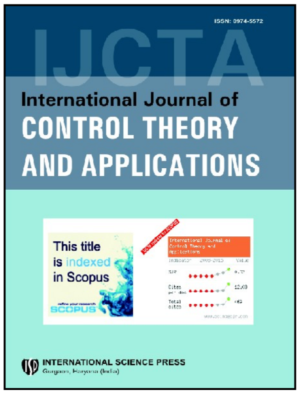

International Journal of Control Theory and Applications

ISSN : 0974-5572

Volume 10 • Number 10 • 2017

A Novel Method for prediction of Parkinson Disease (Voice Dysphonia): Statistical Approach

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Abstract: This paper attempts to estimate the progressiveness of Parkinson disease (PD) using statistical techniques is considered. Various studies reported that, speech is an earliest indicator of PD and 90% of PD patients suffer from some form of vocal impairment. Hence PD dataset that contains voice signal of human is used for statistical analysis. In the proposed system, a mapping between voice signal and UPDRS (Unified Parkinson's Disease Rating Scale) score is explored. Two linear regression techniques, Least Square (LS) and Iteratively Reweighted Least Squares (IRLS) are used to evaluate the regression coefficient between voice measure and actual UPDRS score thereby predicting the UPDRS score. Also, we have computed and compared the errors – Mean Absolute Error (MAE) and Mean Squared Error (MSE) using LS and IRLS. The association strength between the dysphonia measures (voice features) and how these measures are correlated with actual motor and total UPDRS score is determined using Spearman rank correlation coefficients. Kernel Density Estimation (KDE) is used to explore the probability density between dysphonia measures and UPDRS scale using Gaussian kernels (GK).

Keyword: Parkinson disease progression, dysphonia measures, correlation coefficient, probability density, regression coefficient, UPDRS score

I. INTRODUCTION

PD is the most common neurological disorder after Alzheimer [1]. It is a chronic; slowly progressive disease. [2] The first symptom noticed by People with PD (PWP) is tremor which appears in one side of the body and later spread to another side of the body. [3] This symptom also affects the lips, tongue and chin. The other symptoms include rigidity, movement disorder, loss of sense of smell, sleep disorder and vocal impairment. [4] Also there is no cure for PD; its motor symptom can only be medicated.

Of all the symptoms, vocal impairment can be considered for PD detection because 90% of PD patients suffer from some form of vocal impairment.[5] With PD progression, two speech disorders occurs are *dysphonia* (breathiness, creakiness or hoarseness in the voice) and *hypophonia* (reduction in voice volume). Dysphonia is the initial indicators in the detection of the PD.

Dysphonia has either organic or functional causes due to destruction of any one of the vocal organs and hence it regularly observed in the production of vowel sound. UPDRS maps the physical test observations to a *metric* value for tracking progression of the PD symptoms. The total-UPDRS ranges from 0-176, 0 refers to healthy state and 176 refer to total disability. The motor-UPDRS which ranges from 0-108 used to measure various motor symptoms.

Fuzzy k-nearest neighbour approach is used for detecting PD. [6] A system with application of artificial neural network was proposed for voice signal of PD data set to diagnose people with PD. [7] Sang-Hong Lee et al. proposed a system using gait characteristics to detect PD. [8]

D. Wu *et al.* proposed a system based on neural network and particle sworn optimization to predict PD tremor onset. [9] Little *et al.* considered both traditional and non-standard methods to detect dysphonia through which they could distinguish the PD patients from the healthy people and also introduced a new measure called Pitch Period Entropy. [5] Their experiments on 31 people provided 91.4% correct classifications and were also suitable for telemonitoring applications to provide remote diagnosis of patients.

A features selection algorithm, relief-F to reduce no. of attributes and support Vector Machine [10] is built for PD dataset, for detecting the disease with 96.88% accuracy. Indira Rustempasic et al. proposed a system [11] to classify PD dataset (voice dataset) between normal speaking persons and person with PD. The aim of the system is to detect whether PD affected person have speech/voice disorder.

The paper is organized with different sections as given below: Section 2 describes and proposes a system for predicting the PD. Section 3 explains the methods used in the proposed system. Section 4 deals with the experimental evaluation. Section 5 explains the experimental results. Conclusion and extension of the work are provided in section 6.

II. PREDICTION OF PD

Several works have addressed the PD automatic identification. In the proposed system, we have explored a mapping between dysphonia measures and motor-UPDRS/total-UPDRS score. Correlation and regression coefficients are evaluated between the voice signal and both the UPDRS score. Spearman rank correlation coefficients, KDE and two linear regression techniques LS and IRLS [12] are used in our proposed system. Figure 1 exhibits the overall concept of prediction of Parkinson disease.

Figure 1: Overall Structure of Prediction of Parkinson disease

(A) Correlation Analysis and Probability density

The strength of the association between dysphonia measures and UPDRS scores (motor and total) are predicted and analysed. Also, the association strength between the dysphonia measures is examined. The probability density between dysphonia measures and UPDRS scores (motor/total) is explored.

(B) Regression analysis

LS and IRLS methods are used for predicting PD. In both the case, regression coefficient between the 16 dysphonia measures and UPDRS (motor and total) is calculated and then the UPDRS (motor/total) value is predicted accordingly.

Let m_i be the value of i^{th} dysphonia measures and c_i is the regression coefficient between the i^{th} dysphonia measure and UPDRS (motor/total) score. Let Y be the actual UPDRS score and the predicted UPDRS score Y_p is calculated using the equation EQ [1].

$$Y_p = \Sigma\, c_i m_i,\ i = 1 \text{ to } n \text{ …….. EQ} \qquad [1]$$

where n – no. of dysphonia measures.

MAE and MSE are evaluated between predicted UPDRS and actual UPDRS in both the regression methods. The difference between the actual UPDRS and predicted UPDRS is referred as residuals. In LS method, residuals are identically distributed Gaussian random variables and are independent which leads to a poor estimation of the parameters. Thus IRLS method is introduced to overcome the disadvantage of Gaussianity. IRLS achieves lesser prediction error than LS method by minimizing the mean absolute error.

III. METHODS

(A) Spearman Rank Correlation Coefficient

Spearman Rank correlation coefficient, ρ or r_s, is a non-parametric measure suitable for data that is not normally distributed. Pearson correlation coefficient algorithm works better in detecting a linear relationship between 2 variables but spearman rank correlation is for non-linear relationship. The important assumption of this algorithm is monotonic relationship. This correlation coefficient algorithm works by calculating Pearson's correlation on the ranked values of (X_i, Y_i). For a sample of size n, the values X_i, Y_i are converted to ranks rgX_1, rgY_1 and the correlation coefficient r_s is computed from equation EQ [2]:

$$r_s = \rho_{rgx,rgy} = \frac{\operatorname{cov}(rg_x, rg_y)}{\sigma_{rgx}\sigma_{rgy}}$$

where

- ρ - Pearson correlation coefficient applied to the rank variables.
- Cov (rgX_i, rgY_i) - covariance of the rank variables.
- σ_{rgx}, σ_{rgy} - standard deviations of the rank variables.

In our proposed system, a non-parametric statistical test is used as dataset was non-normal and Á-values are computed between each measure and UPDRS. Also correlation coefficient is determined between the dysphonia measures which are used to examine the multicollinearity between the measures.

(B) Kernel Density Estimation (KDE)

KDE, a data smoothing problem, determines probability density function of a random variable. It is a nonparametric way in which inferences on the populations are deducted on the basis of a finite sample.

Let (x_1, x_2…, x_n) be the sample data. The equation EQ [3] used to find kernel density function f is

$$\hat{f}_h(x) = \frac{1}{n}\sum_{i=1}^{n} K_h(x - x_i) = \frac{1}{nh}\sum_{i=1}^{n} K\Big(\frac{x - x_i}{h}\Big),$$

where

K = the kernel, a non-negative function

h = smoothing parameter (>0) It is a trade-off between the bias of the estimator and estimator variance.

$K_h(x)$ = 1/h K(x/h) = scaled kernel.

Mutual information (MI) is a fundamental measure of dependence between two random variables. The mutual information is computed by using appropriate equations. Get the normalized version of MI w.r.t the response variable, allowing direct comparison of MI values amongst the features in the design matrix X. Finally compute the kernel density and normalize the sum of the probabilities between 0 and 1.

(C) Least Square(LS)

LS method is a simple, standard approach in regression analysis. The method is to find the line of best fit. Finding the best fit is minimizing the sum of squared residuals (difference between actual and predicted value).

The two categories of LS methods are ordinary least squares and non-linear least squares. The ordinary LS used for statistical regression analysis. The non-linear problem is an iterative way of linear one and hence the core evaluation is same in both cases.

For the given set of input data **x** and output values f(**x**) = y, determine the regression coefficients b that minimizes the error in predicting output value f(x) over the whole data set. LS determine the coefficients **b** using EQ [4]

$$\hat{b} = \arg\min_{b} \sum_{i=1}^{N} (y_i - f(x))^2 = \arg_b \min \sum_{i=1}^{N} \left(y_i - \sum_{j=1}^{M} x_{ij} b_j \right)^2 \quad [4]$$

where (x_{i1},……….x_{ij}) - input vector, y_i - actual output value, f(x) – predicted output and N is the sample data size.

(D) Iteratively Reweighted Least Square(IRLS)

IRLS is a method to obtain solution for optimization problems. It is useful for the problems which has objective functions in the following form EQ [5]:

$$\underset{\boldsymbol{\beta}}{\operatorname{argmin}} \sum_{i=1}^{n} \left| y_i - f_i(\beta) \right|^p, \tag{5}$$

IRLS is an iteration method. The following weighted least squares equation EQ [6] is solved in iterative manner.

$$\beta^{(t+1)} = \underset{\boldsymbol{\beta}}{\operatorname{argmin}} \sum_{i=1}^{n} w_i(\beta^{(t)}) \left| y_i - f_i(\beta) \right|^2. \tag{6}$$

IRLS is used to find the maximum likelihood estimates of a generalized linear model. The technique minimizes the MAE rather than MSE.

IV. EXPERIMENTAL EVALUATION

The dataset was created by Athanasios Tsanas and Max Little, Oxford University, in collaboration with 10 medical centres in the US and Intel Corporation. [13]

This dataset consists of biomedical voice measurements of 42 people with PD. [14] The voice measurements are automatic voice recordings in the patient's homes were captured every week. These measurements are processed in the clinic to predict the UPDRS score. The UPDRS score value was assessed at baseline and after 3 months and 6 months.

The attributes include subject id, age, gender, motor-UPDRS, total-UPDRS, and dysphonia measures. The total number of voice recording in the dataset is 5,923.

(A) Dysphonia measures

The disorder of voice is termed as dysphonia. The sustained phonation of the vowel "ahh..." is processed using speech signal processing algorithm [15] such as Jitter, Shimmer, Pitch Period Entropy (PPE), Detrended Fluctuation Analysis (DFA) and Recurrence Period Density Entropy (RPDE) to produce the dysphonia measures. Table 1 depicts the attribute list (dysphonia measures) and its description.

Table 1
Description of dysphonia measures

Attribute	*Description*
Subject#	Unique idject
Age	Age
Sex	0' - male, '1' – female
test_time	number of days since hiring.
motor_UPDRS	motor UPDRS score
total_UPDRS	total UPDRS score
Shimmer, Shimmer(dB), Shimmer:APQ3, Shimmer:APQ5, Shimmer:APQ11, Shimmer:DDA	Measures of amplitude variation
Jitter(%), Jitter(Abs), Jitter:RAP, Jitter:PPQ5, Jitter:DDP	Measures of frequency variation
NHR,HNR	noise to harmonic ratio and harmonic to noise ratio
RPDE	A nonlinear dynamical complexity measure
DFA	Signal fractal scaling exponent
PPE	A nonlinear measure of fundamental frequency variation

V. EXPERIMENTAL ANALYSIS

Implementation is performed using statistical Analysis Toolbox in Matlab 2011b. All the built-in functions like spearman rank correlation coefficient, least square, iteratively reweighted least square and Kernel density Estimation are found in this toolbox.

Table 2 shows how the dysphonia measures are significantly correlated with actual UPDRS scores. Although the dysphonia measures are statistically significant with UPDRS score, magnitude of the correlation is not larger.

Table 2
Correlation between measures and UPDRS

S.No	*Measures*	*Motor UPDRS*	*Total UPDRS*
1	MDVP:jitter%	0.12908	0.12928
2	MDVP:jitter ABS	0.0731	0.1042
3	MDVP:Jitter:RAP	0.10568	0.10957
4	MDVP:PPQ5	0.1184	0.11677
5	Jitter:DDP	0.10545	0.10833
6	MDVP:Shimmer	0.13625	0.13862
7	MDVP:Shimmer(dB)	0.1405	0.14117
8	Shimmer:APQ3	0.11352	0.12049
9	Shimmer:APQ5	0.11961	0.1196
10	Shimmer:APQ11	0.16445	0.16113
12	NHR	0.13609	0.14858
13	HNR	0.15675	0.16235
14	RPDE	0.11603	0.15031
15	DFA	0.12953	0.14267
16	PPE	0.16187	0.15523

Table 3 presents the correlations between all the 16 dysphonia measures. All the measures are statistically significantly correlated. If Spearman_coefficent (Á) e" 0.95 then it indicates high correlation exist between the measures. Red color entries in the Table 3 indicate the high correlation between measures.

Table 3 is also used to examine the multi -collinearity between the dysphonia measures. Multi-collinearity exists when two measures are highly correlated. For example, Shimmer: APQ5 and MDVP: Shimmer is highly correlated (0.95).

Table 4 presents the probability density of the dysphonia measures. The mutual information and the normalized version of the mutual information is calculated for both motor-UPDRS and total-UPDRS, then kernel density is computed and the sum of the probabilities is normalized between 0 and 1.

Table 3
Correlation between measures

S. No	*Features*	*MDVP: jitter%*	*MDVP: jitter ABS*	*MDVP: Jitter: RAP*	*MDVP: PPQ5*	*Jitter: DDP*	*MDVP: Shim-mer*	*MDVP: Shim-mer (dB)*	*Shim-mer: APQ 3*	*Shim-mer: APQ 5*	*Shim-mer: APQ 11*	*Shim-mer: DDA*	*NHR*	*HNR*	*RPDE*	*DFA*
1	MDVP:jitter ABS	0.90														
2	MDVP:Jitter: RAP	0.95	0.82													
3	MDVP:PPQ5	0.95	0.88	0.94												

contd. table 3

S. No	*Features*	*MDVP: jitter%*	*MDVP: jitter ABS*	*MDVP: Jitter: RAP*	*MDVP: PPQ5*	*Jitter: DDP*	*MDVP: Shimmer*	*MDVP: Shimmer (dB)*	*Shimmer: APQ 3*	*Shimmer: APQ 5*	*Shimmer: APQ 11*	*Shimmer: DDA*	*NHR*	*HNR*	*RPDE*	*DFA*
4	Jitter:DDP	0.95	0.82	**1.0**	0.94											
5	MDVP: Shimmer	0.65	0.62	0.65	0.68	0.64										
6	MDVP: Shimmer(dB)	0.67	0.63	0.65	0.70	0.66	**0.98**									
7	Shimmer: APQ3	0.61	0.58	0.63	0.66	0.63	**0.98**	0.96								
8	Shimmer: APQ5	0.62	0.62	0.61	0.66	0.62	**0.99**	**0.97**	**0.98**							
9	Shimmer: APQ11	0.63	0.63	0.60	0.66	0.60	0.96	0.95	0.90	0.96						
10	Shimmer: DDA	0.61	0.58	0.63	0.65	0.62	**0.98**	0.96	**1.00**	**0.98**	0.91					
11	NHR	0.79	0.74	0.74	0.74	0.74	0.64	0.68	0.61	0.62	0.62	0.62				
12	HNR	0.76	0.75	0.72	0.72	0.72	0.79	0.78	0.78	0.79	0.79	0.78	0.76			
13	RPDE	0.52	0.63	0.44	0.44	0.45	0.48	0.46	0.43	0.45	0.50	0.43	0.60	0.64		
14	DFA	0.43	0.49	0.43	0.43	0.42	0.28	0.27	0.26	0.26	0.30	0.26	0.15	0.35	0.19	
15	PPE	0.84	0.80	0.77	0.77	0.77	0.64	0.65	0.58	0.58	0.66	0.59	0.72	0.75	0.55	0.41

Table 4
Kernal Density for motor and total UPDRS

Sl. No.	*Measures*	*motor UPDRS True MI*	*motor UPDRS MI*	*total UPDRS True MI*	*total UPDRS MI*
1	jitter%	0.1421	0.1345	0.1421	0.1345
2	jitter ABS	0.1400	0.1365	0.1400	0.1365
3	Jitter:RAP	0.1331	0.1337	0.1331	0.1337
4	Jitter:PPQ5	0.1465	0.1409	0.1465	0.1409
5	Jitter:DDP	0.1345	0.1326	0.1345	0.1326
6	Shimmer	0.1489	0.1306	0.1489	0.1306
7	Shimmer(dB)	0.1526	0.1441	0.1526	0.1441
8	Shimmer:APQ3	0.1540	0.1349	0.1540	0.1349
9	Shimmer:APQ5	0.1390	0.1358	0.1390	0.1358
10	Shimmer:APQ11	0.1363	0.1363	0.1363	0.1363
11	Shimmer:DDA	0.1529	0.1365	0.1529	0.1365
12	NHR	0.1573	0.1322	0.1573	0.1322
13	HNR	0.1394	0.1370	0.1394	0.1370
14	RPDE	0.1556	0.1358	0.1556	0.1358
15	DFA	0.1390	0.1337	0.1390	0.1337
16	PPE	0.1569	0.1334	0.1569	0.1334

Table 5 and Table 6 present MAE and MSE for all dysphonia measures against motor UPDRS and total UPDRS values using two linear prediction methods LS and IRLS. The MAE and MSE are evaluated for both training and testing dataset. Both the errors are calculated between the actual and predicted UPDRS value for all the 16 measures piecewise.

In case of LS method, MAE for training dataset and test dataset remains the same and also there is not much difference in case of MSE.

Table 5
Comparison of MAE and MSE for Motor UPDRS using LS and IRLS

sl.no	*Parameters*	*Methods*	*Mean Absolute Error (MAE)*		*Mean Squared Error (MSE)*	
			Training dataset	*Test dataset*	*Training dataset*	*Test dataset*
1	**jitter%**	LS	0.003170	0.003170	0.000034	0.000034
		IRLS	0.000025	0.003966	0.000025	1.633966
2	**Jitter(ABS)**	LS	0.000025	0.000025	0.000000	0.000000
		IRLS	0.000000	2.036780	21.9888	0.0000
3	**Jitter:RAP**	LS	0.001690	0.001700	0.000010	0.000010
		IRLS	0.0016	0.0016	0.0000	0.0000
4	**Jitter:PPQ5**	LS	0.001820	0.001820	0.000014	0.000014
		IRLS	0.0017	0.0017	0.0000	0.0000
5	**Jitter:DDP**	LS	0.005090	0.005090	0.000095	0.000092
		IRLS	0.0049	0.0049	0.0001	0.0001
6	**Shimmer**	LS	0.017370	0.017350	0.000758	0.000753
		IRLS	0.0170	0.0170	0.0008	0.0008
7	**Shimmer(dB)**	LS	0.157210	0.157380	0.059700	0.059870
		IRLS	0.1547	0.1548	0.0606	0.0605
8	**Shimmer:APQ3**	LS	0.009160	0.009140	0.000201	0.000201
		IRLS	0.0090	0.0090	0.0002	0.0002
9	**Shimmer:APQ5**	LS	0.010760	0.010720	0.000306	0.001986
		IRLS	0.0042	0.0105	0.0003	0.0003
10	**Shimmer:APQ11**	LS	0.013540	0.013560	0.000447	0.000447
		IRLS	0.0257	0.0134	0.0004	0.0004
11	**Shimmer:DDA**	LS	0.027400	0.027470	0.001790	0.001780
		IRLS	0.0236	0.0270	0.0018	0.0018
12	**NHR**	LS	0.024760	0.022710	0.009310	0.003240
		IRLS	0.0215	0.0231	0.0036	0.0035
13	**HNR**	LS	7.704610	7.690700	87.837440	0.000568
		IRLS	0.0219	7.7111	88.0999	88.2613
14	**RPDE**	LS	0.173620	0.160540	0.042550	0.042711
		IRLS	0.1731	0.1736	0.0425	0.0427
15	**DFA**	LS	0.208870	0.208720	0.062970	0.062950
		IRLS	0.0264	0.2079	0.0633	0.0633
16	**PPE**	LS	0.087310	0.087160	0.012290	0.012320
		IRLS	0.0284	0.0869	0.0123	0.0123

Table 6
Comparison of MAE and MSE for Total UPDRS using LS and IRLS

sl.no	*Parameters*	*Methods*	*Mean Absolute Error (MAE)*		*Mean Squared Error (MSE)*	
			Training dataset	*Test dataset*	*Training dataset*	*Test dataset*
1	**jitter%**	LS	0.0032	0.0032	0.0000	0.0000
		IRLS	0.0031	0.0031	0.0000	0.0000
2	**Jitter(ABS)**	LS	0.0000	0.0000	0.0000	0.0000
		IRLS	0.0011	1.9704	1.9710	21.1221
3	**Jitter:RAP**	LS	0.0017	0.0017	0.0000	0.0000
		IRLS	0.0001	0.1515	0.0000	0.0000
4	**Jitter:PPQ5**	LS	0.0018	0.0018	0.0000	0.0000
		IRLS	0.0011	0.0972	0.0963	0.0238
5	**Jitter:DDP**	LS	0.0050	0.0050	0.0001	0.0001
		IRLS	0.0014	0.6867	0.0000	0.0000
6	**Shimmer**	LS	0.0171	0.0171	0.0000	0.0000
		IRLS	0.0014	0.7083	0.0000	0.0000
7	**Shimmer(dB)**	LS	0.1564	0.1561	1.9710	21.1221
		IRLS	0.0014	0.5555	0.0000	0.0000
8	**Shimmer:APQ3**	LS	0.0090	0.0090	0.0000	0.0000
		IRLS	0.0014	0.5818	0.0000	0.0000
9	**Shimmer:APQ5**	LS	0.0106	0.0106	0.0963	0.0238
		IRLS	0.0014	0.6029	0.0963	0.0238
10	**Shimmer:APQ11**	LS	0.0135	0.0135	0.0963	0.0238
		IRLS	0.0014	0.5961	0.0963	0.0238
11	**Shimmer:DDA**	LS	0.0270	0.0270	0.0963	0.0238
		IRLS	0.0014	0.5943	0.0963	0.0238
12	**NHR**	LS	0.0253	0.0254	0.0963	0.0238
		IRLS	0.0014	0.5953	0.0963	0.0238
13	**HNR**	LS	7.4270	7.4293	0.0963	0.0238
		IRLS	0.0014	0.5953	0.0963	0.0238
14	**RPDE**	LS	0.1660	0.1659	0.0963	0.0238
		IRLS	0.0012	0.6545	0.0963	0.0238
15	**DFA**	LS	0.2019	0.2022	0.0963	0.0238
		IRLS	0.0012	0.5170	0.0963	0.0238
16	**PPE**	LS	0.0866	0.0865	0.0963	0.0238
		IRLS	0.0014	0.5613	0.0963	0.0238

In the figure 2, the comparison of Mean Absolute Error (MAE) for LS and IRLS is shown in a bar chart format. As discussed in method description, the IRLS method shows more improvement in MAE than MSE. IRLS achieves the better prediction of UPDRS value by minimizing the MAE value for the following parameter Jitter(%), Jitter:DDP, Shimmer, Shimmer:APQ5, HNR, DFA, PPE. For example, the MAE for HNR using LS is 7.704 and MAE using IRLS is 0.0219.

In case of LS technique, the training MAE for motor UPDRS is 6.7 and for total UPDRS is 8.5. With IRLS, the training MAE for motor UPDRS is 6.4 and for total UPDRS is 8.3. The testing error remains less and nearer to the training error, indicating that the model has attained a reasonable estimate of the performance expected on source data. The difference between actual UPDRS value and predicted UPDRS value is typically low.

VI. CONCLUSION

Better accuracy of estimating UPDRS score is an essential factor in treating the symptoms of Parkinson disease. Linear statistical regression technique, LS and IRLS are applied on the voice dataset to estimate the UPDRS (motor and total) score. It is observed that with both the linear techniques, the testing error is less and nearer to the training error. The performance of IRLS is better in comparison to LS for predicting UPDRS scores.

The correlation and probability density between the dysphonia measures and UPDRS scores is examined. Multi-collinearity exits when two features are highly correlated. Multi-collinearity problem should be eliminated to get the better predicted UPDRS value. When multi-collinearity exists between two measures, one of the measures has to be skipped in predicting the UPDRS value.

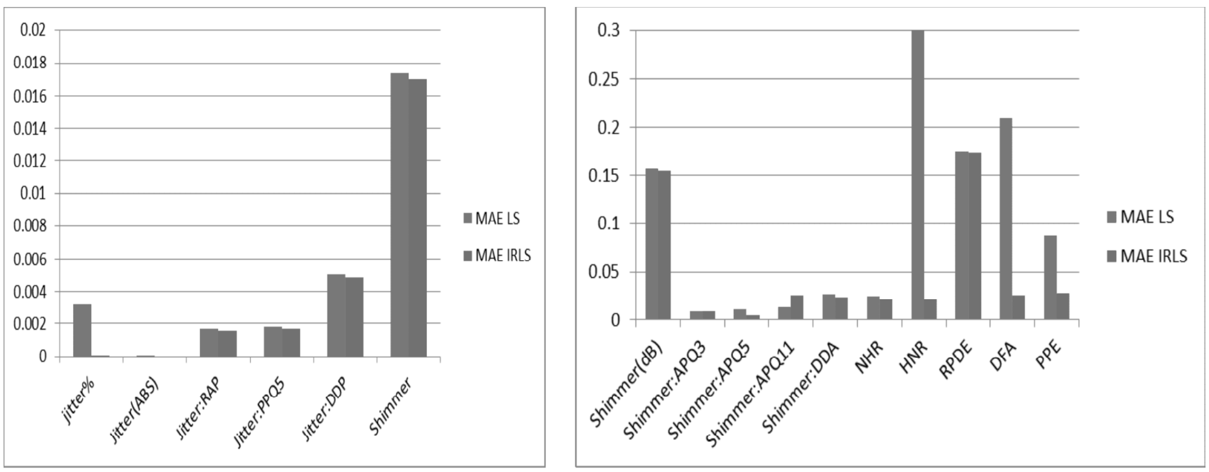

Figure 2: Comparison of MAE for LS and IRLS

For example, MDVP:jitter and MDVP:jitter:RAP are highly correlated (0.95). Here one of the measures has to be skipped in predicting the UPDRS. In this paper, all the 16 dysphonia measures are considered in predicting the UPDRS. Hence as a next step, determine the subset of dysphonia measure which will not have the problem of multicollinearity.

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