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Smartphone based automated detection of freezing of gait in people with Parkinson's disease

Author:
Luigi Borzì

Supervisor:
Dr. Gabriella Olmo

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Abstract

Parkinson's disease (PD) is the second most common neurodegenerative disorder, with serious motor and non-motor complications associated. **Freezing of gait** (FOG) is a form of akinesia (loss of movement) affecting 50-80 % of patients with PD [186]; it has been included among classic characteristics of PD [93] and represents one of the most disabling symptoms of PD [54]. Current therapies are highly effecting in ameliorating the symptoms of the disease [50], but their delivery has to be patient-specific, based on motor fluctuations and progression of the disease in each patient [192]. Objective home and lab-based methods are necessary in order to gather more information about FOG manifestation, its frequency, duration, nature, circumstances and response to therapy [155], thus a long-term monitoring would lead precious benefit. Werable sensors have been recently proposed for providing objective assessment of FOG during the real life [169]. **Aim of this study** was the construction of a system capable of automated FOG detection, in order to prove the feasibility of a simple, small and low cost detection system for home monitoring of FOG episodes in PD patients. **Data acquisition** was executed with a commercial smartphone, which included several inertial sensors (e.g. accelerometers, gyroscopes). A total number of 59 partecipants took part in the study, including PD freezers, PD non-freezers and control sample, leading to acquisition of more than 3 hours of signal, yet only 15 FOG episodes were observed. **Data processing** of acceleration signal was executed offline; FOG was described and differentiated from other activities through a small set of features, both in time and frequency domain, and such features were given as input to two SVM classifiers for a multi-class classification problem. **Results** were promising, with sensitivity, specificity and accuracy reaching values greater than 90 %, while precision was not as good, reaching only 80 %. Despite the smallness of the FOG dataset does not allow to give the results statistical meaningfullness, detection algorithm demontrated great ability of generalization and robustness.

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1 Parkinson's disease

Parkinson's disease (PD) is a chronic, progressive, neurodegenerative disorder whose prevalence increases with age. The overall incidence rate was found to be greater than 17 per 100,000 person-years [85]. PD is characterize by the death of the dopamine[1]-producing neurones in the substantia nigra. The main PD symptoms are bradykinesia, rigidity, tremor and postural instability [161]. However, a number of non-motor symptoms (e.g., sleep disturbances, depression, psychosis, autonomic and gastrointestinal dysfunction as well as dementia) may occur as well [87] [37]. Current PD treatments aim to increase dopamine levels, with levodopa being the most used one. Although this drug temporally reverts the symptoms, it does not prevent disease progression [159]. Many rating scales are available for the evaluation of motor impairment and disability in PD patients; Unified Parkinson's Disease Rating Scale (UPDRS) is the mos uttilised by neurologists to evaluate different aspects of PD.

1.1 Incidence

PD is the second most common neurodegenerative disorder, affecting approximately 0.3% of people in the world. This value rises to 3% for individuals older than 65 years, being **aging** a major risk factor [43]. Mean age at onset is 55 [36], mean age at diagnosis is 70 both for men and women [182], and the incidence[2] ranges from 0.5 per 100,000 in the 30-40 year category to 120 per 100,000 in the oldest age category (over 70) [182]. After aging, the male **sex** is the most prominent risk factor for developing PD at all ages and for all nationalities [45]. Male to female ratios for incidence rates range from 1.37 to 3.7 and generally increases with age, suggesting that twice as many men than women suffer from PD [182]. Incidence of PD also seems to vary by **ethnicity**: highest incidence was found among Whites and Hispanic [35] [182], while both prevalence[3] and incidence are lower in Asians than in Whites [130]. It has been observed an increase of almost 50% in the incidence of both parkinsonism of all types and of PD over the 30-year period from 1976 to 2005, particularly in men older than 70 years. This **time trend** needs to be interpreted with caution. It may be an artifact due to improved access to care of patients, or to increased awareness of signs and symptoms of parkinsonism by physicians [160].

1.2 Pathogenesis

Parkinson's disease is typified by a degenerative process that affetc dopaminergic neurons in the substantia nigra. How the degenerative processes damages both the nigrostriatal system and other brain regions is not completely clear. Studies in literature suggest two major hypotheses regarding the pathogenesis of the disease. One hypothesis indicate **misfolding and aggregation** of proteins to provoke the death of Substantia nigra pars compacta (SNpc) dopaminergic neurons [20],

[1] neurotransmitter required for a correct movement control [93]

[2] number of new cases per population at risk in a given time period

[3] proportion of population with a disease at a specific point in time

while the other proposes the **mitochondrial dysfunction** and the consequent oxidative stress [191], including toxic oxidized dopamin species. The pathological hallmarks of PD are the loss of the nigrostriatal dopaminergic neurons and the presence of intraneuronal proteinacious cytoplasmic inclusions, named Lewy Bodies (LBs) [36]. LBs are α-synuclein inclusions composed of neuro-filament proteins and proteins responsible for proteolysis. These include ubiquitin, a protein playing a primary role in targeting other proteins for dejection. Mutations in the α-synuclein gene are responsible for some familial forms of PD in which LBs are also observed [37]. It has been shown that parkin[4] facilitates the binding of ubiquitin (ubiquination) to other α-synuclein interacting proteins, leading to the formation of LBs [33]. Ubiquitin-proteasome system (UPS) is a potential culprit in the development of cell death. The UPS plays an important role for intracellular proteolysis and several intracellular processes that maintain the viability of cells. Failure of the UPS leads to the abnormal aggregation of proteins including α-synuclein, which are a major component of LBs. The link between UPS and neurodegeneration has been reinforced by the discovery of mutations in genes which code for several proteins belonging to ubiquitin-proteasome system in PD [37].

1.3 Symptoms

The four main features of PD are tremor at rest, rigidity, akinesia (or bradykinesia) and postural instability. Also flexed posture and freezing of gait (motor blocks) have been included among classic characteristics of parkinsonism, with PD being the most common form [93]. Non-motor symptoms are often present before diagnosis, rise with disease progression and contribute to severe disability, impaired quality of life and reduced life expectancy. Non-motor symptoms are often not well recognised and consequently inadequately treated [29]. Some non-motor symptoms (e.g. depression, constipation, pain, and sleep disorders) can be improved with nowdays treatments, while others need the administration of non-dopaminergic drugs. Treatments aim to slow or prevent the progression of Parkinson's disease and provide the best hope of treating non-motor symptoms.

1.3.1 Motor

Tremor can manifest in PD patients in different forms:

- Rest tremor is one of the PD cardinal signs; is often asymmetric, shows moderate amplitude and frequency ranging from 4 Hz to 6 Hz. It is caused by an agonist-antagonist alternate contraction pattern [39]. Typically, it disappears with action and during sleep [93].

- Reemergent tremor represent an action tremor which manifest few seconds after the transition from rest to posture and has a frequency content similar to that of rest tremor.

[4]component of a multiprotein E3 ubiquitin ligase complex which in turn is part of the ubiquitin-proteasome system

- Essential tremor [39].
- Dystonic tremor [167].
- Exaggerated physiological tremor [75].
- Postural tremor is more prominent and disabling than rest tremor and sometimes is the first manifestation of PD [94].

Almost always tremors are prominent in the distal part of an extremity. Tremor frequency ranges from low (4–5 Hz) to high (8–10 Hz) [80]. Pathophysiologically, tremor is linked to altered activity in the basal ganglia circuit, which is affected by dopamine neurons breakdown, and the cerebello-thalamo-cortical circuit, which is also involved in many other tremors [80]. Tremor is not correlated with other PD motor symptoms, such as bradykinesia and rigidity; the magnitude of tremor is not related to the lack of dopamine and does not respond readily to dopamine treatment [76]. Studies in literature indicate tremor to be a marker of benign Parkinson's disease [86]. The occurrence of rest tremor varies among patients and with disease stage. Clinically, tremor is seen in 75 % of patients with PD. Both thermocoagulation and deep brain stimulation provide good to excellent tremor control [80].

Rigidity is defined as an increased resistance during passive mobilization of a body extremity [10], and is one of the main hallmarks of PD. PD rigidity is typified by increased muscle tone, reduced distension to passive movement, increased resistance to stretching [156]. The increase of rigidity during voluntary movement of other body part and during stretching is a feature that helps differentiating PD rigidity from spasticity, which worsens during fast displacement [5]. Similarly to tremor, no direct correlation has been shown between dopamine deficiency and rigidity [156]. The mechanism underling PD rigidity has been suggested to include changes in the passive mechanical properties of joints, tendons, and muscles, and abnormalities in peripheral sensory inputs that may influence the response to muscle stretch [157].

Bradykinesia represents the slowness of a performed movement and is the symptom that best correlates with dopaminergic deficiency [53]. Akinesia and hypokinesia refers respectively to a poverty of spontaneous movement (e.g. in facial expression) or associated movement (e.g. arm swing during walking) and to the low amplitude of movement [13] [93]. Potentially, bradykinesia could be due to slowness in programming or executing movements, given some instructions [47]. However patients with PD demonstrate intact motor programmes but have difficulties in movement performing without an external trigger, which may be a loud noise or a visual cue requiring them to overcome an obstacle [93]. Although muscle weakness and other PD motor symptoms may contribute, the principal deficit was found to be the insufficient recruitment of muscle fibers during the initiation of movement [13]. In current clinical practice, the assessment of bradykinesia is carried by observing the slowness and the amplitude of movements during the

execution of rapid, repetitive, alternating movements of the hand and heel tapping [93].

Postural instability is due to the loss of physiological postural reflexes and commonly manifests in advanced stages of PD, after the onset of other clinical features [93] [21]. Together with freezing of gait, it is the most common cause of falls and leads to high risk of hip fractures [188]. It also may contribute to limitations in gait and decreased mobility [21]. Many studies have indicated rigidity, dystonia, abnormal processing of proprioceptive signals [42], abnormal spatial cognition, and side effects of treatment drugs [27] as causes of postural instability. Abnormal postural response is clinically accessed through the pull test, in which the clinician quickly pulls the patient backward by the shoulders and quantifies the degree of retropulsion: if patient takes more than two steps backwards or does not show postural response, this indicates an abnormal postural response [93]. Treatment (dopaminergic therapy and deep brain stimulation) can improve some axial signs but usually does not robustly improve postural instability [112].

1.3.2 Neuropsychiatric

Depression is a very common condition in patients with PD, with prevalence between 20 % and 70 % [73] [154]. Depression in PD manifests as losing interest, sleep and appetite, decreased energy and motivation, sadness and thoughts of suicide [87]. Prevalence of **Anxiety** disorders is higher in PD patients than age-matched controls (prevalence >40 %) [183] and seems to be related with the motor fluctuations [118]. **Dementia** in PD may manifests in advanced stages. Although PD patients demonstrate cognitive slowing and impaired memory recall, recognition memory remains intact [17]. **Hallucinations** occur in PD, more frequently in the advanced stages. Psychosis and visual hallucinations are common, dose-dependent adverse effects of dopaminergic medications, together with disease progression and medical illnesses [40]. Risk factors include advanced age, presence of dementia, and polypharmacy. **Sleep disturbances** are common in PD patients. Because of depression and/or hallucinations, patients may become restless at night and have difficulty falling asleep. Higher risks for pathologic sleep include male gender, advanced stage of the disease, cognitive impairment and drug-induced psychosis [174].

1.3.3 Other

Orthostatic hypotension induces position-related dizziness, which often leads to falls in PD patients, fatigue or even fainting. This symptom may not manifest as a major problem until later stages [68]. Dopaminergic medications may even worsen the symptoms [101]. Gastrointestinal symptoms are a common problem in PD. **Dysphagia** represents a major risk for polmonite ab ingeris, which is a one of the most common causes of death in PD patients [100]. **Constipation** is the most common problem and often is one of the early signs of PD, even before the appearance of the motor symptoms [147]. At least 59 % of PD patients suffer from constipation as compared with 21 % in age-matched non-PD patients [98].

Nausea affects many PD patients suffering of the side effects of levodopa or other PD medications. Irregular peristalsis is due to the stimulation of dopaminergic receptors, especially receptors of gastrointestinal tract [87]. About one patient out of three experiences incontinence, due to a spastic bladder [190]. Severity of bladder dysfunction is has been correlated with the progression of PD [189]. Finally, patients, particularly those taking dopaminergic medications, may become **obsessive and compulsive** in gambling, shopping, spending or even sex [87].

1.4 Management

Parkinson's disease is typified by the loss of dopaminergic neurons in the substantia nigra. The course of the disease follows the progressive degeneration of the remaining dopaminergic neurons [153]. Until fifty years ago, ablative surgery to the controlateral thalamus was used in patients with severe tremor. Surgical treatment has than been replaced by **levodopa**, a dopamine-replacement therapy highly effective in improving the symptoms of the disease; it is nowdays the standard drug for PD treatment [50]. The introduction of stimulators provided a further development. Deep brain stimulation (DBS) allows specific electrical stimulation of basal ganglia instead of an irreversible lesion. DBS aims to reduce bradykinesia, tremor and rigidity; bilateral subthalamic stimulation also reduces drug-related motor complications [97]. This can produce dramatic benefit. Dopamine agonists[5] and monoamine oxidase (MAO)-B inhibitors[6] have been found to relief motor symptoms of PD and lead to a low risk for motor complications [166]. The **MAO-B inhibitor** selegiline, if administrated early in the course of PD, has been shown to improve PD motor symptoms and activity of daily living (ADLs) score, and the effects persist up to 7 years or more [92]. Although **dopamine agonists** are not as effective as levodopa, they have demonstrated reduced risk of diskinesias [72], and this may be realeted to their longer half-life, compared to levodopa [161]. Current medical and surgical therapies for PD are symptomatic and lack significant disease-modifying effect [161]. At present, there is no proven neuroprotective therapy, and only symptomatic treatments are available [37]. The choice of the therapy has to take into account several factors:

- The age of the patient.
- The presence of cognitive impairment.
- Additional medical conditions.
- Compliance of the patient.

Treatment is carried out in the initial stage to ameliorate symptoms and to allow the patient to be fully independent. Of fundamental importance is that treatment is well tolerated by patient. Since life expectancy, from diagnosis to death, in patients with PD is 17 years [81], a long-term treatment strategy is needed for most patients, and this should be discussed with the patient at an early stage.

[5] compound that activates dopamine receptors

[6] class of drugs that inhibit neurotransmitter degradation, including dopamine, thus increasing their concentration in the CNS

1.4.1 Levodopa

Levodopa (L-3,4-dihydroxyphenylalanine) is the metabolic precursor of dopamine and is combined with carbidopa[7] for reducing the induced side effects (e.g. nausea) and maximizing levodopa transport into the CNS [119]. Levodopa-based treatment led to a significant improvement in both the quality of life (QoL) and life expectancy of patients, although it does not revert disease progression [81]. It represents the most effective drug treatment for Parkinson's disease [37]. Effectiveness of levodopa decreases with disease progression [144] and long-term therapy frequently leads to severe side effects. Levodopa-induced dyskinesias are the most common ones, occurring in more than 50 % of PD patients within 10 years from starting levodopa treatment [28], with pulsatile administration and higher doses being sources of motor fluctuations. For this reason, continuous dopaminergic delivery is necessary in order to minimize motor complications in PD [192]. The time at which the adverse events manifest strongly depends on the severity of dopaminergic neuron loss at the introduction of levodopa [168].

1.4.2 Deep Brain Stimulation

Deep brain stimulation is the most common surgical therapy for motor complications in advanced stages of PD and has demonstrated to be effective in symptomatic PD therapy [19]. Benefits provided by DBS are more constant and predictable, compared with pharmacological therapy [48]. Stimulation of the subthalamic nucleus (STN) was found to reduce motor symptoms of PD, such as dyskinesias, bradykinesia, akinesia, and tremor [143]; it also reduces dopaminergic drug posology [48]. DBS requires an electrode to be inserted through the skull to stimulate the globus pallidus (GPi), STN, or thalamus. A device, similar to a pacemaker, is implanted under the skin and wires connect the device to the electrode. Effective frequency for STN or GPi stimulation has been indicated to be above 100 Hz [187]. The most evident results of this therapy are the reduction of "off" time, increased "on" time without dyskinesia manifestations, reduction of required levodopa dose, and improved tremor [161]. DBS therapy is used for advanced stages of disease, when motor complications have led to an dramatic reduction in quality of life.

1.5 Rating scales

1.5.1 Hoehn and Yahr scale

The Hoehn and Yahr scale (H & Y) is a widely used clinical rating scale for PD, which determine large categories of motor functioning. It is simple and of easy application, capturing typical features of progressive motor impairment, and providing general assessment of disease progression. It ranges from stage 0 (no signs of disease) to stage 5 (wheelchair bound or bedridden unless assisted). HY stages have been found to well correlate with progression of motor complications, reduction of QoL, and neuroimaging studies of dopaminergic loss [64]. However,

[7] aromatic amino acid decarboxylase (AADC) inhibitor

its semplicity and lack of detail ignore other specific aspects of motor deficit, and provides no information about non-motor symptoms of PD. Main focus of this scale are the unilateral versus bilateral manifestations of motor symptoms and impairment of postural reflexes. A modified version of HY is often used.

Hoehn and Yahr Scale	Modified Hoehn and Yahr Scale
1: Only unilateral involvement, usually with minimal or no functional disability	1.0: Unilateral involvement only
	1.5: Unilateral and axial involvement
2: Bilateral or midline involvement without impairment of balance	2.0: Bilateral involvement without impairment of balance
	2.5: Mild bilateral disease with recovery on pull test
3: Bilateral disease: mild to moderate disability with impaired postural reflexes; physically independent	3.0: Mild to moderate bilateral disease; some postural instability; physically independent
4: Severely disabling disease; still able to walk or stand unassisted	4.0: Severe disability; still able to walk or stand unassisted
5: Confinement to bed or wheelchair unless aided	5.0: Wheelchair bound or bedridden unless aided

Table 1: Hoehn and Yahr Scale

1.5.2 UPDRS

The Unified Parkinson's Disease Rating Scale (UPDRS) is the rating scale most employed in current clinical practice to evaluate several aspects of PD, including disability and impairment [64] [150]. It consists of a questionnaire divided into 4 parts: non-motor aspects, motor aspects, motor examination and motor complications; in each part, a score ranging from 0 to 4 is given to each item. Validity, reliability, wide utilization, application across all stages of the disease and wide coverage of motor and non-motor symptoms, make UPDRS the most established rating scale for Parkinson's disease [159]. Ambiguities, lack of enough detailed instructions [63] and poorness to detect small changes [93] led to the necessity of the development of a new version of the UPDRS. In 2001, the Movement Disorder Society (MDS) commissioned a revision of the scale, resulting in a new version, termed the MDS-sponsored UPDRS revision (MDS-UPDRS). The new scale had to keep the strenghts of the previous one, modify not enough clear items and add some new items in order to cover a wider spectrum of features and aspects of the disease [66].

2 Freezing of Gait

2.1 Introduction

Freezing of gait (FoG) is a form of akinesia (loss of movement) that affects 50–80 % of patients with Parkinson's disease [186]; it is one of the most disabling symptoms of PD [55]. It is defined as a "brief, episodic absence or marked reduction of forward progression of the feets despite having the intention to walk" [141] [142], with different features being dominant: "shuffling" steps, "trembling" legs or akinesia [163]. Patients commonly describe this phenomenon as feeling that their feet "are glued to the ground". It can affect various extremities but also the face [93]. The consequences of FOG include high risk of falls [15] [93], reduced functional independence and quality of life [122] [141]. FOG occurs while turning, during the initiation of gait (start hesitation), in narrow spaces, on reaching a destination (destination hesitation) and sometimes during walking in an open space [55] [164]. However it is frequently experienced during turning or step initiation. It can also be triggered by emotional stress [57], environmental constraints [58], dual tasking [16], and directional change [172]. The **duration** of FoG episodes is between 0.5 s and 40.5 s ($7.3s \pm 6.7s$), with 50 % of FoGs lasting for less than 5.4 s and 93.2 % shorter than 20s [114]. Between 20-28 % of patients in the early stages of PD report to have FOG [55] [177]. In the later stages, this number increases up to 80 % [103] [82]. It occurs more frequently in men than in women and less frequently in patients in which the main symptom is tremor [108]. **Risk factors** for the development of freezing include the presence of the primary PD symptoms such as rigidity and bradykinesia [55] [30]. FoG occurs more commonly with increased PD duration, increased disease severity, and long duration of levodopa treatment [127] [103]. Episodes are most common and more severe in the OFF state and are mitigated by **levodopa** therapy [93] [163]. When it occurs during the ON period, it does not usually respond to dopaminergic therapy, but patients treated with selegiline have been found to be at lower risk [59]. Less well recognized types include "unresponsive FOG", which is indifferent to changes in dopaminergic medication [16]; "pseudo-on" FOG, seen during a seemingly optimal "on" state, but which nevertheless improves with stronger dopaminergic stimulation; and "on" FOG, induced by dopaminergic medication [107].

2.2 Assessing FoG

FOG assessment is challenging for several reasons:

- It is an **episodic phenomenon** [172].
- Its observation may require the use of triggering tricks, such as increased cognitive load, as in dual tasking, or stressful situations, such as reacting under time pressure [83].
- FoG may disappear during the examination due to the patient paying extra attention to gait [172].

- Cognitive [137] and affective factors [44] contribute to the episodic nature of FoG.

Assessing FoG is difficult also beacause of the **great variability** of its manifestations among different patients. Several parameters lead to such variability, including: severity of the disease, motor state ("On"/"Off"), visual input, response to variable tricks, and relation to specific gait patterns such as gait initiation or turns, cognitive factors (e.g. attention, anxiety and stress) [49]. The poor correlation of reported FoG with observed FoG during the clinical exam makes it difficult to assess this symptom observationally. Only long-term observation, carried during daily activities, can provide a reliable assessment of FoG. Consequently, researchers have usually to rely on patients' self-reports for quantification of FoG.

2.2.1 Subjective methods

Rating scales

To date, a number of different scales are available to assess FOG [133]. However, the adequacy of these scales in terms of reliability and validity has never been demonstrated. The UPDRS or the Movement Disorder Society(MDS)-UPDRS (UPDRS Part II, item 14: Activities of Daily Living) [65] qustions the patient about the presence and severity of FOG during On and Off states. This is necessary if the examiner is not allowed to perform a levodopa challenge. Knowing if the patient has dopamine-responsive, dopamine-resistant or dopamine-induced FoG is critical for further management [140]. The UPDRS questionnaires does not allow to finely characterize the features of FoG, neither to get details about number of episodes experienced and their duration.

Questionnaires

Apart from MDS-UPDRS items regarding FOG, two validated questionnaires exist: the original Freezing of Gait Questionnaire (FOGQ) [60] and a new version of the former (NFOGQ) [138]. The NFOGQ aims to measure the severity of FoG, asking patients about its frequency of occurrence and intensity, duration of the longest FoG episodes, and reported impact on QoL and ADLs. However, the questions only concern gait initiation and turning, during which often FoG occurs [165], not considering start and destination hesitations, neither FOG episodes in narrow spaces. Moreover, no distinction is made between FoG in the On and/or Off states. Despite the Gait and Falls Questionnaire (GFQ) is not specific enough for FoG assessment [56], it covers a larger range of FoG triggering circumstances and ask patients about the longest FOG episodes experienced and about a typical FoG episode, information that may help for therapeutic adjustments.

Diaries

Since FoG is a phenomenon most commonly experienced at home [136], assessing FoG in a person's home environment may provide detailed information about experience of episodes in the patient's daily life [139]. If patients and caregivers are informed by clinician about which FoG features need to be recorded, a carefully

structured diary may provide important information about the frequency of FOG episodes, most exposed time of day, and possible triggering circumstances [120], and whether the episode resulted in a fall. This informations could lead to drug-therapy and DBS settings adjustment [51]. Drawbacks of a diary include the more subjectivity of the reports, compared to questionnaires, and the fact that only patients with intact cognitive functionality can keep diaries, thus reducing the possibility to record all FOG episodes, especially for later stages of PD. Diaries should hence be combined with other assessment methods.

Clinical examination

It has the goal to objectively verify the presence of FOG, assess its severity, responsiveness to pharmacological therapy, and understand triggering circumstances. The MDS-UPDRS III FOG item assesses the severity of FoG through a 0 to 4 scale, with FoG episodes happening during straight walking (that is a rare case) considered to be more severe than FoG occurring during turning, step initiation or walking in a narrow space [67]. However, a single item is not sensitive enough, and also it does not consider the duration of the episodes. Clinical examination of freezing typically includes 360 degree turns, walking back and forth, stops on command, walking though narrow spaces, dual motor-tasking, and cognitive dual tasking. Caution is required since such tasks may lead to falls. Sometimes, despite these FoG provocation tasks, known freezer patients do not experience any FoG.

The episodic nature of FOG may make difficult its assessment through objective methods, leading to a wide use of subjective assessment methods (e.g. diaries) [84]. Objective home and lab-based methods are necessary to gather more information about FoG and realize how it varies during the course of the disease [54]; test its response to levodopa [165], clinical manifestation [141], triggering circumstances (start hesitation, turn and destination FOG, shuffling forward with short steps) [172], relation to cognitive dysfunction [83], and association with postural instability and falls [16].

2.2.2 Objective methods

Lab assessment

It is required for research on specific effects on FoG. The FoG event(s) can be video-recorded [51] for offline rating by clinician, which is the current gold standard for assessing the severity of FoG [128]. Assessment technology can be synchronized, including motion capture systems, inertial sensors [178] or pressure-sensitive insoles, aiming to detect shorter FOG episodes which may be missed by clinicals [194], as well as abnormal gait parameters in the just-prior phase of an episode. **Video recordings** are used to augment observational gait analysis and provide simultaneusly multiple angle views of the patient while executing tasks or experiencing FOG. **Force plates** measure the force applied to the ground by patient's feet. They measure also the acceleration force and the force directed mediolaterally. The current clinical solutions for motion sensing involve the use of an optical **motion-capture system**, which consists of multiple synchronized cameras, markers attached to specific body location, and computer software that

acquires and process the motion of such markers during walking. **EMG systems** are used to measure muscle activities while walking, a process referred to as "dynamic EMG". It aims to verify the presence of right and useful control, determining whether the activity of muscles is phasic or not, with well defined on and off periods. This above determines the timing and intensity of the EMG during gait cycles, informing neurological control and muscle integration [31]. An **advantage** of assessing FoG in a lab environment is that it allows to assess patients in both On and Off state [105]. Testing a patient in the Off state increases the probability of detecting FoG and allows one to appreciate the effect of medication and its time course. However, lab testing is not suitable for assessing FoG longitudinally. The monitoring process is carried out in a controlled environment, while it is well known that many patients experience the most severe FoG episodes while at home, often due to distraction or inattention to walking [11]. For this reason, lab data should supplemented by information achieved though the use of questionnaires, such as the NFOGQ or a home-based assessment.

Home assessment

At present, FoG has been analysed with several systems and sensors, but some settings can only be used in a laboratory (pressure platforms, EEG [78], EMG, knee-joint goniometers [38], camera and video systems). Thus, since PD monitoring has to be ambulatory and should acquire data for several hours in order to provide useful clinical information [146], many studies have employed wearable technology. The application of non-invasive systems to monitor ADLs and the PD symptoms experienced at home, during daily life may lead to a more accurate and objective evaluation of FoG. It could be possible to monitor the evolution of the disease and to better adjust patients therapy plan [155]. Many different types of sensors have been employed for this purpose. The largely employed method to objectively detect FoG is based on wearable motion sensors, as they are unobtrusive and portable, and provide the best way to evaluate FoG episodes in patients' own homes [155]. Inertial sensors use is a promising method for a more objective assessment of FOG. Most sensor setups involve accelerometers and/or gyroscopes [7] [115] [117]. The recording of gait abnormalities just before of between FOG episodes [185] allow a full description of the FOG events [34].

2.3 Acceleration data for FoG detection

2.3.1 Werable sensors for human activity recognition

Werable sensors (WS) applied to human activity monitoring can provide useful and detailed information about patient's mobility while outside hospital and clinical settings [26]. The collected data provide qualitative and quantitative information about patients disability and its progression, which can be analyzed by engineers and whose results could be very useful for clinicians. Quantification of human motion and energy expenditure [14] [4], for example, may lead to a new and better management of cardiovascular diseases, obesity, diabetes and other widespread diseases [148]. Accelerometers and gyroscopes are small, lightweight, affordable, low power and low cost sensors employed both in clinical

and in home environment, with the aim of a long-term monitoring of patients [62]. The provided acceleration signal could be used to distinguish some specific activity types [9], gait parameters [173] (e.g. walking speed, step cadence, regularity) [111], balance and posture transitions [113], rehabilitation progress [90] and detection of falls [18].
An accurate identification and tracking of the activities of patients with motor disabilities can eneble better treatment plans. Parkinson's disease represents an ideal target, since it responds to an increasing variety of treatment options, including drugs and various exercise therapies [69]. An objective analysis of symptoms both in the clinic and at patient's home may provide functional measures highly correlated with quality of life [46]. Specific activity recognition systems have been developed for the elderly [132], individuals with muscular dystrophy [95], and even PD [158].

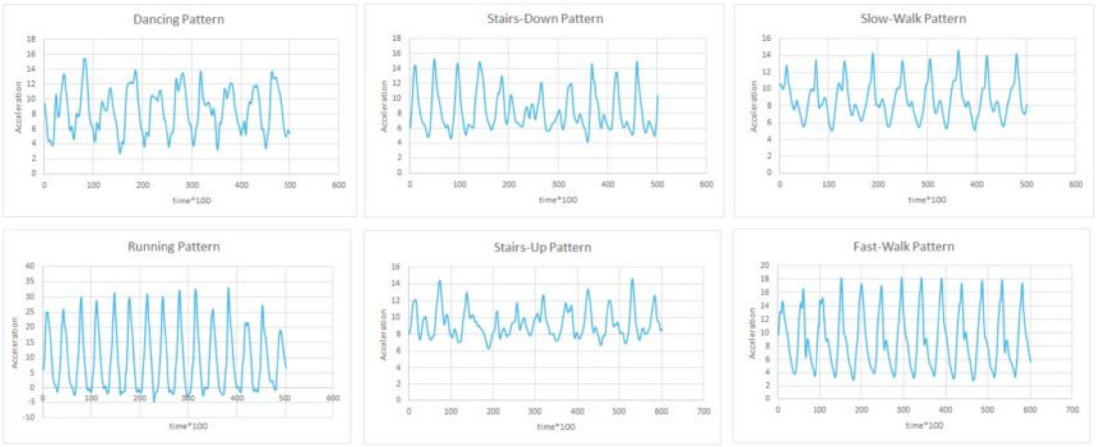


Figure 1: Acceleration plots for the six activities along the z-axis that captures the forward movements. All six activities exhibit periodic behavior but have distinctive pattern. Ref [12]

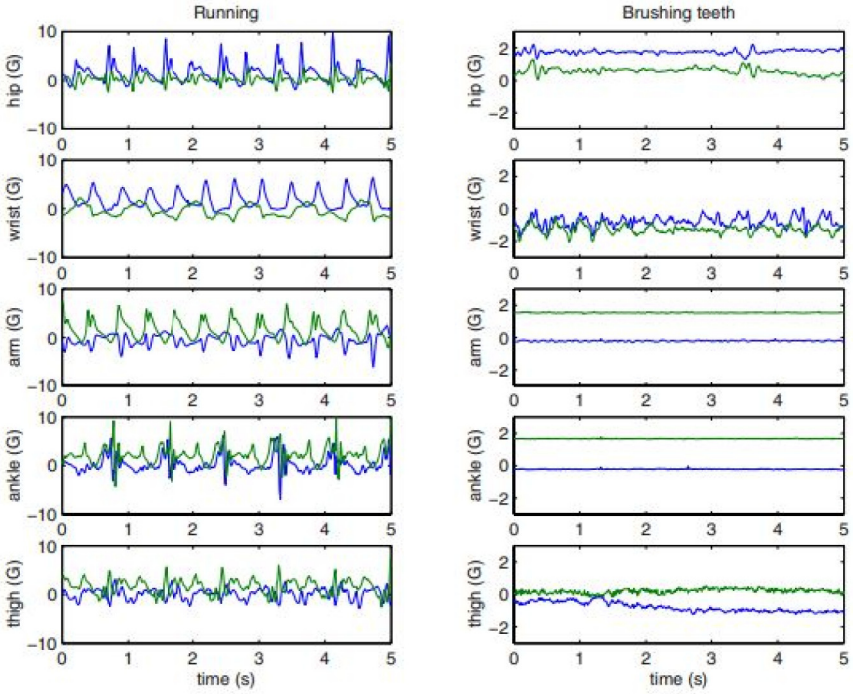


Figure 2: Acceleration signals from five biaxial accelerometers for running and tooth brushing. Ref [88]

2.3.2 Werable sensors for gait disturbances detection

Analysis of the human gait has recently gained a considerable interest, focused on achieving objective measurement of the several parameters characterizing gait. Its application field vary from sports [70] to security purposes [171], and also medicine, since some aspects of people quality of life may be associated with changes in gait patterns [176].

In medicine, it could be useful to monitor the **evolution of different diseases** [176]:

- Neurological diseases, especially multiple sclerosis or Parkinson's;
- Systemic diseases such as cardiopathies;
- Stokes
- Aging correlated disease.

Monitoring and evaluation of gait characteristics over time may allow an **earlier diagnosis** of the disease and analysis of its complications [131]. WS systems aim to capture information about the human gait during patients ADLs. They use sensors located on several parts of the body, such as feet, knees, thighs or waist. Different types of sensors provide different characteristic evaluation of the human gait. These include accelerometers, gyroscopes, magnetometers, force sensors, extensometers, goniometers, active markers, EMG and EEG [131]. Human gait analysis is of crucial importance since gait disorders are widespread woldwide and

represents an important motor complication in many neurodegenerative disorders such as multiple sclerosis, SLA or Parkinson's disease, but also cerebellar ataxia, brain tumors, myopaties. Gait deficiency has been linked to several gait features, in elderly people [99]. PD patients suffering from FOG have been found to show gait abnormalities such as higher gait variability and less solidity, compared to non-freezers [186]. Accurate reliable informations concerning gait features over time, will enable clinicians to find the most suitable treatment [131].

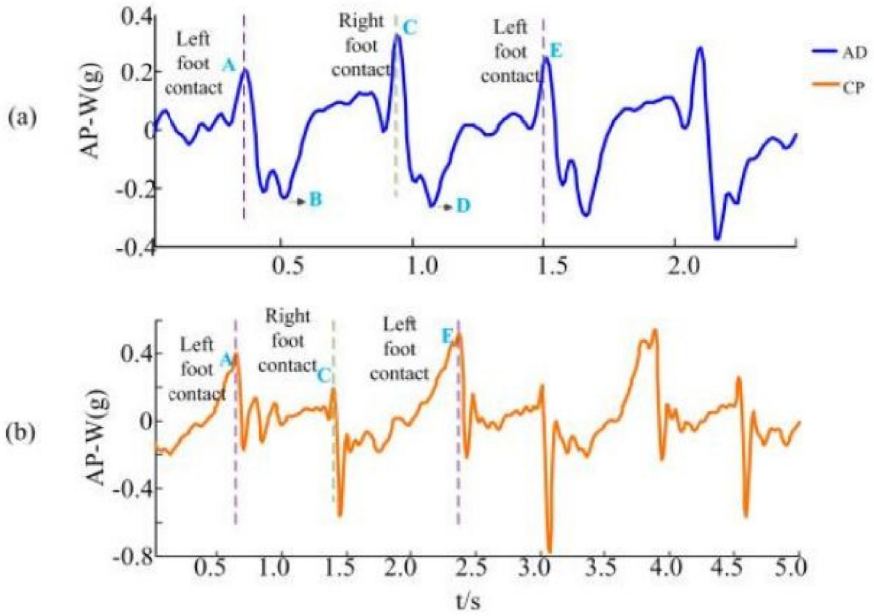


Figure 3: Example of AP waist acceleration (AP-W) of typical gait cycles from a healthy subject (a) and (b) a child with Cerebral Palsy. Ref [32]

2.3.3 FoG detection

Long-term monitoring of FoG could provide crucial information to neurologist, not possible to obtain in a lab environment and having little time. Symptoms are commonly not evident in the clinical environment [135], making it difficult to assess FoG. Thus, a wearable device capable of ambulatory monitoring FoG could lead to precious benefits: from the clinicians point of view, it could provide further information about the disease progression, and this can lead to an improvement of the treatment [162]. From the patient point of view, it has been demostrated that patients are able to improving gait in case specific stimulations are provided, including haptic, visual or auditory cues [106], thus real-time FoG detection may avoid some episodes and, consequently, avoid falls [6]. A great variety of wearable sensors have been recently proposed for providing objective assessment of FoG during the real life [124] [61]. There is yet little agreement concerning the type of sensors to use and their number, location on the body, protocols for data acquisition and signal processing algorithms.

- The **types of sensors** embedded in the devices worn by the participants vary. Tri-axial accelerometers are the most used, either as a single sensor

[1] [152] [195], or combined with gyroscopes [77] [41], or magnetometers [34] [116].

- Both one **location** and a combination of two or more locations have been used. The shin [34] [41] and waist [194] [24] were the most common location on human body, and could be used as single location. When two or more locations were explored, sensors were placed also on feet [126], knee [96], thigh [7], chest [180] or wrist [115].

- Experimental **protocols** include TUG (timed up-and-go) tasks on a standardized 5-m course [25] [126], walking tasks (e.g. walking back and forth, turn) with or without FoG provocation (e.g. walking in straight lines and passing through narrow spaces, walking across crowded halls, negotiate some obstacles) [7] [115] [125] or dual tasking (e.g. carrying a full glass of water while walking) [1] [77], unconstrained ADL simulated in laboratory [7] [1] or at patient's home [181] [155]. Video recordings of patients while data acquisition were used by all studies, with videos labeled by clinicians.

Smartphones are convenient and easy to use; contain several sensors and enough computing power, together with expandable storage space. Thus, smartphones nowadays represent an alternative to dedicated hardware in medical applications requiring wearable assistants [117] since they have several internal sensors used for motion analysis, including accelerometers, gyroscopes and magnetometers. An evident benefit is given by the fact that users do not have to buy additional hardware, since usually they own a smartphone. Smartphones were used in many studies for different purposes: assistants in fitness monitoring [22], heart rate monitoring [2], gait recognition [134], or to promote wellbeing [104]. Also, many human activity recognition (HAR) systems have been recently developed for smartphone use [52] [26] [12]. Smartphone use in FoG detection was recently explored [25] [77] [117], achieving performances comparable to other studies.

2.3.4 FoG acceleration signal charateristics

Acceleration signals during FoG episodes show different patterns, amplitude and frequency content, based on body location of the accelerometer sensor. Furthermore, there are several different types of FoG (e.g. FoG while walk initiation, turning or reaching a destination), as partially shown in figure 5, and the characteristics of signal vary among such types [124]. However, there are some known specific properties that differentiate the sensor data during FoG episodes from normal walking (figure 16c shows also movement patterns just before FoG); the gait of patients with FoG also differs between freezing episodes, compared to patients who do not experience FoG [79]. A feature joining together all kind of FoG episodes, independently of sensor location, is a large increase in the signal energy in the 3-8 Hz frequency band [123]. All other features, such as mean and standard deviation of the signal, its pattern variability, and the exact frequency content depends on several aspects, including patients weight, medication state, disease stage and episode circumstances (e.g. narrow spaces, obstacles, open space). Features

able to well differentiate FoG acceleration signal from other motor activities will be descibed in the next chapters.

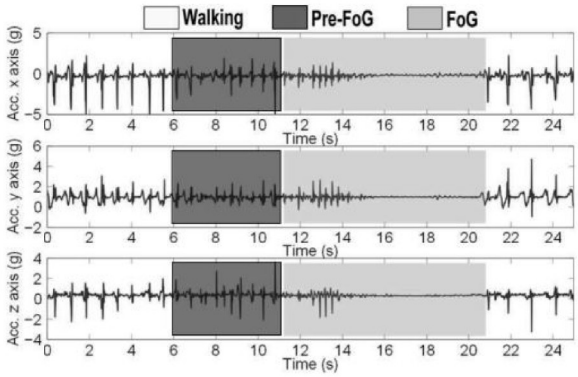


Figure 4: An example of an accelerometer signal, on the three acceleration axes, that captures the motor variations in the gait of a patient with Parkinson's disease. Ref [114]

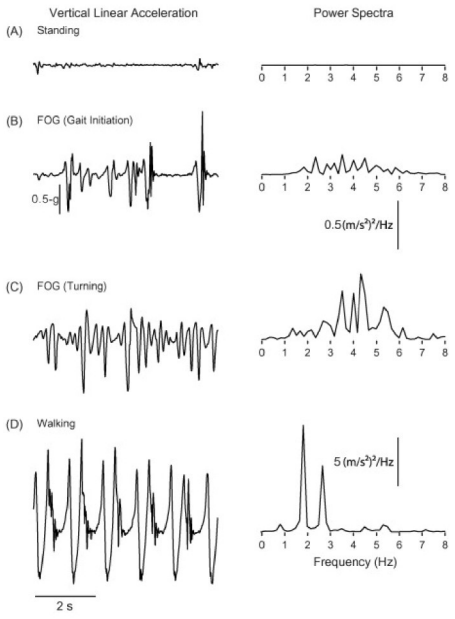


Figure 5: Vertical linear acceleration of the left shank (6 s of data) and corresponding power spectra. Ref [124]

3 Data acquisition for FoG detection

The modalities of data acquitition should be accurately identified and some choices have to be made prior the starting of this process: which sensors to use, based on which physical quantities to be measured; sample composition, with its dimension and variability being of fundamental importance; the experimental protocol require to be accurately choose, considering which is the purpose of the study and at the same time taking into account its duration, execution semplicity, and its feasibility in all places where data has to be acquired.

3.1 Smartphone sensors characteristics

Smartphone sensors characteristics, in terms of sample frequency, range and resolution, were analyzed in order to check if the smartphone was a suitable device for data acquisition, taking into account the activities involved in the protocol and the location of the device on human body.

- Sensors **sample frequency** has to respect the Nyquist sampling theorem, thus having value at least equal to twice the maximum useful frequency in the signal. The activities executed during the protocol (e.g. walking, turning, standing) have different frequency band, with walking band lying in 0-3 Hz and signal during FOG episodes in 3-8 Hz [1] [117] [125] [25]. Anyhow human activity acceleration signal lie in the 0-20 Hz band [146] [23] [184] [151], thus a sample frequency of at least 40 Hz has to be set.
- Acceleration signal **amplitude range** depends on considered direction, location of sensor and body weight. Considering a waist-mounted sensor, acceleration amplitude during walking lie in the range ± 1g, increasing to ± 2g during running [71] [129], with g being the gravitational acceleration.

The table below shows smartphone sensors charateristics, which prove the suitability of the device for data acquisition.

Table 2: Smartphone sensors charateristics

Sensor type	**Range**	**Resolution**	**Sample frequency**
Accelerometer	± 2 g	$4 \cdot 10^{-3}$ g	200 Hz
Gyroscope	± 34.9 rad/s	$1,1 \cdot 10^{-3}$ rad/s	200 Hz
Orientation	360°	1°	200 Hz

Many **smartphone applications** have been developed recently for visualize and record data acquired by smartphone sensors. The one used in this study allow to select all desired sensors for data recording and save recordings in a CSV exportable format. The application also allows to record composite inertial signals, such as linear acceleration, linear angular velocity and linear orientation, which involve the use of a combination of multiple inertial sensors yielding composite single output. Since gravity affects in different proportion inertial signal

components, depending on relative axes orientation, and since smartphone orientation can change during protocol execution, it was considered appropriate to record linear inertial sensors data, in order to remove gravity influence on output signals. Linear acceleration is calculated as the difference between accelerometer and gravity sensors output for each axis and involve the use of both accelerometer and gyroscope, while linear orientation uses data from accelerometer, magnetometer and gyroscope. Data record file contains the following information for each line:

- Session ID: unique number ID identifying data acquisition session. All samples with the same session ID belongs to the same participant.
- Sensor name: specify wich kind of sensor data is taken by.
- Value: 3-element vector containing sampled data in the three space dimensions.
- Timestamp: unix timestamp[8] relative to the sample.

3.2 Sample charateristics

A total number of 59 partecipants were included in this work. The study involved two different samples: the first was made of 38 subjects with Parkinson's disease, with and without past experience of FOG events, while the second consisted of 21 healthy subjects, in terms of neurological disorders, and used as control set. Measurements on control sample were taken at "Orfanelle" nursing home - Chieri (To) while data acquisition on PD subjects was carried out at Center for Parkinson and Movement Disorders - Molinette hospital (To) and "Associazione Amici Parkinsoniani Piemonte Onlus" (To). Geriatricians and neurologists selected participants to be involved in the study, for control and PD sample respectively, and provided clinical information about patients. Subjects with vision problems, dementia and other neurological disorders (apart from Parkinson) were excluded. Subjects needing gait assistence (e.g. walking stick, crutch) were included in the study. Participants were informed about the execution of the test and the purpose of the study, and gave informed consent prior to their inclusion in the study. General information about all participants were noted anonymously; information about disease stage and duration were also obtained for PD partecipants.

A sample containing such groups (control, PD freezers, PD non-freezers) was considered useful both in this study and in future works for the following reasons:

- Increase gait variability for the training of the classifier, in order to obtain a robust system.
- Apply FOG detector system also on control and PD non-freezer groups, to verify that no FOG events were detected (false positives).
- Compare Parkinson's and control group's gait, in terms of symmetry, regularity, frequency content, step cadence and other features.

[8]it is defined as the number of seconds that have elapsed since 00:00:00 UTC, 1/1/1970

- Compare gait of parkinsonian subjects who used to experience FoG in everyday life and PD subjects who did not.
- Study gait alterations, asymmetries and balance both in control and in Parkinson's group.

Table 3: Control sample charateristics

Number of participants	**Gender (% male)**	**Age (years)**	**Gait assistance (%)**
		mean ± std	
21	28.6	85.6 ± 7.2	42.8

Table 4: PD sample charateristics

Participants	**Gender (% male)**	**Age (years)**	**Disease duration**	**H&Y stage**	**Gait assistance (%)**
		mean ± std	mean ± std	mean ± std	
38	66.7	70.7 ± 8.2	9 ± 4.8	2.5 ± 0.8	21.1

3.3 Positioning and protocol

A single location on waist was chosen for data acquisition, due to the following reasons:

- It is confortable, compared to other body locations (e.g. shin, shank, tigh, ankle).
- It is close to the body center of mass, thus better representing body movement [193].
- It allows to monitor other sympthoms of Parkinson's disease, such as bradykinesia and dyskinesia [146].
- It is one of the most suitable placements for detecting FoG [155] [1], leading to high detection performance [195], comparable to those achieved with multiple location sensors [170].

A smartphone belt was used to secure smartphone on partecipants waist, at lower back level, with elastic band ensuring the adherence of the smarthone to the body.

Figure 6: Smartphone belt, smartphone position and reference axes

Experimental protocol consisted on a standard 6-minutes test. This test provides a physical performance measure of functional capacity [8] and has gained clinical acceptance due to its ease of setting up, administration, patient tolerance, reproducibility and similarity to requirements of patient function and participation. It is now also used in clients with cerebral palsy, stroke, multiple sclerosis and Parkinson's disease [175]. Participants were asked to walk back and forth along a hallway for 6 minutes with a waist-mounted smartphone recording inertial data. Participants quit the test if not able to continue. Length of the ride was set to 10 meters in order to ensure repeatability in all places were data had to be recorded. Different from all the other studies in literature, no video recording was carried out, and a chronometer was run at the same time of data recording start; FoG, festination and hesitation episodes were annotated in time. Also gait asymmetries were noted down.

A final consideration has to be done, regarding sample and protocol selection. Four main factors rise the possibility of getting only a small number of FoG events during data acquisition on PD participants:

- No selection on disease stage was done, thus including in the study also participants with mild motor symptoms.
- No selection based on FoG history was done, thus including also participants who have not experienced FoG.
- Most participants were in "daily On" state while data acquisition, thus reducing the chances of detecting FoG events.
- No FoG provocation test was included in the protocol.

3.4 Labeling

Since the classification for FoG detection was intended as a multi-class problem, labeling of different activities was executed offline. A Matlab user interface was used for the purpose, labeling each activity (walk, turn, stand, FOG, hesitation,

others) through a vector of the same length of the signal and containing different numbers (e.g. 1 for walk, 2 for turn, etc) associated to each sample. Data from all three axes of accelerometer and angular velocity around x axis were used for better distinguish activities. Figures 7, 8 and 9 show signal after labeling: label vector is plotted in red, with different heights representing different activities; signal of gyroscope representing angular velocity around x axis is plotted in black, ensuring higher accuracy and temporal resolution in activity recognition process.

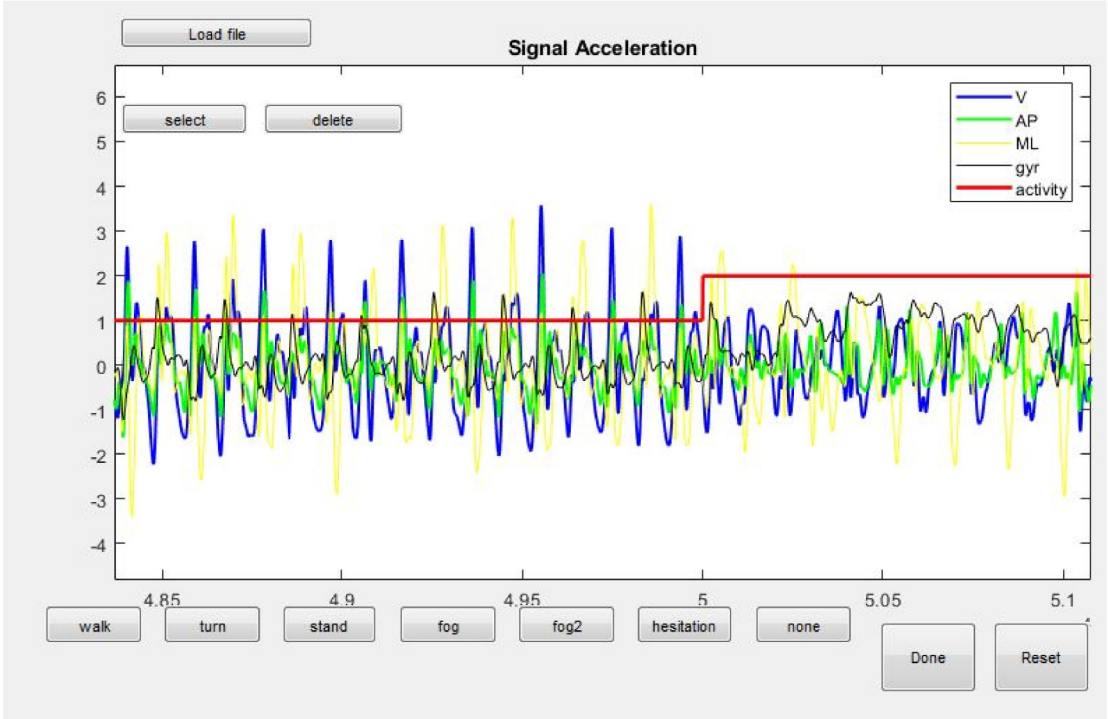


Figure 7: User interface used for signal labeling. Signals relative to walking and turning phases are shown.

Figure 7 shows **walk** (left side) and **turn** (right side) labeling, executed observing that during turning:

- Vertical and antero-posterior components show lower amplitude.
- Vertical and antero-posterion acceleration peaks are no longer in phase.
- Medio-lateral component become predominant among all components, in terms of amplitude.
- Angular velocity around vertical direction shows different shape and its mean value increases.

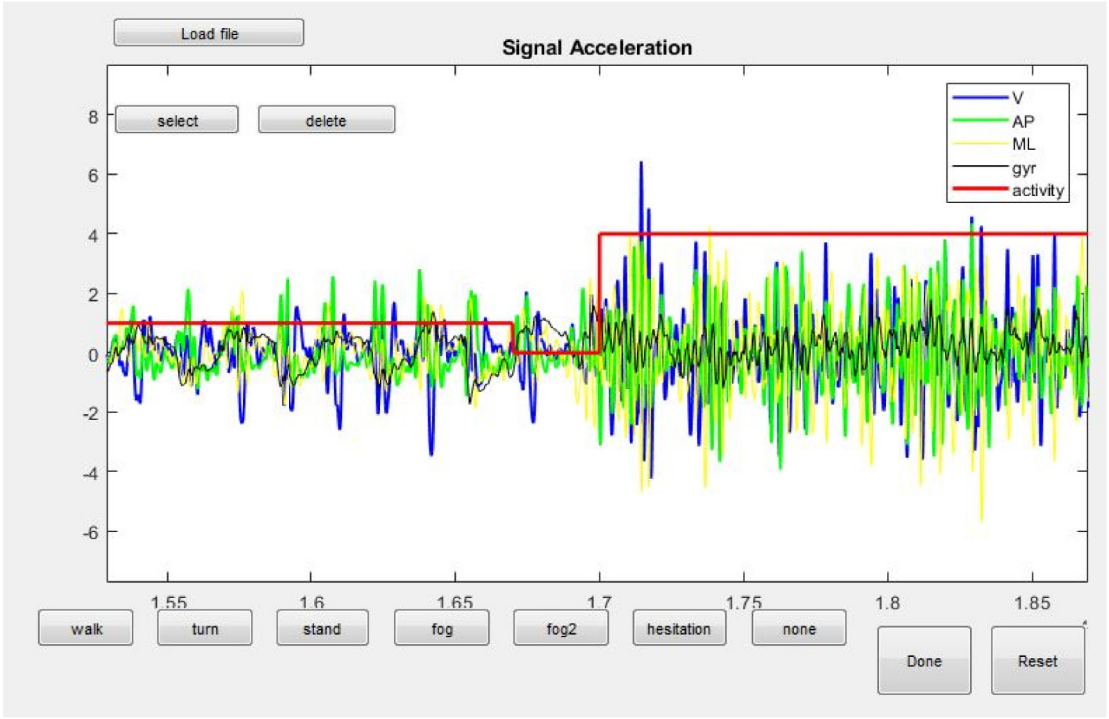


Figure 8: User interface used for signal labeling. Signals relative to walking and a FOG episode are shown.

Despite **FOG** episodes were annotated, for a better temporal resolution, labeling (as shown in figure 8) was realized noting that during FOG events:

- Both acceleration and angular velocity signals lose their periodicity.
- Frequency of all signals rises significantly.

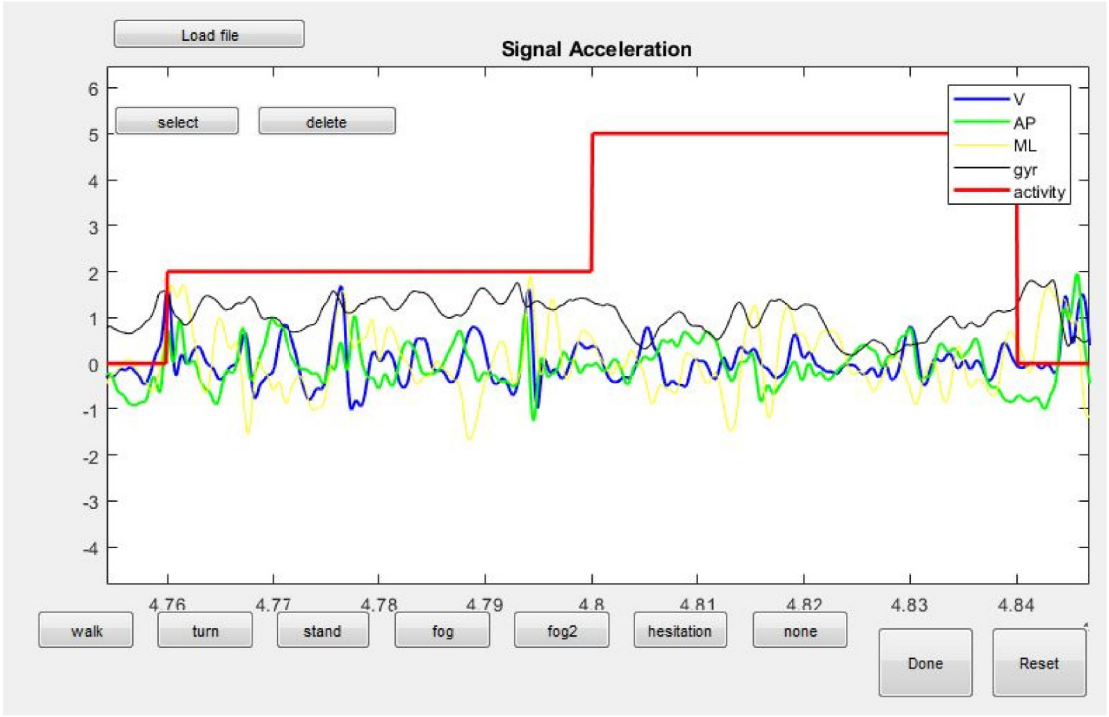


Figure 9: User interface used for signal labeling. Signals relative to turning and a hesitation episode are shown.

Also **hesitation** episodes were annotated during data acquisition and labeled offline. Hesitation was found mostly during turning, leading a longer duration of turning phase, with movements slowing down until a new walking phase was started. As shown in figure 9, hesitation differs from turning in the following features:

- Vertical acceleration peaks amplitude decreases.
- There is a lack of marked forward progression, as the antero-posterior acceleration component does not show marked and differentiated peaks.
- Angular velocity around vertical direction shows a lower mean value, indicating a decreased turning velocity.

4 Detection system

The FoG detection algorithm was realized in Matlab environment. First, acceleration signals were filtered, visualized and analyzed, both in time and in frequency domain, in order to extract some features considered capable to differentiate the signal relative to FoG episodes from all the others. Second, the obtained features were used to train two SVM classifiers, capable of distinguish movement from stand and FOG from other movements, respectively. Finally, the built algorithm was tested on different samples and performance was evalueted. A brief explanation of how SVM works is provided at first, since it is useful for understanding some steps of preprocessing and training phases.

4.1 Algorithm block diagram

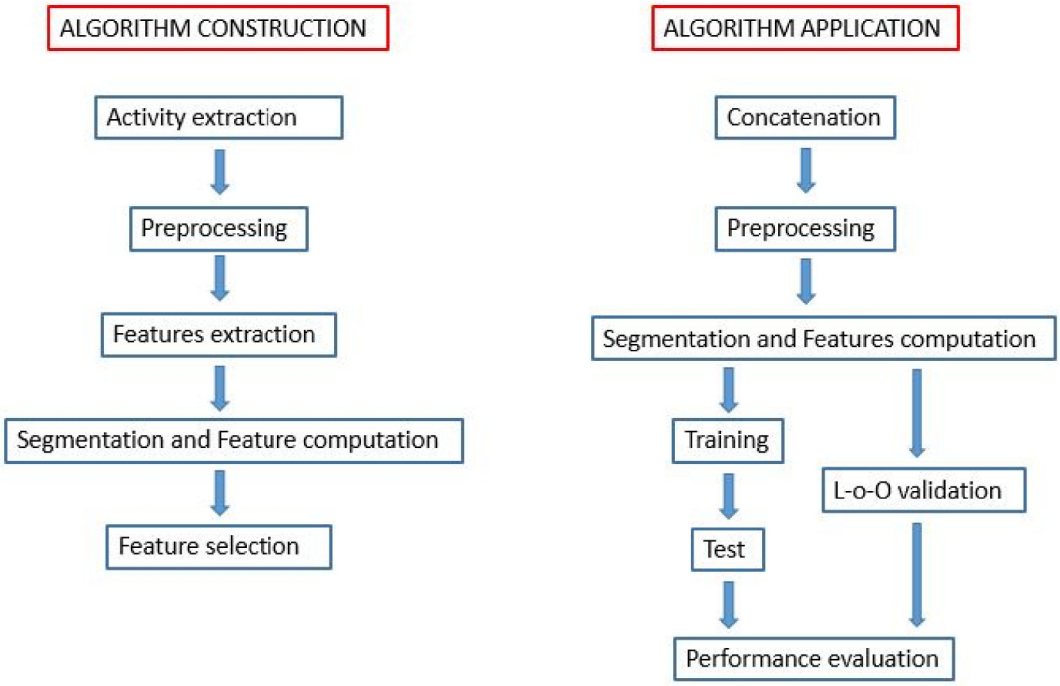
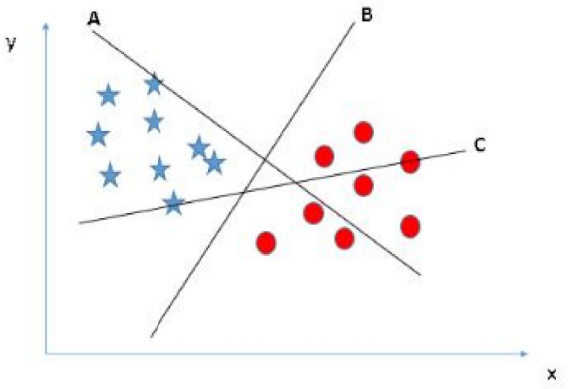


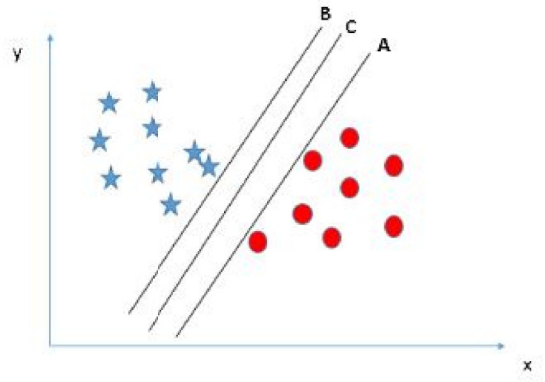
Figure 10: Algorithm block diagram.

4.2 SVM classifier

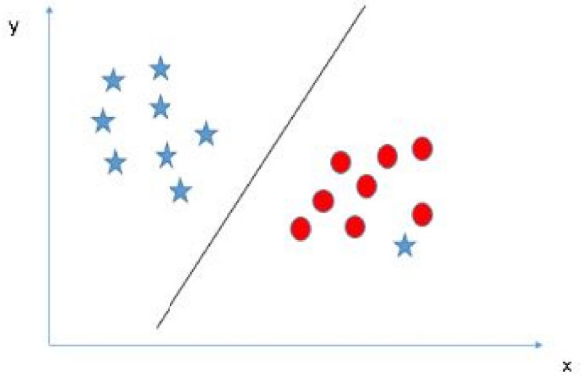
Support vector machine (SVM) is a **supervised** machine learning algorithm, commonly used for binary classification problems but also easily expandable for multiclass classification. A brief explanation of how this algorithm works is reported below. For semplicity, the two-dimensional case is considered. Each data item (red dots and blue stars in the figures below), intented in this study as a temporal window of acceleration signal, is represented as a point in n-dimensional space, with n being the number of features used for signal characterization and with the value of each coordinate being the value of each feature.

1. 

SVM algorithm aims to find the hyperplane that best segregates the two classes, leading to the lowest **missclassification rate** possible. Thus line B will be choosen.

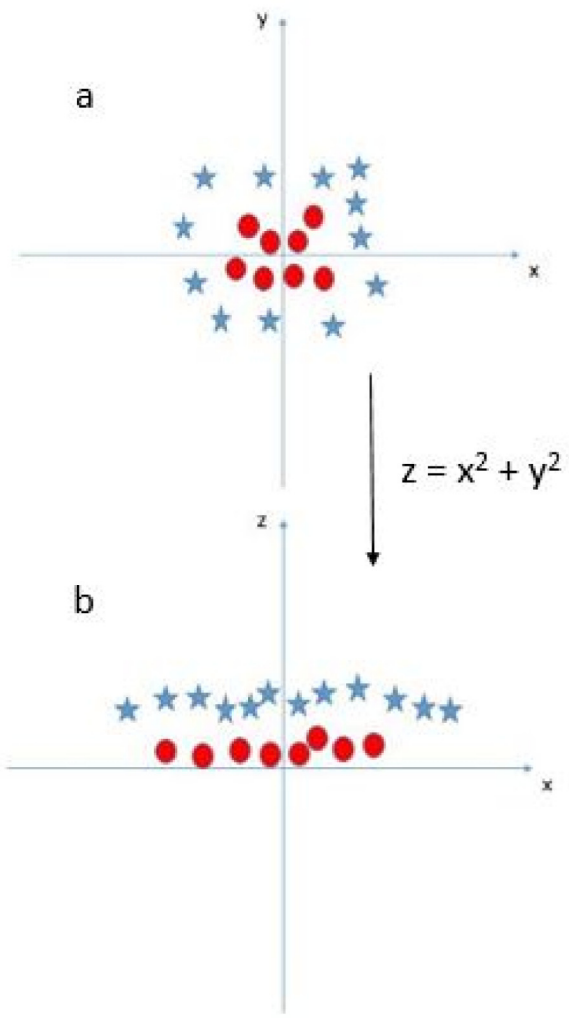
2. 

If more than a hyperplane meets the previous requirement, the one with the highest **margin** is selected, meaning the one with the greater distance from the nearest data points of the two classes. Line C will be selected in this case.

3. 

SVM ignores **outliers**, thus the hyperplane with the highest margin will be choosen also this time, allowing missclassification and thus accepting errors.

4.



In case of **non-linearly separable data**, as in figure (a), it is not possible to find a plane separating the two classes. Hence SVM use a kernel function which transforms the initial space into a higher dimension one, as in figure (b). In this way, not-separable problem is converted into a separable one, thus allowing to find the division hyperplane.

The classificator memory and computational time expensiveness [121] was not considered as a major issue, since the training phase had to be executed offline on a personal computer. The decomposition of the multi-class problem into several two-class problems [109] was achieved using only two classifiers, avoiding an excessive duration of the training and testing phases [109]. The selection of the SVM for the classification problem was due to the following reasons:

- Since SVM classifiers are devised to obtain high performance for unlearned data [102], they have the highest **recognition rate** among many known classifiers [109], leading to a very accurate detection system [179].
- The high generalization capability of the algorithm leads to a desired classifier **robustness** [74].
- SVM was used as classifier in many studies for activity recognition [110] [3], **FOG detection** [155] [1] and monitoring of other PD motor symptoms, such as bradykinesia and diskynesia [146] [159] [181].

4.3 Algorithm construction

4.3.1 Input data

As explained in the previous section, acceleration signal for each partecipant was labeled, with each activity being marked for easy extraction and separation from the others. Algorithm construction required sufficient amount of acceleration data; the more **variability** was in the input data and the more **robust** the algorithm would have been. Variability is intended as different signal pattern, shape, amplitude and frequency content shown by different participants while performing the same activity. The larger is the number of participants involved and the more variable is the input data for the algorithm construction. Acceleration data from all PD participants, both freezers and non-freezers, was loaded and separated based on activities: all signals from different participants relative to the same activity were concatenated, in order to obtain four signals relative to the four activities performed during the protocol (walk, turn, stand, FoG). The final input data was a 4-dimensional cell array, with each dimension being the acceleration signal from all participants and related to the same activity. All the three components of acceleration signal were kept.

4.3.2 Filtering

Bandpass filtering of the input signals was considered necessary. **High-pass filtering** was executed in order to remove gravity component [12], align the three components of acceleration signal (vertical, medio-lateral and antero-posterior) and avoid that any small smartphone displacement could affect the mean value of the signal. **Low-pass filtering** was done for removing possible high frequency noise [155] [91].

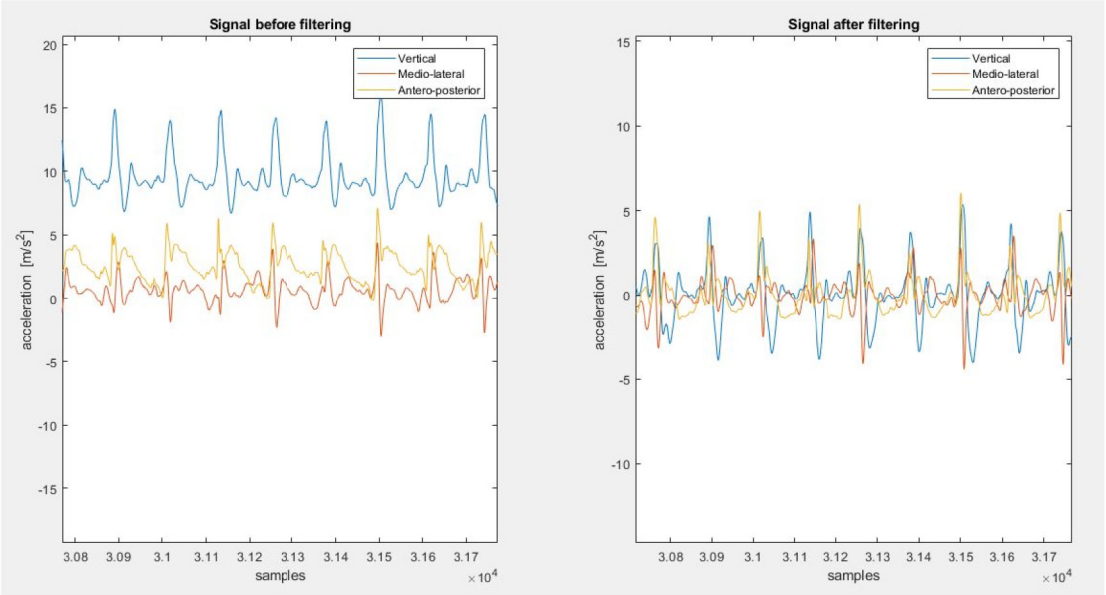
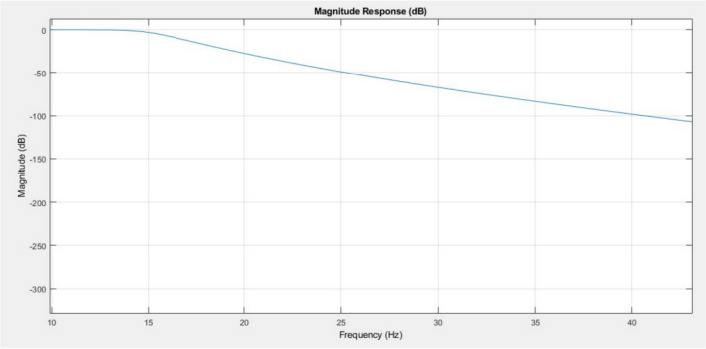


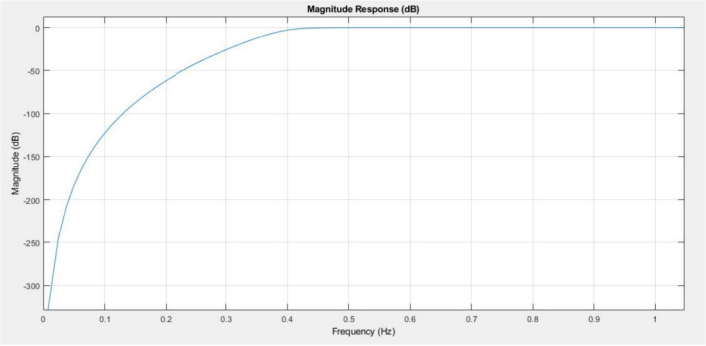
Figure 11: Comparison between signal before and after bandpass filtering.

Cutoff frequencies have to be selected taking into account the band of interest

of the signal. As discussed in the previous chapter, locomotor acceleration signal lies in the 0.5-3 Hz band while signal during freezing shows frequencies up to 8-10 Hz [7] [124]. An IIR Butterworth filter of order 10 with cutoff frequencies of 0.4 Hz and 15 Hz was designed, according to other studies [89] [12] [152] [149]. Such filter order ensured a minimal attenuation of signal with frequency content below 0.2 Hz of a 10^3 factor, a minimal attenuation of factor 10^2 for signal with frequency content over 22 Hz and no alteration of the signal in the band of interest.



(a)



(b)

Figure 12: Frequency response of the designed filter. High (a) and low (b) frequency responses are showed.

4.3.3 Features extraction

Features are any extractable measurement, evaluation or judgment on input data. Classification of signals using a feature-based algorithm requires characterization of the signal with a set of features. Feature extraction aims to build a set of derived values, called features, that attempt to fully describe the input signal, with each feature providing a piece of information. A wide literature research led to the definition of a set features, both in time and in frequency domain, and other features were defined by looking at signal shape, symmetries, amplitude and repetivity in time domain and frequency content band and shape. Acceleration signal in the three space directions was segmented and features computed on each **time epoch (window)**; this process will be better described in the next section. Features, both found in literature and built in this study are listed below and a brief description is provided.

Features in the frequency domain

Power spectral density (PSD) of acceleration signal is shown in figure 13, allowing to understand the differences of the acceleration signal in the frequency domain during different activities. Despite the overlapping of the frequency bands, **power spectral density** shows different magnitude and shape, leading to identify a set of features that well differentiate the signal during FoG episodes from the signal during the other activities. PSD shows a **shift toward high frequencies** for FoG signal, compared to other considered activities.

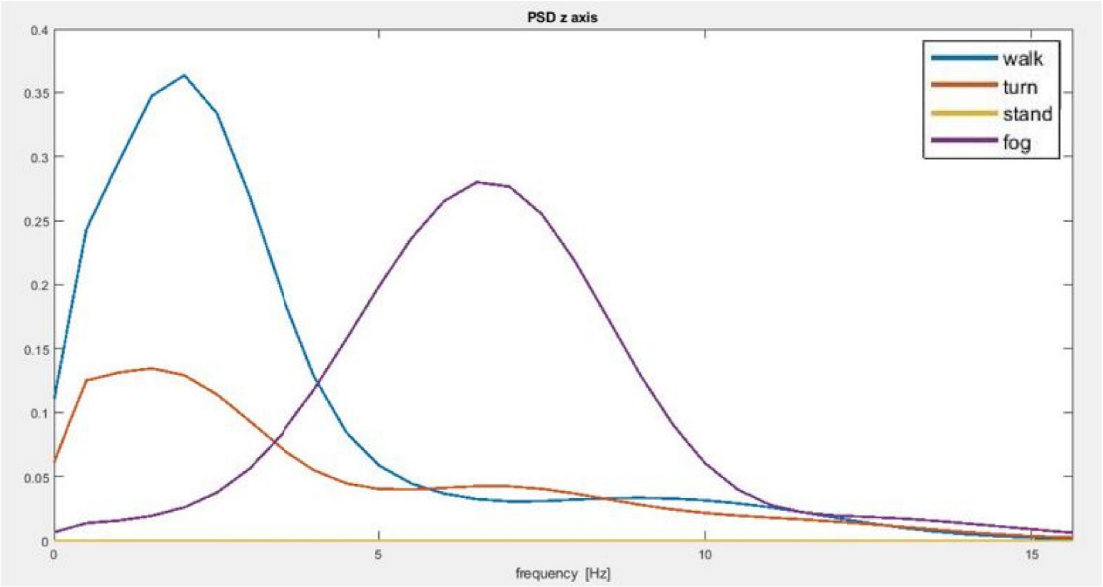


Figure 13: Power spectral density of antero-posterior acceleration signal for different activities.

- **Power in the freeze band** and **locomotor band** are respectively higher and lower for FoG signal than for walk signal (as shown in figure 14), thus leading to the selection of such features [124] [7].
- The ratio between the first and the second feature leads to the definition of a new feature, called **freeze index** (FI), which is probably the most important one for FoG detection [25] [145] since it shows much higher values during FoG episodes than in all the other activities.
- A feature similar to freeze index was used in this study. It was obtained as the percentage of signal power lying in the 3-10 Hz band.
- **Total power** is also considered as a valid feature in many studies, since it allows to distinguish FoG from volitional standing [117] [116] [145].
- In this study, also the frequency value corresponding to the **PSD peak** was added in the set of features.

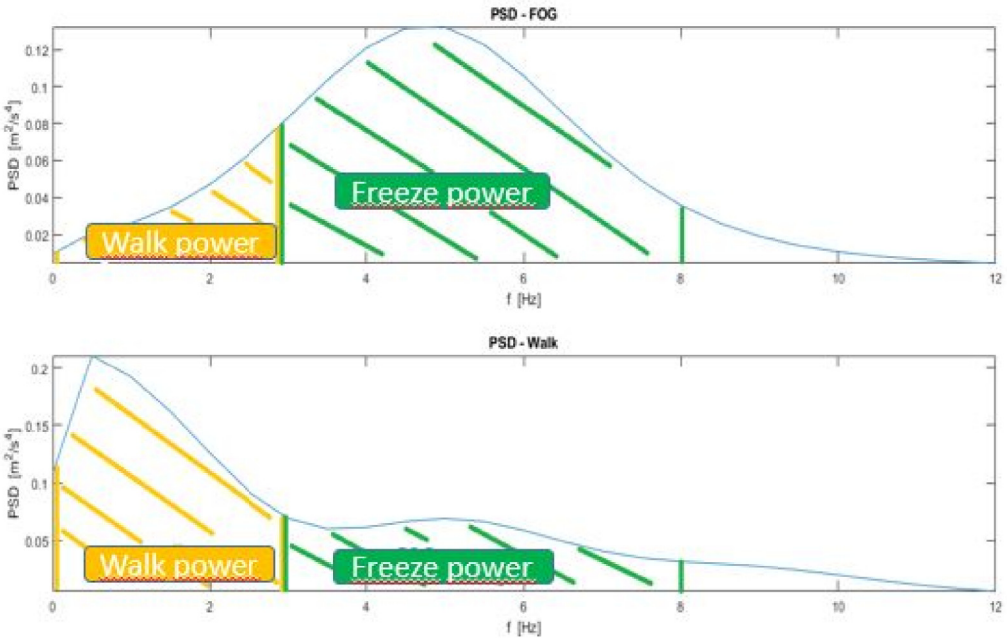


Figure 14: Power in locomotor (0.5-3 Hz) and freeze (3-8 Hz) band for FoG and walk vertical acceleration signals.

- **Kurtosis**[9] and **skewness**[10] are considered useful for the spectral distribution characterization [155].
- **Spectral entropy**[11] aims to provide an estimation of signal's frequency content irregularity and disorder.

Features in the time domain

- **Entropy** in the time domain provide a measure of the distribution of frequency components [117] [114].
- **Correlation** among each pair of axes gives information about linear relation between acceleration signal components, which is useful for detecting normal/continuous gait [155].

[9] measure of the deviation from the normal distribution
[10] measure of lack of simmetry of the distribution
[11] measure of lack of order or predictability

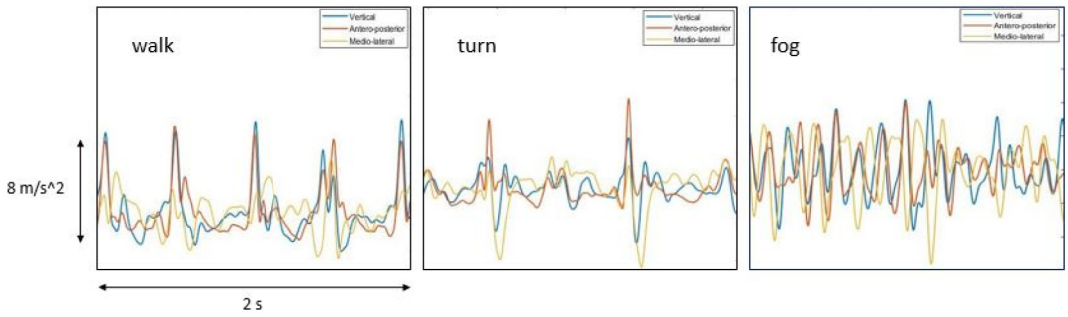
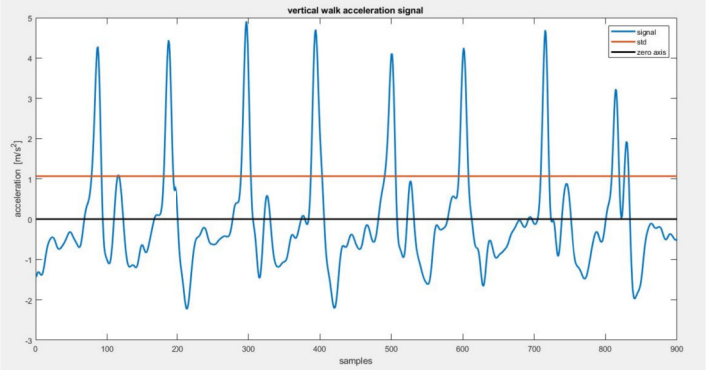
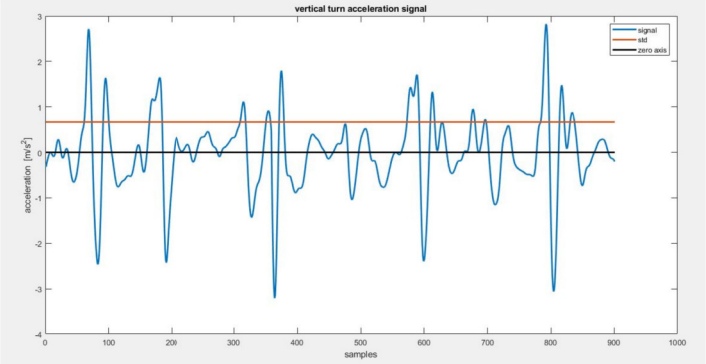


Figure 15: Accleration signals for different activities. All three components of the signal are shown.

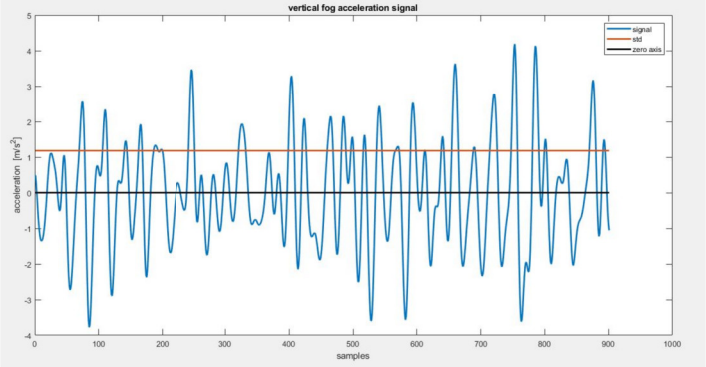
- **Standard deviation** of signal amplitude on each axis indicates the amount of movement performed in a window time [155].
- **Number of signal peaks** over a certain threshold, computed in each time window and with a threshold set in this study equal to 0.8 times the standard deviation of signal amplitude, could well differentiate walk and FoG signals. For this reason, this feature was used in this study.
- **Zero crossing rate** gives a measure complementary to the previous one, counting number of times the signal crosses the zero axis. FoG and standing should show higher values of this feature, compared to walk and turn.
- The **ratio between zero crossing rate and number of peaks** was thought to be a stronger feature in case of not enough reliability of the previous ones.



(a)



(b)



(c)

Figure 16: Vertical acceleration signals during walk (a), turn (b) and FoG episodes (c). Zero level and standard deviations are shown respectively in black and red.

4.3.4 Segmentation and feature computation

FoG detection requires the input acceleration signal to be segmented into windows of the same size, with or without overlap, and features must be computed in each time window. Window size and overlap between windows have to be set taking into account the distribution of FoG episodes duration, the sensitivity and time resolution desired, and the possible real-time implementation of the algorithm.

- Literature studies found 50 % of FoG episodes to last less than 5 s [7] [117], with the majority of them (>90 %) lasting less than 20 s [126] [7] (as shown

in figure 17). In this study, **FoG duration** was found to be <5 s in 80 % of the cases, with only two episodes lasting more than 10 s.

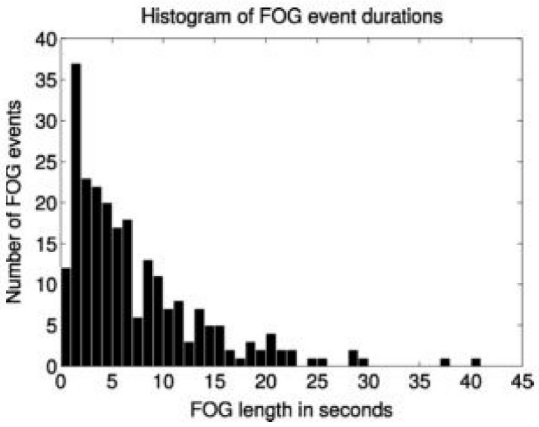


Figure 17: Histogram of FoG episodes duration. Ref [7]

- Optimal window size was found to be twice the duration of the shortest FoG event to be detected [124], and an increase of window size would show a **low-pass filter effect**. Smaller window size reduces both the specificity [126] in signals without FoG and the sensitivity for short-duration FoG episodes detection [124].
- The wider the window is, the lower the **time resolution** will be in identifying FoG episodes duration, as figure 18 shows.

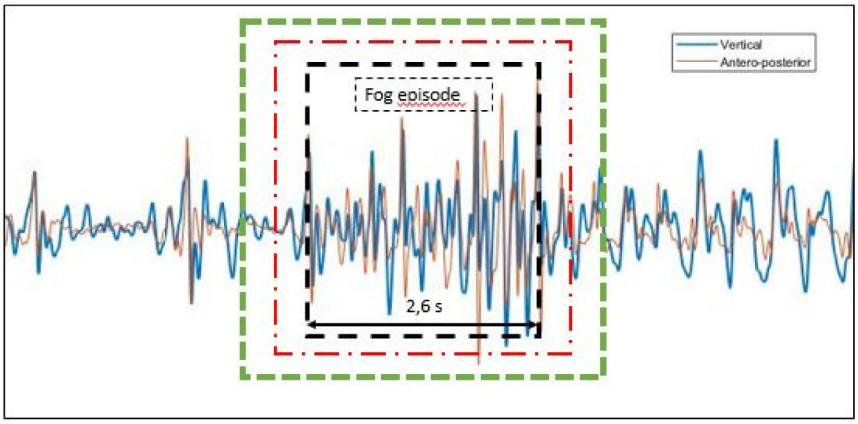


Figure 18: Increasing of windows size leads to a layer uncertainty in FoG duration determination. Black box represents FoG episode length while red and green boxes represent FoG episode detected by algorithm for two different settings of windows length, 1 s and 2 s respectively.

- Possible real-time implementation of the algorithm leads to take into account the **latency**, meaning the time between a FoG episode starting and the time when the system detects it, which is proportional to the window size [117].

- Window size and overlap found in literature ranged from 1 s to 4 s and from 10 % to 50 % respectively [115] [25] [155] [117] [7] [114].

All the considerations above led to the selection of a **2 s window length** for algorithm construction, considering such length as a good compromise between sensitivity and time resolution. Overlap was set to 50 %, ensuring a temporal resolution of $\pm 2s$. Other differents window sizes were explored at the end of algorithm construction and performance were evaluated and compared each other. This will be discussed in the last section of this study.

Features computing was performed as follows: features descibed in the previous section were calculated for each time epoch (2 s-window) and for the three acceleration signal components, and were differentiated based on the activity related to input signal. Power spectral density was estimated using Welch's method. Values of features were calculated using Matlab functions (e.g. std, wentropy, kurtosis, findpeaks) and system objects (e.g. ZeroCrossingDetector). At the end of the process, each feature was represented as a cell array, with each cell dimension representing a different activity. The content of each cell dimension was a 3-colums numeric matrix, with each row being an observation and each column a component of signal (vertical, antero-posterior and medio-lateral), that is the value of the feature in each window of the signal. All features were computed in this phase and their ability to detect FOG was evalueted in the feature selection part.

4.3.5 Feature selection

Feature Selection (FS) aims to select a minimal number of **relevant and informative features** from the initial set of variables. A feature is said to be relevant if it is essential to obtain good performance. An informative feature is one that is highly correlated with the target class but is highly uncorrelated with other features. The benefits of feature selction are:

- Improving prediction performance.
- Decreasing the complexity of the model.
- Facilitating data visualization.
- Reducing the measurement and storage requirements.
- Reducing training and utilization times.

In this study, **supervised** feature selection was used, thus aiming to select the minimum set of features necessary to discriminate which class the objects belong to. This means that the dataset used for FS contained not only the features characterizing each element, but also the information about their class.

Boxplot is a method used in descriptive statistics for graphically representing groups of numerical data through their quartiles[12]. Outliers[13] are plotted as individual points. The distance between minimum and maximumum value and between first and third quartile indicate the degree of dispersion in the data.

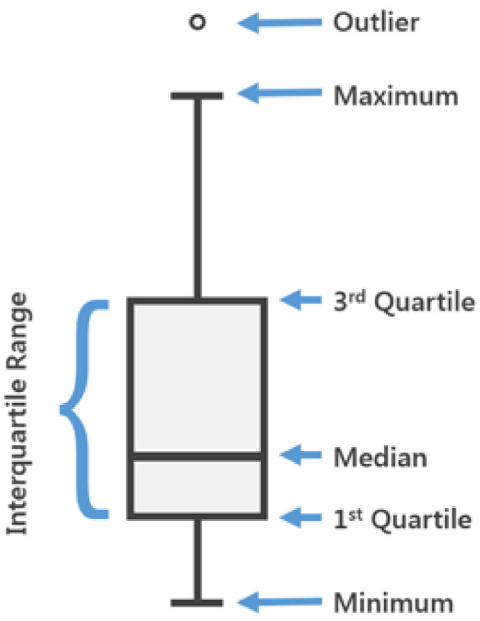
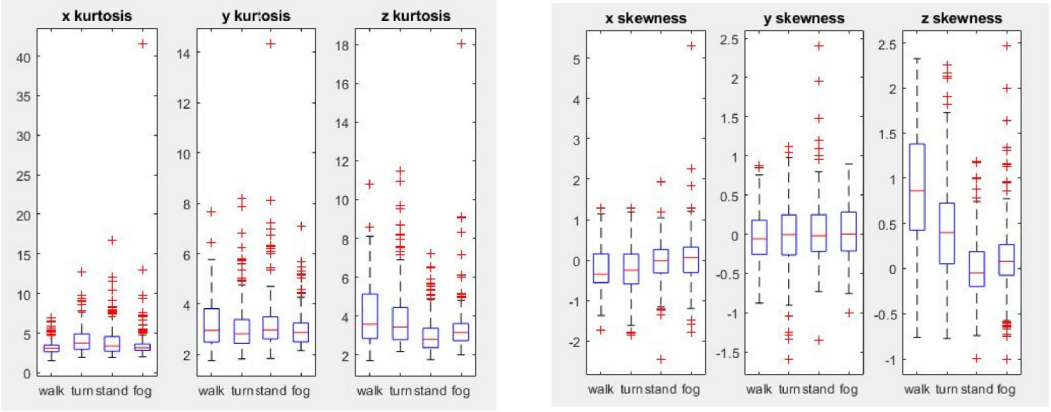


Figure 19: Box plot representation and description.

Boxplots of feature values for different classes (activities) are able to provide a qualitative measure of the goodness of a feature, with better features corresponding to that show well separated ranges for different classes. For each feature, boxplots for the different activities were visualized and analyzed, searching for features that best differentiate the classes. The distance between boxplots of different activities lead to a good differentiation; on the contrary, an overlapping of feature boxplots means that such features are not meaningful for class prediction, with the amount of overlap being a measure of that.

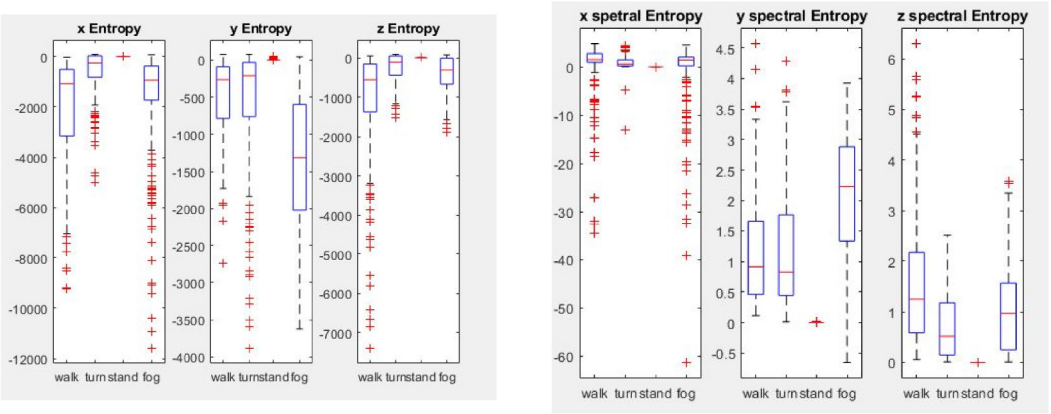
[12]The first quartile (Q1) is defined as the middle number between the smallest number and the median of the data set. The second quartile (Q2) is the median of the data. The third quartile (Q3) is the middle value between the median and the highest value of the data set.

[13]observation that lies outside the overall pattern of a distribution



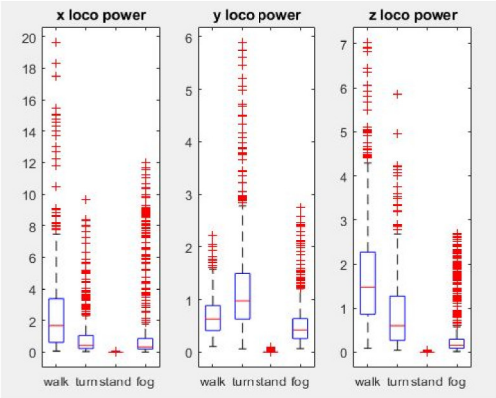
(a) (b)

Figure 20: Boxplots of **kurtosis** (a) and **skewness** (b) for the three components of the acceleration signal. Such features were found not to be meaningful for classes differentiation, because of the amount of overlapping between boxplots of different classes.

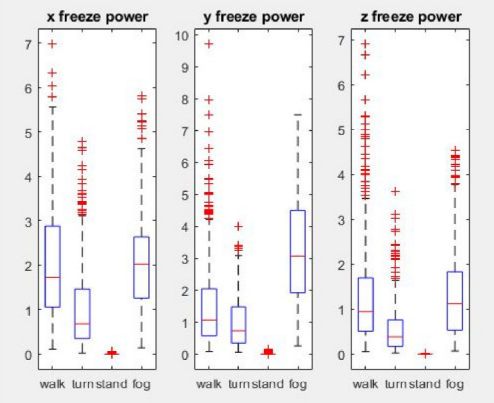


(a) (b)

Figure 21: Boxplots of **entropy** (a) and **spectral entropy** (b) for the three components of the acceleration signal. Neither features was found to be meaningful for classes differentiation, because of boxplots overlapping.

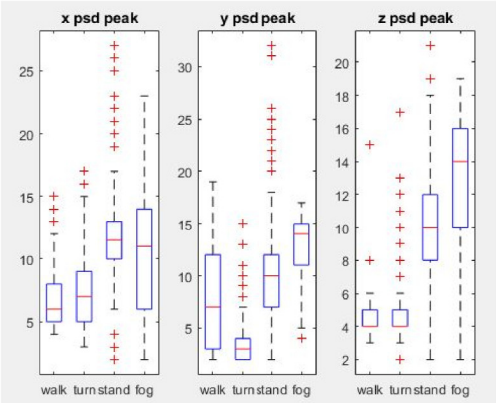


(a)

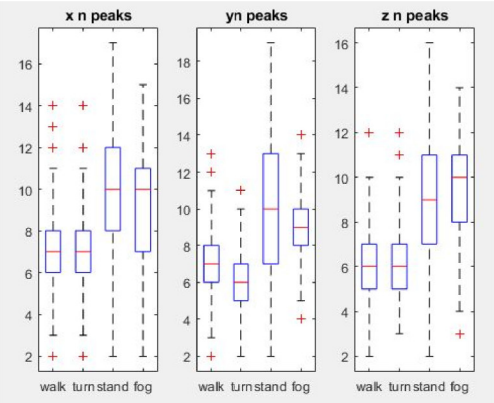


(b)

Figure 22: Boxplots of **power in locomotor band** (a) and in **freeze band** (b) for the three components of the acceleration signal. Also these features are not suitable for class differentiation, due to the overlap of boxplots and to the high number of outliers.

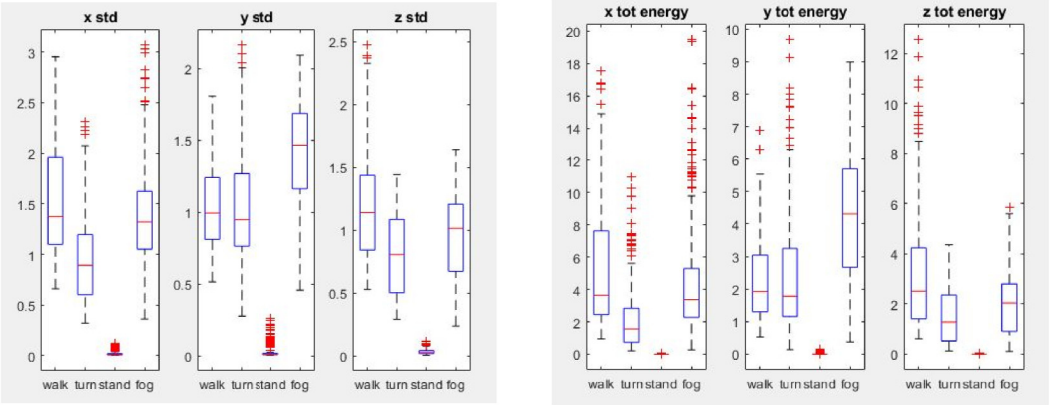


(a)



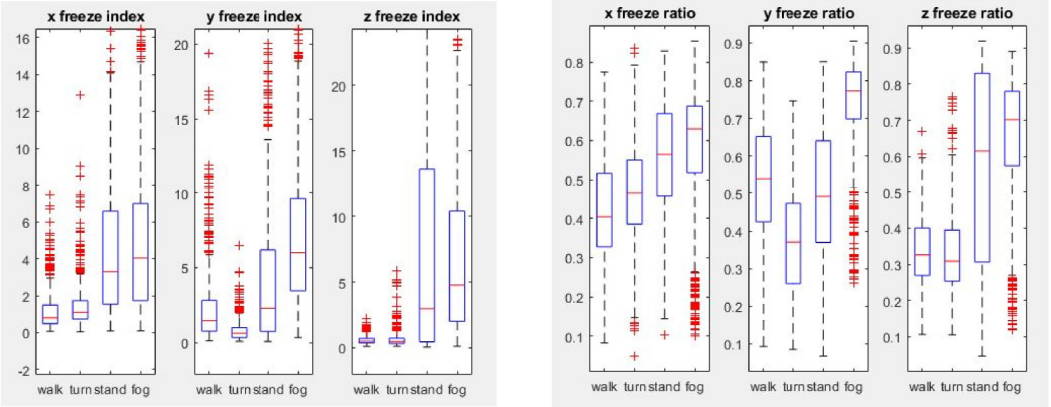
(b)

Figure 23: Boxplots of **PSD peak** frequency value (a) and **number of peaks** of the signals (b) for the three components of the acceleration signal. Boxplots of these features for the z component (antero-posterior acceleration) show high distance between FoG episodes and walk/turn, appearing a good feature for differentiation of such activities. Furthermore the number of outliers is very small, making these features robust. Overlap with stand boxplot has to take into account and new features have to be used in order to separate these two classes.



(a) (b)

Figure 24: Boxplots of **standard deviation** of amplitude (a) and **total energy** of the signals (b) for the three components of the acceleration signal. This features could be useful for differentiation between FoG episodes and stand. The distance between their respective boxplots allows a separation between these two classes, and this is true for all three components of the signal.



(a) (b)

Figure 25: Boxplots of **freeze index** (a) and **freeze ratio** (b) for the three components of the acceleration signal. Boxplots of freeze index in all three axes show a small margin between FoG and walk/turn and a great overlap with stand boxplot. Freeze ratio, meaning the ratio between power in freeze band and total power, show higher margin on y and z component (respectively medio-lateral and antero-posterior acceleration) and no overlap on y component, thus making this a more suitable feature than the previous one.

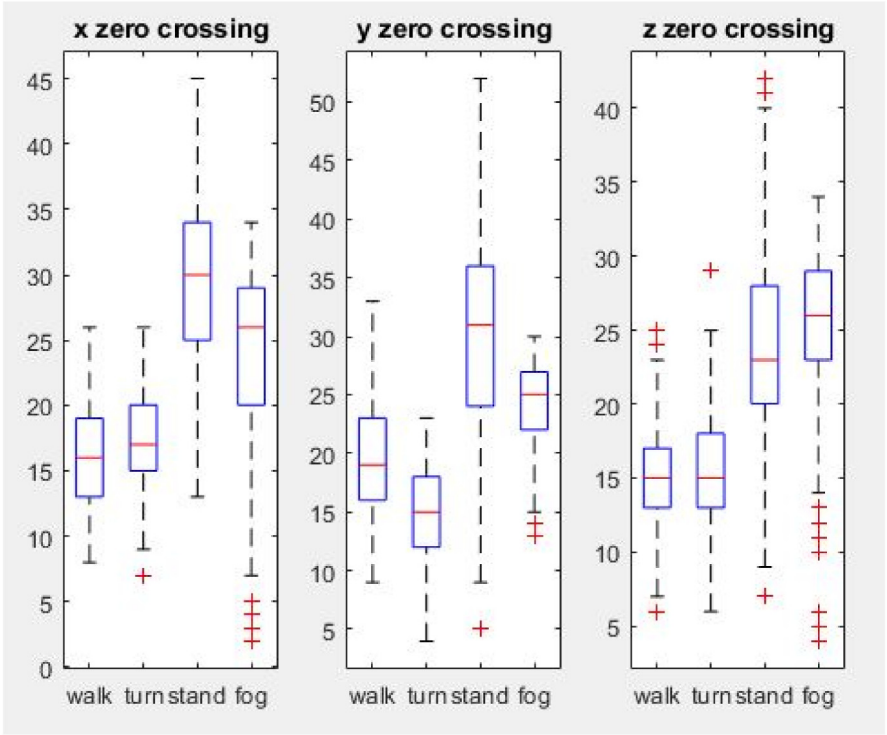


Figure 26: Boxplots for **zero crossing number** for the three components of the acceleration signal. Boxplot of FoG on z component (antero-posterior) show high margin from walk and turn boxplots, thus highlighting the ability of this feature to well differentiate FoG from walk/turn.

All the considerations listed above led to the selection of a small number of features, identifing two sets of features for two different purposes, thus with each set feeding a different SVM.

- **Total power** and **standard deviation of amplitude**, for all the three components of the signal, were chosen with the aim of **differentiating movement** (walk, turn, FoG) **from standing**.
- The antero-posterior component of **frequency value corresponding to PSD peak**, **number of peaks**, **zero crossing rate** and both antero-posterior and medio-lateral component of **freeze ratio** were selected for further **separating FoG from walking and turning**.

Nevertheless, also other features were taken in consideration, for a possible improvement in classificator performances, and will be add in the feature set if a benefit will be shown in training and test phase.

4.4 Algorithm application

4.4.1 Signals organization and concatenation

The purpose of this process is to exploit the maximum possible amount of variability in the acquired data, keeping at the same time a moderate size of input data, avoiding excessive duration of all phases involved in algorithm application.

- From each PD participant, 15 s of signal relative to each activity performed (walk, turn, stand) were extracted, with **15 s of signal** being considered **typical** enough to represent all signal.
- Extracted signals from all PD participants were **concatenated** together, in order to get a signal database relative to walk, turn and stand, and representing all acceleration signals acquired (as shown in figures 28, 29, 30 and 35).
- Acceleration signals relative to FoG events show excessive disparity in duration (as shown in figure 27). Shorter signals were self-concatenated, in order to reach the longest FoG event signal duration. This process aimed to give the same **weight** to all **FoG events**, exploiting the maximum variability and avoiding neglecting of singles and shorter FoG events (these could be considered as outliers by the SVM classifier).
- Obtained FoG signals were concatenated together, thus obtaining a single FoG signal, representative of all FoG events.
- Obtained FoG signal was self-concatenated in order to reach the same size of the signals relative to the other activities.

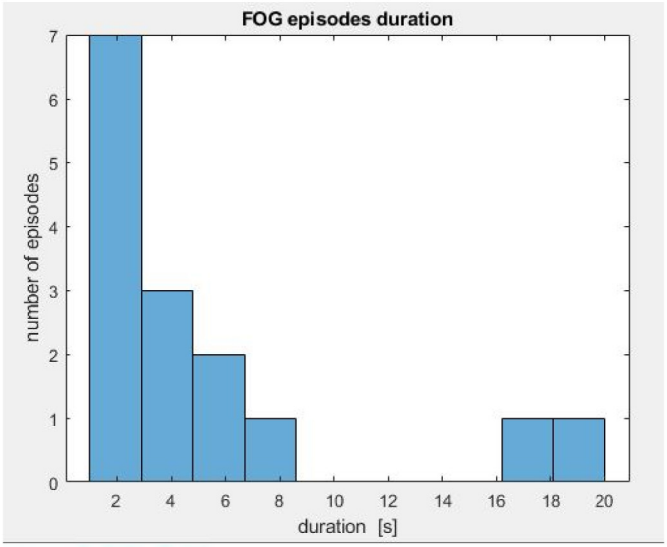


Figure 27: Histogram of FoG episodes duration. Most of episodes last less than 7 s, with only two episodes lasting between 16 and 20 s.

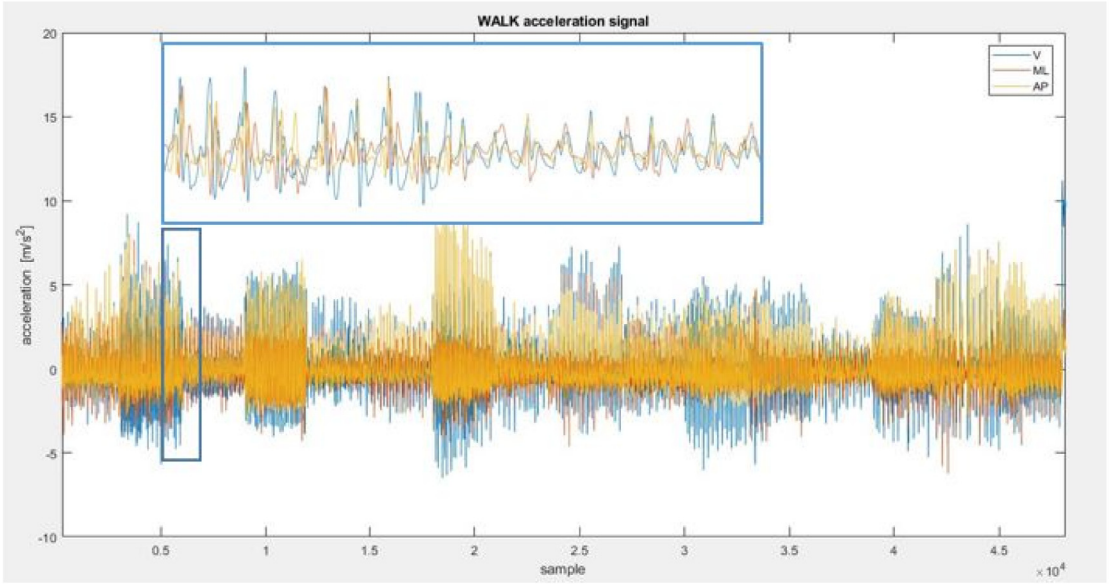


Figure 28: **Walk** acceleration signal obtained from the concatenation of 15 s of walk signal from each PD participant.

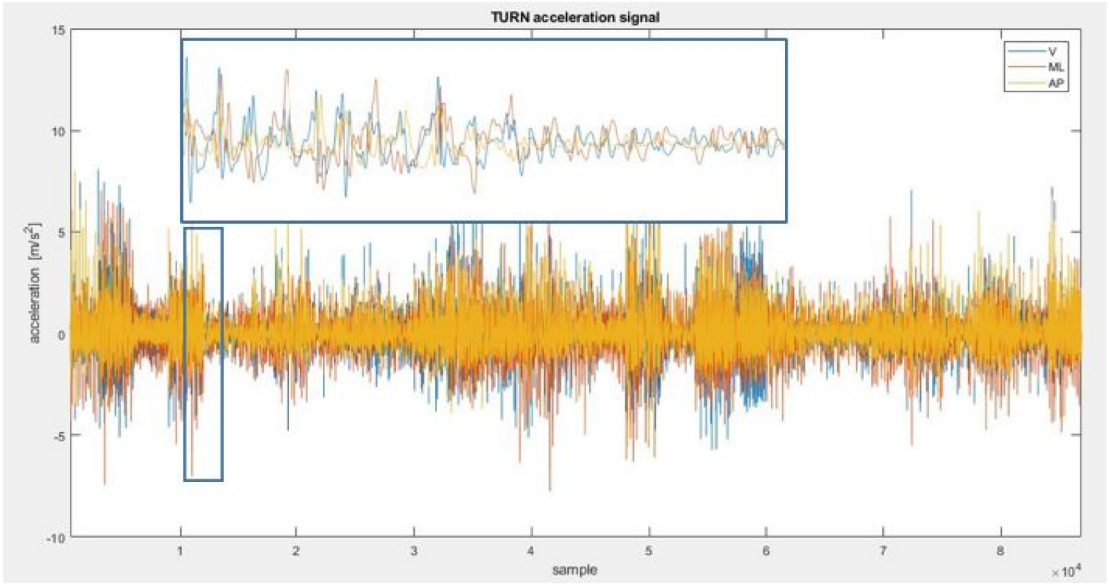


Figure 29: **Turn** acceleration signal obtained from the concatenation of 15 s of turn signal from each PD participant.

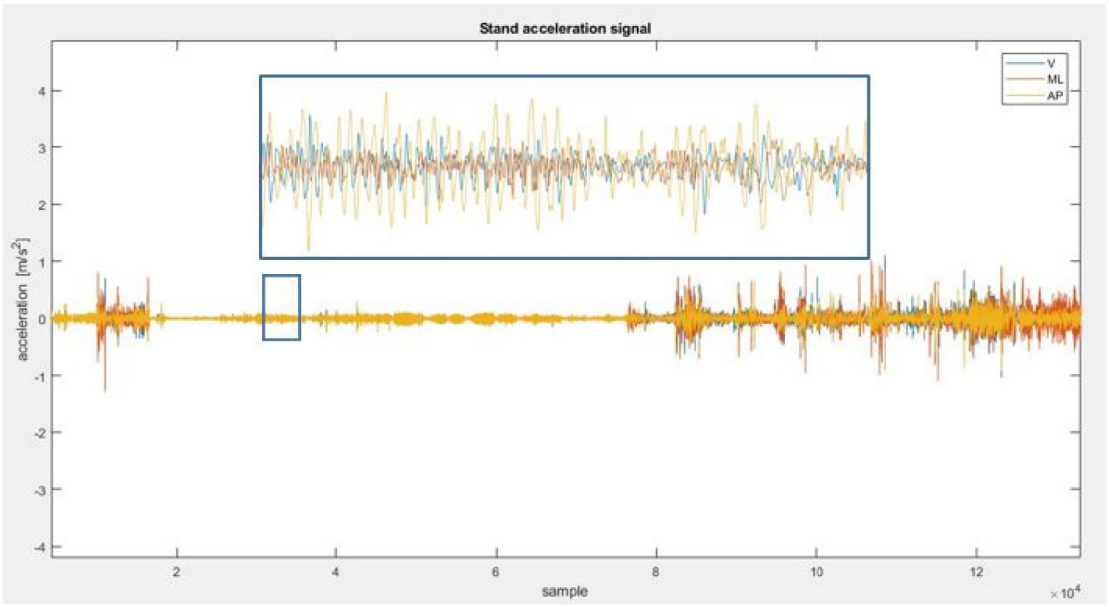


Figure 30: **Stand** acceleration signal obtained from the concatenation of 15 s of stand signal from each PD participant.

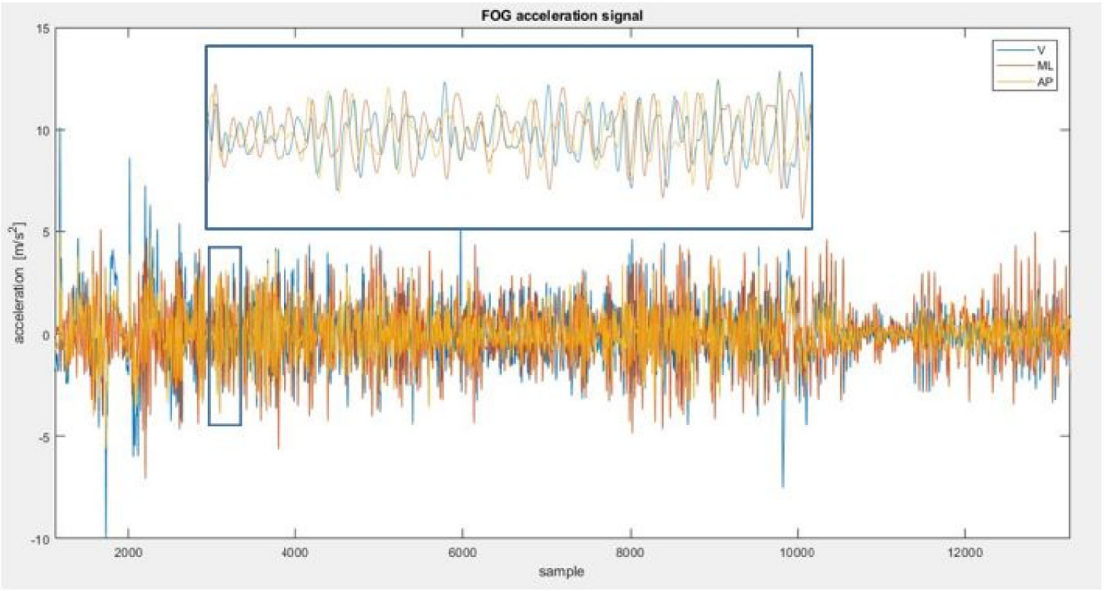


Figure 31: **FoG** accelerations signal obtained from the concatenation of all FoG episodes.

4.4.2 Training and test

Since no feature was able to distinguish FoG events from all other activities, two different SVMs were built: one of them suitable to distinguish movement from stand signals; the other able to detect FoG, differentiating it from other activities (walk, turn). Training and test phases required the same preprocessing (filtering, windowing and feature computing) done for algorithm construction.

Two SVMs were trained using **two training sets**, and required two different processes:

1.
   - All signals relative to movement (walk, turn, FoG) were concatenated and classified as belonging to the first class (movement); stand signals only composed the second class.
   - The two signals were made of the same size, self-concatenating the shorter signal.
   - The set of features computed was that able to **differentiate moving windows from standing windows** (total energy and standard deviation of amplitude for all three components of signals). Despite acceleration signal may show reduced amplidude during some turning, hesitation and FoG, the amount of movement performed is sufficient greater than that during standing; the features above well capture this characteristic.
   - The first SVM was trained with such training data and was able to distinguish acceleration signal relative to movement from signal relative to stand phases.

2.
   - Walk and turn signals were concatenated together and composed the first class (movement non-FoG); FoG signal only composed the second class.
   - The two signals were made of the same size, self-concatenating the shorter signal.
   - The set of features computed was the one able to **detect FoG**, differentiating it from walk and turn (z component of number of peaks, zero crossing rate, frequency relative to PSD peak, y and z component of freeze ratio).
   - The second SVM was then trained with the resulting training data and aimed to distinguish FoG events from other activities.

Table 5: Training input data.

Activity	**Number of participants**	**Total duration (min)**
Walk	38	9.5
Turn	36	8.5
Stand	22	17
FoG	6	1.1

The system was first **tested** on signals non-containing FoG events, in order to evaluate system performance in terms of specificity. Signals from **control and PD non-freezers** were preprocessed and given as input data to the detection system. A **leave-one-out** approach was used for validation of detection system on **FOG events**. This process led to the training of the classifiers using all walk, turn and stand signals, and n-1 FoG events, with n being the total number of

FoG events in the dataset; subsequent testing phase was realized on the single FoG episode excluded in the training. Performance in terms of sensitivity could be analyzed.
Finally, the algorithm was tested on **PD freezer** subjects who esperienced FoG during data acquisition. Sensibility, specificity, accuracy and precision were evaluated for each patient and mean values and their standard deviation were computed.

Table 6: Test input data.

Sample	Number of participants	Total signal duration (min)
Control	21	83
PD non-freezers	33	119
PD freezers	5	18

4.4.3 Performance evaluation

In this study, true positives (TP) were the windows relative to FOG events that have been detected by the system; true negatives (TN) were the windows relative to other activities (walk, turn, stand) that the system did not identified as FoG. False positive (FP) were the windows detected by the system but actually non containing FOG events; false negatives (FN) were the windows containing FoG but not detected by the system.

- Sensitivity, expressed as $\frac{TP}{TP+FN}$, measures the proportion of actual FoG windows that are correctly identified as such.
- Specificity, expressed as $\frac{TN}{TN+FP}$, measures the proportion of non-FoG windows (walk, turn, stand) that are not identified as FoG by the system.
- Accuracy, expressed as $\frac{TP+TN}{TP+TN+FP+FN}$, measures the percentage of the correct classified windows out of the total windows.
- Precision, expressed as $\frac{TP}{TP+FP}$, measures the ability of the system to discriminate FoG from non-FoG events.

Specificity was computed as follow: the detection system was run on acceleration signals relative to control and PD non-freezers partecipants; the number of FP was computed counting the number of windows identified as FoG by the system; the number of TN was calculated as the difference between the total number of windows and the number of FP; specificity was then computed as the ratio between TP and the total number of windows.
Sensitivity was computed as follow: detection system was run on all FoG signals, extracted from PD freezers partecipants; the number of TP was calculated counting the number of windows detected by the system; number of FN was the difference between the total number of windows and the number of TP; sensitivity was then calculated as the ratio between TP and the total number of FoG windows.
Accuracy and Precision were obtained with formulas listed above.

5 Results and discussion

The results of algorithm application were worked out on different test sets as follow:

1. Algorithm was tested on **control** set (partecipant not suffering from Parkinson's disease);
    - every detected window was classified as a false positive;
    - the number of true negatives was computed as the difference between the total number of windows and the number of false positives obtained before;
    - **specificity** was computed and resulted in **99.93 %**.

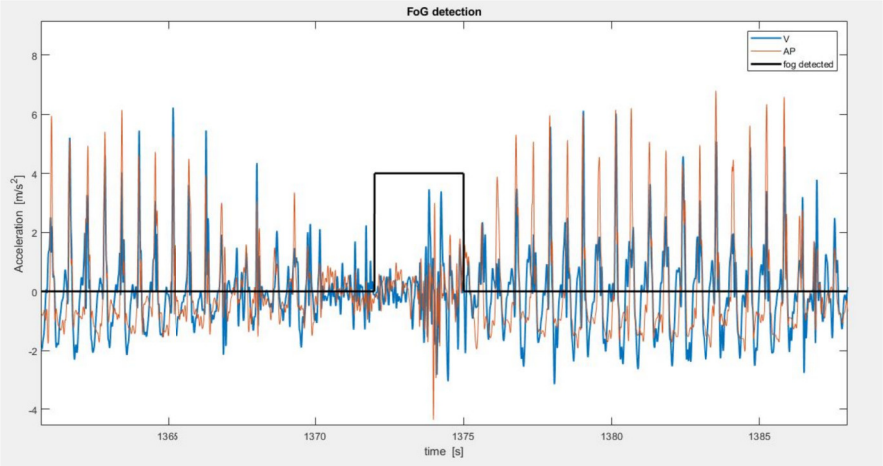


Figure 32: Example of a false positive found in control set.

2. Algorithm was tested on **PD non-freezers** set ;
    - every detected window was classified as a false positive;
    - the number of true negatives was computed as the difference between the total number of windows and the number of false positives obtained before;
    - **specificity** was computed and resulted in **99.44 %**.

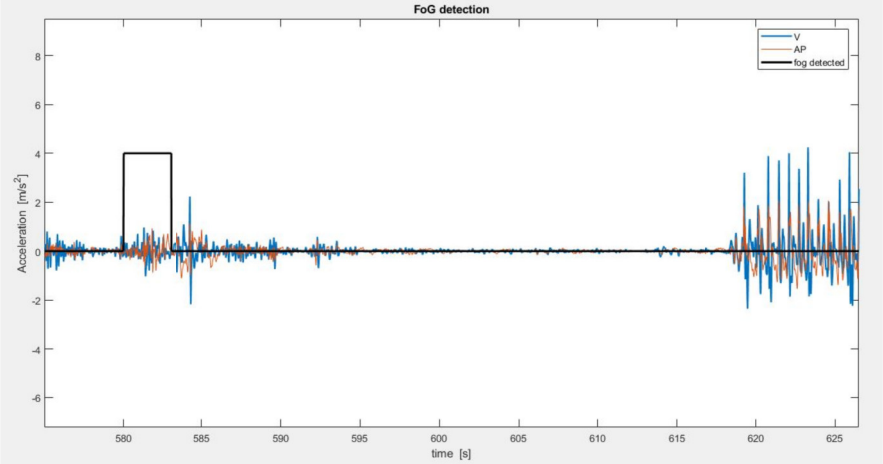


Figure 33: Example of a false positve found in PD non-freezers set.

3. Algorithm was tested on **PD freezers** set ;

   - number of true positives, false negatives and false positives were computed;
   - the number of true negatives was computed as the difference between the total number of windows and the sum of the number of false negatives and the number of true positives obtained before;
   - **sensitivity** resulted in **100 %** while **specificity** was **94.6 %**.
   - **accuracy** was found to be **95.5 %** and **precision** was **79.8 %**.

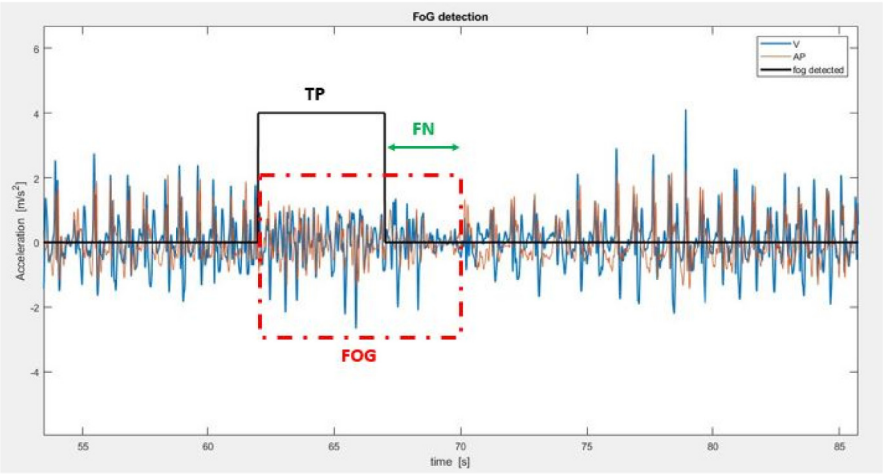


Figure 34: Example of a true positive (TP) and false negative (FN) found on PD-freezers set.

4. A **leave one out** validation was performed on FOG events: it consisted in training the classifier with all walk, turn and stand signals, and n-1 FoG episodes, with 'n' representing number of FoG episodes, and testing on the remaining single FoG episode. For this purpose, shorter FoG signals were

self-concatenated in order to reach a reasonable length. **Detection rate** resulted in **100 %**.

5. **Time resolution** in determining the duration of a FoG episode depends on the length of the windows used for the detection. Since 2 s-windows were used in this study, with overlapping equal to half-window size, it has been expected to have a maximum error of 1 s (half-window size) both at the beginning of the episode and at the end, thus leading to a time resolution of **2 s**.

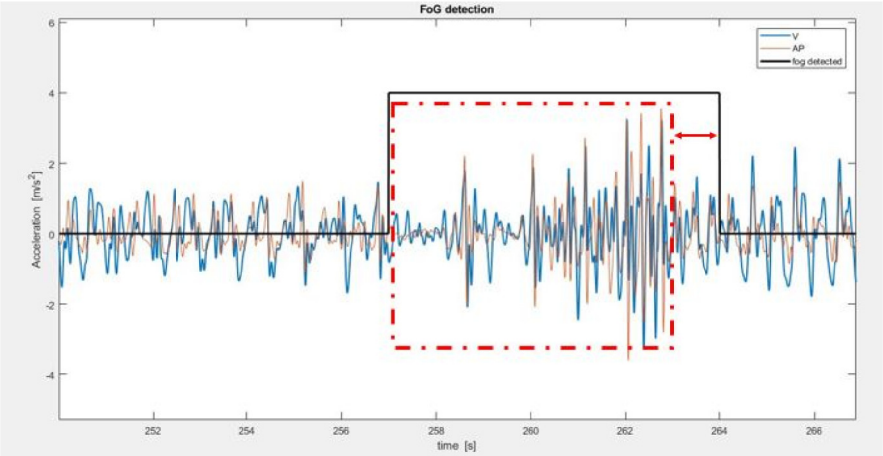


Figure 35: An example of result of application of FOG detection system. Red square indicate FoG episode; black line represent the result of the testing phase of the algorithm. Signals to the left and to the right of FoG event concern respectively turn and walk. **Time resolution** in determine the FoG duration is in this case about 1s.

Table 7: Performance of the classificator.

Sample	**Performance**		**Value (%)**	**Total windows**
Control	Test	Specificity	99.93	4980
PD non-freezers	Test	Specificity	99.44	7140
PD freezers	Test	Specificity	94.6	1200
		Sensitivity	100	
		Accuracy	95.5	
		Precision	79.8	
	L-o-O validation	Detection rate	100	65

Finally, different window sizes were set and new phases of training and test were executed on each participant's set, as done for the 2 s-windows. Results were obtained using the same data and classifiers as before but setting windows size equal to 1 s, 3 s and 4 s. Performance obtained with a 3 s window was very close to that obtained with a 2 s-long window. Both sensitivity and specificity were significantly lower for a 1 s window (92 % and 84 %, respectively). Specificity

only was significantly lower for a 4 s window (75 %), and short-duration FoG were not detected.

Discussion

Performance of the built classifiers proved to be promising.

- Only turning FoGs were observed in this study, thus the suitability of the built algorithm for other FoG types has to be evalueted in future works, when additional FoG data will be included in the dataset.

- On control and PD non-freezers sets, despite the great variability in the activities execution, the number of false positives was found to be extremely low, thus providing a very high specificity, which was considered essential for the purposes of this study. This is an evidence of high **generalization capability** of algorithm, which provided optimal performance, in terms of specificity, on samples not included in the training set.

- On PD freezers set, sensitivity, specificity and accuracy showed values over 90 %, despite gait abnormalities and greater variability have been found on PD freezers subjects, compared to non freezers [186]. Precision demostrated not excellent result, partially due to the small number of FoG episodes detected; This represent an issue that could be easily overcome including in the dataset new partecipants experiencing several FoG episodes of considerable duration (4 s at least).

- Leave-one-out **validation**, executed for FoG episodes, was done in order to prove the **robustness** of the detection system, evaluating FoG episodes that were not used for the training of the classifier, and demostrated optimal results.

- Analysis of algorithm performance, setting different **windows size**, suggests that a 3 s-long window could also be employed, given that it ensures similar performance of a 2 s-long one; however, such choice would lead to a worse time resolution in identification of FoG duration, and the minimum duration of a FoG episode, required to its detection, would increase.

- The large number of partecipants involved in the study has led a great benefit, providing great variability and statistical meaningfulness of performance obtained both on PD non-freezers and control set.

- The **small size of the FoG dataset**, however, is still a huge problem; further FoG episodes have to be included in the dataset, for consolidating the algorithm and giving statistical meaningfulness to the results obtained on PD freezers set, and possibly increasing precision of the system.

- Finally, despite algorithm has demonstrated a good generalization ability, a **patient specific** training would certainly ensure better performance, in terms of precision. This way the system would be able to learn specific gait patterns and FoG manifestation characteristic of the specific subject, and consequently adjust classificator settings.

6 Conclusion

An automated detection system for identification of FoG episodes, their duration and time of day manifestation would lead precious benefit to patients suffering from Parkinson's disease. Home monitoring of FoG would provide fundamental information, useful for monitoring of disease progression, motor fluctuations during the day, and for understanding patient response to drug-therapy, thus making clinicians able to adjust the treatment in a objective, reliable and patient-specific way. The algorithm built in this study demostrated excellent results, robustness and high ability of generalization, despite the poorness of FoG episodes detected; including some more FoG episodes in the dataset would make the algorithm suitable for an implementation in a home environment. At the moment, patient may have two or more sessions of data acquisition during the day, executing the same protocol as done in this study; the data acquired would be analyzed at the end of day and information about FoG episodes could be collected. For a costant and long-term monitoring of patient performing activities of daily living, instead, new data has to be collected, regarding all the set of activities the patient performs during his everyday life. Furthermore, a patient-specific training of the classificator would surely lead to an increase in performace of the detection system, obtaining a even more reliable tool useful both for clinicians and for patients. At last, a real-time implementation of the algorithm may be possible, given the semplicity and the rapidity of execution of the proposed algorithm (processing time for a 10 s signal resulted in less than 0.5 s). Yet, considering time of data trasmission and actuation of some kind of cue (e.g. auditory, haptic), the use of an object oriented programming, together with a programming language faster than Matlab C, would certainly reduce the latency from FoG episode manifestation to its detection.

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