Graph Theory for Dimensionality Reduction: A Case Study to Prognosticate Parkinson's

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I. Summery

The study made its inference on the optimum number of features which might help to get the actual variables influence on the dependent variable like Parkinson's Disease (PD).This research constructs a binary PD prognosticator, upon selection of a relatively noiseless, reduced, representative feature-set using a novel method that transforms the data into a form able to be fed into an NN, a powerful pattern recognizer. It's always been tough to consider multiple regressors as principle and their level of significant correlation to the predicted variable due to the huge dimensionality of the small observations. The study explain its significance by ensuring some methods like Disjoint Set Union (DSU) and dimensionality reduction to show the accurate and precise number of features which are highly explained the predictive variables. DSU is a data structure that may be used on graphs to track a set of features partitioned into a number of non-overlapping subsets. For so, the study undertake computational graph theory which tries to define the construction of a formal mathematical model of real system by the proposition of pruning technique with others. Along with the research highly focused on dimensionality reduction for reducing the number of random variables under consideration, by reducing high dimensional space to the low dimensional space. Principle Component Analysis (PCA), Linear Discriminant Analysis (LDA) and Generalized Discriminant Analysis (GDA) are the participative methods of Dimensionality reduction.Computer scientists have endorsed PCA, LDA for lessening dimensions and the business intelligence community has proposed Apriori [Agrawal and Srikant, 1994] for analyzing huddling tendencies in features. PCA covers the highest possible variance in fewer dimensions with obscure inside intel whereas Apriori rule mining is more popular for nominal itemsets. But here the research narrow down its focus on PCA and LDA for approaching the variables to the linear correlation. The PCA and LDA helps to minimize the variance and maximize the distance between control and predicted variables which are mentioned in the study. Ultimately, the study proposes a means to construct network graphs from features using strong linear correlations, promoting the use of Spearman's r in a current world exalting Pearson's r. Notwithstanding, it's also observe that, dimensionality reduction with PCA does not reveal what features it projected onto another dimension, but DSU can reveal what features have been unified under a root till a timestamp. The elucidation has shown to improve performance through statistical inference on completely randomized, evenly sized k-fold (k = 10) datasets, for each decrement of r, but, multiple iterations are needed to tune r optimally for the most representative set.

II. Linear Discriminant analysis (LDA)

LDA is a supervised ML technique that is mostly used for classification and dimensionality reduction. The working of LDA is based on linear transformation of data (features) into small dimensional space, for maximum discrimination between classes. LDA, in machine learning, is search for the vectors based on linear combination of features in vector space that separates two or more classes. Furthermore, original data values are plotted on the vectors for evaluation of the classes division. When classes are overlapped on the particular data values, then transformation mechanism is adopted by the LDA for better separation of the classes. To achieve the better separation between the classes, LDA deploys a rule known as the Fisher ratio. The maximum value of the Fisher ratio means maximum distance between the two classes.

III. Principal Component Analysis(PCA)

Principal Component Analysis, or PCA, is a dimensionality-reduction method that is often used to reduce the dimensionality of large data sets, by transforming a large set of variables into a smaller one that still contains most of the information in the large set.

Reducing the number of variables of a data set naturally comes at the expense of accuracy, but the trick in dimensionality reduction is to trade a little accuracy for simplicity. Because smaller data sets are easier to explore and visualize and make analyzing data much easier and faster for machine learning algorithms without extraneous variables to process.

IV. Generalized Discriminant Analysis (GDA)

Generalized Discriminant Analysis (GDA) deals with nonlinear discriminant analysis using kernel function operator. The underlying theory is close to the support vector machines (SVM) insofar as the GDA method provides a mapping of the input vectors into high-dimensional feature space. Similar to LDA, the objective of GDA is to find a projection for the features into a lower-dimensional space by maximizing the ratio of between-class scatters to within-class scatter. The main idea is to map the input space into a convenient feature space in which variables are nonlinearly related to the input space.

V. Introduction

Parkinson's disease is a progressive nervous system disorder that affects movement. Symptoms start gradually, sometimes starting with a barely noticeable tremor in just one hand. Tremors are common, but the disorder also commonly causes stiffness or slowing of movement.

In the early stages of Parkinson's disease, your face may show little or no expression. Your arms may not swing when you walk. Your speech may become soft or slurred. Parkinson's disease symptoms worsen as your condition progresses over time.

Although Parkinson's disease can't be cured, medications might significantly improve your symptoms. Occasionally, your doctor may suggest surgery to regulate certain regions of your brain and improve your symptoms.

VI. Objective

Parkinson's disease (PD) is a serious neurodegenerative disorder. It is reported that most of PD patients have voice impairments. But these voice impairments are not perceptible to common listeners. Therefore, different machine learning methods have been developed for automated PD detection. However, these methods either lack generalization and clinically significant classification performance or face the problem of subject overlap.

VII. Methods

To overcome the problems discussed above, we attempt to develop a hybrid intelligent system that can automatically perform acoustic analysis of voice signals in order to detect PD. The proposed intelligent system uses linear discriminant analysis (LDA) for dimensionality reduction and genetic algorithm (GA) for hyperparameters optimization of neural network (NN) which is used as a predictive model. Moreover, to avoid subject overlap, we use leave one subject out (LOSO) validation.

VIII. Who Has Parkinson's?

1.Nearly one million people in the U.S. are living with Parkinson's disease (PD), which is more than the combined number of people diagnosed with multiple sclerosis, muscular dystrophy and Lou Gehrig's disease (or Amyotrophic Lateral Sclerosis). This is expected to rise to 1.2 million by 2030.
2.Approximately 60,000 Americans are diagnosed with PD each year.
3.More than 10 million people worldwide are living with PD.
4.Incidence of Parkinson's disease increases with age, but an estimated four percent of people with PD are diagnosed before age 50.
5.Men are 1.5 times more likely to have Parkinson's disease than women.

IX. Parkinson's signs and symptoms

Parkinson's disease signs and symptoms can be different for everyone. Early signs may be mild and go unnoticed. Symptoms often begin on one side of your body and usually remain worse on that side, even after symptoms begin to affect both sides.

Parkinson's signs and symptoms may include:

1.Tremor. A tremor, or shaking, usually begins in a limb, often your hand or fingers. You may rub your thumb and forefinger back and forth, known as a pill-rolling tremor. Your hand may tremble when it's at rest.

2.Slowed movement (bradykinesia). Over time, Parkinson's disease may slow your movement, making simple tasks difficult and time-consuming. Your steps may become shorter when you walk. It may be difficult to get out of a chair. You may drag your feet as you try to walk.
3.Rigid muscles. Muscle stiffness may occur in any part of your body. The stiff muscles can be painful and limit your range of motion.
4.Impaired posture and balance. Your posture may become stooped, or you may have balance problems as a result of Parkinson's disease.
5.Loss of automatic movements. You may have a decreased ability to perform unconscious movements, including blinking, smiling or swinging your arms when you walk.
6.Speech changes. You may speak softly, quickly, slur or hesitate before talking. Your speech may be more of a monotone rather than have the usual inflections.
6.Writing changes. It may become hard to write, and your writing may appear small.

X. cause of Parkinson's disease

In Parkinson's disease, certain nerve cells (neurons) in the brain gradually break down or die. Many of the symptoms are due to a loss of neurons that produce a chemical messenger in your brain called dopamine. When dopamine levels decrease, it causes abnormal brain activity, leading to impaired movement and other symptoms of Parkinson's disease.

The cause of Parkinson's disease is unknown, but several factors appear to play a role, including:

1.Genes. Researchers have identified specific genetic mutations that can cause Parkinson's disease. But these are uncommon except in rare cases with many family members

affected by Parkinson's disease.

However, certain gene variations appear to increase the risk of Parkinson's disease but with a relatively small risk of Parkinson's disease for each of these genetic markers.

2.Environmental triggers. Exposure to certain toxins or environmental factors may increase the risk of later Parkinson's disease, but the risk is relatively small.

Researchers have also noted that many changes occur in the brains of people with Parkinson's disease, although it's not clear why these changes occur. These changes include:

1.The presence of Lewy bodies. Clumps of specific substances within brain cells are microscopic markers of Parkinson's disease. These are called Lewy bodies, and researchers believe these Lewy bodies hold an important clue to the cause of Parkinson's disease.

2.Alpha-synuclein found within Lewy bodies. Although many substances are found within Lewy bodies, scientists believe an important one is the natural and widespread protein called alpha-synuclein (a-synuclein). It's found in all Lewy bodies in a clumped form that cells can't break down. This is currently an important focus among Parkinson's disease researchers.

XI. Risk factors for Parkinson's disease

Risk factors for Parkinson's disease include:

1.Age. Young adults rarely experience Parkinson's disease. It ordinarily begins in middle or late life, and the risk increases with age. People usually develop the disease around age 60 or older.

2.Heredity. Having a close relative with Parkinson's disease increases the chances that you'll develop the disease. However, your risks are still small unless you have many relatives in your family with Parkinson's disease.

3.Sex. Men are more likely to develop Parkinson's disease than are women.

4.Exposure to toxins. Ongoing exposure to herbicides and pesticides may slightly increase your risk of Parkinson's disease.

XII. Environmental Risk and Protective Factors

Studies consistently suggest that there are environmental

risk factors for PD, although the magnitude of the associations varies. One meta-analysis,21 based on 11 to 16 studies

(depending on the exposure considered), reported an elevated risk for PD with exposure to rural residence (odds ratio [OR] 1.56, 95 percet confidence interval [CI] 1.18Y2.07), use of well water (OR 1.26, 95 percent CI 0.97Y1.64), living on a farm/exposure to farm animals (OR 1.42, 95 percent CI 1.05Y1.91), and pesticide

exposure (OR 1.85, 95 percent CI 1.31Y2.60). Interest in pes- ticides and herbicides as risk factors for PD is high. In

a meta-analysis of case-control studies conducted in North America, Europe, and Asia, 17 of 19 studies reported positive associations between pesticide/herbicide exposure and PD (combined OR 1.94, 95 percent CI 1.49Y2.53).22 Exposures that may protect against the development of PDV-most commonly, cigarette smoking (nicotine intake) and coffee drinking (caffeine intake)Valso have been examined. In a comprehensive meta-analysis, Herna n and colleagues23 examined 48 smoking-related studies and 13 coffee-related studies conducted in North and South America, the Caribbean, and Europe (mainly case-control studies, but also included some

prospective cohort studies). These authors reported strong pro- tective effects for "ever" versus "never" smokers (OR 0.59,

95 percent CI 0.54Y0.63) and for past smokers (OR 0.39, 95 percent CI 0.32Y0.47). Coffee drinkers (compared with non-drinkers) also derived some protection (OR 0.69, 95 percent CI 0.73Y0.84). There were fewer studies of coffee drinking, but they were relatively consistent in showing reduced risk for PD.

XIII. Complications

Parkinson's disease is often accompanied by these additional problems, which may be treatable:

1.Thinking difficulties. You may experience cognitive problems (dementia) and thinking difficulties. These usually occur in the later stages of Parkinson's disease. Such cognitive problems aren't very responsive to medications.

2.Depression and emotional changes. You may experience depression, sometimes in the very early stages. Receiving treatment for depression can make it easier to handle the other challenges of Parkinson's disease.

3.You may also experience other emotional changes, such as fear, anxiety or loss of motivation. Doctors may give you medications to treat these symptoms.

4.Swallowing problems. You may develop difficulties with swallowing as your condition progresses. Saliva may accumulate in your mouth due to slowed swallowing, leading to drooling.

5.Chewing and eating problems. Late-stage Parkinson's disease affects the muscles in your mouth, making chewing difficult. This can lead to choking and poor nutrition.

6.Sleep problems and sleep disorders. People with Parkinson's disease often have sleep problems, including waking up frequently throughout the night, waking up early or falling asleep during the day.

People may also experience rapid eye movement sleep behavior disorder, which involves acting out your dreams. Medications may help your sleep problems.

7.Bladder problems. Parkinson's disease may cause bladder problems, including being unable to control urine or having difficulty urinating.

8.Constipation. Many people with Parkinson's disease develop

constipation, mainly due to a slower digestive tract.

You may also experience:

1.Blood pressure changes. You may feel dizzy or lightheaded when you stand due to a sudden drop in blood pressure (orthostatic hypotension).
2.Smell dysfunction. You may experience problems with your sense of smell. You may have difficulty identifying certain odors or the difference between odors.
3.Fatigue. Many people with Parkinson's disease lose energy and experience fatigue, especially later in the day. The cause isn't always known.
4.Pain. Some people with Parkinson's disease experience pain, either in specific areas of their bodies or throughout their bodies.
5.Sexual dysfunction. Some people with Parkinson's disease notice a decrease in sexual desire or performance.

XIV. Estimated Healthcare Costs Related to PD in the U.S.

The combined direct and indirect cost of Parkinson's, including treatment, social security payments and lost income, is estimated to be nearly 52(United States Dollar) billion per year in the United States alone.

Medications alone cost an average of 2,500(United States Dollar) a year and therapeutic surgery can cost up to 100,000(United States Dollar) per person.

XV. Parkinson's Prevalence

When a large population of people have a disease like Parkinson's disease (PD), it's essential to have accurate numbers of how many people have the disease, where they live and why they have it. This information helps researchers, healthcare professionals and even legislators determine how many resources should be allocated to addressing and treating a disease. Key terms, like incidence and prevalence, are often used when talking about who has PD.

Incidence: A measure of new cases arising in a population over a given period of time, typically incidence is measured as the number of people diagnosed per year.

Prevalence: A measurement of all individuals affected by the disease at a particular time (for example, the number of people with Parkinson's on March 19, 2018).

To calculate an accurate estimate of the prevalence of Parkinson's throughout North America, the Parkinson's Foundation formed the Parkinson's Prevalence Project in 2014. Prior estimates were based on a small number of cases from areas that are not representative of the nation as a whole — like a previous study from 40 years ago that extrapolated the 26 people with PD in a rural Mississippi county

In addition to finding the most comprehensive number to date, the new prevalence study sought to answer two main questions:

Is the prevalence of PD uniform throughout North America or does it vary by study and/or geography? What will the data tell us about the prevalence of Parkinson's and about the disease itself?

The new study draws from larger and more diverse populations. The Parkinson's Foundation Prevalence Project estimates that 930,000 people in the United States will be living with PD by the year 2020. This number is predicted to rise to 1.2 million by 2030.

XVI. Parkinson's Prevalence Facts

1.The last major PD prevalence study was completed in 1978.
2.The new study confirms that men are more likely to have Parkinson's than women and that the number of those diagnosed with PD increases with age, regardless of sex.
3.The new study found that the prevalence of people diagnosed with PD varies by region. Study researchers will now devote more time to find out how.

XVII. Importance of Establishing Parkinson's Prevalence Numbers

Parkinson's Prevalence estimates will help the Parkinson's Foundation attract the attention of federal and state government as well as the pharmaceutical industry to the growing need and urgency in addressing PD. This is an important first step to better understanding who develops PD and why.

The next phase of this study will be to determine the rate of PD diagnosis or incidence, how that has changed over time and what is the rate of mortality among those affected by PD. Determining the prevalence and incidence will allow the PD community to effectively advocate for additional money and resources necessary to support Parkinson's research.

Parkinson's Foundation Prevalence Project numbers highlight the growing importance of optimizing expert Parkinson's care and treatment for people with Parkinson's, which would help future caregivers and ease the strain on health and elder care systems.

By supporting this study, the Foundation works to better understand Parkinson's with the goal of solving this disease. Establishing these numbers and using them to educate PD communities and influence legislation will help the foundation provide tailored resources, outreach advocacy and to the underserved PD populations across the nation.

XVIII. Epidemiology of Parkinson's disease

Parkinson's disease (PD) affects 1-2 per 1000 of the population at any time. PD prevalence is increasing with age and PD affects 1 percent of the population above 60 years. The main neuropathological finding is -synuclein-containing Lewy bodies and loss of dopaminergic neurons in the substantia nigra, manifesting as reduced facilitation of voluntary movements. With progression of PD, Lewy body pathology spreads to neocortical and cortical regions. PD is regarded as a movement disorder with three cardinal signs: tremor, rigidity and bradykinesia. A recent revision of the diagnostic criteria excludes postural instability as a fourth hallmark and defines

supportive criteria, absolute exclusion criteria and red flags. Non-motor symptoms in PD have gained increasing attention and both motor and non-motor signs are now included among the supportive criteria. The cause of PD is unknown in most cases. Genetic risk factors have been identified, including monogenetic causes that are rare in unselected populations. Some genetic factor can be identified in 5-10 percent of the patients. Several environmental factors are associated with increased risk of PD. Autopsy studies show that the clinical diagnosis of PD is not confirmed at autopsy in a significant proportion of patients. Revised diagnostic criteria are expected to improve the clinician´s accuracy in diagnosing PD. Increasing knowledge on genetic and environmental risk factors of PD will probably elucidate the cause of this disease within the near future.

XIX. Treatment of People with PD Who Have Motor Fluctuations and Dyskinesias

Treatment of PD is most frequently based on medical interventions and surgery, including deep brain stimulation (DBS).28 In using medical interventions, both the occurrence of motor fluctuations (ie, "on times," when the medication is demonstrably effective, and "off times," when drugs wear off and PD symptoms return) and dyskinesias (when drug

treatment causes involuntary movements) should be considered. Levodopa combined with carbidopa is the gold standard

treatment for PD; however, adjunctive therapies frequently are combined, with a goal of reducing motor fluctuations and

dyskinesias. Compared with other dopamine agonists, entacapone and rasagiline were most effective in reducing off

times, according to AAN practice parameter guidelines.28 Other agonists were efficacious, although less so, in reducing off times, but the quality of studies supporting this conclusion

was lower. Evidence reviewed in the AAN practice guidelines28 did not establish the superiority of one medicine over

another in reducing off times. Sustained-release carbidopa/ levodopa and bromocriptine were not shown to reduce off times.

DBS is a surgical intervention that has received wide- spread attention and generated enthusiastic responses from

patients and practitioners. In DBS, an electrode is surgically implanted in the subthalamic nucleus (STN), globus thalamus (GPi), or ventral intermediate nucleus, introducing continuous

high-frequency electrical stimulation. DBS usually is indicated for patients with drug-related movements and fluctuations whose condition has not improved after undergoing all

medical management regimens, who show a clear response to levodopa following a levodopa challenge, who do not have a parkinsonian syndrome, who have no other major medical conditions; and who are in the middle (and sometimes late) stages of the illness. Further indications include refractory tremor that is disabling and no cognitive impairment on comprehensive testing. Pahwa and colleagues28 concluded that the DBS of the STN reduces off times and dyskiniseas,

improves motor function, and reduces reliance on medications; however, insufficient data exist regarding stimulation

of the globus thalamus and ventral intermediate nucleus. Research has been conducted to identify predictors of responsiveness to DBS, but conclusions were drawn only about DBS implantation in the STN. Preoperative response to levodopa, younger age, and shorter disease duration (G16 years) may predict greater improvements.28 Pahwa and colleagues28 emphasized that patients should be counseled about the risks and benefits of DBS.

XX. Evaluation and Treatment of Depression, Psychosis, and Dementia

In their evidence-based AAN practice parameter, Miya- saki and colleagues10 recommended using the Beck Depres- sion Inventory I, the Hamilton Depression Rating Scale, and

the Montgomery Asberg Depression Rating Scale to evaluate depression in PD. They concluded that evidence is insufficient

to support the use of any particular rating scale for psychosis in PD.

The efficacy of medical therapies in treating depression in PD is equivocal. Amitriptyline is not recommended for use in older adults because it has anticholinergic properties that can interfere with dopaminergic therapies (Table 2).

Benzodiazepines such as alprazolam, lorazepam, and diazepam may be used to treat anxiety; however, they may be poorly

tolerated, worsen or induce confusion, and worsen motor performance, and there is the potential for dependence with long-term use of this class of medications. Clozapine is effective in treating psychosis in PD. By contrast, olanzapine is somewhat effective but should be avoided because of its concurrent negative effects on motor function. Cholinesterase inhibitors show promise in treating the symptoms of dementia in PD (with relatively short-term effects) as well as DLB. Following publication of the AAN parameter, rivastigmine has been approved by the Food and Drug Administration for the treatment of dementia associated with parkinsonism. Some classes of medications commonly prescribed in the primary care physician setting are contraindicated for use in

PD because they may cancel out the effects of medical interventions in PD or even worsen PD symptoms. Thus, primary

care physicians should be aware that prescribing certain medications could be hazardous to the patient with PD or a PD-related syndrome (Table 2).

XXI. Proposed Methodology

Parkinson's Disease (PD) is a neurodegenerative old-age complication that affects the motor muscular system. It may cause a subject's speech to become monotonous, mumbled, hoarse and conversations often drift away from the topic—endorsing speech as a potential detector of the disease. The progressive nature of the disease merits a longitudinal study, sampling an individual after certain intervals. 2015 witnessed 6.2 million people falling victim to PD, resulting in 117,400 deaths worldwide. The dataset is a square, with a total of 756 examples and 754 features altogether. This type of datasets is an ideal fit for SVMs, but we tune and prune

the feature-space to claim success using an NN. The dataset we analyze for the proposed identification of Parkinson's is enriched with features defining 10 perspectives they are baseline , MFCC, intensity , wavelet , formant frequencies , TQWT, bandwidth , longitudinal study ID , vocal , gender. The study has a longitudinal nature and hence there exists an ID for the ease of tracking, along with different medical metrics.

A. Preparation of Adjacency Matrix

This paper bundles up multiple features applying DSU on a network graph produced on the basis of Spearman's rank correlation coefficient (r Spearman).We know,

$$r_s = 1 - \frac{6\sum D^2}{n\left(n^2-1\right)}$$

Fig. 1. r Spearman

The concept of graph theory has edges linking nodes. Similarly, in this work, we create a network graph that we subsequently represent using a 2D adjacency matrix.
A legit question may arise, as to why the usage of Spearman's (in place of Pearson's) r for defining the edges. It is due to certain advantages of the approach over Pearson's: robustness to extreme observations, ease of calculation and that the two variables can be ranked separately. We know r Person is:

$$r = \frac{\sum(x-\bar{x})(y-\bar{y})}{\sqrt{\sum(x-\bar{x})^2\sum(y-\bar{y})^2}}$$

Fig. 2. r Person

Graphs are simple models representing relations between pairs of objects. Contextually, oral features can play the objects and correlations can play the relations in a unidirectional graph. In statistics, Spearman's Rank Correlation Coefficient (Spearman's r) tells the magnitude and direction of a monotonic relationship between two variables, essentially outputting Pearson's r with additional advantages. However, the concept of correlation is bidirectional in nature and outputs a value within -1 to +1 (inclusive).
Firstly demolish boundaries 10 features. Then set a tolerable threshold for spearman's r and calculate Spearman's r for each features against all other features. After calculate consider absolute values of r Spearman. Then prepare a unidirectional network graph basis Pearson's r. Prepare an upper triangular matrix of Spearman's r. The output count of connections.

B. Performing DSU on Features

We assume a connection to be there between any two features if they are highly correlated. The threshold of the said high correlation is alterable and its tuning leads to different counts of features in the final feature-sets.The main routine eventually invokes the subroutines for the purpose. From Preparation of Adjacency Matrix the connections induct features and initialize features to their own roots. Then input the edges from the adjacency matrix. From disjoint sets until the list of edges is exhausted. After exhausted extract out the final roots. And lastly finalize the set of roots as a constructed feature set.

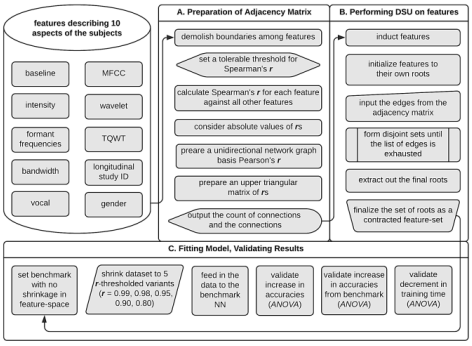

Fig. 3: a mindmap of the overall process followed for the proposed detection of *Parkinson's*

Fig. 3. a mindmap of the overall process followed for the proposed detection of Parkinson's

C. Fitting Models, Validating Results

Representative features (roots) from all disjoint sets are found by running DSU until the list of r-based connections (edges) is exhausted. With this output, we manually transfer the feature-sets to Tensor flow for predictive analysis. The higher the tolerance for r Spearman, the more the features. We first set a benchmark accuracy and incrementally improve on this by tuning the r-threshold 5 times. For results free of bias, specifications are kept the same for all cross validation. The features have been scaled via normalization for a smooth convergence of Gradient Descent (GD).

XXII. Parkinson's Disease Detection Using Dynamic Writing Traces Warping

Parkinson's disease (PD) is a kind of brain damage arising from diminishing in dopamine production. As conventional diagnostic methods are time-consuming, expensive and somewhat subjective, there is a need to propose a cost-effective and reliable detection system. Since one of the most prominent features of PD is impaired performance of motor skills, online handwriting analysis can provide a useful tool for detection of disease. In this study, a nonlinear method based on dynamic writing traces warping (DWTW) in combination with support vector machine classifier was developed. It was evaluated on a database of 32 healthy and 29 PD infected samples. Further, effects of eight handwriting tasks were investigated. The proposed method achieved high average accuracy rate of 88.33 percent , sensitivity of 86.43 percent and specificity of 89.5 percent . This study demonstrated the capability of DWTW features as a cost effective and discriminative measure for diagnosis of PD.

XXIII. Automated Detection of Parkinson's Disease

Automated Detection of Parkinson's Disease Based on Multiple Types of Sustained Phonations Using Linear Discriminant Analysis and Genetically Optimized Neural Network.

Objective:Parkinson's disease (PD) is a serious neurodegenerative disorder. It is reported that most of PD patients have voice impairments. But these voice impairments are not perceptible to common listeners. Therefore, different machine learning methods have been developed for automated PD detection. However, these methods either lack generalization and clinically significant classification performance or face the problem of subject overlap.

Methods: To overcome the problems discussed above, we attempt to develop a hybrid intelligent system that can automatically perform acoustic analysis of voice signals in order to detect PD. The proposed intelligent system uses linear discriminant analysis (LDA) for dimensionality reduction and genetic algorithm (GA) for hyperparameters optimization of neural network (NN) which is used as a predictive model. Moreover, to avoid subject overlap, we use leave one subject out (LOSO) validation. Results: The proposed method namely LDA-NN-GA is evaluated in numerical experiments on multiple types of sustained phonations data in terms of accuracy, sensitivity, specificity, and Matthew correlation

coefficient. It achieves classification accuracy of 95 percent on training database and 100 percent on testing database using all the extracted features. However, as the dataset is imbalanced in terms of gender, thus, to obtain unbiased results, we eliminated the gender dependent features and obtained accuracy of 80 percent for training database and 82.14 percent for testing database, which seems to be more unbiased results. Conclusion: Compared with the previous machine learning methods, the proposed LDA-NN-GA method shows better performance and lower complexity.

Clinical Impact: The experimental results suggest that the proposed automated diagnostic system has the potential to classify PD patients from healthy subjects. Additionally, in future the proposed method can also be exploited for prodromal and differential diagnosis, which are considered challenging tasks .

XXIV. DIAGNOSIS OF THE PARKINSON DISEASE BY USING DEEP NEURAL NETWORK CLASSIFIER

Parkinson disease occurs when certain clusters of brain cells are unable to generate dopamine which is needed to regulate the number of the motor and non-motor activity of the human body. Besides, contributing to speech, visual, movement, urinary problems, Parkinson disease also increases the risks of depression, anxiety, and panic attacks, disturbances of sleep. Parkinson disease diagnosis via proper interpretation of the vocal and speech data is an important classification problem. In this paper, a Parkinson disease diagnosis is realized by using the speech impairments, which is one of the earliest indicator for Parkinson disease. For this purpose, a deep neural network classifier, which contains a stacked autoencoder and a softmax classifier, is proposed. The several simulations are performed over two databases to demonstrate the effectiveness

of the deep neural network classifier. The results of the proposed classifier are compared with the results of the state-of-art classification method. The experimental results and statistical analyses are showed that the deep neural network classifier is very efficient classifier for Parkinson disease diagnosis.

XXV. Diagnosis of Parkinson's Disease Based on Gait, Speech Analysis and Machine Learning Techniques

Parkinson's disease (PD) is a long-term degenerative disorder of the central nervous system. The common symptoms are tremor, rigidity, slowness of movement, and difficulty with walking at early stages. Currently, PD can't be cured. And there are not really effective methods to diagnose it. However, machine learning is a new way for the diagnosis of PD. It can build a model from PD patients dataset, which can help classify PD and healthy people. In this review, the applications of machine learning for PD diagnosis by algorithms and data are analyzed. Several machine learning classifiers are briefly introduced, including artificial neural network (ANN), support vector machine (SVM), Naive Bayes (NB), K-Nearest Neighbor (k-NN). Next, the basis

of gait analysis is introduced, including gait circle and gait data, and then, each step of the machine learning processing is focused on. Two ways are concentrated to analyze speech signals - support vector machine (SVM) and artificial neural network (ANN). This review presents that machine learning has good performances for the diagnosis of PD. However, it can only be a diagnosis tool to help doctors because of its limited generalization. In the future, people should explore more effective algorithms with better generalization.

XXVI. Classification of Parkinson's Disease Using NNge Classification Algorithm

One of the most widely spread diseases around the world is Parkinson's disease (PD). This disease affects the human brain and results in sudden and random body movements. It progresses slowly and differently at every stage. Moreover, the disease has few known symptoms. Therefore, it is difficult for doctors to discover it in its initial stages. One of the main symptoms that can help researchers to predict the disease as early as possible is speech disorder. Many researchers have conducted several studies using voice recordings to produce an accurate

PD diagnosis system. One unique promising way to use the speech disorder as a helping factor to predict PD is by using machine learning techniques. In this paper, we used NNge classification algorithms to analyze voice recordings for PD classification. NNge classification is known to be an efficient algorithm for analyzing voice signals but has not been explored in details in this area. In this paper, a literature review of previous research papers about PD prediction was briefly presented. Then, an experiment using NNge classification algorithm to classify people into healthy people and PD patients

was performed. The parameters of the NNge algorithm were optimized. Moreover, SMOTE algorithm was used to balance the data. Finally, NNge and ensemble algorithms specifically, AdaBoostM1 was implemented on the balanced data. The final implementation of NNge using AdaBoost ensemble classifier had an accuracy of 96.30 percent .

XXVII. An efficient dimensionality reduction method on Parkinson's disease classification

An efficient dimensionality reduction method using filter-based feature selection and variational autoencoders on Parkinson's disease classification Parkinson's disease (Pd) is a progressive disease caused by the loss of brain cells and brings about speech and pronunciation defects during the early stages. This study revealed a Pd classification system based on vocal features extracted from the voice recordings of the individuals and proposed a hybrid dimensionality reduction methods to extract robust features. Proposed method took advantage of the prominent aspects of Variational Autoencoders (VAE) and filter-based feature selection models. Relief and Fisher Score were selected as filter-based methods for their effective performance in handling noisy data while VAE was used as a feature extractor due to the capability of preserving the regular latent space properties during the feature generation. In order to assess the effectiveness of the devised method, multi-kernel Support Vector Machines (SVM) classifier were trained with obtained deep feature representations. The combination of deep Relief features and SVM with multiple kernels distinguished Pd individuals from healthy subjects with an accuracy of 0.916 with 0.772 Matthews Correlation Coefficient (MCC) rates using only 30 features. Compared to results obtained without dimensionality reduction, proposed model provided approximately 9 percent and 22 percent improvements on accuracy and MCC rates, respectively.

All experimental results showed that models trained with the deep features had higher accuracy and MCC rates with those trained with Fisher Score and Relief selected features. In addition, all models trained with reduced features had higher classification performance than the model without selection. It was also concluded that using multiple kernels in the SVM boosted the classification performance.

XXVIII. Local discriminant preservation projection embedded ensemble learning based dimensionality reduction of speech data of Parkinson's disease

Speech has been widely used in the diagnosis of Parkinson39;s disease (PD). However, the collected PD speech data has the characteristics of high data redundancy, high aliasing and small sample size, which brings great challenges to PD speech recognition. Dimensionality reduction (DR) can effectively solve these problems. However, the existing methods for PD speech DR methods ignore the high noise and high aliasing characteristics of PD speech. In order to alleviate these problems, a weighted local discriminant preservation projection embedded ensemble algorithm is proposed to detect PD. The proposed algorithm preferentially reduces the intra-class variance of PD speech samples, and simultaneously increases the inter-class variance and maintains the neighborhood structure

of PD speech samples. In addition, the idea of ensemble learning is introduced to increase the stability of the model. Two widely used PD speech datasets for diagnosis and a treated Parkinson patient speech dataset collected by ourselves were used to verify the effectiveness of the proposed algorithm. Compared with existing PD speech DR methods, the proposed algorithm always has the highest Accuracy, Precision, Recall and G-mean in PD speech datasets. This shows that the proposed algorithm not only has excellent performance in classification of PD speech data, but also can handle imbalanced PD samples well. Even compared with the state-of-the-art DR methods, the proposed method was improved by at least 4.34 percent. In addition, the proposed algorithm not only achieved the highest detection accuracy, but also achieved the highest AUC in most case.

XXIX. Using deep neural networks along with dimensionality reduction techniques to assist the diagnosis of neurodegenerative disorders

The analysis of neuroimaging data is frequently used to assist the diagnosis of neurodegenerative disorders such as Alzheimer's disease (AD) or Parkinson's disease (PD) and has become a routine procedure in the clinical practice. During the past decade, the pattern recognition community has proposed a number of machine learning-based systems that automatically analyse neuroimaging data in order to improve the diagnosis. However, the high dimensionality of the data is still a challenge and there is room for improvement. The development of novel classification frameworks as TensorFlow, recently released as open source by Google Inc., represents an opportunity to continue evolving these systems. In this work, we demonstrate several computer-aided diagnosis (CAD) systems based on Deep Neural Networks that improve the diagnosis for AD and PD and outperform those based on classical classifiers. In order to address the small sample size problem we evaluate two dimensionality reduction algorithms based on Principal Component Analysis and Non-Negative Matrix Factorization (NNMF), respectively. The performance of developed CAD systems is assessed using 4 datasets with neuroimaging data of different modalities.

XXX. Machine Learning for PD Classification

The success of the PD classification studies is directly related to the selection of relevant feature extraction and artificial learning methods. In literature, many studies have used the same publicly available dataset consisting 31 instances (23 PD patients and 8 healthy individuals) with 195 sound recordings. Another PD dataset has 40 examples of 20 PD patients and 20 healthy individuals with multiple speech recordings. Both datasets have commonly extracted features such as vocal fundamental frequency, measures of variation in fundamental frequency, measures of variation in

amplitude etc. Since most of the PD detection studies are conducted experiments with these datasets, obtained features from both datasets generally are known as baseline features. Apart from the baseline features, other features that are based on signal processing techniques were also employed in PD detection. Signal-to-noise ratio (SNR), Mel-frequency cepstral coefficients (MFCC) and Tunable Q-factor Wavelet Transform (TQWT) are important tools for extracting relevant features in PD classification [18]. Rather than using separate feature types in model training, most studies use the combination of individual feature types to perform classification task. Extended feature space in these studies can be reduced via feature selection methods. Although, there are lots of symptoms among the people subjecting to the PD including slowed movement, posture and balance deficiencies, dysphonia which is defined as the changes in speech and articulation, is the most meaningful forerunner of PD. This is the reason why many studies are focused on speech based PD classification.

PD patients mainly face vocal defections which directly influence the vocal loudness, instability and frequency abnormality. Voice breaks and impaired vocal quality are also the other impairments that can be seen in PD patients. Speech processing techniques is commonly used to detect anomalies in speaking and it is often preferred in automated extraction of PD-related vocal features. During the last decade, several machine learning based studies have been performed in the detection of PD using vocal features. Tsanas et al. proposed a novel PD detection model with vocal features and they applied several feature selection techniques to select the top 10 features with high relevance scores as the inputs of such model. Least Absolute Shrinkage and Selection Operator (LASSO), Minimum Redundancy Maximum Relevance (mRmR), Relief and Local Learning-Base Feature Selection (LLBFS) were the methods used for feature selection and the performance of the selected features were evaluated with Random Forest (RF) and Support Vector Machines (SVM) classifiers. These classifiers resulted the performances up to 98.6 percent of precision rate using features from the shimmer, HNR and vocal fold excitation. Their study was also found out that the feature set with the lowest classification error was obtained from the Relief selection.

Rouzbahani and Daliri suggested a model for the detection of PD using voice signals. The inputs of the proposed model were based on parameters such as fundamental frequency, jitter, shimmer, pitch, HNR and several statistical measures based on these parameters. In order to select informative features among whole feature set, several feature selection methods such as correlation rates, Fisher's Discriminant Ratio, t-test and ROC curves were utilized. The number of optimal features was specified by wrapper approach that used SVM classifier to form a feature-performance curve. After the determination of optimal features, SVM, KNN and Discrimination-Function-Based classifiers were trained. The performances of the classifiers were measured with accuracy, error rate, sensitivity and specificity, and the best performance was obtained using the KNN classifier (with an accuracy rate of 93.82 percent).

Vikas and Sharma extractedee the different sets of features from voice signals with Praat software for distinguishing PD patients from healthy individuals. They compared MFCC, pitch, jitter and shimmer features along with the individual's glottal pulse. It was concluded that MFCC and glottal pulse did not show similar characteristics and had higher fluctuations when comparing PD patients and healthy individuals. When the values of jitter and shimmer features were examined, it was also found out that PD patients had higher feature values than healthy subjects.

In Parisi et al., they aimed to built a system based on a novel hybrid Artificial Intelligence-based classifier for the early diagnoses of PD. The data used in the study was obtained from the University of California-Irvine (UCI) Machine Learning repository which had 68 instances with dysphonic measures and clinical scores. Multi-Layer Perceptron (MLP) with custom cost function (function includes both accuracy and Area Under Curve (AUC) scores) was trained to assign the importance scores of the features. Thus, 20 features with high importance scores were given as inputs to a Lagrangian Support Vector Machine (LSVM) for classification. The overall performance of the proposed hybrid classification framework (MLP-LSVM) was compared against available similar studies and the results showed that the proposed feature-driven algorithm (MLP-LSVM) achieved 100 percent of accuracy rate.

In a recent study, the tunable Q-factor wavelet transform (TQWT) was applied to vocal signals of the individuals for the diagnoses of PD. The success of extracted TQWT features was compared with commonly used vocal features in PD studies. Experiments were conducted with the multiple voice instances of 252 individuals and different types of features sets were extracted from these instances. The feature subsets were given to numerous classifiers as input data and the outputs of such classifiers were combined with the majority voting scheme. This study concluded that TQWT features resulted better or close performance than the state-of-the-art voice features frequently used in PD classification. In addition, it was found out that the combination of MFCC and TQWT features boosted up the classification performance when the mRmR selection was performed on.

When aforementioned studies are examined, it is clear that related PD studies generally use voice-based features with machine-based learning algorithms. Although these studies make use of vocal-based features to deal with PD classification, there are some recent studies that extract features from different data sources such as electroencephalogram (EEG), smart pens and wearable sensors.

XXXI. Advantage

1. The paper precisely done on linear data correlation and firmly defines the principle variables influences on Parkinson disease.

2. Helps to remove data redundancy and compress the dataset precisely.

3.The interdisciplinary field, Clinical Data Mining, helps practitioners gain qualitative and quantitative insights from stored

medical health records using AI, statistics.
4. In this paper, using so many graph and table so, the reader read easily and understood properly.

XXXII. Disadvantage

1. The research didn't consider Generalized Discriminant Analysis (GDA) which certainly reject some random variables might influence predicted variable; Parkinson Disease.
2. The PCA LDA solely focused on linear correlation among the control and predicted variables mentioned in the paper are quite undesirable to presume the optimum number of control variables.
3. Higher possibility of data loss, mean and covariance might not enough to define dataset precisely.
4. PCA shows a 'black box' tendency by not clarifying which features have contributed the most/least to the final projections.

XXXIII. Every terminology of the paper used

Disjoint set union, dimensionality reduction, Spearman's r, Pearson's r, Parkinson's disease, statistical inference.

XXXIV. Why this paper is unique

This paper has introduced a novel feature-exclusion method based on the application of DSU, an algorithm belonging to computational graph theory. The research proposes a means to construct network graphs from features using strong linear correlations, promoting the use of Spearman's r in a current world exalting Pearson's r. In order to optimize computational costs regarding r calculation and DSU, the study seeks to make the network graphs unidirectional and reduces the corresponding matrix to an upper triangular form. The solution has shown to improve performance through statistical inference on completely randomized, evenly sized k-fold (k = 10) datasets, for each decrement r. Dimensionality reduction with PCA does not reveal what features it projected onto another dimension, but DSU can reveal what features have been unified under a root till a timestamp.

XXXV. Experimental Result section explanation

The documented research attempts to justify the effectiveness of a novel application of graph theory for a reduction in dimensionality. The course of this discussion starts out by demonstrating success in optimally training, eventually making its way to show the significant positive impact on incrementally increasing accuracies—using statistical inference. The discourse is concluded by comparative studies involving other dimensionality-reducing technologies and related literature. Before putting forth the argument bolstering the supremacy of our method, it is imperative to set a fair field for experimentations with all alterations. For all alterations, we cross-validate the results k-fold where k = 10, a widely-accepted numeric for validating medical diagnosis. Qualitatively, PCA shows a 'black box' tendency by not clarifying which features have contributed the most/least to the final projections; whereas DSU has the capability to reveal features that have flocked up.

XXXVI. Conclusion

Parkinson disease is a neurodegenerative disorder that is clinically diagnosed based on its motor features, with nonmotor symptoms being recognized commonly. The etiology remains unknown, but includes a combination of genetic and environmental risk factors, most commonly age and sex. Factors associated with increased mortality may include severity of parkinsonism, rate of worsening of parkinsonism, poor response to levodopa, early gait dysfunction and symmetry of parkinsonism. Some of these features may account for the possibility of a misdiagnosis of a Parkinson-plus syndrome as idiopathic Parkinson disease, and it is important to recognize this challenge in the differential diagnosis.

Although no neuroprotective treatments are yet available, many medical and surgical therapies exist that may be used in different stages throughout the course of disease for symptomatic treatment of both motor and nonmotor features. With the variety of ongoing trials on emerging therapies, we may see better options in the near future.

Key points 1.Parkinson disease is the second most common neurodegenerative disorder after Alzheimer disease; its cause is unknown.

2.Parkinson disease remains a clinical diagnosis, based on motor symptoms and signs; nonmotor symptoms, such as constipation, anosmia, rapid eye movement sleep behaviour disorder and depression, may precede motor symptoms by years.

3.Factors such as symptom severity, degree of functional impairment and patient preference should be taken into account when choosing treatment. Levodopa remains the gold-standard therapy for treatment of motor symptoms of Parkinson disease.

4.Motor fluctuations and dyskinesia will develop in most patients five to ten years into the disease while taking levodopa; many adjunctive oral therapies are available to reduce motor fluctuations.

5.Surgical therapies, including deep brain stimulation and levodopa–carbidopa intestinal gel, may be offered to patients who continue to have troublesome motor fluctuations and dyskinesia.

XXXVII. Future work of the paper

The future research may find out some non-linear correlations and undertake GDA methods to show the random relationships among the considering number of predicted and control variables.

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