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Analysis of Parkinson's Disease Dysgraphia Based on Optimized Fractional Order Derivative Features

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***Abstract*—Parkinson's disease (PD) is a common neurodegenerative disorder with prevalence rate estimated to 1.5 % for people age over 65 years. The majority of PD patients is associated with handwriting abnormalities called PD dysgraphia, which is linked with rigidity and bradykinesia of muscles involved in the handwriting process. One of the effective approaches of quantitative PD dysgraphia analysis is based on online handwriting processing. In the frame of this study we aim to deeply evaluate and optimize advanced PD handwriting quantification based on fractional order derivatives (FD). For this purpose, we used 37 PD patients and 38 healthy controls from the PaHaW (PD handwriting database). The FD based features were employed in classification and regression analysis (using gradient boosted trees), and evaluated in terms of their discrimination power and abilities to assess severity of PD. The results suggest that the most discriminative and descriptive information provide FD based features extracted from a repetitive loop task or a sentence copy task (maximum sensitivity/specificity = 76 %, error in severity assessment = 14 %, error in PD duration estimation = 22 %). Next, we identified two optimal ranges for the order of fractional derivative, α = 0.05 – 0.45 and α = 0.65 – 0.80. Finally, we observed that inclusion of pressure, azimuth, and tilt together with kinematic features into mathematical modeling has no influence (positive or negative) on classification performance, however, there was a notable improvement in the estimation of PD duration.**

***Index Terms*—online handwriting; Parkinson's disease; dysgraphia; fractal calculus; fractional derivatives; classification; regression**

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I. Introduction

Parkinson's disease (PD) is a common neurodegenerative disorder affecting approximately 1.5 % of the world population aged over 65 years [1]. The risk of being affected by PD increases with age. Therefore, as populations age, the incidence rate is expected to be doubled in the next 15 years [2]. The exact pathophysiological cause of PD has not yet been discovered, though a rapid degeneration of dopaminergic cells in the substantia nigra pars compacta is the most significant biological finding linked with PD. Tremor at rest, rigidity, bradykinesia and postural instability are considered as the primary motor symptoms of PD [3]. Non-motor symptoms such as cognitive impairment, sleep disturbances, depression, etc. may also arise [4], [5]. Moreover, PD patients usually develop additional axial motor symptoms, e.g. hypokinetic dysarthria, dysphagia, and gait freezing [5].

Considering the primary motor symptoms of PD to be in line with cognitive, perceptual and motor requirements of handwriting, the disrupted handwriting of PD patients may be used as a significant biomarker in PD diagnosis [6]. Especially, by detecting micrographia (progressive decrease of letter's amplitude or width), which is the most commonly observed handwriting abnormality in PD patients [7]. Nevertheless, some PD patients never develop micrographia, but they still exhibit some other handwriting disabilities. Due to this complexity, Letanneux et al. [8] started to use the term PD dysgraphia. To be able to effectively quantify manifestations of PD in handwriting, more advanced approaches were introduced [9], [10]. They are based on digitizing tablets that are able to acquire x and y trajectories along with temporal information (this kind of signal is called online handwriting). Therefore, we are not limited to analyze the spatial features only, but we can process temporal, kinematic or dynamic characteristics.

Researchers have been exploring the influence of many

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handwriting/drawing tasks in PD dysgraphia analysis, from the simplest ones (loops, circles, lines, Archimedean spiral, etc.) to more complex (words, sentences, drawings, etc.) [10]–[15]. The importance of kinematic features was confirmed by most of the recent works, however, temporal, spatial, dynamic or other more advanced features play their significant role as well. For instance, Drotar et al. [10]–[12] achieved PD classification accuracy up to 89 % using a combination of kinematic, pressure, energy or empirical mode decomposition (EMD) features. Average accuracy of 91 % was achieved by Kotsavasilogloua et al. [16] using kinematic and entropy based features extracted from simple horizontal lines. Some other works reported even higher classification accuracies ($\approx$97 %) [17], [18], but based on a very small dataset. Moetesum et al. [19] published a promising advanced approach by applying convolutional neural networks (CNN) on handwriting data transformed into the offline mode, which resulted in 89 % accuracy. Next, Taleb et al. [9] reported up to 94 % accuracy of PD severity prediction using kinematic and pressure features in combination with adaptive synthetic sampling approach (ADASYN) for model training. Finally, in our recent works [14], [15], [20] we introduced and evaluated a new advanced approach of PD dysgraphia analysis exploiting a fractional order derivative (FD) as a substitution of conventional differential derivative during basic kinematic feature extraction (i.e. velocity, acceleration, and jerk parameters). We achieved up to 90 % classification accuracy employing only 5 FD-based kinematic parameters in these works. Nevertheless, in comparison to conventional parameters, the newly proposed FD-based features yielded better performance only in specific tasks (continuous and/or repetitive movement) and in specific applications such as PD severity estimation.

Therefore, the main objective of this study is to extend our previous findings and perform a deeper and more sensitive analysis of FD-based features, especially in terms of their discrimination power and descriptive abilities. More specifically, we aim to:

- explore the utilization of FD in the other dimensions of online handwriting (i.e. pressure, azimuth, and tilt),
- identify an optimal combination of handwriting/drawing tasks and the FD-based features in terms of discrimination power and descriptive abilities,
- identify an optimal range of FD order α for classification and regression analysis.

The rest of this paper is organized as follows. Section II describes the used dataset and methodology. Results are summarized in Section III. In Section IV the discussion related to the results can be found and the conclusions are drawn in Section V.

II. Dataset and Methodology

A. Dataset

For the purpose of this work, we used the Parkinson's disease handwriting database (PaHaW) [11]. The database consists of several handwriting or drawing tasks acquired in 37 PD patients and 38 age- and gender-matched healthy controls (HC). Demographic and clinical data of the participants can be found in Table I. The participants were enrolled at the First Department of Neurology, St. Anne's University Hospital in Brno, Czech Republic. All participants reported Czech language as their native language and they were right-handed. The patients completed their tasks approximately 1 hour after their regular dopaminergic medication (L-dopa). All participants signed an informed consent form approved by the local ethics committee.

TABLE I
Demographic and clinical data of the enrolled participants.

Gender	N	Age [y]	PD dur [y]	UPDRS V	LED [mg/day]
Parkinson's disease patients					
Females	18	71.23 ± 8.03	9.55 ± 5.29	2.17 ± 0.84	1124.03 ± 535.84
Males	19	67.52 ± 13.15	7.26 ± 4.12	2.37 ± 0.86	1724.12 ± 733.03
All	37	69.32 ± 10.97	8.38 ± 4.80	2.27 ± 0.85	1432.19 ± 704.78
Healthy controls					
Females	18	61.44 ± 9.89	-	-	-
Males	20	63.30 ± 12.79	-	-	-
All	38	62.42 ± 11.39	-	-	-

[1] N – number of subjects; y – years; PD dur – PD duration; UPDRS V – Unified Parkinson's disease rating scale, part V: Modified Hoehn & Yahr staging score [21]; LED – L-dopa equivalent daily dose.

B. Data Acquisition

The PaHaW database [11] includes multiple handwriting tasks, namely: Archimedean spiral; repetitive loops; letter *l*; syllable *le*; Czech words *les*, *lektorka*, *porovnat*, and *nepopadnout*; Czech sentence *Tramvaj dnes už nepojede.* During handwriting tasks performance, the participants were rested and seated in a comfortable position with a possibility to look at a pre-filled template. In case of some mistakes, they were allowed to repeat the task. A digitizing tablet (Wacom Intuos 4M) was overlaid with an empty paper and the participants wrote on that using the Wacom Inking pen. Online handwriting signals were recorded with $f_\mathrm{s} = 150$ Hz sampling rate. The following time sequences were acquired: x and y coordinates – $x[t]$, $y[t]$; time-stamp – t; on-surface (i.e. on paper movement) and in-air (i.e. movement up to 1.5 cm above the paper) status – $b[t]$; pressure – $p[t]$; azimuth $az[t]$; and tilt $al[t]$.

C. Fractional Derivative

We discovered the potential of FD-based kinematic features in PD dysgraphia analysis in our previous works [14], [15], [20]. By substitution of the conventional differential derivative during feature calculation, we have developed a new advanced approach of handwriting parametrization. Generally, FDs can have wide range of settings and several approaches of approximation (e.g. Caputo, Grünwald-Letnikov) [22]. In this work, we utilized the Grünwald-Letnikov approximation implemented by Jonathan Hadida. A direct definition of FD $D^\alpha y(t)$ is based on finite differences of an equidistant grid in $[0, \tau]$ assuming that the function $y(\tau)$ satisfies certain smoothness conditions in every finite interval $(0, t), t \leq T$. Choosing the grid [22]

$$0 = \tau_0 < \tau_1 < ... < \tau_{n+1} = t = (n+1)h \tag{1}$$

with

$$\tau_{k+1} - \tau_k = h \tag{2}$$

and using the notation of the finite differences

$$\frac{1}{h^\alpha}\Delta_h^\alpha y(t) = \frac{1}{h^\alpha}\left(y(\tau_{n+1}) - \sum_{v=1}^{n+1} c_v^\alpha y(\tau_{n+1-v})\right), \tag{3}$$

where

$$c_v^\alpha = (-1)^{v-1}\binom{\alpha}{v}. \tag{4}$$

The Grünwald-Letnikov implementation is defined as:

$$D^\alpha y(t) = \lim_{h\to 0}\frac{1}{h^\alpha}\Delta_h^\alpha y(t), \tag{5}$$

where $D^\alpha y(t)$ denotes a derivative with order α of function $y(t)$, and h represents sampling lattice.

D. Handwriting Features

The first set of parameters consists of conventional kinematic features extracted from all tasks of the PaHaW database for both on-surface and in-air movement. It means we calculated: *velocity* (rate at which a position of pen changes with time [mm/s]), *acceleration* (rate at which the velocity of pen changes with time [mm/s^2]), *jerk* (rate at which the acceleration of pen changes with time [mm/s^3]), and their horizontal and vertical variants [11], [23]. Next, we calculated the kinematic features based on FD. Moreover, to further extend and improve our previous research, FD was also similarly applied to pressure, azimuth and tilt.

In the first step, the FD-based features were calculated for different values of α in range from 0.1 to 1.0 with the step of 0.1. Next, the most discriminative handwriting tasks were selected and deeper analysed with a finer step of α (0.01). This selection was made in order to reduce computational cost of the analysis. Statistical properties of all extracted handwriting features were expressed using mean, median, standard deviation (std), and maximum (max).

E. Statistical Analysis

To evaluate the discriminative power of the handwriting features, a multivariate binary classification analysis based on the state-of-the-art Gradient Boosted Trees (10-fold cross-validation with 50 repetitions) was employed. More specifically, the famous XGBoost algorithm [24] was used in light of its ability to achieve good performance on a small dataset. Classification performance was evaluated by the Matthew's correlation coefficient (MCC), classification accuracy (ACC), sensitivity (SEN), and specificity (SPE). Next, in order to evaluate the power of handwriting features to estimate values of PD duration and UPDRS V, regression analysis was performed. The same boosting tree algorithm (XGBoost) with the same supervised learning setup was used. Regression performance was evaluated by mean absolute error (MAE), root mean square error (RMSE), and estimation error rate (EER).

III. Results

The results of classification and regression analysis for the FD-based handwriting features extracted from all tasks can be found in Table II. Selection of the most discriminative/descriptive handwriting tasks for the consequent optimization of FD was performed based on feature importances of trained models (feature importance quantifies the relative importance of the feature in an ensemble of the trained XGBoost model [24]). Distribution of particular tasks and derived features for all classification/regression scenarios can be found in Figure 1. Results of the classification/regression analysis after the fine tuning of FD are reported in Table III. Finally, distributions of the FD order α among the fine-tuned parameters are visualized in Figure 2.

TABLE II
RESULTS OF CLASSIFICATION AND REGRESSION ANALYSIS BASED ON ALL TASKS

Classification				
MCC	ACC [%]	SEN [%]	SPE [%]	Feat
0.62 ± 0.14	80.60 ± 9.87	79.41 ± 14.52	80.56 ± 7.25	18
Regression				
Scale	EER [%]	MAE	RMSE	Feat
UPDRS V	12.98 ± 7.01	0.55 ± 0.29	0.66 ± 0.42	3
PD duration	25.23 ± 3.65	4.42 ± 0.64	5.33 ± 0.89	30

[1] MCC – Matthew's correlation coefficient; ACC – accuracy; SEN – sensitivity; SPE – specificity; Feat – number of features important for the trained model; MAE – mean absolute error; RMSE – root mean squared error; EER – estimation error rate; UPDRS V – Unified Parkinson's disease rating scale, part V: Modified Hoehn & Yahr staging score [21].

TABLE III
RESULTS OF CLASSIFICATION AND REGRESSION ANALYSIS FOR SELECTED TASKS

Classification					
Task	MCC	ACC [%]	SEN [%]	SPE [%]	Feat
Sentence	0.34 ± 0.18	66.67 ± 12.45	65.79 ± 18.12	65.79 ± 21.58	21
Rep. loops	0.52 ± 0.11	76.00 ± 11.98	75.68 ± 12.36	76.32 ± 19.54	11
Regression					
Task	Scale	EER [%]	MAE	RMSE	Feat
Sentence	UPDRS V	14.67 ± 7.44	0.63 ± 0.32	0.78 ± 0.40	1
Rep. loops	UPDRS V	13.94 ± 7.61	0.61 ± 0.33	0.75 ± 0.41	2
Sentence	PD duration	23.73 ± 10.67	4.05 ± 1.82	4.62 ± 1.83	33
Rep. loops	PD duration	21.97 ± 8.97	3.75 ± 1.53	4.36 ± 1.60	39

[1] MCC – Matthew's correlation coefficient; ACC – accuracy; SEN – sensitivity; SPE – specificity; Feat – number of features important for the trained model; MAE – mean absolute error; RMSE – root mean squared error; EER – estimation error rate; UPDRS V – Unified Parkinson's disease rating scale, part V: Modified Hoehn & Yahr staging score [21].

IV. Discussion

Firstly, we performed the analysis using all tasks of the PaHaW database utilizing features calculated for α from 0.1 to 1.0 with step 0.1 (10 FD-based features for one handwriting parameter). As can be seen in the upper part of Table II, ACC (80.60 %) corresponds with our previous results (81.43 %) [14], while SEN and SPE were improved by approximately 10 %. Number of features involved in the trained model is 18, and as can be seen in Figure 1 (bottom part of column a), besides the kinematic features the pressure

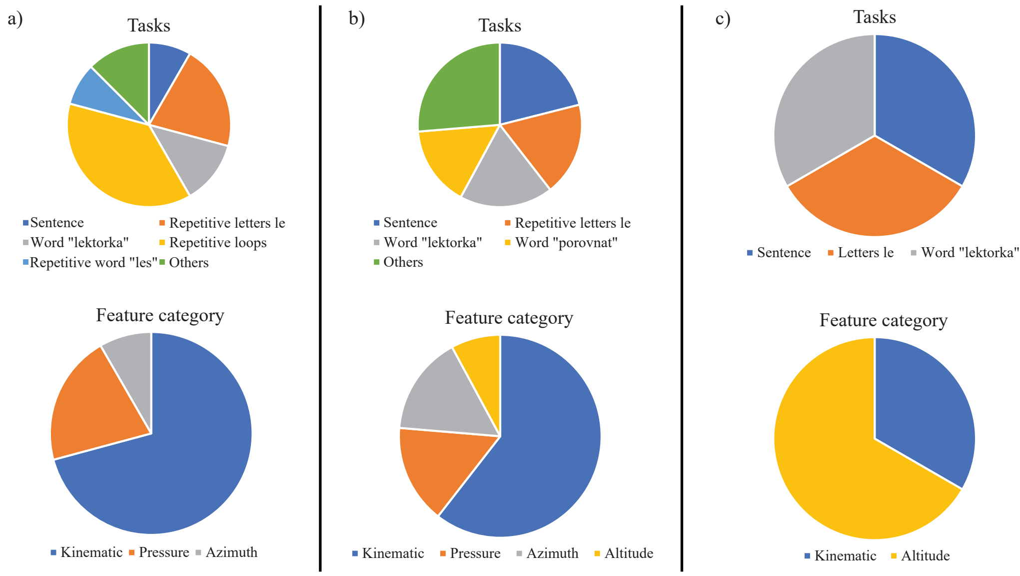

Fig. 1. Distribution of particular tasks and derived features in the trained XGBoost models: a) classification analysis; b) regression analysis (PD duration); c) regression analysis (UPDRS V).

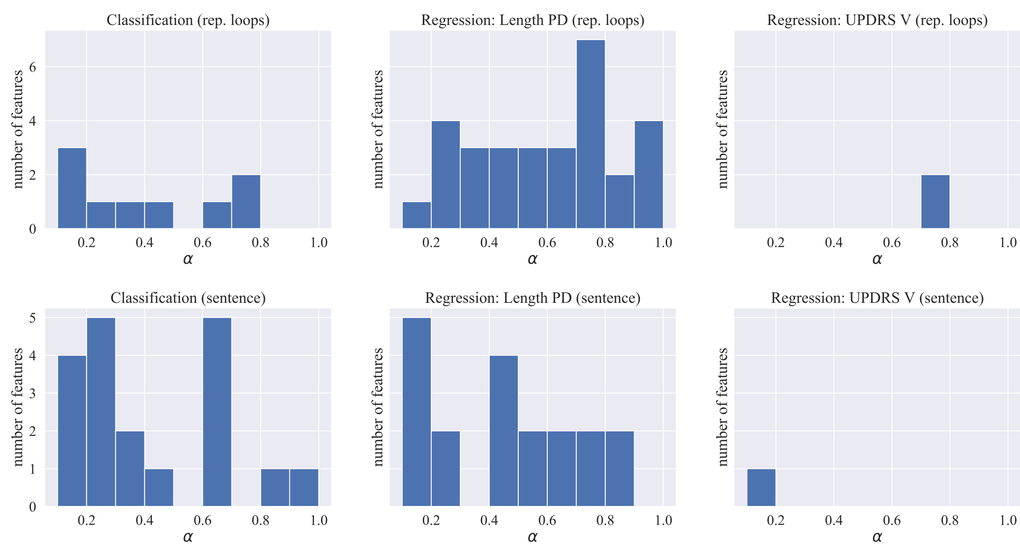

Fig. 2. Distributions of FD order α among the fine-tuned parameters.

and azimuth parameters are also modeled. Based on the distribution reported in the upper part of column a) (see Figure 1), it is noticeable that the highest discriminative power provide repetitive loops. Regarding the results of regression analysis, the most suitable task for further optimization of the FD-based features is the sentence (see the upper part of column b) and c) in Figure 1). In comparison with our previous results [14], the estimation error of PD duration differs minimally, however, the resulted models include parameters coming from all feature categories. In the case of UPDRS V, the value of EER is similar again, but in this case, most of the features are tilt-based instead of kinematic-based. Considering the facts mentioned above, we can conclude that utilizing FD analysis of pressure, azimuth and tilt does not have any noticeable effect on model's performance.

Secondly, we performed the optimization of FD-based features extracted from the repetitive loops and sentence. We recalculated these features for α from 0.01 to 1.00 with 0.01 step (100 FD-based features for one time sequence) in order to identify the optimal values of α. As can be seen in the upper part of Table III, ACC for both tasks is lower in comparison with the all task classification. It is the consequence of using just a single task for classification, and it corresponds with previous works [10], [11], [14], [20]. Nevertheless, we have to point out that the main objective of this step is not to increase the classification accuracy but to identify the optimal values of α. It is visible from the first column of Figure 2 that the optimal α for PD classification is in ranges from 0.05 to 0.35 and 0.60 to 0.75. Regarding the results of regression analysis, in the case of UPDRS V estimation, EER is slightly worse in comparison with the first step. In the case of PD duration estimation, EER is slightly better (by $2-3.5\,\%$) than in the first step and also in comparison with our previous work [14] it was improved by 5 %. These results are probably caused by the usage of fine-tuned FD-based features. From the middle and last column in Figure 2, we may conclude that the optimal value of α for PD severity assessment and duration estimation is in ranges from 0.05 to 0.45 and from 0.65 to 0.80. By intersectioning optimal α ranges of classification and regression analysis, we created a final optimal range of α from 0.05 to 0.45 and from 0.60 to 0.80, that is recommended to be used in the field of PD dysgraphia analysis.

V. Conclusion

Based on the results we can conclude that applying FD on pressure, azimuth and tilt profiles has no influence (negative or positive) on classification performance. However, there was a notable improvement in the estimation of PD duration by 19 %. Next, in the field of PD dysgraphia analysis, we identified the optimal values of the FD order, which should be in the range from 0.05 to 0.45 or from 0.60 to 0.80. Identification of these ranges enables significant reduction of computational cost (by approximately 50 %), because researchers do not have to explore the full range of possible values of the FD order during quantitative analysis of PD dysgraphia.

This study has several limitations and possible parts, that could be further improved/explored. Since the processed dataset is small, further studies on this topic should be held in order to generalize the results. Next, the FD order could be further tuned for horizontal and vertical movement separately. And finally, some other approximations of FD (e.g. Caputo's) can further improve classification or regression performance.

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