A New Modality for Quantitative Evaluation of Parkinson's Disease: In-Air Movement

Peter Drotár, Jiří Mekyska, Irena Rektorová, Lucia Masarová, Zdeněk Smékal and Marcos Faundez-Zanuy

Abstract— **Parkinsons disease (PD) is neurodegenerative disorder with very high prevalence rate occurring mainly among elderly. One of the most typical symptoms of PD is deterioration of handwriting that is usually the first manifestation of Parkinsons disease. In this study, a new modality - in-air trajectory during handwriting - is proposed to efficiently diagnose PD. Experimental results showed that analysis of in-air trajectories is capable of assessing subtle motor abnormalities that are connected with PD. Moreover, conjunction of in-air trajectories with conventional on-surface handwriting allows us to build predictive model with PD classification accuracy over 80%. In total, we compute over 600 handwriting features. Then, we select smaller subset of these features using two feature selection algorithms: Mann-Whitney U-test filter and relief algorithm, and map these feature subsets to binary classification response using support vector machines.**

I. Introduction

Parkinson's disease (PD) is progressive neurodegenerative disorder characterized by tremor, riginity, bradykinesia and loss of postural reflexes. PD usually affects people with the average age of 60, although 5% to 10% of patients may develop symptoms even before age 40 [1]. The particular causes of PD are not known, but there is ongoing research evaluating genetics, ageing and toxins. From the pathological point of view there is no objective quantitative method for clinical diagnosis. It is thought that PD can only be definitively diagnosed at postmortem that further highlights the complexities of diagnosis. Therefore there is intensive effort to develop expert systems and decision support systems for the assessment and diagnosis of PD.

Previous research has shown that one of the frequent syndromes of PD is significant vocal impairment such as dysphonia (impairment in the vocal production of normal sounds) and dysarthia (problems with normal articulation) [2],[3],[4]. These findings grasped attention of the speech processing community and motivated further research on link between PD and impaired speech. Several new and traditional voice measures has been proposed to discriminate healthy people from people with PD [5]. Recent studies for detection of PD with machine learning tools using acoustic measurement of voice impairment achieved different levels of PD prediction accuracy [6], [7]; where the latest reported results showed as high as 98% overall classification accuracy [8].

Not only speech, but also handwriting is affected by the PD [9],[10],[11],[12],[13]. Parkinson's Disease patients tend to move more slowly than healthy subjects and reduce movement amplitude when they are required to make movement with upper extremities. Slowness of movement and reductions in movement amplitude in clinical observations of PD patients are called bradykinesia and hypometria, respectively. Several studies have documented that handwriting provide numerous features that display statistically significant differences between healthy subjects and subjects with PD [11]. Statistical significance only is not sufficient, as this does not provide a complete picture of the extent to which any one measurement or set of measurements is useful in predicting and diagnosis of PD. Therefore we propose classification model for diagnosis of PD and test it on relatively large dataset consisting of 75 individuals. In addition, minimal subset of the most predictive features is selected.

The fact, that has been rarely taken into account is, that hand movement during handwriting a text consist of two components: an on-surface component, comprising the movements executed while exerting pressure on the writing surface, and an in-air component, comprising the movements performed without touching the writing surface. The amount of information is similar in both types of trajectories and, even if they share some information, in-air and on-surface trajectories appear to be notably non-redundant [14]. In-air movement has been so far used only for biometric application, but here we show that it has meaningful application also for medical analysis.

The rest of the paper is organized as follows. In Section 2., the database of handwriting samples is introduced and described, followed by initial feature analysis. Application of feature selection and machine learning methods to problem of PD classification is described in Section 3. Finally, conclusions are drawn in the last section.

II. Data and Methods

A. Parkinson's Dataset

37 Parkinsonian patients (19 men/18 women) and 38 (20 men/18 women) age matched healthy controls took part in this study. Dominant hand of all participants was the right hand. Parkinsonian patients completed the session in the ON state (under medication by L-DOPA). Mean and standard deviation of age, Unified Parkinsons Disease Rating Scale-Part V., score and disease duration are summarized in Table I.

P. Drotár, J. Mekyska and Z. Smékal are with Department of Telecommunications, Brno University of Technology, Technická 12, 61200 Brno, Czech Republic drotarp@feec.vutbr.cz

I. Rektorová and L. Masarová are with the First Department of Neurology, Faculty of Medicine, St. Ann's University Hospital , Pekarska 664, 66591 Brno, Czech Republic and Central European Institute of Technology, Masaryk University, Brno, Czech Republic

Marcos Faundez-Zanuy is with Escola Universitaria Politecnica de Mataro, Tecnocampus, Avda. Ernest Llunch 32, 08302, Mataro, Spain

978-1-4799-3163-7/13/$31.00 ©2013 IEEE

TABLE I

PARKINSON'S HANDWRITING DATASET CHARACTERISTICS

	Age		UPDRS (part V)		Years since diag.	
	mean	*std*	*mean*	*std*	*mean*	*std*
PD	69.3	10.9	2.27	0.84	8.37	4.8
H	62.4	11.3	-	-	-	-

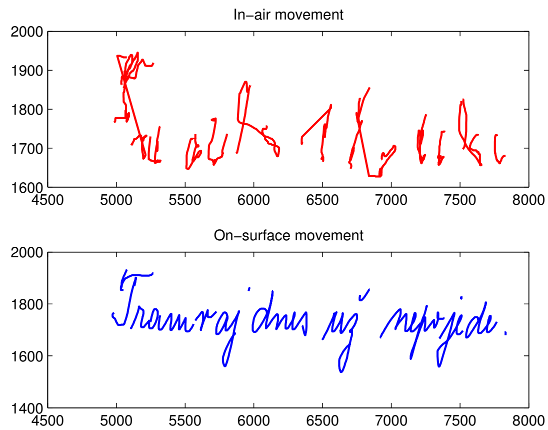

Fig. 1. Handwriting sample of PD patient.

Each subject was asked to write sentence in Czech language (native language of participants) "Tramvaj dnes u nepojede" (The tram won't go today). Handwritten signals were acquired using digitizing tablet Intuos 4M (Wacom technology) in the x-y plane, and in the pressure axis. An inked writing pen was held in a normal fashion without constraints to allow for full visual feedback during writing. As was already mentioned, signals were acquired not only during movements executed while exerting pressure on the writing surface, but also during movement performed without touching the writing surface. Fig. 1 and Fig. 2 show example of on-surface and in-air trajectories taken from executions of the sentence performed by PD patient and healthy control, respectively.

B. Measured feature sets

The recordings starts when the pen touched the surface of digitizer and finishes when task is completed. Digitazing tablet captures following dynamic features (time-sequences): *x*-coordinate, *x(t)*; *y*-coordinate,*y(t)*; time stamp, *s(t)* and button status, *b(t)*. Button status is binary variable being 0 for pen-up(in-air movement) and 1 for pen-down(on-surface movement), this means that tablet captures pen movement while on surface, but also in close proximity of surface - in-air. The x and y components are segmented into on-surface and in-air strokes and analyzed in terms of handwriting measures. The feature calculation stage involves the application of the traditional and nonstandard measurement methods to all handwriting signals. Each method produce either a single value or vector of numbers for each of 75 signals. List of computed features is provided in Tab. II, where single value features are denoted as s and vector features are denoted

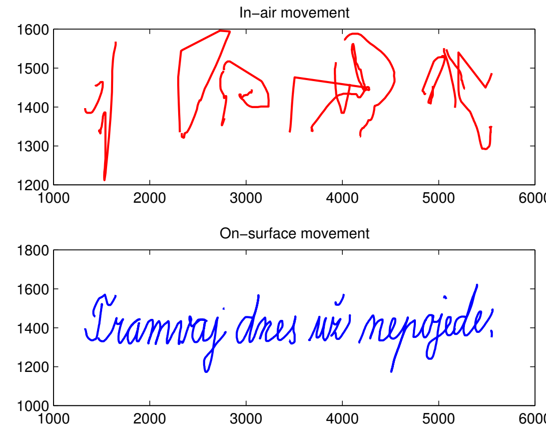

Fig. 2. Handwriting sample of healthy control.

as v. Additionally 30 statistical functionals of the vector features were computed. These include minima, maxima, range, outlier robust range(percentile *99th* - percentile *1st*), geometrical mean, median, mode, mean, standard deviation, statistical moments (3, 4, 5, 6), trimmed means (5, 10, 20, 30, 40, 50), percentiles(1, 5, 10, 20, 30, 90, 95, 99), quartiles(25/lower, 75/upper), kurtosis.

C. Feature analysis

Previous processing stages produce together more than six hundred features for in-air and on-surface movement. In order to obtain some preliminary insight into statistical properties of handwriting features we computed Pearson correlation coefficients and mutual information between feature vectors and associated response. Pearson correlation express measure of linear dependence between features vectors and associated response. Mutual information is a measure of the amount of information shared by two random variable X and Y. It is defined as:

$$I(X;Y) = -\sum_{x\in X}\sum_{y\in Y} p(x,y)\cdot\log_2\left(\frac{p(x,y)}{p(x)p(y)}\right) \tag{1}$$

where x and y are possible variable values with a joint probability distribution function $p(x,y)$ and marginal distribution functions $p(x)$ and $p(y)$, respectively [16].

Table III sumarizes ten handwriting measures with largest relevance to response sorted according absolute correlation coefficient. All correlations are statistically significant ($p < 0.05$). Eight of ten features are in-air movement related features, that give us some initial confirmation of our hypothesis that in-air features contain information relevant for predicting PD. The Mann-Whitney test indicated significant differences ($p < 0.05$) between control group and PD group for all features listed in table.

III. CLASSIFICATION RESULTS

A. Selection of candidate feature set for classification

After removing all features that did not pass the Mann-Whitney U test for significant differences there are still 262

TABLE II

PLEASE WRITE YOUR TABLE CAPTION HERE

Feature	(s)/(v)	Description
stroke speed	v	trajectory during stroke divided by stroke duration
speed	s	trajectory during handwriting divided by handwriting duration
velocity	v	rate at which the position of a pen changes with time
acceleration	v	rate at which the velocity of a pen changes with time
jerk	v	rate at which the acceleration of a pen changes with time
horizontal velocity/acceleration/jerk	v	velocity/acceleration/jerk in horizontal direction
vertical velocity/acceleration/jerk	v	velocity/acceleration/jerk in vertical direction
number of changes in velocity direction (NCV)	s	the mean number of local extrema of velocity [15]
number of changes in acceleration direction (NCA)	s	the mean number of local extrema of acceleration [15]
relative NCV	s	NCV relative to writing duration
relative NCA	s	NCA relative to writing duration
in-air time	s	time spent in-air during writing
on-surface time	s	time spent on-surface during writing
normalised in-air time	s	time spent in-air during writing normalised by whole writing duration
normalised on-surface time	s	time spent on-surface during writing normalised by whole writing duration
in-air/on-surface ration	s	ratio of time spent in-air/on-surface

TABLE III

DESCRIPTION OF CALCULATED FEATURES

Feature	Mutual Information	Correlation Coefficient
stroke speed (on surface, standard dev.)	6.09	-0.388
velocity (in air, standard dev.)	5.94	-0.387
vert. jerk (in air, min.)	5.7	0.383
acceleration (in air, standard dev.)	5.92	-0.38
horz. jerk (in air, range)	5.72	-0.379
jerk (in air, standard dev.)	5.96	-0.389
horz. acceleration (in air, range)	5.81	-0.375
horz. velocity (in air, range)	5.87	-0.371
horz. velocity (on surface, quantile 75%)	4.46	-0.37
vert. acceleration (in air, min.)	5.74	-0.369

candidate features left. Even if many classification algorithms are fairly robust to the inclusion of potentially irrelevant features, their performance in speed (due to high dimensionality) and predictive accuracy (due to irrelevant information) may be severely degraded. Feature selection algorithms aim to choose a small subset of features that ideally is necessary and sufficient to describe target concept. From many feature selection algorithms we decided to use Relief algorithm [17], that has been shown to achieve promising results in problems similar to ours [8]. Relief is feature weighting algorithm that relies entirely on statistical analysis and employs only few heuristics. It selects most of the relevant features even though only a small number of them is necessary for prediction. In most cases it does not help with redundant features. Since we want all relevant features to be included for prediction even at the cost of higher dimensionality Relief appears to be promising candidate.

B. Support Vector Machines

The underlying idea of SVM classifiers is to calculate a maximal margin hyperplane separating two classes of the data. To learn non-linearly separable functions, the data are implicitly mapped to a higher dimensional space by means of a kernel function, where a separating hyperplane is found. New samples are classified according to the side of the hyperplane they belong to. We used RapidMiner Java implementation of the mySVM with radial kernel. The parameters kernel gamma γ, penalty parameter C and convergence epsilon ϵ were optimized using grid search of possible values. Specifically, we searched over the grid (C, γ, ϵ) defined by the product of the sets $C = [10^{-5}, 10^{-4}, \ldots, 10^{3}, 10^{4}]$, $\gamma = [10^{-5}, 10^{-4}, \ldots, , 10^{2}, 10^{3}]$ and $\epsilon = [10^{-5}, 10^{-4}, \ldots, 10^{2}, 10^{3}]$. Classifier validation was conducted using a leave-one-out approach. That is, we left out the sample of one individual to be used for validation as if it is an unseen individual. The process was repeated a total of 50 times, where in each repetition the original dataset was randomly permuted prior to splitting into training and testing subsets. Training and testing features were normalized to have zero mean and a standard deviation of one on a per-feature basis before classification.

C. Numerical Results

Classification performance for different number of features was computed for three different scenarios: using only features based on in-air movement; using only features extracted from on-surface movement and using fusion of both groups of features. By fusion we mean that both feature groups were merged prior to feature selection. Fig.3 shows prediction accuracy of PD using SVM classifier for increasing number of features. Features were selected by application of Relief algorithm. Classification features based on in-air movement provide classification accuracy similar or higher then accuracy of features based on on-surface movement.

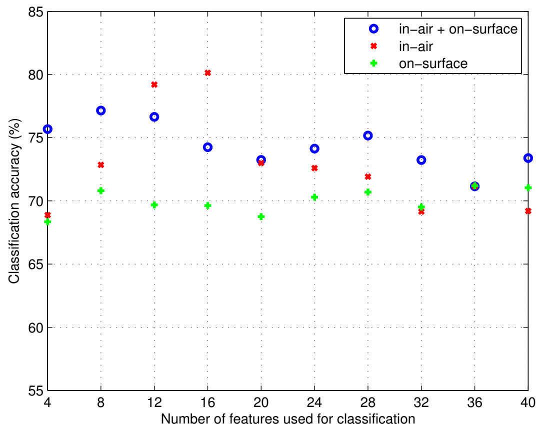

Fig. 3. Classification accuracy of SVM for different modalities.

This confirms our initial hypothesis that in-air movement holds significant information with regards to diagnosis of PD. The highest classification accuracy, 80.09%, was achieved for 16 features selected from in-air. Merging of both modalities brings in most of the cases improvement in classification accuracy indicating amount of non-redundant information in in-air and on-surface movement. As can be seen from Fig. 3 increasing number of features is not always beneficial.

IV. Conclusion

It was shown that proposed scheme can be used for diagnosis of PD with classification accuracy over 80%. Besides conventional on-surface handwriting also in-air trajectories during writing were utilized for PD prediction task. Results indicate that novel in-air features outperform conventional on-surface features in separating healthy controls from subjects with PD. Conjunction of both modalities to built predictive model can be used for quantitative recording for the treating doctor in order to detect and predict long term changes in the individual disease history. Beside the PD classification and disease tracking the handwriting analysis can be also used during an evaluation of modern non-invasive treatment methods such as high-frequency repetitive transcranial magnetic stimulation (rTMS), see e.g. [16]. In our future work, we will analyse new features that can more efficiently capture tremor, micrographia and other medically relevant information. We believe that merging handwriting features with e.g. voice features can further improve diagnosis, evaluation and tracking of PD.

Acknowledgment

This work was supported by the project NT13499 (Speech, its impairment and cognitive performance in Parkinsons disease), CZ.1.07/2.3.00/20.0094, project CEITEC, Central European Institute of Technology: (CZ.1.05/1.1.00/02.0068) from the European Regional Development Fund and by FEDER and Ministerio de Economa y Competitividad TEC2012-38630-C04-03. The described research was performed in laboratories supported by the SIX project; the registration number CZ.1.05/2.1.00/03.0072, the operational program Research and Development for Innovation. Peter Drotár was supported by the project CZ.1.07/2.3.00/30.0005 of Brno University of Technology.

References

[1] L. M. de Lau and M. M. Breteler, "Epidemiology of Parkinson's disease," *The Lancet Neurology*, vol. 5, no. 6, pp. 525 – 535, 2006.

[2] A. K. Ho, R. Iansek, C. Marigliani, J. L. Bradshaw, and S. Gates, "Speech impairment in a large sample of patients with Parkinson's disease," *Behav. Neurol.*, vol. 11, no. 3, pp. 131 – 137, 1998.

[3] K. M. Rosen, R. D. Kent, A. L. Delaney, and J. R. Duffy, "Parametric quantitative acoustic analysis of conversation produced by speakers with dysarthria and healthy speakers," *J Speech Lang Hear Res*, vol. 49, no. 2, pp. 395–411, 2006.

[4] J. Mekyska, Z. Smekal, M. Kostalova, M. Mrackova, S. Skutilova, and I. Rektorova, "Motor aspect of speech impairment in parkinsons disease and their assesment," *Czech and Slovak Neurology and Neurosurgery*, vol. 74, no. 6, pp. 662–668, 2011.

[5] M. Little, P. McSharry, E. Hunter, J. Spielman, and L. Ramig, "Suitability of dysphonia measurements for telemonitoring of parkinson's disease," *Biomedical Engineering, IEEE Transactions on*, vol. 56, no. 4, pp. 1015–1022, 2009.

[6] P.-F. Guo, P. Bhattacharya, and N. Kharma, "Advances in detecting parkinsons disease," in *Medical Biometrics*, ser. Lecture Notes in Computer Science. Springer Berlin Heidelberg, 2010, vol. 6165, pp. 306–314.

[7] C. Sakar and O. Kursun, "Telediagnosis of parkinsons disease using measurements of dysphonia," *Journal of Medical Systems*, vol. 34, no. 4, pp. 591–599, 2010.

[8] A. Tsanas, M. Little, P. McSharry, J. Spielman, and L. Ramig, "Novel speech signal processing algorithms for high-accuracy classification of Parkinson's disease," *Biomedical Engineering, IEEE Transactions on*, vol. 59, no. 5, pp. 1264–1271, 2012.

[9] C. Marsden, "Slowness of movement in parkinson's disease," *Movement Disorders*, vol. 4, no. 1, pp. 26–37, 1989.

[10] R. Saunders-Pullman, C. Derby, K. Stanley, A. Floyd, S. Bressman, R. B. Lipton, A. Deligtisch, L. Severt, Q. Yu, M. Kurtis, and S. L. Pullman, "Validity of spiral analysis in early parkinsons disease," *Movement Disorders*, vol. 23, no. 4, pp. 531–537, 2008.

[11] M. Broderick, A. Van Gemmert, H. Shill, and G. Stelmach, "Hypometria and bradykinesia during drawing movements in individuals with parkinsons disease," *Experimental Brain Research*, vol. 197, no. 3, pp. 223–233, 2009.

[12] M. Wang, B. Wang, J. Zou, L. Chen, F. Shima, and M. Nakamura, "A new quantitative evaluation method of parkinson's disease based on free spiral drawing," in *Biomedical Engineering and Informatics (BMEI), 2010 3rd International Conference on*, vol. 2, 2010, pp. 694–698.

[13] P. Drotár, J. Mekyska, I. Rektorová, L. Masarová, Z. Smékal, and M. Faundez-Zanuy, "Prediction potential of different handwriting tasks for diagnosis of Parkinsons disease," in *IEEEE International Conference on e-Health and Bioengineering (EHB 2013)*, Iasi, Romania, November 2013.

[14] E. Sesa-Nogueras, M. Faundez-Zanuy, and J. Mekyska, "An information analysis of in-air and on-surface trajectories in online handwriting," *Cognitive Computation*, vol. 4, no. 2, pp. 195–205, 2012.

[15] T. Eichhorn, T. Gasser, N. Mai, C. Marquardt, G. Arnold, J. Schwarz, and W. Oertel, "Computational analysis of open loop handwriting movements in parkinsons disease: a rapid method to detect dopamimetic effects," *Movement Disorders*, vol. 11, no. 3, pp. 289–297, may 1996.

[16] T. M. Cover, *The elements of Information Theory*. Wiley, 1991.

[17] K. Kira and L. A. Rendell, "A practical approach to feature selection," in *Proceedings of the ninth international workshop on Machine learning*, ser. ML92. San Francisco, CA, USA: Morgan Kaufmann Publishers Inc., 1992, pp. 249–256.