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**ORIGINAL ARTICLE**

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| Analysis of Hand Tremor in Parkinson’s Disease: Frequency Domain Approach | |
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| **Abstract**  **Purpose:** Parkinson's Disease (PD) is a neuro-degenerative interminable issue causing dynamic loss of dopamine-creating synapses, which is one of the most far reaching ailments after Alzheimer's infection. In this paper, a system for the classification of Parkinson’s disease tremor using noninvasive measurement and frequency domain features is represented.  **Materials and Methods:** Tremor time-series of Parkinson's disease patients were recorded via a smartphone’s accelerometer sensor. Short-Time Fourier Transform (STFT) was applied to transform the time-domain signal into the frequency domain with high time-frequency resolution. Several frequency features, including mean, max of power spectral density and side frequency have been extracted and by using the FDR algorithm combinations of features carried enough information to reliably assess the severity of tremor in Parkinson patients were determined.  **Results:** Four different classifiers were implemented to estimate the severity of tremors based on the Unified Parkinson's Disease Rating Scale (UPDRS) in Parkinson's disease patients.  **Conclusion:** Classifiers’ estimation was compared to clinical scores derived via neurologist UPDRS annotation on Parkinson's disease patients’ tremor. The best accuracy achieved was 95.91±1.51.  **Keywords:** Accelerometer; Parkinson’s Tremor; Unified Parkinson's Disease Rating Scale; Classification; Evolutionary Algorithm. | |

# Introduction

Parkinson’s Disease (PD) is a neuro-degenerative chronic disorder causing progressive loss of dopamine-producing brain cells, which is one of the widespread illnesses after Alzheimer’s disease. The loss of dopamine in the midbrain often induces characteristic motor symptoms such as rigidity, tremor, bradykinesia and, hypokinesia [[1]](#Ref1). The predominant method for evaluating the status of PD patients, such as their tremor, is the Unified Parkinson’s Disease Rating Scale (UPDRS). According to this method, neurologists can assess the PD patient’s tremor from 0 (absence of tremor) up to 4 clinically [[2]](#Ref2). [Table 1](#table1) shows the UPDRS rating system. There are several types of tremulous movements in PD; the Resting Tremor (RT), and action tremor which are split into Kinetic Tremor (KT) and Postural Tremor (PT). The characteristic tremor of PD is indisputably the resting tremor, however, it is extremely important to analyze the possible presence of other sorts of tremors as might be the PT or KT, so physician can diagnose more accurately and prescribe the most optimal treatment method [[3,](#Ref3) [4]](#Ref4).

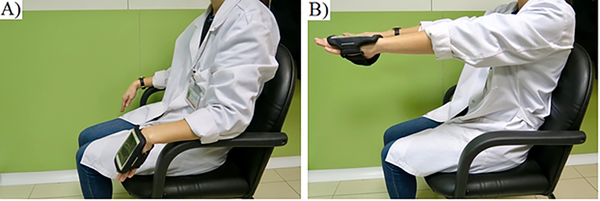
### **Table 1.** Unified Parkinson’s Disease Rating Scale (UPDRS) Mark Interpretation

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| **UPDRS** | **Interpretation** |
| 0 | Without tremor |
| 1 | Weak tremor |
| 2 | Mild tremor |
| 3 | Mean tremor |
| 4 | Excessive tremor |

According to this point that evaluating and discriminating the severity of tremor in the proportion of the UPDRS method, which has been performed clinically as an error-prone task. The presence of at least one expert neurologist is required to design a system or a piece of equipment to assess tremor severity for PD patients. Advantage of using this equipment belongs not only to the PD patients who suffer from tremors and do not have adequate access to neurologists through their medication, but also to the neurologists who want to monitor their patients. The other advantages, which such a system brings to neurologists, are providing the capability of making a comparison between different methods of tremor medication in their research and treatments.

Many studies [[5-](#Ref5)[7]](#Ref7) have demonstrated the convenience of acceleration signals in the instrumental diagnosis and assessment of neuromuscular disorders and the identification of tremor kinds. A favored machine-learning method for acceleration data classification is the Artificial Neural Network (ANN). In [[8]](#Ref8), Khezri and Jahed applied ANN to discriminate against a variety of hand movements. They employed Principal Component Analysis (PCA) to minimize data dimensions for faster processing. In [[9]](#Ref9), based on acceleration values, extracted features, mainly based on Power Spectral Density (PSD) from STFT, was employed to separate each kind of tremor. In [[10]](#Ref10), Lingmei designed a classification algorithm based on hand acceleration signal for PD by using Empirical Mode Decomposition (EMD) and Discrete Wavelet Transform (DWT) for feature extraction, and Support Vector Machine (SVM) in the classification block. Nowostawski [[11]](#Ref11) has developed an application based on a smart-phone that uses DWT and SVM to distinguish Parkinson’s and Essential postural tremors with over 96% accuracy. Palmes *et al.* [[12]](#Ref12) has developed an Instrumental Method (IM), machine learning system, based on time-domain features extracted and SVM classifier by the appropriate kernel, to replace the Clinical Method (CM) of diagnosing the presence of different kind of tremor. Palmerini *et al.* [[13]](#Ref13) used acceleration signal, including tremor records, postural acceleration records, and postural displacement records within the classification procedure to carry out a feature selection technique to identify the subset of measures that best discriminate between early-mild PD subjects and control subjects during and on the medication by Levodopa.

In the present research, a pattern recognition-based method for PD patient’s tremor assessment is reported to implement a classification algorithm. This experiment was performed with real and available data set that can be easily recorded, and the strength of this

The structure of the paper is as follows: in the next section, the database and the algorithm are described. In the result section, the outcomes of the classifiers are presented. Then the discussion section explains the results and finally, there is a conclusion part. In this original research was focusing on a set of frequency features which all possible combinations were examined by the algorithm and the best combinations **were selected. In this way, the accuracy and precision of the classifier increased by selecting the distinguishing features. Moreover, conducting experiment with different classifiers and comparing their performance is another advantage of this research. It also revealed the PD patient’s tremor discrimination by numerical results, which was presented and discussed in the following sections.

# Materials and Methods

## 2.1. Data Collection

In this original research, 50 PD subjects with the age of 58±7.4 years old and 7±2 years of duration of disease were analyzed. PD subjects were chosen as train and test subset by k fold method. All patients were suffering from PD tremor, labeled UPDRS 0 to 4. The data was collected in the psychology of information processing lab at the Technical University of Darmstadt. Sony Xperia SP Android smartphone has been employed. The sampling rate was 100 Hz. To make the device wearable, it was inserted into a bracelet fitted with a strap that allowed convenient use. In order to evaluate the rest, postural and kinetic tremor, three different tests have been applied. One-minute recording in a rest condition just sat on the chair for RT. For postural tremor evaluation, patients were asked to straighten their arm horizontally for another one minute. In kinetic tremor measurement, the patients were seated on the hospital’s chair with their eyes closed, while carrying out an index-nose test, stretching the arms forward, then performing a sort of forward and backward hand movements bringing the index figure to the nose touching its tip. All three tests were performed by both hands and the neurologists (of Psychology of Information processing Lab at the Technical University of Darmstadt) determined the UPDRS score for each patient. [Figure 1](#fig1) illustrates a subject during the test.

## 2.2. Algorithm Description

To eliminate noise and other undesired frequency band signals, earlier works such as [[12]](#Ref12) for Parkinson's tremor suggested three bandpass FIR Equiripple filter to be applied in three frequency bands: 3-6 Hz for RT, 6-9 Hz in case of PT as well as 9-12 Hz for KT.

### **Figure 1.** Signal Recording, A) rest tremor, B) postural tremor

Frequency and intensity are the major characteristic features for the classification of Parkinson’s tremors that have been widely utilized in literature [[11]](#Ref11). Hand tremor is a non-stationary signal with periodic oscillations [[15]](#Ref15); hence, spectral analysis to extract fundamental frequency components is an efficient way to assess each class of Parkinson's tremor. The fundamental frequency extraction is indispensable for tremor classification.

Tremor time series generates a stochastic signal, but its randomness is not completely arbitrary. This kind of signal contains numerous transitory or non-stationary features such as drift, trends, and abrupt changes [[14]](#Ref14). These features are often the most important part of a signal like a tremor having non-uniform changing such as magnitude and period with time. It could disappear sharply and appear again. Being capable of providing spectral-temporal signal information at the same time, the STFT processing is highly practical in the case of classifying patient tremor, which was adopted in this paper for analysis. If the time windows are narrow enough, each extracted frame can be selected as a stationary signal for the Fourier analysis. By moving the time windows on the time axis, the relationship between frequency and time changes is determined.

For STFT analysis, the Hamming window with 50% overlap and 4 seconds length was applied to the signals. Since tremor signal changes abruptly and PD subjects usually show higher tremor amplitude during stressful conditions, the STFT processing block provided the feasibility of separating tremor and non-tremor in 4 seconds epochs.

The amplitude of hand tremor fluctuation was the second fundamental factor, which was determined for essential tremor patients through logarithmic relationships by considering the Tremor Rating Scale (TRS) method [[16]](#Ref16). To scale tremor amplitude as a classification factor, PSD function was calculated which illustrates the power of the signal at different frequencies across the spectrum. The tremor fundamental frequency was obvious from a visible peak in the power spectral density, while the area under the peak could be considered as average tremor amplitude [[17]](#Ref17). To obtain a numerical scale of PSD, for each window of the patient’s acceleration signal, the mean absolute value of the PSD weighted average was calculated in each frequency band.

Another feature accounting for an indication of hand tremor amplitude was the maximum PSD of each band. The observation result has shown that for Parkinson's disease patients who suffer from tremors with less severity, up to the higher level of severity, the width of frequency spectrum, which contained fundamental frequency and the peak value of PSD, was getting narrower. Other features based on the speed and intensity of hand tremor in Parkinson's disease patients that have been used to differentiate patients were frequency features such as Side Frequency with 50% power in the left half and 50% in the right half of the power spectrum graph (This Gaussian-like distribution is not observed in Parkinson's disease patients) [[18]](#Ref18). 50% Frequency, which divides the power spectrum graph into two equal parts, Base Frequency, which represents the frequency at which the maximum value of the power spectrum density occurred in the desired frequency band and the difference between base frequency and 50% frequency to investigate the extent of power amplitude in the density spectrum graph [[18]](#Ref18).

To reduce the high-dimensionality, feature selection was done and it was divided into two general types: scalar feature selection and vector feature selection. In this pattern recognition problem, the scalar method was not adequate and using the vectorial method as a complement is essential to reduce the number of features by keeping the more informative ones and ignoring the less informative ones; in this way the best combination set was obtained. Fisher’s Discriminant Ratio (FDR) for the scalar part and Sequential Forward Selection (SFS) for vector selection has been chosen. To quantify the discriminatory ratio of individual features between two classes FDR is employed [[19]](#Ref19). As can be seen in [Table 2](#table2), the parameter with a higher Fisher value is more important in distinguishing features. Based on FDR result, the PSD weighted average and Mean PSD have the best discriminative power.

### **Table 2.** FDR values

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| **Feature** | **FDR** |
| Mean PSD | 0.912 |
| Max PSD | 0.731 |
| Side Frequency(SF) | 0.636 |
| SF-F50% | 0.623 |
| Fifty Percent Frequency (F50%) | 0.1102 |
| Base Frequency(F0) | 0.1333 |

Furthermore, by combining the Fisher Ratio and WEKA software [[20]](#Ref20) and defining the SVM classifier as the criterion classifier, the final sequence of attribute effects was depicted in [Table 3](#table3).

### **Table 3.** The final ranking of features

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| --- | --- |
| **Rank** | **Feature** |
| 1 | Mean PSD |
| 2 | Max PSD |
| 3 | Base Frequency(F0) |
| 4 | Fifty Percent Frequency (F50%) |
| 5 | Side Frequency (SF) |
| 6 | SF-F50% |

To achieve more accurate results, various combinations of classifier algorithms have been used with different methods. The techniques were developed around the optimal Bayesian classifier based on the probability calculation of each class using statistical features of training data. Alternatively, the other techniques focused on designing a decision boundary that separates the classes from the training data set, such as SVM, so both techniques have been put to the test. As well as the fact that the dimension of training data contained an acceptable number of patients for each class, Naive Bayesian has been examined considering its advantages. It only required a small amount of training data to estimate the parameters necessary for classification. K-Nearest Neighbor (KNN) also has been applied as a case of Bayesian classifiers, besides ANN and SVM as a case of decision boundary classifiers.

# Results

The proposed algorithm has been applied in all three axis values, and the result was shown in [Table 4](#table4). As it was shown in [Table 4](#table4), the different types of classifiers were applied to extracted features. In order to perform cross-validation, the K-fold algorithm was used. Based on K-fold, the dataset were divided into 10 groups (fold) randomly. Each fold contains 5 subjects. So, each classification (employing a different combination of features and classifiers) was done 10 times. Consequently, each fold was used as a test group once and nine times was used as training data. Then the accuracy of classifiers was calculated by averaging ten result and were illustrated in [Table 4](#table4) in the form of mean and standard deviation. The features names correspond to the assigned numbers in [Table 3](#table3). For example, instead of Mean PSD, sign “(1)” has been used. Also, all the numbers were shown in percentage.

[Table 4](#table4) represented the result of the classification utilizing different combination of features and classifiers. Regardless of the combination of features the performance of Naïve classifier was better and the combination of features hasn't had much impact on its output. Also the best performance belonged to Naïve classifier with just 2 features. The biggest fluctuations were for the neural network and the nearest neighbor. Although the support vector machine was not good in accuracy, but did not fluctuate much. Due to the fact that the classification included 5 classes and test and training data (20%) were changed randomly, most of the results were good and acceptable.

### **Table 4.** Accuracy of classification results using k-fold method. Each column shows different combination of features and the number corresponding to each feature is defined in [Table 3](#table3)

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|  | **Naive** | **KNN** | **ANN** | **SVM** |
| (1),(2),(3),(4),(5), | 91.7±1.61 | 41.95±1.19 | 90.83±1.27 | 59.81±1.17 |
| (1),(3),(4),(5), | 90.7±1.26 | 45.41±1.21 | 62.95±1.31 | 65.95±1.18 |
| (1),(2),(3),(4),(5), | 92.35±1.62 | 42.63±1.54 | 91.53±1.03 | 68.98±1.57 |
| (1),(2),(3),(4), | 93.01±1.21 | 56.7±1.48 | 92.15±0.84 | 69.37±1.07 |
| (1),(3),(4),(5) | 93.46±0.94 | 52.04±0.94 | 39.2±1.45 | 68.77±0.65 |
| (1),(5) | 95.91±1.51 | 64.35±1.11 | 43.77±1.43 | 65.37±1.62 |
| (1),(2),(3) | 95.24±1.39 | 90.9±1.35 | 42.06±1.28 | 68.36±0.95 |
| (2),(3),(4) | 94.76±1.08 | 89.94±1.31 | 92.18±1.27 | 55.97±1.11 |
| (2),(3),(4),(5) | 92.46±2.43 | 85.77±1.77 | 90.7±1.21 | 61.3±1.06 |
| (2),(5) | 89.6±1.42 | 81.19±1.69 | 47.63±1.37 | 63.54±0.68 |

The main aim of implementing the feature selection and classification blocks was reducing the dimension and increasing the accuracy. Thanks to these two blocks, by only processing the acceleration values in RT band, 3-6 Hz band, 95.91±1.51 accuracy, and 95.8±1.21 % specificity as well as 93.87±0.95 % sensitivity can be obtained. Observations indicated that all of the patients, RT, PT, and KT had a dominant PSD peak in 3-6 Hz and depending on their kind of tremor, they also had subordinate PSD peak in their frequency band.

# Discussion

Most of the classification research has been done on designing different algorithms to distinguish different types of tremors such as Parkinson's, essential and so on. Due to the inaccessibility of patients in all groups, working on specific types of tremors, like Parkinson's tremor under the UPDRS standard rarely has been done. This paper has revealed a classification method to assess Parkinson's disease patients' tremors based on the UPDRS scale. There were several related studies with different objectives to analogous problems that have been presented for performance comparison. Jakubowski *et al.* [[21]](#Ref21) have presented a method with polyspectra statistical characterization of the tremor acceleration signals. The classification accuracy of Jakubowski MLP neural network for recognition Parkinson, essential and physiological tremors was 97%.

Palmes *et al.* [[12]](#Ref12) developed an Instrumental Method. His study has been developed based on 38 different patients' Electromyography (EMG) signals. Palmes applied different types of classifiers to, first, separated normal patients suffering from tremor, then among tremor patients discriminated Parkinson and essential and others forms. For his first separation step, he has obtained 98.4% accuracy and for the second step, the 99.2% accuracy has been taken.

Nowostawski *et al*. [[11]](#Ref11), to discriminate Parkinson's tremor and essential tremor, used DWT as a processing block and SVM as a classifier block in their smartphone-based application. They achieved over 96% accuracy.

A precise assessment of Parkinson's tremor is extremely important especially during treatment of the disease where it must be determined to prescribe drug or tune the electrodes of that stimulate brain patients deeply who had Deep Brain Stimulation (DBS) surgery to diminish their hand tremors. Furthermore, the highly proved correlation with the UPDRS scale allowed physicians to have a report objectively and universally identified and approved for the evaluation of patients with PD.

The most important limitation of this research was a few numbers of patients with a higher order of tremor in the UPDRS scale. Because of that the data acquisition process to make a balance in each class of the UPDRS scale has requested a long time.

In the future, working on the compilation of other UPDRS factors is suggested. Furthermore, experiments including other symptoms of Parkinson such as rigidity or dyskinesia will be appropriate studies. The designed system will make remote controlling possible for Parkinson's disease patients, allowing the neurologists to calibrate and regulate drug therapy based on a long-term observation rather than a simple outpatient visit.

# Conclusion

The developed system was very appropriate for using in assessment, diagnosis and remote control of Parkinson's disease patient’s both ambulatory and remote controlling. This work was based on a set of algorithms for obtaining an objective classification of tremors according to the UPDRS scale and it was done with high accuracy.

For the implementation of each classifier, all types of conditions of that classifier have been considered, for instance, SVM had been tested by its different kernels such as linear, polynomial, radial basis and bipolar sigmoid, and the best result by 70% accuracy came from the polynomial kernel. Examination on ANN varied in the number of neurons based on features and especially its functions, and the best result is obtained using five neurons, two hidden layers with linear function and an output layer with sigmoid function. To find out the best network structure, different numbers of hidden neurons have been utilized for training the algorithm. All trained networks have been tested by test data, which were chosen by k-fold method. The network provided the smallest value of the testing error with the smallest possible number of hidden neurons and the combination of extracted features has been selected as the optimal one. Back Propagation (BP) algorithm has been utilized to determine appropriate weights minimizing the error function of our ANN structure.

In consequence of successful result prediction of the Naïve classifier, sensitivity (True Positive Ratio: TPR), specificity (True Negative Ratio: TNR), and accuracy for all four classifiers (True Ratio: TR) were calculated by analyzing the confusion matrix elements coming from the classifier’s outputs. It was worthwhile to mention that evaluation of accuracy, specificity, and sensitivity of our system in all four different classifiers has been obtained based on test data which was different from test data with K-fold method.

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