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Real-Time Quantification of Resting Tremor in the Parkinson's Disease

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Abstract—Resting tremor (RT) is one of the most frequent signs of the Parkinson's disease (PD), occurring with various severities in about 75% of the patients. Current diagnosis is based on subjective clinical assessment, which is not always easy to capture subtle, mild and intermittent tremors. The aim of the present study is to assess the suitability and clinical value of a computer based real-time system as an aid to diagnosis of PD, in particular the presence of RT. Five healthy subjects were asked to simulate several severities of RT in hands and feet in three static activities. The behaviour of the subjects is measured using tri-axial accelerometers, which are placed at four different positions on the body. Frequency-domain features, strongly correlated with the RT activity, are extracted from the accelerometer data. The classification of RT severity based on those features, provided accuracy 76%. The real-time system designed for efficient extraction of those features and the provision of a continuous RT severity measure is described.

I. Introduction

THE parkinson's disease (PD) is a disorder of certain nerve cells in the part of the brain which produces dopamine. These nerve cells break down, dopamine levels drop and brain signals which are responsible for the movement become abnormal. PD usually begins in the middle or late life (after age 50). It progresses gradually for 10-15 years. This results in more and more disability. Patients suffering from PD present major clinical abnormalities of movement like resting tremor, rigidity, bradykinesia and postural instability [1].

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Resting tremor (RT) is the second most common sign of PD, after bradykinesia [1]. It is usually the first symptom noticed by the patient or by the family members; it is often the direct cause of the visit to the physician. In the early stage of the disease, RT is visible in the distal part of the limb (fingers, hand) and it gradually involves the whole limb thereafter. The cause of RT in PD has not been explained unequivocally. It is suggested that some areas responsible for the generation and inhibition of RT are located within the thalamus, while the amplitude and the frequency of RT are modulated at the level of the spinal cord and peripherally [1].

RT has a number of characteristics that make it easy to differentiate from other causes of tremor: it is slow with frequency of 3.5-7.5 Hz [1] and affects asymmetrically upper and lower limbs [1,2]. On the other hand, the presence and severity of RT can change during the day and as such, detection, assessment and following the changes of these signs during daily activities are of great interest [2].

Currently assessment of RT is mainly clinical, based on subjective methods, such as clinical scales (Unified Parkinson's Disease Rating Scale, Schwab and England Activities of Daily Living Scale, Hoehn and Yahr scale, and Webster scale) [1,2] and assessment of hand-writing or drawing of an Archimedes spiral [2]. Although administered under clinician observation, these largely subjective scales lack validation against actual RT amplitude. Furthermore, the coarse resolution of the ratings is insufficient for assessing minute changes in RT severity. Finally, the extent of inter-clinician and inter-subject rating variability is unknown [1,2].

Several researchers have proposed objective methods to detect and quantify RT [2-13]. More specifically, quantification of RT has been achieved by numerical methods such as time-domain analysis [3,4], spectral analysis [4,5], time-frequency analysis [6] and nonlinear analysis [4]. Recently, there has been a growing interest in applications of body-fixed sensors (BFS) [7] and in particular kinematic sensors for long-term monitoring of PD patients [3,8]. Several groups have used accelerometry [5,8], electromyography (EMG) [9], computer tracking [10], digital tablets [11], infrared video cameras [12] and laser transducers [13] in order to objectively assess RT. All these solutions have demonstrated limited usability in clinical settings due to deficiencies in wearability, fidelity, and flexibility.

In this study, we report the first results obtained from an easily applicable system using accelerometers. It is based on frequency-domain features and artificial neural networks (ANN). Using simulated data for the severity of RT obtained by patients, our results indicate that the identification of different severities of RT in several static activities is feasible. This system can be employed for clinical diagnosis of Parkinsonian tremor patients as it can provide with real-time quantitative assessment of the RT severity.

II. MATERIALS AND METHODS

A. Experimental Setup

In this study, five subjects, two males (aged 31 and 28 years) and three females (aged 31, 27 and 44 years) were enrolled. All the subjects are medical doctors in the Department of Neurology at the University Hospital of Ioannina with experience in PD and movement disorders, and agreed to participate in the study voluntarily. Subjects were asked to simulate Parkinsonian RT with a severity of 1 to 4 accordingly to the definition for RT severity in their Unified Parkinson's Disease Rating Scale (UPDRS) [1,2].

Four accelometers were placed on the right and left forearm, and on the right and left chin. The recordings were made consecutively starting first with a period with the tested limb resting and presenting no activity. Then a RT of severity 1 was simulated followed by a period of rest/inactivity, then a tremor of severity 2 was simulated, followed by rest, then severity 3, rest and finally severity 4. Each session lasted for 10 sec. The whole series of recordings for each subject was repeated three times for three static activities: with the subject sitting on a chair, lying on a bed, and standing.

B. Measurement System

Accelerometer data were recorded using the SHIMMER platform [7]. SHIMMER is a small wireless sensor platform designed by Intel for health-sensing applications. All sensors' trasmit data using Bluetooth to a portable PC equipped with data acquisition hardware and software to collect and store the signals. The sensor size is no bigger than a small matchbox. Sensors on the arms and legs are attached on specially designed elastic bands with Velcro, which allow fixation to any wrist or ankle size. Sampling rate is set to 100Hz for each signal. During the measurement, the activities of the subjects were recorded using a portable video camera.

C. Resting Tremor Metric

In the experimental protocol, the subjects were asked to emulate parkinsonian RT for different severities. The annotation consists of the sample points where RT starts and ends, as well as the severity of the RT. Thus, a pulse signal is produced:

$$s(t) = \begin{cases} k_i & when\ t > a_i\ and\ t < b_i \\ 0 & otherwise \end{cases}, \tag{1}$$

where a_i and b_i are the start and the end of periods of RT, i, and k_i is the RT severity of the specific period. In order to accumulate the transition from the non-tremor region to the tremor region we produce a smoother annotation signal convolving $s(t)$ with a hamming window $h(t)$ of length $5 \cdot Fs$, where Fs is the sampling frequency of the signal.

The RT metric is thus given by:

$$RT(t) = h(t) \otimes s(t). \tag{2}$$

D. Feature Extraction in Real Time

To our knowledge, RT assessment relies on time-domain and frequency-domain features [3-6]. However, in order to make a more robust system which is user independent, we ignore the statistical features of the signal which are very sensitive to sensor configuration and the subject. Thus, we concentrate on features from the frequency domain (in the frequency range of interest, 4-10 Hz according to the literature [2,3]). More specifically, we split the frequency band of interest in four equally distributed bins:

$$B = \{B_1, B_2, B_3, B_4\}.$$

The features extracted according to the proportion of energy signal contained in each one of the four bins:

$$H_i = \frac{\sum_{k \in B_i} |X(k)|^2}{\sum_{j \in \mathbf{B}} |X(j)|^2}, \quad i = \{1, ..., 4\}, \tag{3}$$

where X is the DFT of the signal and

$$\mathbf{B} = B_1 \cup B_2 \cup B_3 \cup B_4.$$

However, instead of using DFT for energy estimation we use an alternative method, more convenient for real-time application. It is possible to determine the energy of the signal in a specific frequency band after proper filtering, isolating the proper frequency band. Having a signal containing energy only on a specific band R then according to Parseval's theorem we have:

$$\begin{gathered} E(R) = E = \sum_{k=0}^{N-1} |X'(k)|^2 = N \sum_{n=0}^{N-1} x(n)^2 \quad, \\ X'(k) = \begin{cases} X(k), & k\ \ in\ \ R \\ 0, & otherwise \end{cases} \quad, \end{gathered} \tag{4}$$

where X is the DFT of the signal, $E(R)$ is the energy on the specific frequency band and E is the energy on the whole frequency domain. Thus, we needed to derive a filtering schema which isolates the four frequency bins of interest. This can be achieved with a combination of symmetric FIR digital filters. In order to reduce filter complexity, we down sampled the raw signal at a factor of 2. First, the signal was passed through a high pass filter with cutoff frequency at 2-4 Hz. Then a low pass filter at 10-12

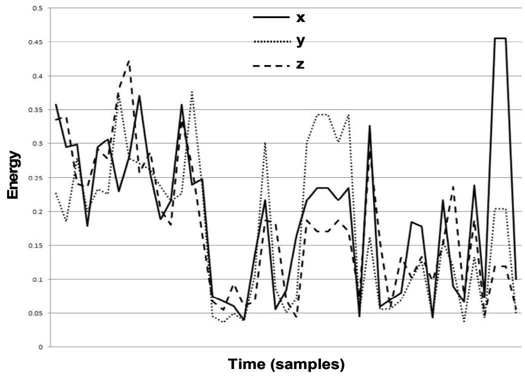

Fig. 1. Energy on B_1 bin (4-5.5Hz) for the three axes (x-y-z) for an accelerometer.

TABLE I
CORRELATION OF EXTRACTED FEATURES WITH THE RT

	RT activity
Total Energy	0.8182
Frequency Bin 1	-0.2573
Frequency Bin 2	-0.3105
Frequency Bin 3	-0.4272
Frequency Bin 4	0.6373

Hz is applied in order to remove the noise. The remaining signal contains the signal in frequencies from 4 to 10 Hz. Next, we apply a low pass filter with the desired cutoff frequency and the filtered signal propagates to the next filter. Subtracting the filtered signal from the input signal, delayed according to the filter length, we obtain the signal with energy only on the desired band.

Each accelerometer has three signals; the accelerations produced on the three axes x-y-z. All axes must have the same frequency distribution in the band of interest but in different amount of energy. This assumption was also confirmed by our data (Fig. 1). Taking that into account, we fuse the information of the three axes by simple taking the average energy in each bin from all accelerometer axes:

$$H_i^a = \frac{\frac{1}{3}\{H_i^x + H_i^y + H_i^z\}}{\sum_j \frac{1}{3}\{H_j^x + H_j^y + H_j^z\}}, \quad i = 1, \ldots, 4. \tag{5}$$

The correlations of the features with the RT activity are given in Table I. The total energy is the sum of energies in the four bins. We observe that total energy has high correlation with the RT, however we ignore this feature as is not affine transformation invariant and thus subject and sensor dependent.

E. Classification

According to the experimental protocol, the RT is recorded for four different severities. In order to determine the differentiability of the RT severities, we first treat the problem as a classification one. Initially, we equalize our dataset taking all the samples from the class with the less sample number and choose randomly equal number of sample from each other class. Thus, we produce a dataset with equal distributed classes. Then, in the new dataset we perform 5-cross validation using K-NN and decision tree classifiers [14] obtaining the confusion matrices. The above procedure is performed 50 times.

TABLE II
CONFUSION MATRICES FOR K-NN (3-NN) & C4.5 DECISION TREE CLASSIFIER

	K-NN Classifier		
Results/Class	No RT	RT severity 1 & 2	RT severity 3 & 4
FNs per Class	0.84	0.72	0.72
TPs per Class	0.97	0.63	0.74
Accuracy	0.7622		
	C4.5 Classifier		
Results/Class	No RT	RT severity 1 & 2	RT severity 3 & 4
FNs per Class	0.78	0.69	0.75
TPs per Class	0.89	0.61	0.76
Accuracy	0.7427		

RT = Resting Tremor, FN = False Negative, TP = True Positive.

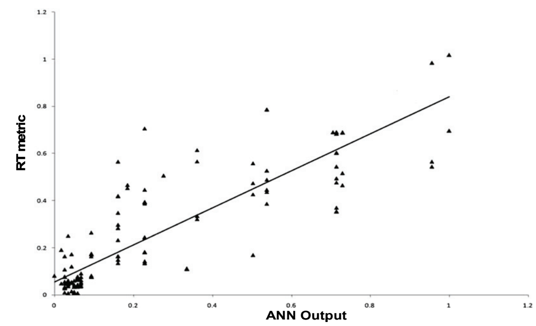

Fig. 2. Correlation between RT metric vs. ANN output.

F. Regression using Artificial Neural Networks

The focus of this work is the development of a real-time system obtained to provide a continuous metric of RT based on the features from the accelerometers. As an estimator we use an artificial neural network (ANN) [15], having as input the energy proportion contained in each bin and as a desired output the metric described in Section II-C. The hidden layer has sigmoid nodes and the output node is linear.

III. RESULTS

A. Classification

Classification results are presented in Table II for K-NN (K=3) and C4.5 decision tree classifiers [14]. Note that both classifiers have similar performance (the slightly better results of the 3-NN probably are due to similarity of the data from the same subject) and the source of confusion is between the RT severity classes, probably due to incapability of the control subjects to emulate different RT severities in the same way every time. At this point, we must notice that in our experiments using additional features, as statistical ones and the total energy of the four bins much higher accuracy is achieved (above 91%). However, we believe that this accuracy is biased due to the experimental

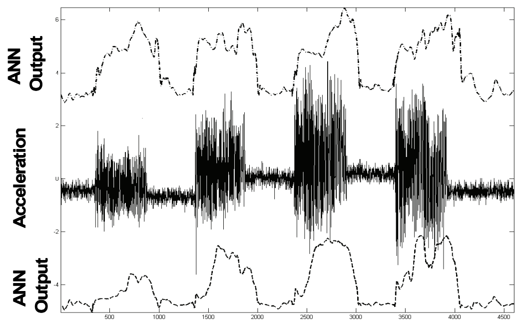

Fig. 3. The output of the ANN for a raw signal (x-axis). The ANN output without total energy (top), the raw signal (middle) and the ANN with total energy (bottom).

protocol, a case which will be examined given more experimental data, and data from real Parkinson patients.

B. Regression using Artificial Neural Networks

We have tested various architectures. The architecture with four input nodes, one hidden level with eight nodes and one output node (4-8-1) provides with the best results. In Fig. 2 the correlation between RT metric and the ANN output is illustrated. The correlation with the RT activity is 0.88, which is quite promising, as a preliminary result. Fig. 3 shows the ANN output for an example input signal (only for the x-axis). Note that the output captured the start and the end of the RT activity. For comparison purposes, the output of an ANN trained with the total energy of the four bins is also depicted. Note that the later differentiates better the four states. This differentiation is based mainly in the amplitude of the RT (as observed from the signal), thus the energy of the signal. However, the subjects when asked to simulate higher severity tremor, tend to accommodate higher frequency with higher amplitude, which is not necessary in true Parkinson patients [1,2].

C. Execution time

The filtering schema and the ANN are implemented in Matlab/Simulink. We investigated two possible analysis, one in 50 Hz with energy taken in buffers of 128 samples (~2.5 sec) and another in 25 Hz with energy taken in buffers of 75 samples (2.5 sec). Fig.4 shows the execution times of the filtering process and the whole system, as well as the execution time of a FFT on the equal sized buffers, for comparison. Note that the execution time of the whole system is comparable to a simple FFT's and thus is easily applicable to a real-time system.

IV. Conclusions

In this paper, an initial evaluation of the proposed system for real-time quantification of RT provides with promising results. Recording and quantification of the severity of RT in PD could have direct clinical implications for the diagnosis and therapeutic management of PD. In early stages of PD the RT may be very mild and intermittently present making diagnosis difficult if one relies for the detection of RT in the short office visit. Having a real-time system that can record reliably the existence of the typical Parkinsonian RT may help the early diagnosis of the disorder. Current effort is concentrated on the confirmation of these results using patients.

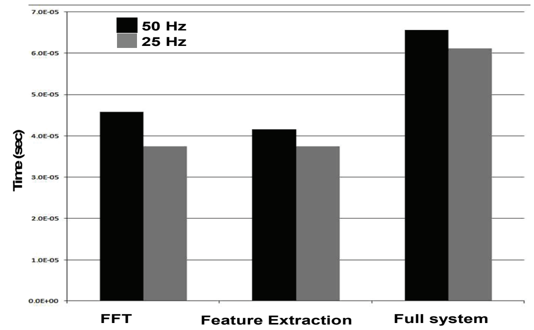

Fig. 4. Comparison of execution times of the FFT the filtering process, and the whole system.

References

[1] J. Jankovic and E. Tolosa. *Parkinson's Disease and Movement Disorders*. 3rd ed. Williams & Wilkins, Baltimore 1998.

[2] A. Budzianowska and K. Honczarenko. "Assessment of rest tremor in Parkinson's disease," *Neurologia i Neurochirurgia Polska*, vol.42, pp. 12–21, 2008.

[3] A. Salarian, H. Russmann, C. Wider, P.R. Burkhard, F.J.G. Vingerhoets and K. Aminian, "Quantification of tremor and bradykinesia in Parkinson's disease using a novel ambulatory monitoring system," *IEEE Trans. Biomed. Engin.*, vol. 54, pp. 313-22, 2007.

[4] J. Timmer, C. Gantert, G. Deuschl, and J. Honerkamp, "Characteristics of hand tremor time series," Biol. Cybern., vol. 70, pp. 75–80, 1993.

[5] C.N. Riviere, S.G. Reich, and N.V. Thakor, "Adaptive Fourier modelling of quantification of tremor," *J. Neurosci. Methods*, vol. 74, no. 1, pp. 77–87, 1997.

[6] P.E. O'Suilleabhain and J.Y. Matsumoto, "Time-frequency analysis of tremors," *Brain*, vol. 121, pp. 2127–134, 1998.

[7] S. Patel, R. Hughes, N. Huggins, D. Standaert, J. Growdon, J. Dy, and P. Bonato, "Using wearable sensors to predict the severity of symptoms and motor complications in late stage Parkinson's Disease," in *Conf. Proc. IEEE Eng. Med. Biol. Soc.* 2008, pp.3686-9.

[8] M. Smeja, F. Foerster, G. Fuchs, D. Emmans, A. Hornig, and J. Fahrenberg,"24-h assessment of tremor activity and posture in Parkinson's disease by multi-channel accelerometry," *J. Psychophysiol.*, vol. 13, pp. 245–56, 1999.

[9] M. Bacher, E. Scholz, and H.C. Diener, "24 hour continuous tremor quantification based on EMG recording," *Electroencephalogr. Clin. Neurophysiol.*, vol. 72, pp. 176–183, 1989.

[10] S. Yu, C.R. Allen, D. Geng, D. Burn, U. Brechany, G.D. Bell, and R. Rowland, "3-D motion system ("data-gloves"): application for Parkinson's disease," *IEEE Trans. Instr. Measur.*, vol. 52, pp. 662-74, 2003.

[11] M. Rudzipska1, A. Izworski, K. Banaszkiewicz1, S. Bukowczan, M. Marona1 and A. Szczudlik, "Quantitative tremor measurement with the computerized analysis of spiral drawing," *Neurologia i Neurochirurgia Polska*, vol.41, pp. 510–16, 2007.

[12] P. Bain, "Clinical measurement of tremor," *Mov. Disord.*, vol. 13, pp. 77–80, 1998.

[13] K.E. Norman, R. Edwards, and A. Beuter, "The measurement of tremor using a velocity transducer: comparison to simultaneous recordings using transducers of displacement, acceleration and muscle activity", *J. Neurosci. Meth.*, vol. 92, pp.41-54, 1999.

[14] M. Kantardzic, "Data Mining Concepts, Models, Methods, and Algorithms", *IEEE Press*, John Wiley & Sons, 2003.

[15] C.M. Bishop, "Neural Networks for Pattern Recognition", *Oxford*, University Press, 1995.