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Angular velocity analysis boosted by machine learning for helping in the differential diagnosis of Parkinson's Disease and Essential Tremor

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ABSTRACT Recent research has shown that smartphones/smartwatches have a high potential to help physicians to identify and differentiate between different movement disorders. This work aims to develop Machine Learning models to improve the differential diagnosis between patients with Parkinson's Disease and Essential Tremor. For this purpose, we use a mobile phone's built-in gyroscope to record the angular velocity signals of two different arm positions during the patient's follow-up, more precisely, in rest and posture positions. To develop and to find the best classification models, diverse factors were considered, such as the frequency range, the training and testing divisions, the kinematic features, and the classification method. We performed a two-stage kinematic analysis, first to differentiate between healthy and trembling subjects and then between patients with Parkinson's Disease and Essential Tremor. The models developed reached an average accuracy of 97.2±3.7% (98.5% Sensitivity, 93.3% Specificity) to differentiate between Healthy and Trembling subjects and an average accuracy of 77.8±9.9% (75.7% Sensitivity, 80.0% Specificity) to discriminate between Parkinson's Disease and Essential Tremor patients. Therefore, we conclude, that the angular velocity signal can be used to develop Machine Learning models for the differential diagnosis of Parkinson's disease and Essential Tremor.

INDEX TERMS Differential diagnosis, Parkinson's disease, Essential tremor, Gyroscope, Kinematic analysis, Machine learning.

I. INTRODUCTION

TREMOR is a compulsory and oscillatory movement of a part of the body [1]. Its effects are primarily visible in the limbs, head, and voice [2]. Physiological tremor is usually of low amplitude and interferes only with fine motor control. In most cases, it is not visible or symptomatic, except when increased by fatigue or anxiety [1], [3]. On the contrary, pathological tremor is usually visible and constant [1]. Parkinson's disease (PD) and Essential Tremor (ET) are the most common tremor syndromes worldwide [4], [5]. Distinguishing between PD and ET can be difficult in the early stages of the diseases or for patients without a family history of PD. The risk of incorrect diagnosis is high; even specialists in movement disorders may have a rate of up to 25% false positives or negatives [4], [6]–[8]. Typically, resting tremors are associated with PD, whereas postural or kinetic tremors associate with ET [5]. However, some PD patients may develop postural tremor [5], and some ET patients may develop resting tremors during the progression of the disease [9], [10]. Early diagnosis is fundamental to ensure adequate treatment of the patient and to prevent harmful side-effects [4], [5], [9]. Nowadays, dopamine transporter (DAT) imaging using Single Photon Emission Computed Tomography (SPECT) with appropriate tracers (^{123}I-FP-CIT) is the most reliable technique for diagnosing PD [4], [5], [11]. However, the test is costly and therefore limited to economically developed countries. Additionally, it is an invasive test with a radioactive fluid that requires patient compatibility, which may limit its applicability.

Therefore, it is a current topic of research to develop fast and non-invasive techniques for the early and reliable diagnosis of PD. Unlike the kinematic position information captured with optical movement detection systems [12], the accelerometry analysis is currently a hot topic in the biomechanical field. It records the motion information of physical activity based on wearable devices. [13]. In this sense, extensive research on the use of wearable devices in the field of movement disorders is underway, with numerous papers published on these topics. Uchida et al. [10] employed a triaxial accelerometer to measure the severity and frequency of hand tremors in patients with ET and PD under conditions of rest, posture, writing, and walking. They observed that resting tremor is attenuated during walking in patients with ET and increased in patients with PD. Recently, Bernhard et al. [14] studied the gait and balance deficit by using wearables fixed at the lower back and the ankle. They denoted that wearable gadgets could assess the progression of movement disorders and the response to the treatment of the disease. Wile et al. [15] classified patients with PD and ET via calculation and analysis of the Mean Harmonic Power using a smartwatch accelerometer. They noted that, compared to an analog accelerometer, a smartwatch device could provide accurate and relevant information for the differential diagnosis between PD and ET subjects. Locatelli et al. [5] recorded hand tremors during resting, postural, and kinematic tasks using a wearable sensor to differentiate PD and ET patients. They observed that, in the frequency domain, the execution of resting tasks showed a predominance of PD over ET tremors. In contrast, the data provided by postural and kinetic tasks stand out in ET subjects.

Some researchers have used Machine Learning (ML) to differentiate between the two tremor conditions. Woods et al. [3] developed an offline application that uses a mobile phone accelerometer to perform the diagnosis and classification of PD and ET patients. Surangsrirat et al. [9] classified PD and ET patients based on temporal angular velocity fluctuations, recorded with a 6-DOF inertial measurement unit. Kramer et al. [16] combined Electromyography (EMG), and Accelerometry (ACC) signals to distinguish between different types of tremor through Wavelet Coherence Analysis (WCA). They stated that WCA is superior to a standard coherence analysis and could be a useful additional tool for discriminating between tremor types when the result obtained with other methods is inconclusive. Nanda et al. [7] used the Wavelet transform to extract EMG and ACC signal features. These features, combined with an Artificial Neural Network, were used to perform a quantitative classification of ET and PD. Finally, Raza et al. [17] compared the diagnosis obtained by using wearable devices with the early diagnosis made by a specialist. They also used ML methods to perform the differential classification between PD and other movement disorders. Besides, in previous works, we proposed different methods for the differential diagnosis of the two diseases using the mobile phone's built-in triaxial accelerometer [4], [18], [19]. The developed methods allow to characterize and recognize the discriminative features of hand tremor in PD and ET patients and to use ML algorithms to improve the differentiation between them.

This work aims to use the same methodology to evaluate the angular velocity data, recorded with the mobile phone's built-in gyroscope, and to build ML models to differentiate healthy subjects (HS) and tremor patients (TP) and, subsequently, within the subjects identified as TP to discriminate PD patients from ET patients. These models are performed based on two different frequency ranges and three group divisions. We expect this method to be an additional tool to help the physician in case of uncertainty and undecided diagnosis of the diseases.

II. MATERIALS AND METHODS

Fig. 1 illustrates the different steps that compose the methodology developed in this work: Signal recording with a mobile phone, data analysis, and model training and testing. The demographic characteristics of the subjects, the method of recording, and the preprocessing of the dataset are described in Barrantes et al. [4]. The whole process was carried out in Matlab v. R2019b (MathWorks Inc., USA) on a computer with an Intel i5-9600K processor at 3.70 GHz, 16 GB of RAM and an NVIDIA GeForce GTX 1650 graphics card with 4 GB of V-RAM.

A. PATIENTS AND DATASET DESCRIPTION

The dataset used in this study includes recordings of 19 PD patients, 20 ET patients, and 12 HS from the Movement Disorders Unit of the Hospital Clinic of Barcelona between October 2015 and December 2016 [4]. All the patients had visual evidence of hand tremors and were diagnosed with strong indications of PD or ET. Patients had scores of 1 or 2 on the Fahn-Tolosa-Marín scale for ET and the Unified Parkinson's Disease Rating Scale (UPDRS) for PD patients. A SPECT test confirmed all the patients with PD.

The angular velocity signals were collected with the built-in triaxial gyroscope of an iPhone 5S using SensorLog application [20]. The smartphone was placed on the dorsum of the most affected hand in TP or the dominant hand in HS while sitting in an armrest chair. Tremor signals were recorded with a frequency of 100 Hz and an average duration of 35.66±4.08 s, 35.42±3.42 s, and 33.30±3.27 s for HS, ET, and PD subjects, respectively. As shown in Fig. 1, two-arm positions were studied: 1) Rest (Position A), the subject rests his forearm on the upper part of the armrest, and 2)

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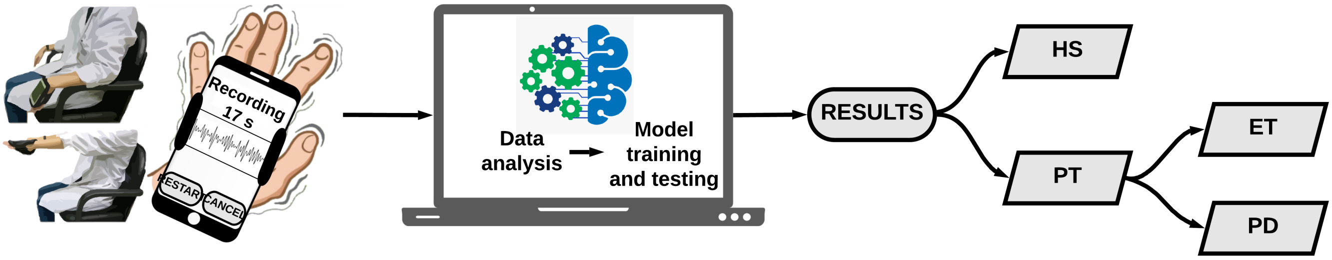

FIGURE 1. Schematic of the methodology for the differential diagnosis of PD and ET patients.

Posture (Position B), the subject keeps both upper limbs fully extended.

B. DATA ANALYSIS

One of the clinical signs and symptoms of PD is tremor at rest with moderate amplitudes and low frequencies from 4 to 6 Hz [9], [21]. In contrast, ET is characterized by postural or kinetic tremors with mean frequency values between of 5 to 8 Hz [15], [22]. Furthermore, physiological tremor is in the frequency band of 8 to 12 Hz [23]. Based on this, the dataset is preprocessed as follows in order to extract the kinematic features: artifacts generated by starting and ending the signal recording were eliminated by cutting approximately 2 seconds on both sides of the signals. Two 10th order Butterworth filters with cut-off frequencies of 3 to 10 Hz [11] and 1 to 16 Hz [24], where PD and ET are found, were implemented separately in order to identify an optimal frequency range for feature extraction. Additionally, these filters allow reducing the sensor offsets and drifts due to various physical phenomena such as motion artifacts [17], [25]. Figure 2 shows the time-domain signal of PD, ET, and HS subjects in posture position before and after signal processing.

Since the analysis was performed in the frequency domain, Power Spectral Density (PSD) was calculated. For each of the three spatial directions, a Welch's periodogram averaging segments of the signal recording of 3s with a 50% overlap of Hanning's window was applied. The PSD average of the angular velocity components was calculated and normalized. The resulting average was used to calculate kinematic indexes that allow the identification and classification of subjects with pathological tremor and differentiate them between PD and ET. The kinematic features are briefly explained below:

- **Median Power Frequency (MPF):** Frequency at which the PSD is halved.
- **Power Bandwidth (PB):** Frequency band, centered around the MPF, which contains 90% of the total power.
- **Peak Power Frequency (PPF):** Frequency at which the maximum power is located.
- **Harmonic Index (HI):** Quotient between the area under the PSD curve and a rectangle bounded on the sides by the frequency band of interest (f_l - f_h) and the Peak Power (PP).

$$HI = \frac{\int_{f_{th}}^{f_h} PSD(f) \cdot df}{PP \cdot (f_h - f_l)} \tag{1}$$

- **Relative Power Contribution to the first harmonic (RPC):** Quotient between the PSD of harmonics found between a frequency division threshold (f_{th}) and f_h and the PSD between f_l and f_h.

$$RPC = \frac{\int_{f_{th}}^{f_h} PSD(f) \cdot df}{\int_{f_l}^{f_h} PSD(f) \cdot df} \tag{2}$$

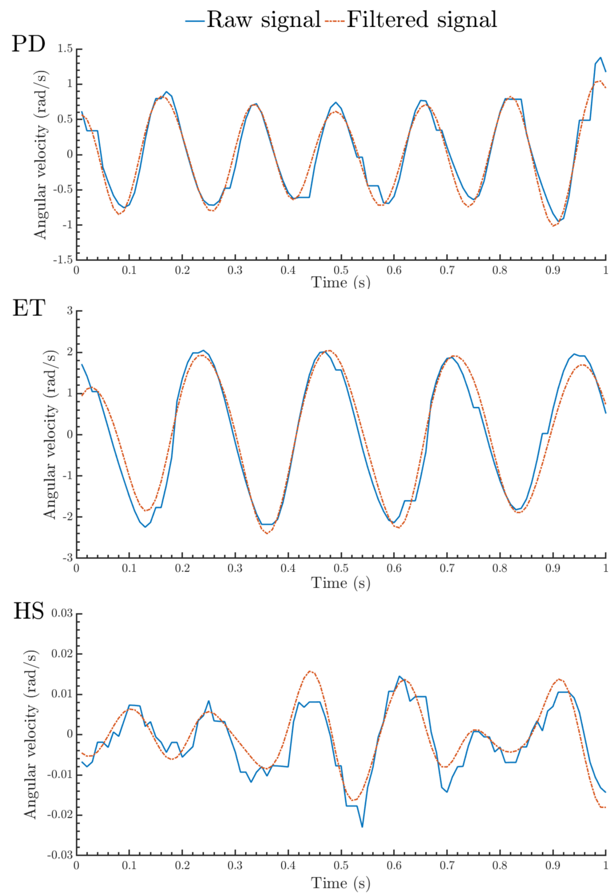

FIGURE 2. Time-domain signal of PD, ET and HS subjects in posture position before and after signal processing.

- **Relative Energy (RE):** Quotient between the normalized PSD of resting ($\mathrm{PSD_A}$) and posture ($\mathrm{PSD_B}$) in the frequency range of f_l to f_h.

$$RE = \frac{\int_{f_l}^{f_h} PSD_A \cdot df}{\int_{f_l}^{f_h} PSD_B \cdot df} \tag{3}$$

- **Harmonic Index Ratio (HIR):** Quotient between the harmonic indexes of resting and posture position.

$$HIR = \frac{HI_A}{HI_B} \tag{4}$$

- **Sum of Maximum Power (SMP):** Sum of the power value at the PP of resting and posture position.

$$SMP = PP_A + PP_B \tag{5}$$

After extracting the feature matrix of the subjects, they were labeled as follows:

1) **Case 1: TP vs. HS**
   - **TP** (Tremor patients) - Positive Class.
   - **HS** (Healthy subjects) - Negative Class.
2) **Case 2: PD vs. ET**
   - **PD** (Parkinson's Disease) - Positive Class.
   - **ET** (Essential Tremor) - Negative Class.

Since thirteen features have been extracted per subject, we used feature selection algorithms [26] to reduce the dimensionality of the resulting matrix and to select a subset of a maximum of five features to create the classification models. This allows to reduce the training time of the models and to focus on the features that provide the highest differentiation between both Cases' classes. We used the Chi-square test and the Unbiased Tree method to estimate, separately, the importance of each feature [27], [28]. For each test, the five features with the highest importance values were identified. The features that matched in both tests were chosen for further analysis. This process was carried out in two frequency ranges: 1-16 Hz and 3-10 Hz.

C. MODEL TRAINING AND TESTING

The classification models designed differ in four aspects:

1) **The frequency range of analysis.** As mentioned in the previous subsection, the kinematic features were extracted in two different frequency ranges (1-16 Hz and 3-10 Hz) to identify which range is optimal for differentiating between physiological and pathological tremors and, subsequently, between pathological tremors.
2) **The proportion of training and testing data.** For each of the cases presented, the dataset was randomly divided into three different proportions (30/70, 50/50, and 70/30), ensuring that both positive and negative classes were distributed at the same ratio in each training and testing set. Table 1 details, for both cases in all proportions, the class ratios obtained in the training and testing sets.

TABLE 1. Training and testing set class ratios.

Division	Case 1: TP vs. HS				Case 2: PD vs. ET			
	Training		Testing		Training		Testing	
(%)	PC	NC	PC	NC	PC	NC	PC	NC
30 / 70	12	4	27	8	6	6	13	14
50 / 50	20	6	19	6	10	10	9	10
70 / 30	27	8	12	4	13	14	6	6

PC, Positive class. NC, Negative class.

The reason why we decided to use three different divisions and not one, as commonly implemented in ML, was to evaluate the influence of the data distribution to obtain high-performance models.

3) **The kinematic features used.** Using the features extracted and selected during the data analysis, we identified all the possible combinations of features that can be generated, from a single feature to the whole of them. Since we set 5 as the maximum number of features, for some cases, up to 31 combinations of features were obtained. These feature combinations allowed us to evaluate the discriminatory ability the features can reach individually or in combination using the classification methods that implement them.
4) **The classification method used to train the model.** The classification methods used for training the models were developed based on the Matlab *Classification Learner* app. This app offers a variety of supervised ML methods to classify data, including decision trees, discriminant analysis, Support Vector Machines, Logistic Regression, Nearest Neighbors, Naive Bayes, and ensemble classification. There are several default configurations of hyperparameters of these methods in the app, offering a total of 25 different configurations for the training of classification models. We integrated all configurations into a script and applied them to the dataset.

Given the number of combinations of features that were possible to obtain and the diverse configurations of the classification methods, we obtained 775 different classification models for some cases. After setting the training sets, the testing sets were used to calculate Accuracy, Sensitivity and Specificity. We defined Sensitivity as the capacity of a classification model to identify positive cases, that is, to identify TP in Case 1 or PD subjects in Case 2. On the contrary, Specificity is defined as the ability of the classification model to identify negative cases, being HS in Case 1 or ET subjects in Case 2. All training and testing processes were randomly iterated 100 times for the same combinations of features and classification methods in each of the three training/testing divisions. Consequently, a different level of performance was obtained in each iteration for each model. After all iterations, the average values of Accuracy, Sensitivity, and Specificity obtained for each classification model were calculated. The three best classification models for Cases 1 and 2 were identified based on the output classification metrics. Fig. 3 summarizes the whole process that was implemented for the

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development and selection of the classification models.

III. RESULTS

We divide the results of this work into two subsections. In the first part, we evaluate the model's capacity to differentiate TP from HS. In the second part, we analyze the model's ability to differentiate patients with PD and ET.

A. DIFFERENTIATION OF TREMOR PATIENTS AND HEALTHY SUBJECTS

Table 2 shows the results of the evaluation and selection of features for distinguishing between TP and HS. In the 3 to 10 Hz frequency analysis, the five features with the highest values were identical in both tests. These features were: SMP, RPC_B, HI_B, HI_A, and PB_B. In the 1-16 Hz frequency analysis, four of the five features identified by both tests coincided: SMP, RPC_B, HI_B, and PB_B.

TABLE 2. Evaluation and selection of kinematic features for the differentiation of tremor and healthy subjects.

Feature	Position	3 - 10 Hz		1 - 16 Hz	
		CS	UT	CS	UT
MPF	A	3.23	0.04	3.02	0.07
	B	3.36	0.02	3.98	0.03
PB	A	3.98	0.03	3.98	0.06
	B	**8.12**	**0.07**	**11.74**	**0.14**
PPF	A	3.49	0.01	3.73	0.06
	B	4.76	0.03	8.12	0.08
HI	A	**4.76**	**0.06**	4.76	0.07
	B	**9.01**	**0.08**	**9.01**	**0.14**
RPC	A	3.42	0.01	4.96	0.10
	B	**6.97**	**0.07**	**10.82**	**0.15**
RE	A/B	1.87	0.00	3.98	0.00
HIR	A/B	0.78	0.01	0.35	0.00
SMP	A+B	**11.74**	**0.12**	**10.82**	**0.16**

A, rest position. B, postural position. CS, Chi-square test. UT, Unbiased Tree method. Bolded values correspond to the five features with the highest discriminative values in both tests.

The upper and left side of Figure 4 shows the best models for the differentiation of TP and HS in the frequency range of 3-10 Hz, sorted by the three training/testing divisions. For each division, the top 3 models were identified and listed based on their average metrics. The SMP feature is present in all nine models, while PB_B, HI_B, and RPC_B are present in two of them. The best performing classification model shows an average accuracy of 94.3±5.6% (95.9% sensitivity, 89.5% specificity), and an average computational cost of 6.7±0.7 ms. This model was achieved in a 70/30 division, using the SMP feature and the Linear SVM method. Although there are a variety of classification methods among the nine listed, in both the 30/70 and 50/50 divisions, the best model implemented the Logistic Regression method and the SMP feature. On the right side, the figure visualizes the best models obtained in the frequency analysis from 1 to 16 Hz in all training/testing divisions. Again, the three best models were selected based on their average performances. All models in this frequency range use SMP as a discriminatory feature, while the PB_B feature is applied in eight of them. The best model shows an average accuracy of 97.2±3.7% (98.5% sensitivity, 93.3% specificity), and an average computational cost of 105.8±1.9 ms. There is only one model that implements a single feature, SMP, using a 70/30 division and the Medium Tree method. The rest of the models implement Ensemble Subspace KNN method and combine various features. Note that the average computational cost of the models that use the Medium Tree method with a single feature is considerably smaller than those obtained with the models that use the Ensemble Subspace KNN method and multiple features.

B. DIFFERENTIATION OF PARKINSON'S DISEASE PATIENTS VS. ESSENTIAL TREMOR PATIENTS

Table 3 shows the evaluation and selection of features for the differentiation of PD and ET patients. In the 3-10 Hz frequency analysis, the for each test separately identified tests were identical: SMP, HIR, RE, RPC_A, and MPF_A. In the frequency range of 1-16 Hz, only three of the five features coincided: HIR, RE, and RPC_A.

TABLE 3. Evaluation and selection of kinematic features for the differentiation of tremor subjects: PD vs. ET.

Feature	Position	3 - 10 Hz		1 - 16 Hz	
		CS	UT	CS	UT
MPF	A	**2.70**	**0.03**	0.54	0.02
	B	0.13	0.00	0.12	0.00
PB	A	0.62	0.03	1.12	0.05
	B	1.12	0.02	0.62	0.01
PPF	A	0.62	0.02	0.62	0.01
	B	0.05	0.01	0.01	0.00
HI	A	0.62	0.02	0.62	0.04
	B	1.63	0.03	0.34	0.02
RPC	A	**1.91**	**0.04**	**1.37**	**0.05**
	B	0.12	0.01	1.63	0.02
RE	A/B	**3.79**	**0.07**	**5.20**	**0.09**
HIR	A/B	**3.34**	**0.07**	**2.10**	**0.06**
SMP	A+B	**1.91**	**0.04**	1.91	0.01

A, rest position. B, postural position. CS, Chi-square test. UT, Unbiased Tree method. Bolded values correspond to the five features with the highest discriminative values in both tests.

The bottom left side of Figure 4 depicts the best models for the differentiation of PD and ET in the frequency range of 3-10 Hz. The top 3 models in each training/testing division are listed, sorted by their average performance values. The HIR feature seems to provide significant information for the differentiation of tremor patients, since it is present in all the models depicted. The best overall performance was achieved in the 70/30 division, combining the HIR and MPF_A features and using the Linear SVM method. This model showed an average accuracy of 77.8±9.9% (75.7% sensitivity, 80.0% specificity), and an average computational cost of 5.4±0.3 ms. The right side of the figure visualizes the models with the best performances for the differentiation of PD and ET in the frequency range from 1 to 16 Hz. Again, the best model can be found in the 70/30 division, with an average accuracy of 76.1±11.8% (72.5% sensitivity, 79.7% specificity) and an average computational cost of 26.5±1.7 ms. The feature that

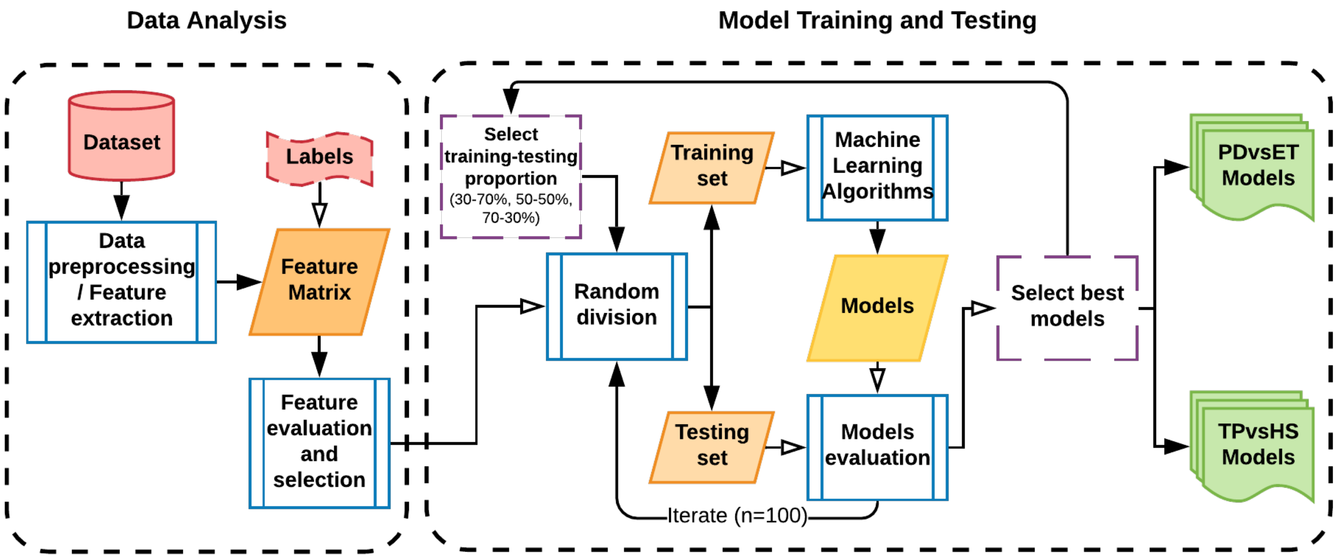

FIGURE 3. Process diagram for the development and selection of classification models.

is present in most of the models is RE, being used in eight of the nine models shown. In the 30/70 and 50/50 divisions, the two best classification models use the Gaussian Naive Bayes method. In contrast, in the 70/30 division, the two best performances were obtained with two different configurations of the KNN method, obtaining the same average accuracy.

IV. DISCUSSION

The results obtained in this work show that the characterization and differentiation between tremor in PD and ET are possible with a mobile phone's built-in gyroscope. The accuracy of the tremor differentiation using this sensor is comparable to the performance obtained using a mobile phone's built-in accelerometer [4], [19]. Although there is a clear difference between the number of TP (39 in total) and HS (12 in total), the accuracy of the models differentiating the two conditions is high. This is due to the differences in the frequency components of the tremors that characterize both classes. By analyzing the entire data in the frequency domain, we were able to highlight these differences. Since the PSD in HS can be up to 1000 times lower than in trembling subjects, we obtained higher accuracy values than in [17], (82.43%), even though their dataset was considerably larger than ours. Other studies [27], [29] reported accuracy values of 82% to 100%; however, their groups of trembling subjects only included PD patients. In [8], [30], wearable sensors (accelerometers and gyroscopes) were used to extract features that allowed the implementation of ML algorithms for the differentiation between PD and ET, reaching accuracies of 96% to 100%. In [8], the analysis was performed in the time domain and kinetic tremors instead of tremors in posture were analyzed. The study performed in [30] uses accelerometry data, registers each patient for a recording time of five minutes, and uses a newly introduced posture as well as statistical analysis of the data's frequency components to differentiate the subjects. Compared to those studies, our classification models were developed to be used during clinical follow-up, where simple postures and short recording times are required. The accuracy values reaches in our study are lower than those in [8], [30], for two reasons. Firstly, they both registered more subjects which improves the predictive ability of the models. Secondly, the accuracy values we represent in this study are average values of 100 random iterations in three training/testing divisions. In single iterations, the classification models developed for PD/ET differentiation reached similar values. Moreover, since the aim of this work was to evaluate whether the angular velocity signal could help to differentiate tremor subjects using ML, we considered the use of the default configurations of the ML methods to be enough. In future works, we intend to analyze in detail how to adjust the hyperparameters of the implemented models to optimize their discriminative capacity.

The frequency ranges used to develop the models generated significant differences regarding their performance. For the differentiation of TP and HS, the average accuracy values obtained in the frequency analysis from 1 to 16 Hz are higher than those obtained in the analysis from 3 to 10 Hz. These differences could exist because the frequency range from 3 to 10 Hz includes only a part of the area in which physiological tremors occur (8 to 12 Hz) [23], whereas the analysis of 1 to 16 Hz includes its full range. Nevertheless, the models generated in the 1 to 16 Hz range require complicated methods and more kinematic features. For the differentiation of PD and ET patients, the models analyzed in the 3-10 Hz frequency range show better performance compared to those in the 1-16 Hz frequency range. These performance differences could be directly related to the dominant frequencies of the two tremor types. As mentioned in the Data Analysis subsection,

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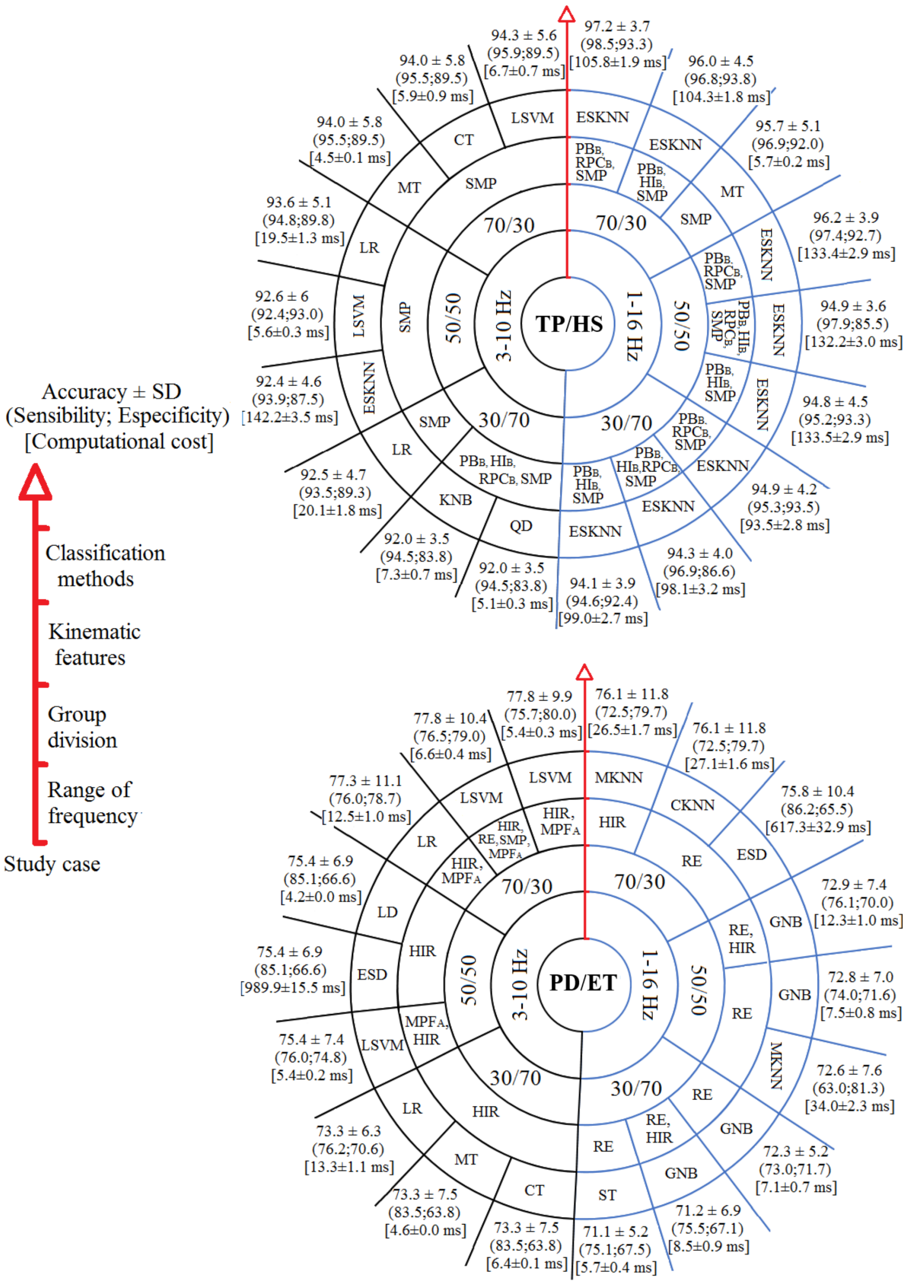

FIGURE 4. Output results of the machine-learning algorithm based on study case, range of frequency, kinematic features, and classification methods.

ST - Simple Tree, MT - Medium Tree, CT - Complex Tree, LR - Logistic Regression, LD - Linear Discriminant, QD - Quadratic Discriminant, KNB - Kernel Naive Bayes, GNB - Gaussian Naive Bayes, LSVM - Linear Support Vector Machine, MKNN, Medium k-nearest neighbor, CKNN - Cubic k-nearest neighbor, ESD - Ensemble Subspace Discriminant, ESKNN - Ensemble Subspace KNN.

both PD and ET tremors are located in a frequency range between 4 and 8 Hz [9], [15], [21], [22]. Thus, the extraction of kinematic features within a frequency range of 3 to 10 Hz eliminates unwanted effects that are introduced by frequencies outside the area of interest.

It is noticeable that the variability in the performance of the PD/ET models listed is relatively high (5.2% to 11.8%). This variability is influenced by the presence of atypical patient data in each iteration since, as mentioned previously, there are PD patients who experience postural tremors [5] and ET patients who show tremors at rest during disease progression [9], [10]. Other variability factors are the training/testing divisions, as the data distribution influences the performance of the classification models. As expected, the classification models show better performances the higher the percentage of data in the training set. Analyzing Figure 4, the models for differentiating TP and HS exhibit a difference of 3.1% when comparing 30/70 and 70/30 divisions combined with identical features (SMP, RPC_B, and PB_B) and the same classification method (Ensemble Subspace KNN). The models for differentiating PD and ET show a difference of 4.0% when comparing 30/70 and 70/30 divisions combined with the same features (HIR) and classification method (Logistic regression).

Based on the presumption that the frequency components of the pathological tremor are higher in either of the two positions studied, SMP and HIR were introduced to improve the differentiation between the tremor types. RE and RPC features were proposed in [4] to improve the differentiation between PD and ET patients, as their tremor frequency components are different under resting or postural conditions. Theoretically, PD patients should have higher amplitudes of tremor at rest (position A) than postural tremor (position B), and vice versa for patients with ET. The results obtained in this work supported the above, the most significant feature for the differentiation of patients with PD and ET seems to be the novel HIR feature, as it was implemented in 12 of the 18 best models depicted in Figure 4. Also, as already observed in previous works [4], [19], RE and RPC features provide essential information. The RPC feature also contains relevant information for the differentiation of TP and HS in both analyzed frequency ranges. However, the SMP feature introduced in this study was most discriminative in several of the best models; high accuracy values were reached by only using this relative feature. Analyzing the implemented features, it is noticeable that some of them provide more accurate information for the differentiation of the subject according to the Case. The features extracted in the posture position were predominant in the models that differentiate between subjects in Case 1. In Case 2, there is a higher presence of features extracted in the resting position, which is consistent with the works of [5], [8].

As it was the intention to develop high-performance classifiers and avoid classification errors, only patients with a confirmed diagnosis of PD or ET were used to implement the ML models. However, this also means that the patients were already on treatment when they were registered, so their tremors intensity was remarkably low. For this reason, we consider that additional records should be performed on early-stage tremor patients to prevent the effects of medication [31] or surgical suppression [32], as these are possible causes of misclassification of patients. Another important topic regarding the development of high-performance models is the dataset size. Since the dataset for training and testing of the models was small, the ML models implemented in this study are limited in their performance. The dataset needs to be increased to develop highly accurate models. Therefore, in the second phase of the project, we aim to introduce a mobile application linked to a web server that allows adding new patient records to the already registered data. This phase will be realized through the collaboration of an international network of physicians and biomedical engineers using the application. By enlarging the dataset, we expect to improve the accuracy of the developed models or to create new models with even higher performance and lower computational cost.

V. CONCLUSION

The angular velocity signal recorded by the gyroscope and boosted using ML algorithms has proven to be an effective method to differentiate between healthy subjects and tremor patients as well as between Parkinson's disease patients and Essential Tremor patients. This differentiation is substantially dependent on the correct selection and evaluation of classification methods and kinematic features, as well as on the processing and the size of the training data. The best model to differentiate HS and TP has an average accuracy of 97.2±3.7% (98.5% Sensitivity, 93.3% Specificity). The average accuracy of the best model to differentiate tremor patients with PD and ET was 77.8±9.9% (75.7% Sensitivity, 80.0% Specificity).

During the training of the models, we were able to identify outstanding performance for some combinations of kinematic features, such as SMP, PB_B, and RPC_B, for TP and HS differentiation, as well as HIR and MPF_A for PD and ET differentiation. Regarding the classification methods, for the differentiation of TP and HS (Case 1), the best performances were reached with the Linear Support Vector Machine and Ensemble Subspace KNN methods. For the differentiation of PD and ET (Case 2), in the frequency analysis from 3 to 10 Hz, the best performance was also obtained with the Linear Support Vector Machine method. In contrast, in the 1-16 Hz range, the best performance was obtained with Medium K-nearest Neighbor method. In both cases, the Linear Support Vector Machine models present a lower computational cost compared to the KNN methods.

In future works, we want to combine the recordings of accelerometer and gyroscope sensor to obtain higher classification performances and reduce the training times. The optimized ML models developed in this research will be used to design a low-cost and non-invasive tool (mobile app) to support physicians in the differential diagnosis of the two diseases, particularly in developing countries where sophisticated diagnostic techniques such as ^{123}I-FP-CIT SPECT are not available. Additionally, we expect that the use of this tool will help in patients with undecided diagnosis and, consequently, in choosing appropriate and opportune therapeutic actions.

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