence is the rate at which the individual feet contact the ground, measured in steps per minute.

- Velocity is the distance the whole body takes to move forward in a given time, measured in meters per second

Further measurements of temporal space parameters can be obtained for the identification of gait disorders. For example, gait alterations and postural instability in a group of patients with advanced Parkinson's disease are described from the acquisition of gait cycle parameters such as frequency, number of cycles, and percentage of monopodal and bipodal support among others. In the case of typical Parkinson's disease, gait disorders include shortened stride length and generally slow gait, with shuffling steps and reduced speed despite normal cadence [31, 21, 46].

Kinematic features

In gait, kinematic features correspond to the pattern of movement from the different segments of the body referring to variables such as angular displacement of the hips, knees and ankle joints over time, and postural alignment of body segments throughout the gait cycle. Figure **1-2** shows the typical pattern of the sagittal plane angles in normal adults in a study performed with young adults by a simple external marker system and algorithms for computing lower extremity.
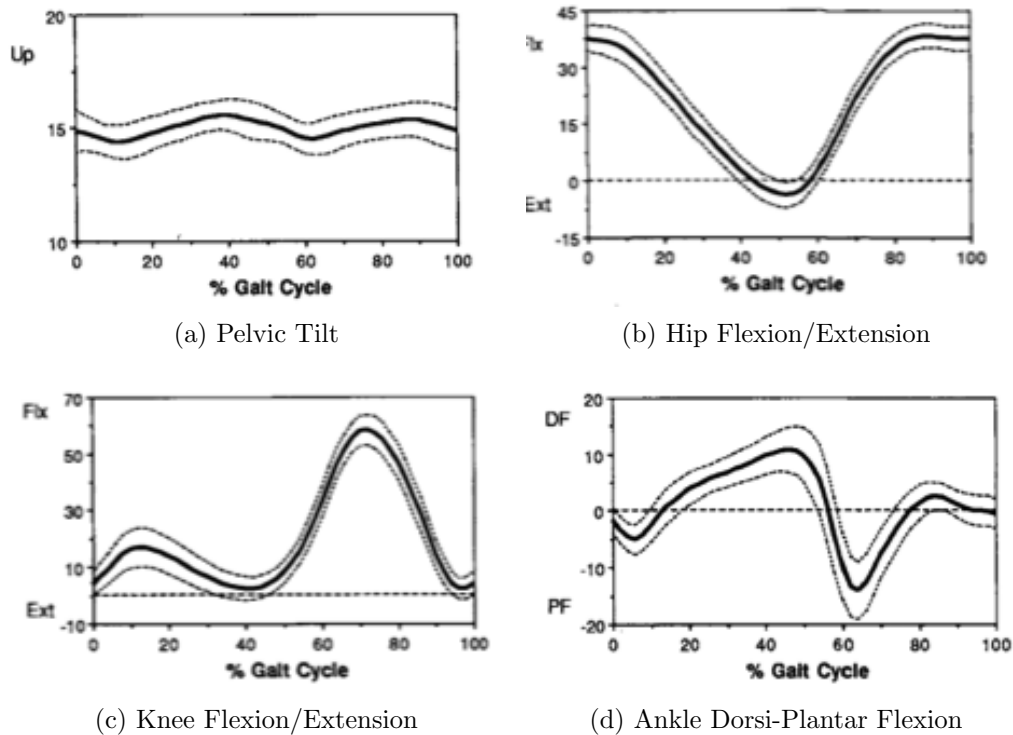
(a) Pelvic Tilt

(b) Hip Flexion/Extension

(c) Knee Flexion/Extension

(d) Ankle Dorsi-Plantar Flexion

Figure 1-2.: Sagittal plane angles of normal adults
(mean is thick line and the standard deviation are the dotted lines). From: Kadaba, M. P.,
Ramakrishnan, H. K., & Wootten, M. E. (1990). Measurement of lower extremity
kinematics during level walking. Journal of orthopaedic research, 8(3), 383-392.

Kinetic features

Kinetics refer to the underlying forces, powers and energies of the lower limbs and trunk that enable the person to walk [48]. That is to say, the cause of movement. Ground reaction forces (GRF) defined as the force exerted by the ground when the body is in the stance phase, describe the magnitude of the impact during the foot contact which varies depending on factors such as step velocity, cadence and even contact style [17].

1.2.2. Methods for gait analysis

Methods for gait analysis are based on the use of different devices to capture and measure kinematic and kinetic data that describe displacements, angles, and forces on the lower limbs and their joints during the gait cycle [1]. Then, the mechanisms used to obtain the gait data can be classified into different sources such as video cameras, wearable sensors and floor sensors.

It is stated that the first methods for analyzing and recording gait parameters involved a te-

levision camera interconnected with a PDP minicomputer in the year of 1975 [8]. Its authors report that the oldest methods with the use of stroboscopic photography and electrogoniometers date back to 1901 in 1969 respectively. Besides, different image processing techniques based on the extraction of silhouettes are used for extracting information from human walking cycle in normal and pathological gait [1, 11]. Easily-accessible tools like Microsoft (MS) Kinect [23, 73] and smart-phones, provide means to the quantification and the delivery of personalized rhythmic auditory cueing [19].

Additional wearable sensors are commonly used to capture different parameters of the gait [54], range of pressure (Pressure and Force Sensors), velocity, acceleration, orientation, gravitational forces (Inertial sensors), angles (goniometers) and contraction of the muscle (electromyography). Lastly, floor sensors such as force platforms and pressure sensors, able to quantify the components of the applied forces and the pressure patterns when the foot is in contact with the ground, evaluate the pattern in different modalities such as walking, running or jumping, both in normal (including studies with athletes) and pathological gait. Considering the info mentioned above, commercial gait analysis systems have been developed to analyze gait parameters such as running cycle time, stride length, speed and cadence, step length, time of support and swinging [11, 10]. With regards to a specific case of Parkinson's disease the effectiveness of the GAITRite system in the evaluation of bradykinesia in Parkinson's was evaluated, analyzing spatio-temporal gait parameters with On-Off medication status, finding the correlation to the results obtained in the UPDRS-III test [10].

1.2.3.   Modeling human gait

In order to know the complex dynamics of human motion, several studies have approached the gait analysis from the development of different models which achieve to describe some kinematic patterns during locomotion. Following the mechanic approach, the gait dynamic was represented by a double inverted pendulum system [24, 43, 44] (see figure **1-3**), an inverted pendulum that follows the pattern produced when muscles are weakened, a three-dimensional pendulum model adapted to normal gait [63].

Similarly, a general formulation of a motion equation that is applied to modeling the gait in young healthy subjects was introduced [52]. Nevertheless, these models are ineffective in actual clinic scenarios since they remain really far from characterizing gait dynamic patterns in pathologic conditions [12]. Consequently, to characterize patterns of Parkinson gait, another model describes the center of gravity trajectory during a gait cycle in patients with Parkinson's disease in stages 2, 3 and 4 (see figure **1-4**). This model represents the gait cycle phases by a coupled-pendulum, that it is attached to damper and spring elements, which is described by a system of two non-linear differential equations [5]. Results of this approach
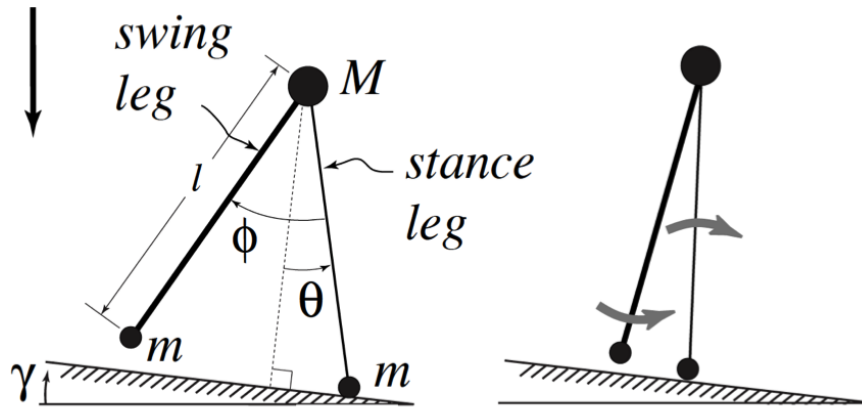
Figure 1-3.: Inverted pendulum model
It has two rigid legs connected by a frictionless hinge at the hip. Ilustration From Garcia et al. (1998)
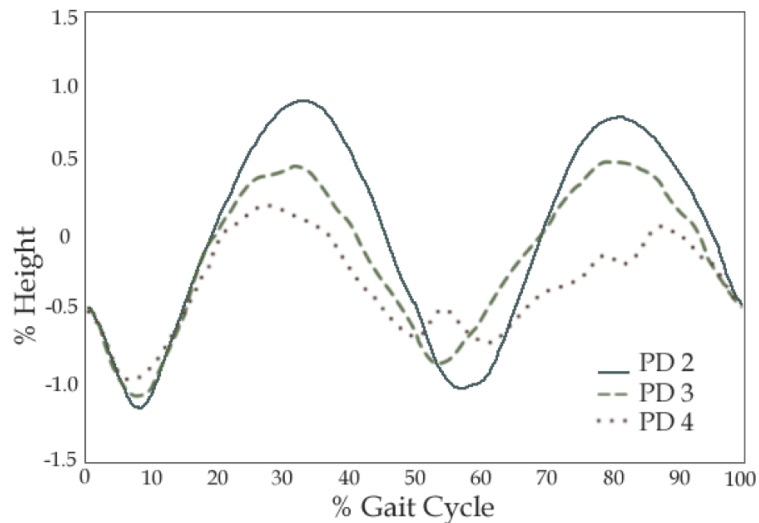
Figure 1-4.: Mean curve of the CoG trajectory in PD
Illustration from Cardenas et al. 2016

report a decrease in the amplitude of the real CoG trajectory as well as the greatest value of k and b parameter in patients with Parkinson's disease while the disease progress. With this physical gait model is possible understanding the disease with physiological interpretability. Even though the physical model represented the single support phase as a couple of rigid pendulums and the double instance phase as a damper spring system.

1.3.   Proposed Approach

This thesis proposed a methodology that characterizes gait patterns in Parkinson's disease through a simple computational model, estimating the force generated at each gait cycle by a single grounded pendulum developed by the Euler- Lagrangian equation which describes the gait patterns in control and Parkinson subjects. This approach was previously published in the 13th International Conference on Medical Information Processing and Analysis (See chapter 2).

Contribution

The following are the main contributions of this study:

- Design of a simple computational model to estimate a force that characterize the gait dynamics in Parkinson's Disease.

- A reproducible objective measurement of the disease progression that may support therapeutic interventions.

2. Quantifying Gait Patterns in Parkinson's Disease

Parkinson's disease (PD) is constituted by a set of motor symptoms, namely tremor, rigidity, and bradykinesia, which are usually described but not quantified. This work proposes an objective characterization of PD gait patterns by approximating the single stance phase a single grounded pendulum. This model estimates the force generated by the gait during the single support from gait data. This force describes the motion pattern for different stages of the disease. The model was validated using recorded videos of 8 young control subjects, 10 old control subjects and 10 subjects with Parkinson's disease in different stages. The estimated force showed differences among stages of Parkinson disease, observing a decrease of the estimated force for the advanced stages of this illness.

2.1. Introduction

Parkinson's disease (PD) is worldwide the second most common neurodegenerative disorder of the central nervous system [74][50]. Specifically, this illness is caused by a loss of dopaminergic neurons in the substantia nigra [7], resulting in a motor deterioration with symptoms such as restring tremor, rigidity, bradykinesia and postural instability [69][66]. These motor changes are a major cause of morbidity and mortality among these patients[74].

PD diagnosis and follow up depend on a proper assessment of the progression of these symptoms [47][34]. One of them, the rigidity, is also crucial to evaluate the treatment efficacy[60]. Currently, both diagnosis and monitoring are performed with scales that require a high degree of expertise at evaluating or interpreting results [12]. Moreover, a reliable PD test is not yet available [15]. Hence, there exists an actual necessity of supporting the clinic assessment with objective measures of motor symptoms such as rigidity and walking limitation [20].

Several works have developed different kinds of models that approximate the dynamic of human body motion during the gait with different pendulum models. García M. et al [24] represent the gait dynamic by a double inverted pendulum system, producing a periodic motion applied to design anthropomorphic robots, prosthetic devices, and rehabilitation procedures. Kuo et al. [43, 44] evaluate the hypothesis of optimizing the spent energy using a model with a coupled inverted pendulum. Komura et al. [40] simulates the gait motion by an inverted pendulum that follows the pattern produced when muscles are weakened. Sakka et al. [63] represent human walking by a three-dimensional pendulum model adapted to normal gait. Likewise, Mcgrath et al. [52] introduce a general formulation of a motion equation that is applied to modeling the gait in young healthy subjects. Nevertheless, these models are ineffective in actual clinic scenarios since they remain really far from characterizing gait dynamic patterns in pathologic conditions [12]. In contrast, Cárdenas et al. [5] introduced a physical model that emulates the double stance phase when both legs touch the ground. This study reported a larger difference for the vertical displacement of the CoG trajectory during the double stance phase in patients with Parkinsoń disease.

This work proposes a simple characterization of gait patterns at any stage of the PD by estimating the force generated during the single stance phase. The main contribution of this work is the introduction of a method that quantifies different stages of the Parkinson's disease, facilitating the design of prognosis indexes and the development of rehabilitation protocols. This method estimates the force generated at each instant of time during the single stance phase from the gait data.

2.2. Methods

Gait is essentially a periodic sequence of movements that transfer the body weight from one limb to the other [58]. A sequence of these movements is called the gait cycle and is divided into two phases: the single stance phase and the double stance phase. The former is the period during which one leg is on the ground and the other is swinging (correspond to 70-80 % of the gait cycle) while
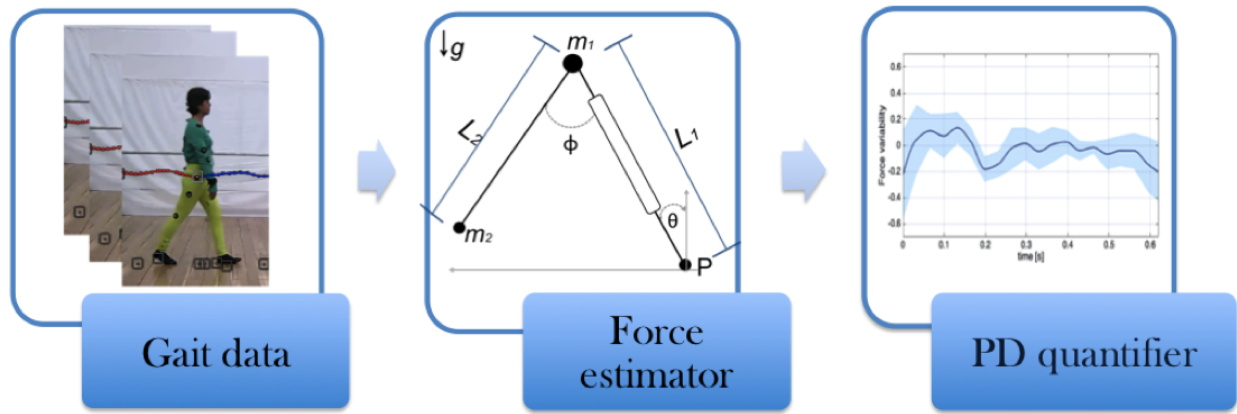
Figure 2-1.: PD quantifier methodology
Gait is captured in videos, sacral and foot markers are tracked and recorded for later
analysis. Using the marker trajectory the force is estimated and quantified in PD subjects

the other phase spans the interval in which both feet are touching the ground (about 20-30 %). Interaction of these two phases is defined by the Center of Gravity (CoG), which is a sensitive indicator of postural stability changes [30].

The approach herein proposed emulates the support phase by estimating the force by a 2D physical gait model that characterizes the gait pattern of PD at each gait cycle. The movement is close to an inverted and grounded pendulum. Which it has a moving rod as illustrated in the pipeline in Figure **2-2** which approximates the global dynamics of the leg motion seen in the sagittal plane during a gait cycle.

2.2.1. Gait data acquisition

Gait data were obtained by recording the gait in the sagittal plane in non-controlled conditions. The experimental setup corresponded to a walkway of $3,8\,m$ long and a video camera placed $1,5\,m$ perpendicular to that walkway. Gait data were captured at a sampling rate of $30\,\frac{fr}{s}$ for Parkinson subjects and a Control Group at a resolution of 1920×1080 pixels. Reflective markers were placed on the subject under the Plug in Gait protocol. The gait data acquisition consisted in extracting the (x,y) sagittal plane coordinates of the marker placed on the posterior superior iliac spine (left and right) and the marker located on the lateral malleolus. Once these coordinates were set, a distance between the markers is calculated at any time of the recorded sequence, in particular for the support leg, noted as L_1 in figure **2-1**. Subsequently, velocity ($\dot{L}_1$) and acceleration ($\ddot{L}_1$) were also obtained.

2.2.2.   Force estimator

The motion description is extracted under a Lagrangian approach assuming the energy cost is a continuous function which continues in a cycle per cycle analysis for greater interpretability of the gait patterns of PD. The proposed force estimator (see Figure **2-2**) consists of a point mass (m_1) that represents the 50 % the body weight and it is attached to two weightless rods which symbolize the lower limbs (L_1 and L_2). The first limb (which is the support leg) is represented by a moving rod of length L_1 fixed at a pivot point (P). This moving rod approximates the global dynamic of motion of leg during the support phase, which it is forming an angle of θ with the vertical. The second limb (which is the swinging leg) is represented by a rigid rod of length L_2 attached to a second mass (m_2) which it is the foot mass (1.5 % body weight) that it does not having any contact with the floor.
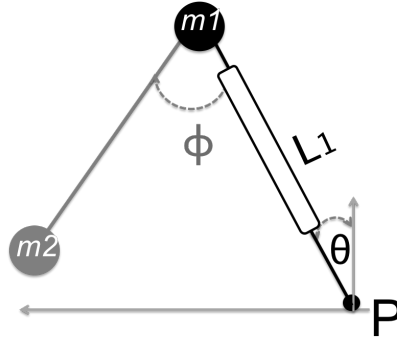

Figure 2-2.: The force estimator

It is assumed three degrees of freedom: two kind of rotational movements, defined as θ that corresponds to the angle of the advancement of the support leg and ϕ as the angle between the legs, and a translational movement which takes place along by L_1.

Total Kinetic energy of the system is $E_K = \frac{1}{2}m_1\dot{\theta}^2L_1^2 + \frac{1}{2}m_1\dot{L_1}^2 + \frac{1}{2}m_2\dot{\phi}^2L_2^2$ and total potential energy is: $E_P = m_1gL_1cos\theta + m_2gL_1cos\theta - m_2gL_2cos(\phi - \theta))$. Since the full Lagrangian is: $\mathcal{L} = \frac{1}{2}m_1\dot{\theta}^2L_1^2 + \frac{1}{2}m_1\dot{L_1}^2 + \frac{1}{2}m_2\dot{\phi}^2L_2^2 - m_1gL_1cos\theta - m_2gL_1cos\theta + m_2gL_2cos(\phi - \theta)$.

Now, the Euler-Lagrange's relation applies $\frac{d}{dt}\left(\frac{\partial \mathcal{L}}{\partial \dot{q}}\right) - \frac{\partial \mathcal{L}}{\partial q} = F_i$ being in this case $\mathcal{L}$ the total system energy q position, $\dot{q}$ the velocity observed from sagittal plane and F_i a non-conservative force of the system . For detail of solution of motion equation of the force estimation see Annex A.
The solution for L_1 coordinate is obtained:

$$F_{L_1} = \quad m_1\ddot{L_1} - m_1\dot{\theta}^2L_1 + m_1gcos\theta + m_2gcos\theta \tag{2-1}$$

The position (L_1), velocity ($\dot{L_1}$) and acceleration ($\ddot{L_1}$) data were extracted from the gait videos, and subsequently, a value of the force (F_i) was estimated at each instance of time using equation 2-1.

2.2.3.   Characterization of gait patterns

Quantification of gait patterns in Parkinson's disease is achieved by estimation of the force F_{L_1} during the translational movement L_1 in the support phase at each gait cycle using the extracted gait data obtained from each subject for each time of the whole gait cycle, as it was described in subsection 2.2.1.

2.2.4.   Data collection

Eighteen healthy subjects (8 young subjects and 10 old subjects) and ten patients with Parkinson's disease (PD) have been studied. All of them gave their informed consent approved by the ethics committee of the Universidad Nacional de Colombia, according to the Helsinki Declaration [80]. The age of the subjects was $57,3 \pm 5,51$ years for the old control group, $26,75 \pm 2,36$ years for the young control group and $63,60 \pm 10,15$ years for Parkinson patients. Anthropometric characteristics as height (m) and weight (kg) were specified in Table **2-1** for each group. Parkinson patients group were classified on the Hoehn & Yahr scale (see: Table **2-2**).

Table 2-1.: Dataset characteristics

	Young group		Old group		Parkinson Group	
Gender	F	M	F	M	F	M
N. subjects	3	5	5	5	6	4
Age	$27,66 \pm 2,36$	$26,20 \pm 3$	$57,8 \pm 2,8$	$56,8 \pm 7,25$	$63,60 \pm 10,15$	$56 \pm 10,56$
Height (m)	$1,59 \pm 0,05$	$1,76 \pm 0,08$	$1,54 \pm 0,03$	$1,72 \pm 0,07$	$1,53 \pm 0,05$	$1,65 \pm 0,06$
Weight (kg)	$59,66 \pm 7,41$	$75,20 \pm 11,62$	$66,2 \pm 5,15$	$68 \pm 8,8$	$56,30 \pm 5,79$	$68,25 \pm 7,50$

Table 2-2.: The Hoehn and Yahr (H&Y) score

Stages	N. videos
1	2
2	3
3	4
4	1

2.3.   Results

Gait data corresponding to the single stance phase was extracted and an average of the estimated force was obtained per experimental group, namely the two controls and each different stage of PD. Figures **2-3** and **2-4** shows the curve of the estimated mean force and its standard deviation per

group as a function of the gait cycle. The first part of the curve $(0 - 15\%)$ was calculated during the heel contact while the last part $(80 - 100\%)$ corresponds to the final contact before swinging.

Control subjects were classified by gender (see Figure **2-3**) since the gait pattern is definitely dependent on the body weight and this factor may clearly influence the force estimation. This claim is observed in the right upper panel, where the curve of the young men group (see Figure **2-3**b) when compared to the young women group, is in general higher and performs a larger amplitude. Interestingly, the variance for the male group is also larger. In contrast, this difference is not observable for old control subjects. In this case, a remarkable observation is that the estimated force is overall larger for the old group and with oscillations that probably are compensatory movements of the gait in the frontal plane. Both variances look alike in this case. These results are consistent with a study where explore the ground reaction force in young and old people [36], which was evidence an increase of the value of the force in old people compared to the young subjects.
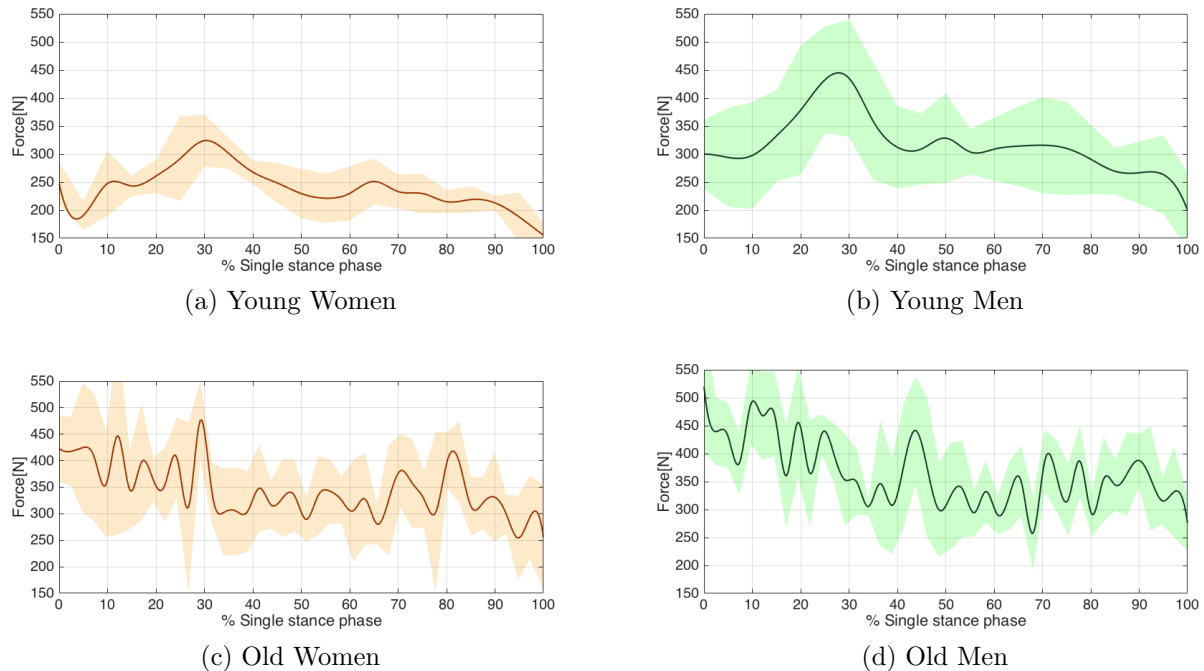

(a) Young Women

(b) Young Men

(c) Old Women

(d) Old Men

Figure 2-3.: Estimated force control subjects

On the other hand, the estimation of the force in the Parkinson group is shown in Figure **2-4**. These estimated results illustrate different patterns of the force for the different stages of the illness. Note how the amplitude of the force curve decreases on the first 10%, which corresponds to the instant of the gait initiation. This factor is consistent with a study that explores the ground reaction forces in patients with PD at different stages [67], it demonstrated a decrease in the average value of force while the disease progresses. Meanwhile, for the first stage (left upper panel) shows higher values for the first $(0-10\%)$, that corresponds to the instance of gait initiation, and last $(80-100\%)$ parts of the curve, evidencing the progressive rigidity of the gait. The pattern is also smoother in the two

early stages of the disease (upper left and right panels) when compared with the two other ones (bottom left and right panels).

The transition between stages 2 and 3 (see figures **2-4**b and **2-4**c) turns out to be characterized by a more oscillating pattern, probably necessary to compensate the rigidity progression, yet less evident than the pattern at the beginning and end of the cycle. Finally, stage 4 shows a very oscillating pattern with a very small value at the beginning the smallest value also at the end. It should be strengthened out that the number of the subject per group is different and this of course influences these observations, for instance, the graph for stage 4 corresponds to a single patient in an advanced stage and the variance to the different captures performed for this patient.
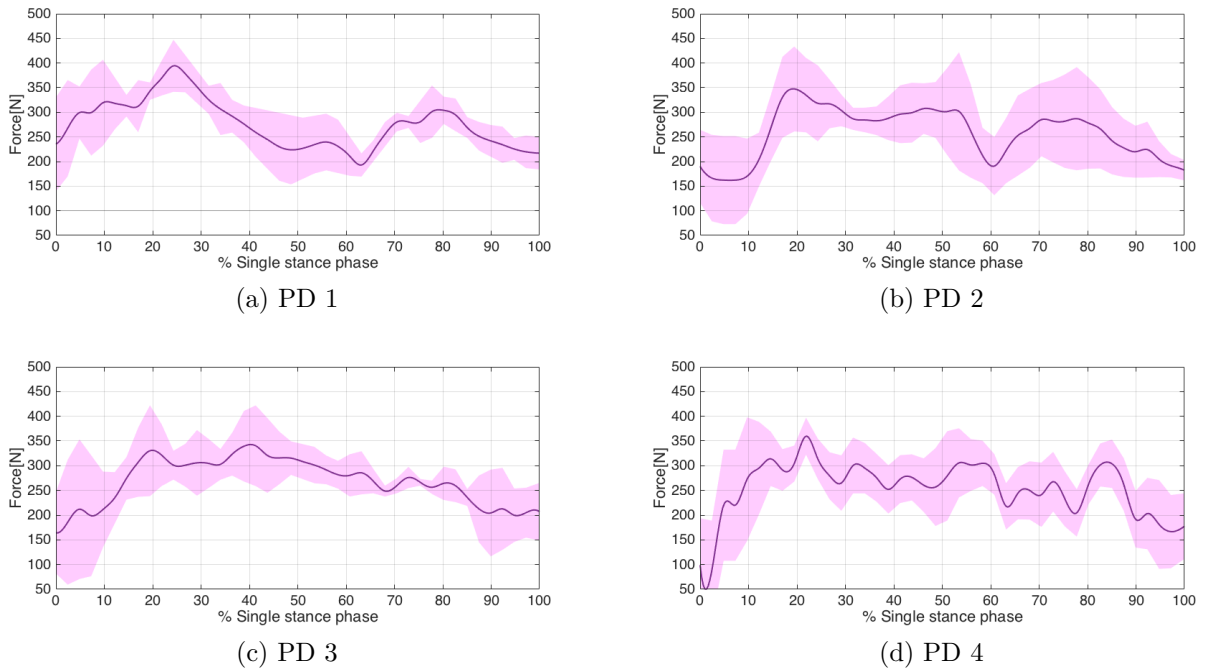

(a) PD 1   (b) PD 2

(c) PD 3   (d) PD 4

Figure 2-4.: Estimated force Parkinson group

An interesting observation is the force variability along the time. The variability of the estimated force was then obtained for each of the groups following the equation: $(F_{i+1} - F_i)/F_{i+1}$ where F_i is the estimated force for each time.

In the young control group, although there are different estimated forces between men and women, it can be observed a low variability. In the old control group, there is a higher oscillation and a larger variability with respect to the young group. While the Parkinson group showed the largest variability (See: Figure **2-5**c), above all for the first and last parts of the curve, which corresponds to the initial and final contact of the foot during the single support.

Figure **2-6** shows the force for the young control group. In the x-axis, the different shown subjects are as follows: 1, 2 and 3 correspond to women and 4-8 to men. The distribution of the estimated force is similar in the boxes with values between −0,2 and 0,1. Figure **2-7** shows the force variability

(a) Young Controls

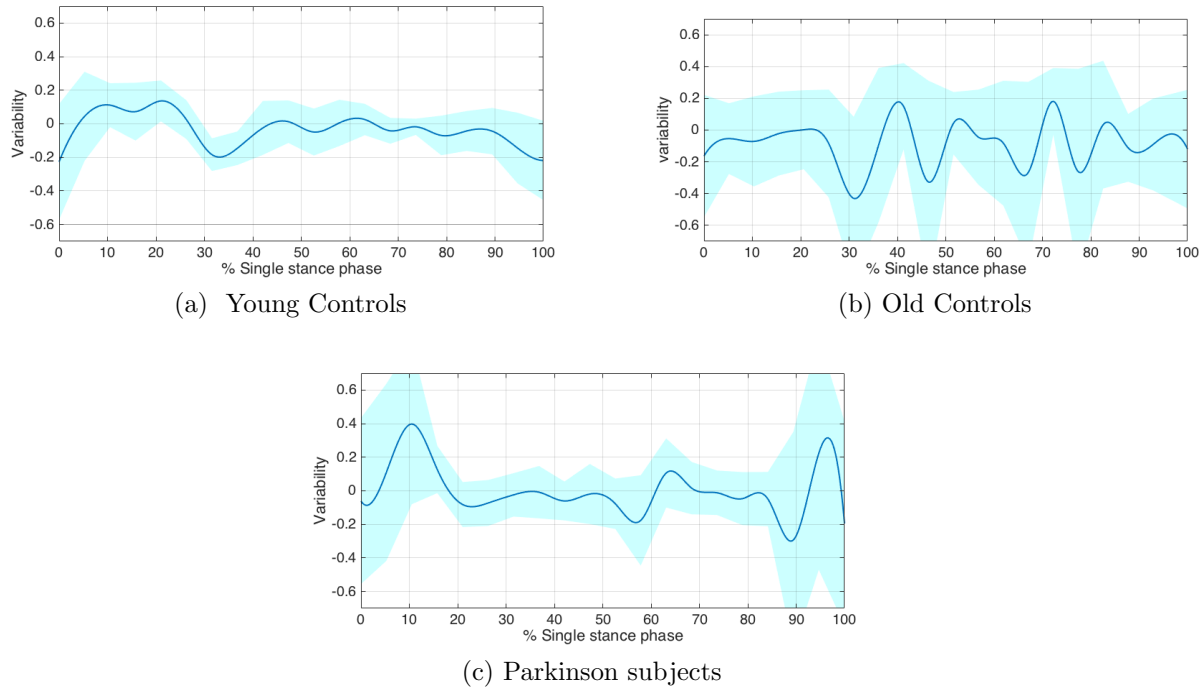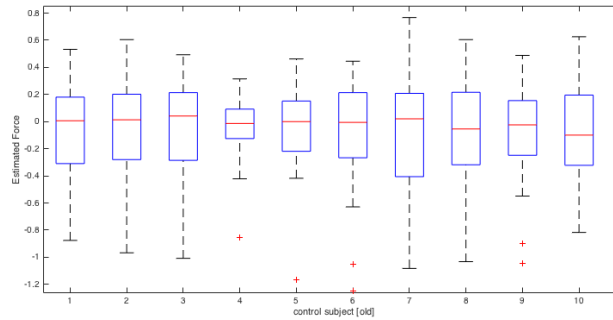(b) Old Controls

(c) Parkinson subjects

Figure 2-5.: Force variation along the time

for the old control group. Again data 1 to 5 correspond to women and 6 to 10 to men. The distribution of the estimated force is similar in the boxes with values between $-0,4$ to $0,2$. Finally, The variability of the estimated force in Parkinson group is shown in figure **2-8**. The subjects were organized by stage (PD1: 1-2; PD2: 3,4,5; PD3: 6,7,8,9 and PD4: 10). This group presents the largest variation when compared with the control subjects.
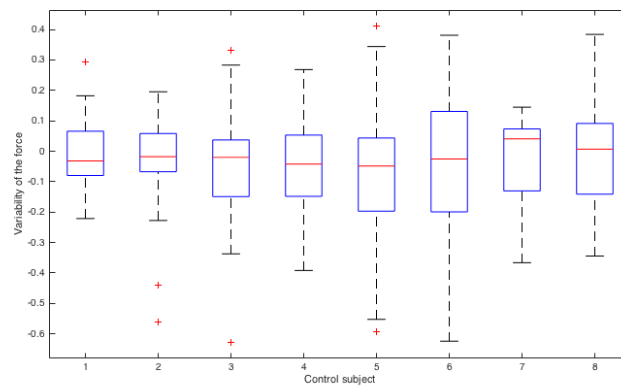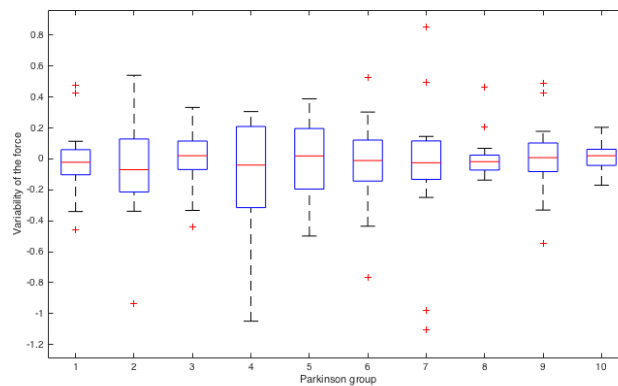

In the x-axis, the data: 1, 2 and 3 correspond to women and 4, 5, 6, 7 and 8 are men subjects.

Figure 2-6.: Variability of the force Young control group

In the x-axis, the data: 1, 2, 3, 4 and 5 correspond to men; 6, 7, 8, 9 and 10 are women.

Figure 2-7.: Variability of the force Old control group.

In the x-axis, the data: 1, 2 correspond to PD subjects in stage one; 3, 4 and 5 the stage two; 6, 7, 8 and 9 stage three; and 10 stage four.

Figure 2-8.: Variability of the force Parkinson group.

Stage 1 (PD1) shows a different distribution between subjects, while data distribution is similar between the subjects 4 and 5, compared with subject 3 stage 2 (PD2) for stage 2. This difference may be attributed to the anthropometric characteristics by gender. In stage 3 (PD3), there is less data dispersion. Likewise, there is less force variability in subject 7, which can be related to the gait pattern of this subject, i.e., a decrease of the gait speed and the step length when compared to the other subjects of the same stage. The subject in stage 4 (PD4) shows the lowest gait variation, i.e., a constant pattern of the force curve (see figure **2-5**c).

2.4. Conclusion

In this work, a method that quantifies gait patterns in Parkinson's disease is presented. A simple model estimates the force estimator for the single stance phase. The estimated force allows deter-

mining objective differences between different stages of the disease. In this study, a decrease of the estimated force amplitude is observed while the disease progresses, especially during the first foot contact. This fact is likely related to the muscle stiffness associated with different Parkinson stages.

2.5. Future work

Future work includes more extensive experimentation with a greater number of patients with Parkinson's disease in different stages. Likewise, it will be proposed to approximate of the gait dynamics from a model with a minimum number of parameters by ignoring the swinging leg and concentrating the modeling on the support leg, which has been shown in this study capable to characterize the gait in EP with a force estimator. In addition, damper and spring elements will be added. which represent the behavior of the rigidity in the different stages of Parkinson's disease.

3. Conclusions and Perspectives

3.1. Conclusions

The problem of quantifying gait patterns in Parkinson's disease even in advanced stages has been studied. For this, the main contribution of this work was the design of a simple computational model to estimate a force at each gait cycle that characterize the gait dynamics in Parkinson's Disease. Wherewith, a simple measure could support medical decisions and facilitate the design of prognosis indexes and the development of rehabilitation protocols. On the other hand, it is possible to find differences between groups due to the variability of the gait patterns. For instance, the results of the force variation along the time suggest an increase of the force variation during the first foot contact that corresponds to the period of gait initiation which is affected in Parkinson patients.

3.1.1. Future work

Taking in to account the development of this thesis, it could be implemented an automatic tool that easily extracts the relevant and specific information of the gait videos. Likewise, to explore another human gait models or complementary information of the human motion that it can predict the progress of the disease.

A. Annex: Motion equation of force estimator

The proposed physical gait model (See figure **A-1** was obtained under the Euler-Lagrange energy analysis,i.e., the system must meet three conditions for its applicability. The system must satisfy specifically: the generalized coordinates must be independent and the system is holonomic and complete.

- Independence: Note that in this system when fixing any two coordinates, the remaining coordinate is free to move, for instance if θ and ϕ are fixed, motion in L_1 is still possible, or the other way around, by fixing L_1 and any of the two angles, the motion in the remaining angle (θ or ϕ) is still possible

- Holonomic: this requirement is clearly met since the three generalized coordinates (L_1,θ and ϕ) correspond of the number of degrees of freedom, three in this case.

- Complete: The motion of this pendulum system is completely determined by the generalized coordinates (L_1,θ and ϕ).

Once this conditions are verified, the rest of the section presents in detail how the model was developed. The system is composed of two weightless rods: L_1 and L_2 where the first rod has a motion along its axis, while the second is a rigid rod. The rod L_1 correspond to an inverted pendulum which is fixed to a pivot point P with a mass m_1 concentrated on the extreme. The second rod, L_2, is a simple pendulum fixed to the extreme of the pendulum L_1 with a mass m_2. The movements of L_1 are described by the angle θ respect to the vertical which describe the advance of the support leg, and the movement along to the rod L_1. The pendulum L_2 motion is described by the angle ϕ that corresponds to the angle between legs.

To estimate the motion equation, firstly the total kinetic energy E_K and potential energies E_P are obtained:

$$E_{K1} \quad = \frac{1}{2}m_1\dot{\theta}^2 L_1^2 + \frac{1}{2}m_1\dot{L_1}^2 \tag{A-1}$$

$$E_{K2} \quad = \frac{1}{2}m_2\dot{\phi}^2 L_2^2 \tag{A-2}$$
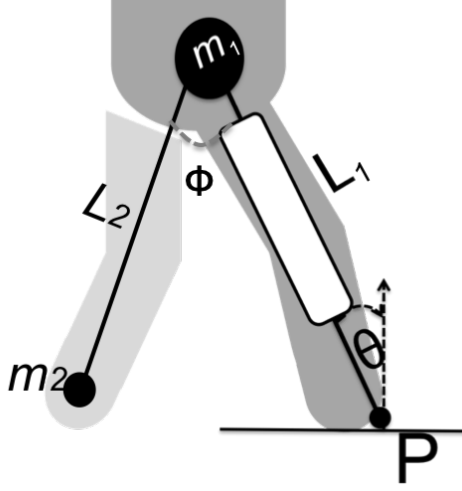
$$E_{P1} \quad = m_1 g L_1 cos\theta \tag{A-3}$$

Figure A-1.: Inverted Pendulum for stance phase

$$E_{P2} \quad = m_2 g L_1 cos\theta - m_2 g L_2 cos(\phi - \theta)) \tag{A-4}$$

Afterward, it proceeds to resolve the Lagrangian, defined by the difference of the total kinetic and potential energies:

$$\mathcal{L} \quad = \sum E_{K_i} - \sum E_{P_i} \tag{A-5}$$

$$\mathcal{L} \quad = \frac{1}{2} m_1 \dot{\theta}^2 L_1^2 + \frac{1}{2} m_1 \dot{L_1}^2 + \frac{1}{2} m_2 \dot{\phi}^2 L_2^2 - m_1 g L_1 cos\theta - m_2 g L_1 cos\theta + m_2 g L_2 cos(\phi - \theta) \tag{A-6}$$

Now, the Euler-Lagrange's equation defined in eq. A-7 is applied.

$$\frac{d}{dt} \left(\frac{\partial \mathcal{L}}{\partial \dot{q}} \right) - \frac{\partial \mathcal{L}}{\partial q} = F_i \tag{A-7}$$

Where $\mathcal{L}$ is the full Lagrangian, q and $\dot{q}$ corresponds to the components of position and velocity of each coordinate of the system seen from a sagittal plane (L_1, θ and ϕ). F_i denote a non-conservative force of the system that is a quantity applied to the system, it is the result of introducing specific inputs of position and velocity extracted from gait data to the physical gait model.

And three non-linear differential equations are obtained for this system. To L_1 see equation A-8, to θ see equation A-9 and to ϕ see equation A-10:

To F_{L_1}:

$$F_{L_1} = \frac{d}{dt} \left(\frac{\partial L \frac{1}{2} m_1 \dot{\theta}^2 L_1^2 + \frac{1}{2} m_1 \dot{L_1}^2 + \frac{1}{2} m_2 \dot{\phi}^2 L_2^2 - m_1 g L_1 cos\theta - m_2 g L_1 cos\theta + m_2 g L_2 cos(\phi - \theta)}{\partial \dot{L_1}} \right)$$

$$- \frac{\partial(\frac{1}{2} m_1 \dot{\theta}^2 L_1^2 + \frac{1}{2} m_1 \dot{L_1}^2 + \frac{1}{2} m_2 \dot{\phi}^2 L_2^2 - m_1 g L_1 cos\theta - m_2 g L_1 cos\theta + m_2 g L_2 cos(\phi - \theta))}{\partial L_1}$$

$$F_{L_1} = \frac{d(m_1\dot{L}_1)}{dt} - (m_1\dot{\theta}^2 L_1 - m_1 g cos\theta - m_2 g cos\theta)$$

$$F_{L_1} = \quad m_1\ddot{L}_1 - m_1\dot{\theta}^2 L_1 + m_1 g cos\theta + m_2 g cos\theta \tag{A-8}$$

To θ coordinate:

$$F_\theta = \quad m_1\dot{\theta}\dot{L}_1^{\;2} + m_1\ddot{\theta}\dot{L}_1^{\;2} + m_2 g L_2 sen(\phi - \theta) - m_1 g L_1 sen\theta - m_2 g L_1 sen\theta \tag{A-9}$$

To ϕ coordinate:

$$F_\phi = \quad 2m_2\dot{\phi}L_2 + m_2\ddot{\phi}L_2^2 - m_2 g L_2 sen(\phi - \theta) \tag{A-10}$$

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