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INTERNSHIP REPORT

Analysis of Anticipatory Postural Adjustments of Parkinson's Patients Using Inertial Sensors

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Preface

This report presents my practical work within the Project “Analysis of anticipatory postural adjustments of Parkinson’s patients using inertial sensors” at the Research Centre for Information and Communications Technologies of the University of Granada (CITIC-UGR). The Münster University of Applied Sciences required an internship of at least ten weeks prior to the final bachelor’s thesis.

This is a conjoint project between the University of Granada and the Department of Neurology of the Klinikum Großhadern in Munich, which is part of the Ludwig-Maximilians University. The goal of the project was to carry out an analysis of the so called anticipatory postural adjustments, which are the movements by a human subject between the moment he initiates gait and the first step. The medical community is interested in this procedure, as it can assist the diagnosis of neurodegenerative diseases such as Parkinson’s.

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Abbreviations

APAs	Anticipatory Postural Adjustments
COM	Centre of Mass
COP	Centre of Pressure
GRF	Ground Reaction Force
HMM	Hidden Markov Model
HY	Hoehn and Yahr scale
IMU	Inertial Measurement Unit
LS-SVM	Least Squares Support Vector Machine
MIMU	Magnetic Inertial Measurement Unit
MJFF	Michael J. Fox Foundation for Parkinson's Research
PD	Parkinson's Disease
TUG	Timed Up and Go Test
UPDRS	Unified Parkinson's Disease Rating Scale

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Introduction

1.1 General

1.1.1 Parkinson's Disease

According to Patients Medical [4],

“Parkinson’s disease is a progressive, neurodegenerative disease that occurs when the neurons within the brain responsible for producing the chemical dopamine become impaired or die. Dopamine is essential for the smooth control and co-ordination of the movement of voluntary muscle groups. Once approximately 80% of the brain’s dopamine producing cells no longer function, the symptoms of Parkinson’s disease begin to appear. [...] Parkinson’s disease may be termed as a progressive movement disorder that is distinguished by marked slow movements, tremors, and unstable posture.”

Especially in advanced stages of the Parkinson’s disease (PD) many patients exhibit an episodic, brief inability to step that delays gait initiation or interrupts ongoing gait. This phenomenon is called freezing of gait and is often associated with an alternating shaking of the knees, called knee trembling. However, these clinical signs of balance or gait problems are not evident in early stages of the disease [5][6].

1.1.2 Anticipatory Postural Adjustments

A major challenge to the human balance control system is the fact that we are bipeds having only one foot in contact with the ground while walking, and that two-thirds of our body

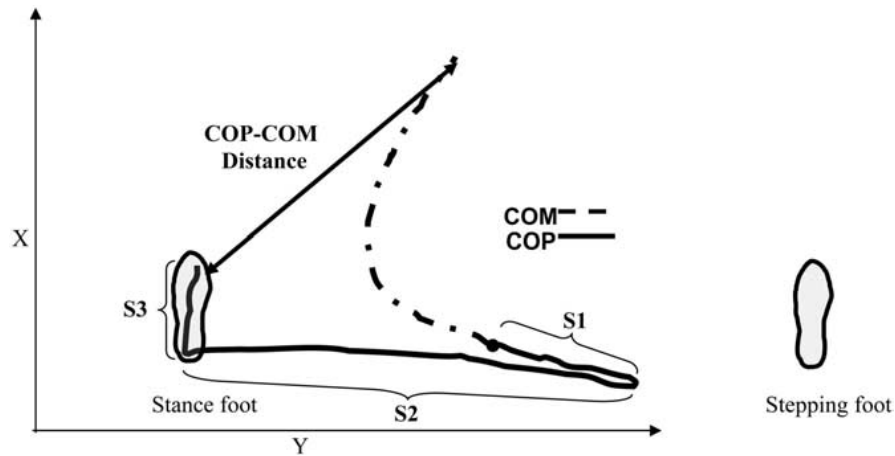


Figure 1.1: Representative anticipatory postural adjustments during forward-oriented gait initiation when stepping with the right foot [1].

mass is located two-thirds of body height above the ground [7]. Thus, to induce stable gait anticipatory postural adjustments (APAs) are necessary. The Encyclopedia of Neuroscience [8, p.133] defines APAs as "A predictive motor response that acts to counter, in a preemptive manner, the postural destabilisation associated with a forthcoming movement." As seen in Figure 1.1 the centre of body mass (COM) is accelerated forward and laterally over the stance foot to make sure that the body does not fall laterally toward the stepping foot during the swing phase [8]. The curve of the centre of pressure (COP) is divided in three periods. First, in the S1 period the COP moves posteriorly and toward the intended stepping limb, while the deliberate uncoupling of the COP and COM generates forward momentum. Then, in the S2 period, the COP displaces mediolaterally toward the stance foot. Finally, during the S3 period the COP moves anteriorly under the stance foot [1].

1.2 Goals

The goal of the project was to analyse anticipatory postural adjustments prior to step initiation and subsequently build a classifier using MATLAB[®], which is fed with data from both a force plate and a magnetic inertial measurement unit (GaitWatch [2]), in order to distinguish between Parkinson patients and healthy subjects. To gather the data the subject stood in front of the force plate. Then, the GaitWatch and force plate record was started and the subject made a step onto the force plate. After standing upright for a variable time of two to ten seconds the subject left the force plate, made a few steps, turned left, and stopped in front of it again. This sequence was repeated ten times. From now on we will refer to one of these ten gait cycles as simply a cycle.

1.3 Motivation

Advanced PD can increasingly diminish the quality of life, due to patients being more dependent on help from others to accomplish daily tasks. New neuroprotective medications are currently being developed and are expected to decelerate or stop the progression of the disease in early stages prior to significant loss of neurons [9][10]. Thus, a quantitative PD classification, enabling early diagnosis of the disease, could optimise early treatment and could furthermore help to validate new treatment methods. Additionally, an objective evaluation of longterm treatment success was ensured.

1.4 State of the Art

There are several rating scales as well as technical equipment that has been used to assess Parkinson's disease and to analyse anticipatory postural adjustments. They differ in terms of practicability, accuracy, validity, portability, and cost. The state of the art at the beginning of the project is described below.

1.4.1 Rating Scales

A commonly used rating scale is the Unified Parkinson's Disease Rating Scale (UPDRS), which is a short test performed by a physician [11]. The patient is rated on 31 different items (see Table 1.1) with a score of 0 (normal) to 4 (severely affected) [3]. Another method is the rough, but widely utilised and accepted Hoehn and Yahr scale (HY). Parkinsonian motor impairment is categorised in 5 stages: Unilateral (Stage 1) to bilateral disease (Stage 2) without balance difficulties, to the presence of postural instability (Stage 3), loss of physical independence (Stage 4), up to being wheelchair- or bed-bound (Stage 5) [12]. Finally, there is the Timed Up and Go Test (TUG). This clinical test consists of rising from a chair, walking three metres, turning, walking back, and sitting. The total duration then represents the clinical outcome. It is widely used to rate balance, mobility, and fall risk in PD in its entirety, but does not give information about the particular impairments [13].

Without the need for complex technical devices these tests are relatively simple to perform. Klerk et al. [11] mentioned their disadvantages, including subjectivity, short observation periods, and unfamiliarity of the environment that these rating methods bring along. Further limitations are caused by clinician's bias and insensitivity to mild impairments (floor effect) [10].

Mentation, mood and behaviour	Activities of daily living	Motor examination
Intellectual impairment	Speech	Speech
Thought disorder	Salivation	Facial expression
Depression	Swallowing	Tremor at rest
Motivation/initiative	Handwriting	Action or postural tremor of hands
	Use of eating utensils	Rigidity
	Dressing	Finger taps
	Hygiene	Hand movements
	Turning in bed	Rapid alternating movements of hands
	Falling	Food agility
	Freezing when walking	Arising from chair
	Walking	Posture
	Tremor	Gait
	Sensory Complaints	Posture stability
		Body bradykinesia and hypokinesia

Table 1.1: Unified Parkinson's Disease Rating Scale items adapted from [3].

1.4.2 Instrumentation

In addition to the aforementioned subjective rating scales, there are different devices used to quantify gait and posture to assess them objectively. All of them come with certain pros and cons. The following devices have been used:

1.4.2.1 Electromyographs

Electromyography is a technique for evaluating the electrical activity of skeletal muscles. Successive action potentials generated by muscle cells are measured, by means of needle electrodes inserted into the muscles, and displayed on a cathode-ray oscilloscope. Thus medical abnormalities can be detected. The instrument used to capture the visual recording, termed electromyogram, is called electromyograph [14]. Electromyography is constrained to clinical application only, but in return gives indication about the contribution of specific, individual muscles to APAs.

1.4.2.2 Force Plates

Force plates quantify the ground reaction force (GRF), that is, the force exerted to the human body by the ground. The GRF is a three-dimensional vector with three orthogonal components. One component along the direction of gravity, one parallel to the ground in the sagittal plane, and one parallel to the ground in the frontal plane. Those are vertical planes

that divide the body in left and right halves, and ventral and dorsal sections, respectively. A force plate usually gives an electrical voltage proportional to the force in each of the three directions. Force plates can be characterised according to the following criteria: Sensitivity in Volts per Newton, crosstalk (indication of vertical force if a horizontal force is applied and vice versa), repeatability (similar results under the same load), and time- and temperature drift [15]. Usually force plates are embedded in the ground to place minimum constraints on subjects [16]. Therefore they are limited to clinical application. They have the advantage that they don't need to be calibrated before each use.

1.4.2.3 Inertial Measurement Units

Devices that use a combination of inertial sensors like accelerometers and gyroscopes are referred to as inertial measurement units (IMUs). If they also include magnetic field sensors (magnetometers), they are called magnetic inertial measurement units (MIMUs). With these devices the orientation of the body can be obtained with up to nine degrees of freedom, provided that triaxial accelerometers, gyroscopes and magnetometers are used, respectively [17].

- **ACCELEROMETERS** measure the acceleration of an object relative to an inertial frame. Since acceleration cannot be measured directly, the force exerted to a reference mass is obtained and the resultant acceleration is computed according to Newton's second law $\mathbf{F} = m \cdot \mathbf{a}$ [18].
- **GYROSCOPES** measure angular velocity and are based on the Coriolis Effect. By means of integration of the angular velocity the rotation angle is obtained [17].
- **MAGNETOMETERS** measure the strength and the direction of the magnetic field in a point in space, using the relationship between magnetic fields, movement and induced currents [17].

MIMUs are portable and relatively inexpensive. They can be easily attached to the body and thus allow non-clinical longterm application. Their drawbacks are complex calibration procedures and drift behaviour over time, depending on intensity and duration of the movement. Hence, in order to maintain a satisfactory degree of precision, periodical recomputation of the calibration parameters is required [17]. Moreover, Mancini et al. [10] pointed out the need of data pre-processing and the question of how to generate a clinically understandable presentation of the movement data.

1.4.3 Classification

There are several research works in the literature dealing with APA analysis and PD classification, as the examination of posture and gait are key components of the clinical evaluation of PD [19].

Klerk et al. [11] developed a measurement system based on accelerometry, called PD Monitor, implementing an Activity Classifier that quantifies tremor and bradykinesia in the arm, thigh, and trunk, in an ambulant way and over long periods of time. They validated their measurements with video records, which were rated by physicians using the UPDRS and concluded that “the PD monitor can be used for a detailed evaluation of the PD motor symptoms in order to optimise treatment.” [11].

Mancini et al. [5] found that the eleven untreated early-to-moderate stage Parkinson’s patients that took part in their study have a significantly smaller peak COP displacement towards the stepping leg and peak trunk acceleration towards the stance leg compared to the twelve age-matched healthy control subjects. Even though step velocity and step length were not different. The results showed that lateral APAs are impaired in early, untreated PD and that they are detectable with inertial sensors. As well as force plate-based, also acceleration-based extracted features could be used to detect impairments equally well. Due to the fact that the acceleration signal can be easily obtained via a sensor on a belt, no matter if in clinical or home environment, APA detection by means of accelerometers is considered as a useful way to characterise patients in early stages of PD without evident clinical symptoms. Additionally in [5] it is proposed to carry out further studies to determine the relationship between small APAs and the probability to develop start hesitation and freezing.

Palmerini et al. [19] states that PD classification could deliver a tool to follow the progression of the disease during the entire course to examine the efficiency of treatment. They studied classification of PD subjects using triaxial accelerometers on the lower back at L5 level and an ad hoc wrapper feature selection technique designed in [13]. Linear discriminant analysis was used to obtain a classifier that permits clinical interpretation of the results. Twenty early-mild PD subjects and twenty healthy age-matched control subjects had to perform two simple tests (quiet standing, Timed Up and Go test), in two evaluations over a one-year follow-up, to test accuracy and robustness over time. They achieved satisfactory accuracy of 93.75% and considered feature selection to be essential in this kind of data set. As well as [5] they found that lateral dynamics i.e. range of motion are impaired in early-mild PD and suggested further investigation on validity of measures in later stages.

Hass et al. [1] investigated the magnitude of the separation between the centre of pressure and the centre of body mass during gait initiation and its correlation with the severity of PD. They collected these data with a force plate and observed that the peak COP-COM distance during the S3 period (see Figure 1.1), of the 20 participating patients with H&Y score of 2.5 or higher, was 16% smaller than the one of the 23 patients with H&Y score of

2.0 or less. The results showed that this approach can quantify impairment of balance in PD at various stages of the disease.

On 13th of August 2014, the Michael J. Fox Foundation for Parkinson’s Research (MJFF) and Intel Corporation [20] announced a collaborative research study on objective measurement of PD symptoms. They aim to collect movement data of thousands of patients twenty-four seven at over 300 samples per second by means of unobtrusive wearable devices and store them on a big data analytics platform. The data platform, deployed on a cloud infrastructure, supports an analytics application that processes the data and detects changes in real time. Thus, by detecting anomalies, the progression of the disease can be measured objectively without the need for scientists to focus on the underlying computing technologies. Physicians and researchers are intended to have access to the data as well as be able to submit their own anonymised patient data for analysis. According to [20] the correlation of data that quantifies symptoms such as slowness of movement, tremor, and sleep quality with molecular data could advance drug development and provide a deeper insight into the clinical course of PD. At the end of 2014 Intel and MJFF plan to launch a mobile application, with which patients can report medication intake and how they are feeling to permit medical researchers to assess the effects of medications on motor symptoms. The extraordinary large scale of this project makes it unique in this research area.

Khorasani and Daliri [21] compared a Hidden Markov Model (HMM) based classifier against a sophisticated nonlinear classifier. The raw gait data corresponding to sixteen healthy and fifteen PD subjects was preprocessed and the stride interval i.e. length of gait cycle served as the input for the HMM classifier. Their results showed that the HMM method can distinguish between healthy subjects and PD patients with an accuracy of 90.3%, similar to the accuracy obtained with the least squares support vector machine (LS-SVM) implemented in [22].

Mancini et al. [10] found that untreated PD affects postural control, even if it is not clinically apparent. They measured the acceleration on the posterior trunk at L5 level of thirteen patients recently diagnosed with PD, but not taking anti-parkinsonian medications, and twelve healthy, age-matched control subjects to quantify the active postural corrections. To assess the smoothness of postural sway they calculated the jerk, which is the time derivative of the acceleration. At the same time they measured the COP with a force plate and determined, in contrast to [5], an increased magnitude of both COP and acceleration signal in subjects with untreated PD in comparison with the control subjects. On top of this both signals contained a larger jerk, i.e. showed faster components in the untreated PD subjects. They concluded that acceleration based parameters as well as COP parameters are able to distinguish between the two groups.

1.5 Methodology

The team in which I was integrated worked using the agile software development methodology. Working software was delivered frequently and was the principal measure of progression. Our self-organising team consisted of three members meeting regularly. Parts of the software were developed doing pair programming. To follow the progress of other team members at any time we used Pivotal Tracker, a tool for agile project management and GitHub, a repository hosting service based on the distributed version control system Git. I used the document markup language \LaTeX to write this report.

Hardware and Data Preprocessing

As aforementioned, we used a MIMU (GaitWatch) and a force plate (Zebris FDM-S) to gather the raw gait data. In this chapter we will describe the employed hardware in detail. Subsequently, we will elaborate on the necessary synchronisation of both systems.

2.1 GaitWatch

The GaitWatch device [2] is designed to monitor the motion of patients by means of inertial sensors while attached to the body. It was developed at the Department of Neurology of the Ludwig-Maximilians University in Munich in conjunction with the Department of Signal Theory, Telematics and Communications of the University of Granada. The system is composed of a set of embedded magnetic and inertial sensors wired to a box containing a microcontroller. This microcontroller is in charge of collecting data from the embedded box sensors, as well as from the external measurement units, and storing them on a memory card. The various units are placed at the patient's thighs, shanks, arms and trunk as shown in Figure 2.1. The components of the three different kinds of subunits are described below:

- TYPE A (thighs and shanks):

IMU Analog Combo Board with 5 Degrees of Freedom from SparkFun Electronics [23] containing an IDG500 biaxial gyroscope (from which only Y axis is actually used) with a measurement range of $\pm 500^\circ/\text{s}$ [24] and a $\pm 3\text{ g}$ triaxial accelerometer, ADXL335 from Analog Devices [25].

- TYPE B (arms):

IDG500 biaxial gyroscope with a measurement range of $\pm 500^\circ/\text{s}$ from SparkFun Electronics [24].

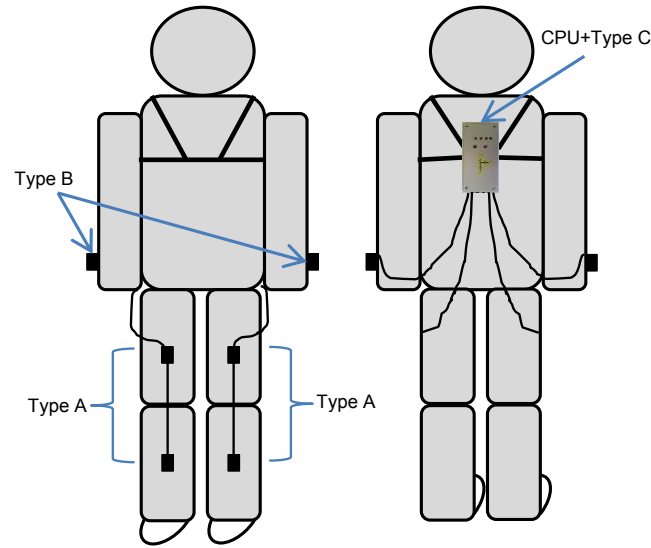


Figure 2.1: Placement of GaitWatch components at the body [2].

- TYPE C (trunk):

ADXL345 triaxial accelerometer with programmable range of $\pm 2\text{ g}/\pm 4\text{ g}/\pm 8\text{ g}/\pm 16\text{ g}$ from Analog Devices [26], IMU3000 triaxial gyroscope with programmable range of $\pm 250/\pm 500/\pm 1000/\pm 3000\text{ }^\circ/\text{s}$ from InvenSense [27], Micromag3 triaxial magnetometer with a measurement range of $\pm 11\text{ Gauss}$ from SparkFun Electronics [28], AL-XAVRB board containing an AVR ATxmega processor from ALVIDI [29].

2.2 Zebris FDM-S

The Zebris FDM-S [30] is a force measuring plate for stance and gait analysis with a sensor area of 540 x 330 mm accommodating 40 x 64 force sensors, which results in 1.4 sensors per square centimetre and 2560 sensors in total. The data was sampled at a frequency of 120 Hz.

2.3 Synchronisation

According to the data gathering protocol in 1.2 the raw data that was collected with the MIMU and the force plate had distinct time axes, which is why a synchronisation of both systems was necessary. In order to achieve this we created a MATLAB[®] routine that read both the raw force plate and GaitWatch data, calibrated the GaitWatch signals and carried out the synchronisation for all patients in a data set.

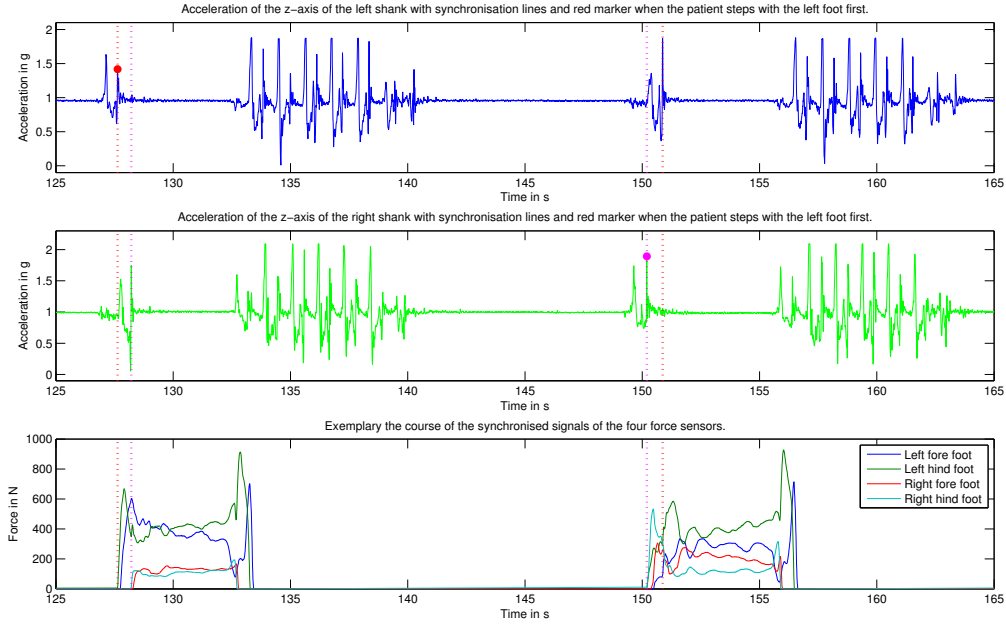


Figure 2.2: Left-right detection of stepping limb and synchronised signals of the four force sensors.

The single data sets of each patient that we received from the clinic in Munich consisted of one .mat-file containing the GaitWatch signals and ten text files with the force plate signals of one cycle, respectively. An Excel-file for all patients of one complete data set stated the order of the separate text files, the corresponding GaitWatch .mat-file, their file names as well as additional hints and characteristics in respect of the patient, e.g. ‘patient with freezing’ or ‘deep brain stimulation’. To read the force plate data in the right order and to associate the correct GaitWatch file we evaluated this Excel-file, so that the rest of the synchronisation could be automatised.

We used the z-axis of the acceleration signals of both shanks for synchronisation, since those had a large peak at the point in time when the patient touched the force plate. That was also the time when the force plate signals attained nonzero values. First we detected the second peak pointing upwards of each separate gait cycle in the aforementioned signals. We detected the second one since when the patient initiated the step onto the force plate there was a peak pointing upwards while accelerating his leg upwards, then a one pointing downwards at the point in time when the motion changes its direction and the patient lowers his leg. Finally, there was a second peak pointing upwards when the foot touches the force plate and thus the shank decelerates strongly. Patients could step with an arbitrary limb onto the force plate, in order to keep the procedure as natural as possible. As seen in the upper two graphs in Figure 2.2 we distinguished between stepping with the left foot first and stepping with the right foot first and used the sooner peak as synchronisation line.

Next, we computed the differences between the time vectors of the force plate signals and the GaitWatch signals and corrected the force plate time vector, accordingly. Then the force plate signals were resampled at the GaitWatch sampling frequency of 200 Hz. Eventually the signals were grouped in time series objects, separated in chunks of one cycle and stored in cell arrays, in which one cell contained one cycle, as a .mat-file. The lower graph in Figure 2.2 shows exemplary the synchronised signals of the four force sensors.

Conclusion and Future Work

3.1 Conclusions

Summarising the above, I can say that I have learned a lot in the four month that I spent in Granada. Amongst others I have come to know many new work methods, not only due to being exposed to people from a different culture, but also due to the fact that scientific research differs strongly from the work as a student at university. I gained a deeper understanding of Parkinson's disease and how various gait analysis techniques are used to quantify its effects. Therefore I had to study the principles of force plates and inertial measurement units as well as the basics of classification. I was able to improve my MATLAB[®] skills and have realised how important it is to write understandable and well commented code, if it is for a larger project and not only for a coursework. I am now familiar with tools such as GitHub and Pivotal Tracker which make working in a team much easier and significantly more efficient. Beside my work at the research centre, where I obtained a valuable insight into scientific research, I read a book about scientific writing that helped me to improve my oral and written English skills during my stay. Furthermore I now know the fundamentals of L^AT_EX.

The above will hopefully serve as a good foundation for my subsequent bachelor's thesis. All in all it was a great experience, professionally as well as personally. I truly recommend such a stay to every university student.

3.2 Future Work

Biomedical research is a very interesting blend of both my major interests, that is, working in the medical field as a paramedic and in the technical field as an electrical engineer. I

would like to keep working in this field and write my aforementioned bachelor's thesis here in Granada. There is a variety of possible future work. One related topic would be the validation of the pitch angles of the body measured with the GaitWatch by means of cameras that record the trace of visual markers. From these markers one could compute the pitch angels and compare them to those of the GaitWatch to validate its performance. Another option would be the implementation of an new Kalman filter based orientation algorithm proposed by Bennett et al. in [31] to fuse the calibrated GaitWatch signals and thus improve the accuracy of the orientation estimates. Also a visual interface for the entire gait analysis process would be a reasonable improvement of the existing system.

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