PROJECT PROPOSAL

Gait assessment of patients with Parkinson's disease using inertial sensors and non-linear dynamics features

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1 Research Problem

Parkinson's disease (PD) is a progressive disorder of the nervous system that affects movement. It develops gradually, sometimes starting with a barely noticeable tremor in one hand. Besides tremor, which is, the most well-known sign of PD, the disease also commonly causes stiffness or slowing of movement [1]. In the early stages of PD, the face may show little or no expression, or the arms may not swing when walking. The speech may become soft or slurred.

PD is usually diagnosed and clinically characterized by the four major motor symptoms: bradykinesia, tremor, rigidity, and postural instability. The assessment of these motor symptoms is performed according to the Unified Parkinson Disease Rating Scale (UPDRS) [2]. The therapy mainly focuses on treating the symptoms of the patients with individual medication. This medication always has to be adjusted according to the current stage of disease. To assess the continuous course of locomotive disorders in PD on a daily basis and over a long period of time, the only possibility is to rely on a patient's diary. In these diaries, the patient registers the current state of motion disorder at regular intervals. Since these ratings are always subjective, it is necessary to find a way to provide the physicians with objective parameters from long term studies [3]. An accurate monitoring of PD patients could help making timely decisions regarding their medication and their therapy. Additionally, if such a screening is performed from bio–signals like gait, their treatment could be followed remotely. Due to this fact, there is an interest worldwide to develop technology for the automatic monitoring of the neurological state of PD patients considering different bio–signals.

For instance Astrum IT GmbH developed a system for gait analysis of PD patients called eGait [4], which consists of inertial sensors (acelerometers and gyroscopes) attached to the patient's shoes with the aim of analyzing the gait impairments of the patients.

The aim of this work is to evaluate gait deficits of the patients using several feature extraction methods with the aim of discriminating the walking of PD patients vs. healthy controls, and also to evaluate and predict the neurological state of patients according to the UPDRS scale.

2 State of the Art

PD is caused by the loss of dopaminergic cells in the mid brain which are in charged of controlling movement and emotions. This leads to a reduction in a chemical called dopamine in the brain. Dopamine plays a vital role in regulating the movement of the body. A reduction in dopamine is responsible for many of the symptoms of PD. It is unclear the cause of the loss of nerve cells, but a combination of genetic and environmental factors is the most probable responsible [5].

Gait changes are a hallmark of PD, with reductions in speed, decreased step length, altered cadence, and increased gait variability. While gait abnormalities are not pronounced in the early stages, their prevalence and severity increases with the disease progression. Within three years of diagnosis, more than 85% of people with clinically probable PD develop gait problems. The potential consequences of gait impairments in PD are significant and include increased disability, increased risk for falls, and reduced quality of life. As the disease progresses, people with PD typically exhibit shuffling gait with a forward-stooped posture and asymmetrical arm swing (festinating gait). These characteristics make the patient to use a lot of energy, which causes that routine walking places a person at or near to their maximum metabolic capacity. Gait impairments are compounded by the presence of bradykinesia, rigidity, and postural instability. Balance and gait abnormalities can lead to reduced quality of life. In fact, people with PD consider mobility and walking limitations to be among the worst aspects of the disease. Patients consistently identify improvement in walking as the most relevant outcome when rating the success of a Parkinson's treatment[6].

In related studies, the scientific community has shown a growing interest about the gait analysis and other bio–signals to detect the PD and monitoring the neurological state of PD patients.

In [7] the authors performed a classifications of 42 patients and 39 controls using the eGait sensors [4], using features related to non-linear dynamics features in three aspects of each stride (impulse, heel support and all foot support). The authors achieved an accuracy of up to 81% for the detection of all patients and 91% when considering only the most affected patients.

In [8] the authors proposed an algorithm for the segmentation of the stride for patients with PD based on Dynamic Time Warping (DTW). The authors developed a stride template using gait information from 25 controls and performed tests conducted for the stride segmentation of 40 controls, 15 PD patients and 25 geriatric patients. The results show that they can be segment the individual strides of patients can be segmented with an accuracy of 98%.

In [9], The authors proposed a body area network formed by several inertial sensors in the higher and lower extremities, with the aim of monitoring the neurological state of PD patients according to the UPDRS score. The authors analyzed several tasks including continuous gait. They computed kinematic-based features such as the standing time, the stride length, the stride velocity and the acceleration, among others. The database used for the authors is formed by 34 PD patients. A Spearman's correlation coefficient of 0.60 is obtained between the predicted UPDRS score and the real one assigned by a neurologist, using an algorithm based on k-nearest neighbors (KNN).

In [10] the authors by speech analysis of the five Spanish vowels, they performed a feature extraction based on NLD analysis to classify using SVM, PD patients and healthy controls with classification accuracy up to 76,81%.

In previous studies [11] was computed kinematics features from gait signals captured with the same inertial sensors [12] to evaluate the neurological state of the patients. A Spearman's correlation of up to 0.72 was reported between the MDS-UPDRS-III score of the patients and the predicted values obtained with a support vector regressor.

Recently in [13] the authors proposed new features to assess gait impairments in PD patients. Those new features were the peak forward acceleration in the loading phase and peak vertical acceleration around heel-strike, which encode the engagement in stride initiation and the hardness of the impact at heel-strike, respectively. The results indicated that the proposed features correlate with the disease progression and the loss of postural agility/stability of the patients.

3 Hypothesis

Gait signals captured with inertial sensors help in the assessment of the neurological state of patients with PD in several stages of the disease (low, intermediate, and severe).

4 Objectives

4.1 General Objective

To develop a methodology based on gait analysis and pattern recognition techniques, to perform the automatic classification and monitoring of the neurological state of PD patients according to the MDS-UPDRS-III scale [2].

4.2 Specific Objectives

1 To evaluate the discriminant capability of Non-linear Dynamics features in gait tasks.
2 To analyze the suitability of classification and regression m ethods to model the neurological state of Parkinson's disease patients.
3 To evaluate the developed methodology with several performance metrics.

5 Theoretical background

5.1 Feature extraction

In a non-linear system the response is not proportional to the inputs of the system. In some circumstances, when the response has a lot of sensibility to the initial conditions of the model, it is called chaos. If this happens and is not possible to know the initial conditions, the behaviour of the system will be unpredictable.

The dynamical side of chaos which manifests itself in the sensitive dependence of the evolution of a system on its initial conditions. This strange behaviour in time of the deterministically chaotic system has its counterpart in the geometry of the set in phase space formed by the (non-transient) trajectories of the system, attractors[14].

In general terms, non-linear dynamic measures indicate how chaotic and complex is a system. People with motor disorders have larger variations about the standard parameters and it can cause that a system is not linear. The list of non-linear dynamics measures to compute in this study is described in Table 1.

Table 1: Non-linear dynamic measurements

Measures
Approximate entropy
Sampled frequency
Approximate entropy with Gaussian kernel
Sample entropy with Gaussian kernel
DFA-Detrended fluctuation analysis
RPDE-Recurrence period density entropy
Correlation dimension
Largest Lyapunov exponent
Hurts exponent
Lempel-ziv Complexity

In addition, we will extract features from Poincaré sections[14], which are a low dimensional representation of the attractor. This application takes each point of this section at the first point at which the orbit containing it returns to it, as it is shown in the figure 1.

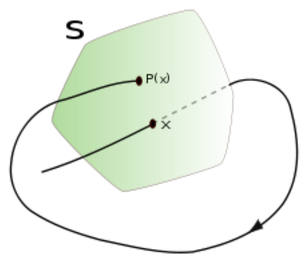

Figure 1: Poincaré Section

5.2 Classification

Two classification strategies will be performed: (1) a 2-class approach to discriminate between PD patients and HC subjects, and (2) the classification of PD patients in several stages of the disease (low, intermediate, advance) according to the UPDRS scale. Three classification algorithms will be used: K-Nearest-Neighbors (KNN), Support Vector Machine (SVM) and Random Forest (RF).

5.2.1 K-Nearest-Neighbors (KNN)

KNN algorithm [15] belongs to the family of competitive and lazy learning algorithms. This store all possible cases data and new data depending on a similarity measure (distance functions). A new data x is classified using a majority vote among the $\mathbf{k}$ instances, defining competencies as a distance measure d in equation 1, and the most likely class is assigned to the input between their k-neighbors as is shown in the figure 2.

$$d(\boldsymbol{x}, \mathbf{x}') = \sqrt{(x_1 - x_1')^2 + (x_2 - x_2')^2 + ... + (x_n - x_n')^2} \tag{1}$$

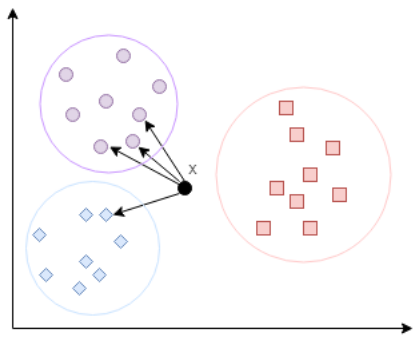

Figure 2: New input data in accordance with their distances

Then, the conditional probability in equation 2 is estimated for each class, it means, the points fraction in the given class.

$$P(Y = j|X = x) = \frac{1}{k} \sum I(Y^{(i)} = j) \quad (2)$$

Where $I(x)$ is the indicator function to evaluate 1 when the argument is true. Finally for the input x, the class with the highest probability is assigned.

5.2.2 Support Vector Machine (SVM)

Support Vector Machine can be an efficient classifier for a lot applications such that in classification problems and pattern recognition, being the second most popular method to classify[16].

The algorithm for lineal SVM was proposed by Vapnik in [17]. The aim of this algorithm is to find a hyperplane with maximum margin given a training set S of l training points as following:

$$S = \left\{ \mathbf{x}_i, y_i \right\} \ , i = 1, 2, ..., l \quad (3)$$

Where each point $\mathbf{x}_i \, \epsilon \, \mathbb{R}^N$ belongs to two different classes and a label is assigned for each one $y_i; \epsilon \, \left\{ -1, 1 \right\}$.

With this, what it is trying to do is to model the above training set by means of the hyperplane with the best fitting, being this hyperplane defined by the following equation:

$$\boldsymbol{w} \cdot \boldsymbol{x} - b = 0 \quad (4)$$

Where $\boldsymbol{w}$ is the vector to the hyperplane.If the SVM predicts that the positive class is given when $\boldsymbol{w} \cdot \boldsymbol{x} - b > 0$ and the negative class by $\boldsymbol{w} \cdot \boldsymbol{x} - b < 0$ as is showed in the figure 3

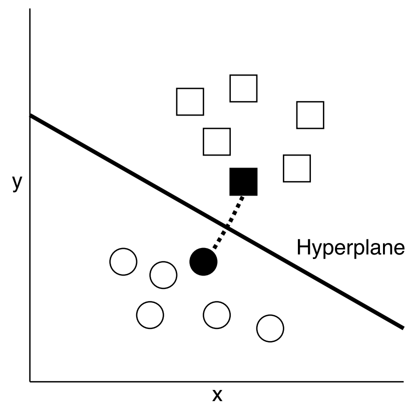

Figure 3: Best fitting hyperplane for the example training set S

5.2.3 Random Forest (RF)

RF consists in a set of classification trees, where each tree contributes with a single vote to the assignation of the most frequently class. It uses a combination of features at each node to grow a tree. To achieve the above is employed Bagging method to generate a training data-set by means of original data-set re-sample in a randomly way as is shown in the figure 4.

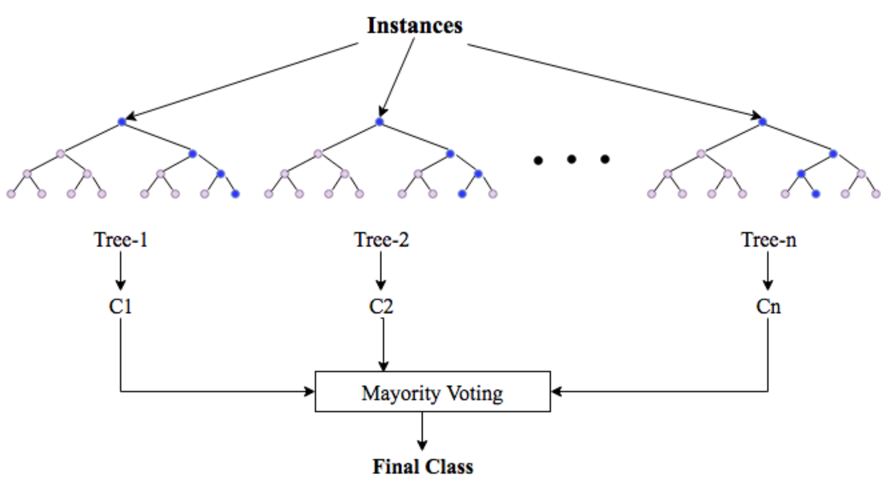

Figure 4: Architecture of the random forest model

To design the decision tree is required the choice of an attribute selection measure, being one of the most frequently used attribute in the selection measures in decision tree induction are the Gini Index[18]. Gini in equation 5, measures the impurity of a given element with regard to the other classes. Thus, using a given combination of features is made to grow up until their maximum depth.

$$\sum \sum_{j \neq i} (f(C_i, \boldsymbol{T})/|\boldsymbol{T}|)(f(C_j, \boldsymbol{T})/|\boldsymbol{T}|) \tag{5}$$

Where T is the given training set, C_i is the class and $f(C_i, \boldsymbol{T})/|\boldsymbol{T}|$ is the probability that the selected case belongs to C_i.

5.3 Regression to predict the neurological state

The prediction of the neurological state of patients according to the UPDRS scale is performed using a support vector regressor (SVR) with Gaussian or lineal kernel. This technique lets to predict the value of the scale ($\widehat{y}$) using a loss function $L(y, \widehat{y})$ that ensures the existence of global optimum. This function is calculated with the equation 6.

$$L(y, \widehat{y}) = \begin{cases} 0 & if\, |y - \widehat{y}| \leq \varepsilon \\ |y - \widehat{y}| - \varepsilon & in\, other\, cases. \end{cases} \tag{6}$$

The feature vectors $\mathbf{x}$ are mapped into a m$-$dimensional space using a lineal kernel g($\mathbf{x}$) The predicted values $\widehat{y}$ are estimated using the equation 7, where ω_j establishes the weight of each support vector, and b is the independent term.

$$\widehat{y} = \sum_{j=1}^{m} \omega_j g_j(\boldsymbol{x}) + b \tag{7}$$

5.4 Performance metrics

A performance metric is a tool that gives quantitative information according to the a comparison between this set goals and the achieved performance. In [19] is defined as, “the process of quantifying the efficiency and effectiveness of past actions”.

To evaluate results of Machine Learning experiments several metrics will perform. This metrics are related to the measure of effectiveness, efficiency or correlation [20].

To understand the following metrics, it is defined some concepts:

- True positive (TP): the number of cases correctly identified as PD patient.
- True negative (TN): the number of cases correctly identified as healthy control.
- False positive (FP): the number of cases incorrectly identified as PD patient.
- False negative (FN): the number of cases incorrectly identified as healthy control.

5.4.1 Confusion Matrix

The confusion matrix is a tool that allows visualization of the algorithm performance a a supervised learning. The number of class predictions are represented by columns, while the instances of the real classes are representing by rows. The above is shown in table 2.

Table 2: Confusion matrix structure

	Actual Class	
Predicted Class	TP	FN
	FP	TN

5.4.2 Accuracy

The accuracy in equation 8 is its ability to differentiate the patient and healthy cases correctly. To compute it, we should estimate the proportion of true positive and true negative in all evaluated cases.

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \tag{8}$$

5.4.3 Sensitivity

The sensitivity in equation 9, is its ability to determine the patient cases correctly. To compute it, we should estimate the proportion of true positive in patient cases.

$$Sensitivity = \frac{TP}{TP + FN} \tag{9}$$

5.4.4 Specificity

The specificity in equation10, is its ability to determine the healthy control cases correctly. To compute it, we should estimate the proportion of true negative in healthy control cases.

$$Specificity = \frac{TN}{TN + FP} \tag{10}$$

5.4.5 Receiver Operating Characteristic curve (ROC curve)

ROC curve is a graphical representation which shows the binary classifier performance, since its discrimination threshold is varied. In ROC curve the $Sensitivity$ is plotted in function of $1 - Specificity$ for different threshold settings.

The labels will be called as, y-label is True positives ($Sensitivity$) and x-label is False positives ($1 - Specificity$).

5.4.6 Precision and Recall

Precision or positive predictive value in equation 11, is the ability of that have the classifier to not predict a label as positive a sample which is negative, it means which proportion of positive identifications was actually correct.

$$Precision = \frac{TP}{TP + FP} \tag{11}$$

While Recall (sensitivity for multi-class classification) in equation 12 is the ability to find all the positive samples, being this concerning the proportion of actual positives was identified correctly.

$$Recall = \frac{TP}{TP + FN} \tag{12}$$

5.4.7 F-score

F1-score in equation 13 is a weighted average of the two above metrics, being a measure of test's accuracy. It ranging since 0 until 1.

$$Fscore = 2 * \frac{Precision * Recall}{Precision + Recall} \tag{13}$$

5.4.8 Cohen's Kappa

Cohen's Kappa (κ) in equation 14 measures the level of agreement between two raters on a classification problem, adjusting the random effect.

$$\kappa = \frac{p_o - p_\epsilon}{1 - p_\epsilon} \tag{14}$$

Where p_o is the empirical probability of agreement on the label assignedto any sample. and p_ϵ is te expected agreement when both raters assign labels randomly.

5.4.9 Spearman's Correlation

Spearman's is a correlation metric that measures the extent to which two variables tend to change together. It has the following characteristics:

- Its value ranges from -1 to 1.
- The Spearman's correlation advantage over Pearson correlation is that Spearman leave to find out nonlinear correlations between variables.

As following, this correlation is define:

$$\rho = 1 - \frac{6 \sum D^2}{N(N^2 - 1)} \tag{15}$$

Where D is the difference between the statistics corresponding and N is the number of data couples.

6 Methodology

This proposal consists in monitoring the neurological state of PD patients by means of features extracted from gait signals of the patients captured from inertial sensors. The gait signals will be captured with the eGait platform [4] (it was developed at the company Astrum IT GmbH with cooperation of the Pattern Recognition Lab in the University of Erlangen)[1]. The system consists of two inertial sensors

[1]Embedded Gait analysis using Intelligent Technology, `http://www.egait.de/`

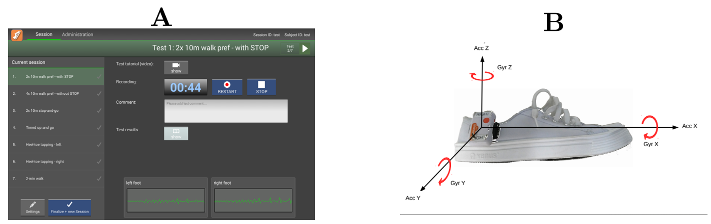

Figure 5: Interface and shoe to use in the project.

containing three axes accelerometers and gyroscopes. Each sensor is attached to the outer side of the feet as it is shown in the figure 5. At the moment we have a database of more than 38 PD patients and we also have data from 89 healthy control subjects to perform comparisons and train the classification algorithms. Figure 6 summarizes the methodology to address this study.

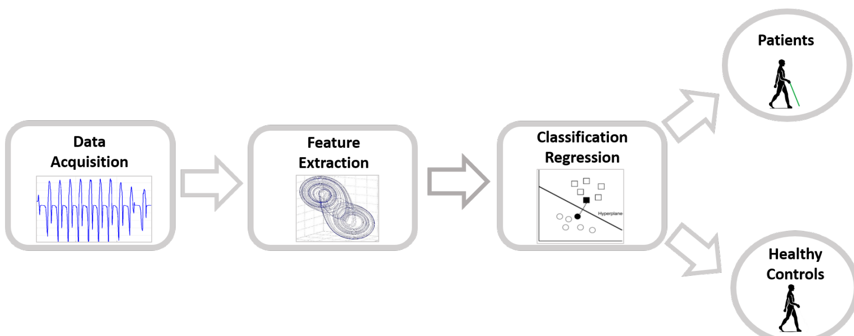

Figure 6: Summary of the methodology to assess in this study

To achieve the objectives, the state-of-the-art will be reviewed with special attention to contributions in non-linear dynamics. Classical and non-linear dynamics features based on embedded attractors and Poincaré sections will be implemented in the feature extraction stage. Then, classification and regression algorithms will be implemented, and finally, the performance of the system will be evaluated in terms of accuracy, sensitivity, specificity, Cohen Kappa, f-score, precision, recall and Spearman's correlation.

7 Schedule (in months)

Table 3: Schedule

Activity	M1	M2	M3	M4	M5	M6
Additional data acquisition						
State-of-art revision						
Development algorithms to model gait using non-linear dynamics features						
Development algorithms to model gait using Poincaré Section						
Implement Classification algorithms						
Write the final report						

8 Expected Results

Using NLD features it is expected to get more information about the walking process of patients vs healthy controls. In addition, it is expected to automatically classify in several stages of the disease according to the MDS-UPDRS-III score. We hope this methodology to contribute in the development of tools for the automatic monitoring of the disease progression.

The suitability of the automatic systems for classification and monitoring of the neurological state will be evaluated according to the following metrics:

- 2-class classification: confusion matrix, accuracy, sensitivity and specificity. It is expected to obtain accuracies higher 70%.
- Multi-class classification: confusion matrix, Cohen Kappa, f-score, precision and recall. It is expected to obtain a Cohen Kappa (ranging [-1,1]) of about 0.4. Finally, it is expected to obtain an F-score of at least 60%.
- Regression: it is expected to obtain Spearman's correlations of at least 0.3.

9 Research team and supporting partners

1 The research group GITA from the University of Antioquia.

2 The Pattern Recognition Lab (LME) from the Friedrich Alexander University of Erlangen-Nuremberg.

10 Budget

Table 4: Budget

	In kind	**In cash**	
Item	GITA	UdeA	GITA
Equipment			
Computer	$3.000.000	———	———
eGait plataform	$12.000.000	———	———
Personal-power			
Student expenses	———	———	$1.932.000
Advisor: Prof.Dr.-Ing. Juan Rafael Orozco-Arroyave (1 hour/week)*	———	$1.650.000	———
Total	$15.000.000	$1.650.000	$1.932.000

Values in COP (Colombian peso)

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