Data Analysis and Prediction of Alzheimer's Disease in patients using new and existing algorithms[1]

Deborup Sanyal[2]
[2]*Department of Computer Engineering,*
Netaji Subhas Institute of Technology, University of Delhi

Abhinav Bhushan, PhD[3]
[3]*Department of Biomedical Engineering,*
Illinois Institute of Technology

Abstract

Alzheimer's disease is the most common cause of dementia worldwide, with the prevalence continuing to grow. This is a disease for which there is no diagnosis or cure. The last decade has witnessed a steadily increasing effort directed at discovering the etiology of the disease and developing pharmacological treatment. Recent developments include improved clinical diagnostic guidelines and improved treatment of both cognitive disturbance and behavioral problems. Here, we have data from a prospective clinical study given by a proprietary clinic that has recorded hundreds of biomarkers with Alzheimer's as the primary outcome. We aim to develop or use existing algorithms to analyze the given dataset and produce a model that predicts whether a patient has Alzheimer's disease or not. This research can be used as a contribution towards the data analysis of biomarkers that lead to Alzheimer's disease.

I. INTRODUCTION

Alzheimer's is a neurodegenerative disorder affecting adults over the age of 60 years and continues for a long period. It is a global health issue and its early detection could slow the progression of the disease. One out of every three people dies with Alzheimer's [1]. It kills more than Breast Cancer and Prostate Cancer combined. Alzheimer's leads to nerve cell death and tissue loss throughout the brain. With time, the brain shrinks dramatically, affecting nearly all its functions. Right now, there is no cure for this disease. But its early diagnosis could slow the progression of symptoms. It also prevents possible harmful treatment resulting from misdiagnosis.

II. METHODS

In our proposed work, the tabular dataset is collected from a Disease Center. The dataset contains Longitudinal Clinical data of Alzheimer's and Non-Alzheimer's patients. We have applied more than ten classification techniques starting from Naïve Bayes to Neural Networks to the dataset using multiple Python frameworks like Scikit-Learn, TensorFlow, etc. The attributes in the dataset include age, follow-up years of individual patients, blood biomarkers, medication status, and cognitive assessment tests.

The following are the steps involved in the proposed work:

1. Data Cleaning and Formatting

In this study, jupyter notebook, based on python, was used throughout the whole data analysis. The dataset contains 3309 unique subjects with each having multiple follow-up years. We started by importing the packages pandas, numpy, torch, matplotlib.pyplot, seaborn & graphviz. To get a unique patient's lists, we narrowed each patient to their last follow-up year. Several attributes including cognitive assessment tests and many medications, which were not a part of our research were removed. Attributes causing the problem of Data Leakage were also removed. Separated and filtered the raw data by only having numbered features as descriptive 'string' features weren't required. Each unique patient has come for a certain no. of follow-up years at the medical center. Only the latest follow-up has been taken into account since that provides the latest stance on AD for a patient.

2. Data Imputation

Imputation is one of the most fundamental parts of the data pre-processing due to the incompleteness and inconsistency of real-world data. The missing entries were filled up using the K-Nearest Neighbor algorithm. It uses feature similarity to predict values of new data points. The new point is assigned a value on how closely it resembles the points in the dataset. Sorted out the columns(features/biomarkers) with missing values by using means(average) and K-Nearest Neighbor depending upon the nature of each such feature.

3. Data Balancing

Most machine learning classification algorithm is sensitive to unbalance in predictor class. They tend to bias towards the majority class while predicting using an unbalanced dataset. In our case, the ratio of Alzheimer's to Non-Alzheimer's patients was around 3 to 1. We used Sampling Techniques like Under-Sampling (reduces the majority class with respect to

[1] July 2019

minority class) and Over-Sampling (create dummy sets for minority class to make it equal to the majority class) to balance the dataset.

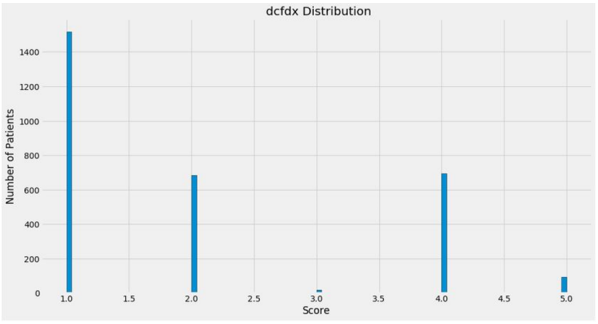
4. *Scaling*

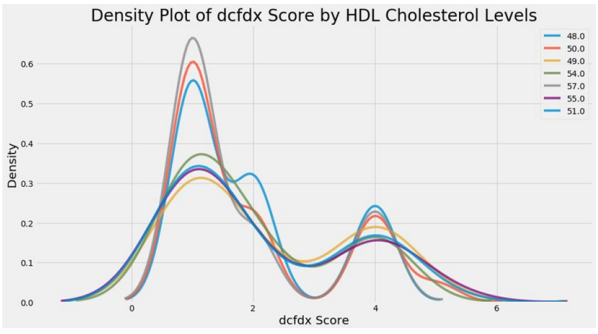
Scaling of data ensures that features whose numerical values are much greater than the others, the machine learning models won't use them as the main predictor. The numerical features in our dataset were scaled to the range of [0,1] using MinMax Scaler. The MinMax Scaler uses the following formula:

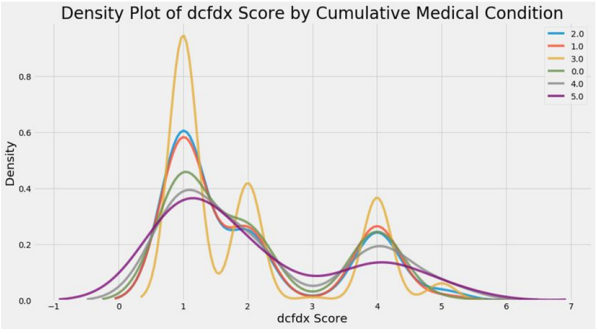
$$Xi - min(i)/max(i) - min(i)$$

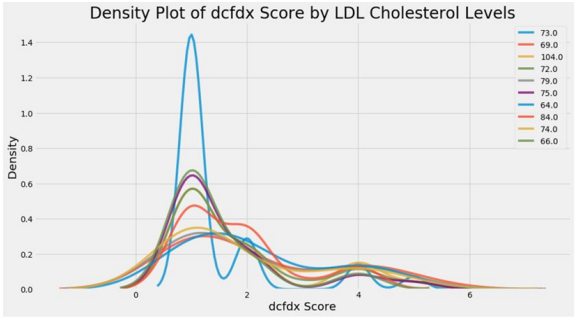
5. *Exploratory Data Analysis*

It is the process of selecting the attributes in our dataset that are relevant to the predictive modeling we are working on. Given the dataset had 203 features, we opted for EDA. It is an open-ended process where we calculate statistics and make figures to find trends, anomalies, patterns, or relationships within the data. After thoroughly reading the biomarkers codebook, through EDA we learned different features that we will use for our models.





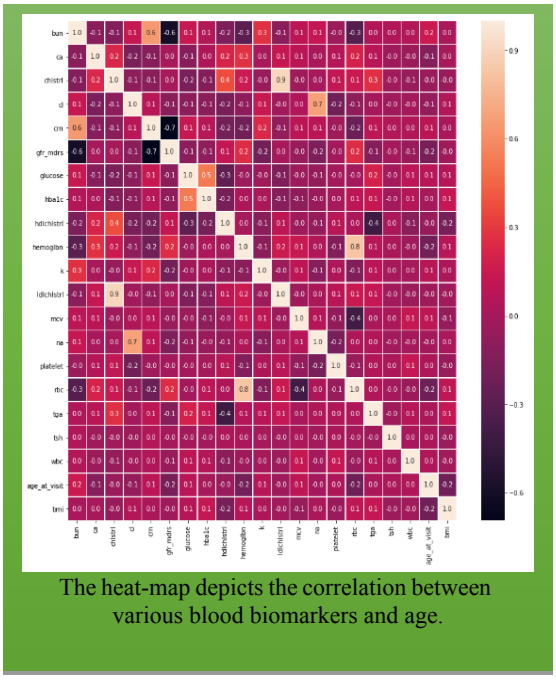




6. *Feature Engineering and Selection*

It is the process of selecting the attributes in our dataset that are relevant to the predictive modeling we are working on. We used the Recursive Feature Elimination (RFE) method to list out the optimal no. of features. RFE fits a model and removes the weakest feature(s) until the specified no. of features is reached.

- Identified dcfdx as the outcome variable of our prediction model.
- Eliminated all the patients who had dcfdx value as 6 in their latest follow-up(38 patients) because there is no clinical evidence of AD .
- Classified dcfdx(referred as Alzheimer's hereafter) into binary outcome variable(0&1).
- Dropped all cognitive tests and medications as required by our problem definition. Also dropped 'projid' and 'fu_year'.
- Reduced the 203 features to 39 by conducting research and feature engineering and also developed a set of features that we will use.



The heat-map depicts the correlation between various blood biomarkers and age.

7. *Classification*

We used multiple classifiers in our model. Some of them are as follows:

- Logistic Regression

It is a statistical method for analyzing a dataset in which there are one or more independent variables that determine an outcome. The outcome is measured with a dichotomous variable [2].

$$p = b0 + b1X1 + b2X2 + \dots$$

$$odds = p/1 - p$$

$$logit(p) = ln(p/1 - p)$$

- Random Forest

A random forest is a classifier consisting of a collection of tree-structured classifiers {h(x,Θ_k),k=1, ...} where the {Θ_k} are independent identically distributed random vectors and each tree casts a unit vote for the most popular class at input x[3].

- Gradient Boosting

Boosting is a method of converting weak learners to strong learners, typically decision trees. It begins by training a decision tree in which each observation is assigned an equal weight. After evaluating the first tree, we increase the weights of those observations that are difficult to classify and lower the weights for those that are easy to classify.

- LightGBM

It is a fast, distributed, high-performance gradient boosting framework based on the decision tree algorithm [4]. Unlike other boosting algorithms, it splits the tree leaf wise with the best fit.

- XGBoost

It is a decision tree-based ensemble Machine Learning algorithm that uses a gradient boosting framework [4]. It provides a parallel tree boosting method.

- Neural Networks

Neural Networks consist of input and output layers, as well as a hidden layer(s) consisting of units that transform the input into something that the output layer can use. A layer is called a node which has neuron-like switches that turn on or off as input is fed to the network. Each unit has its own set of parameters, called the weight(w) and bias(b). In each iteration, the neuron calculates a weighted average of the values of the vector x, based on its current weight vector w and adds bias [5].

$$\check{Z} = w1x1 + w2x2 + w3x3 + \dots$$

$$Z = \check{Z} + b$$

$$\hat{Y} = g(z)$$

8. *Calculations*

Finally, the classification accuracy, specificity, sensitivity and confusion matrix were calculated.

$$Tp - True\ PositiveFFp - False\ Positive$$

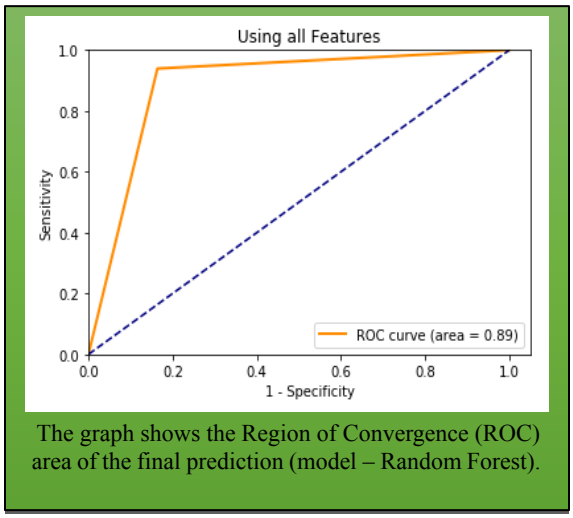
$$Tn - True\ NegativeFFn - False\ Negative$$

$$Accuracy = Tp + Tn/(Tn + Tp + Fp + Fn)$$

$$Specificity = Tn/(Tn + Fp)$$

$$Sensitivity = Tp/(Tp + Fn)$$

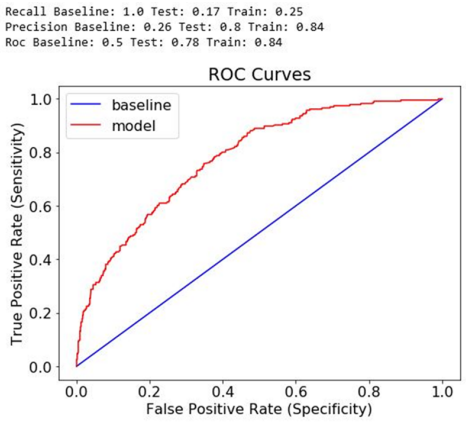
III. RESULTS

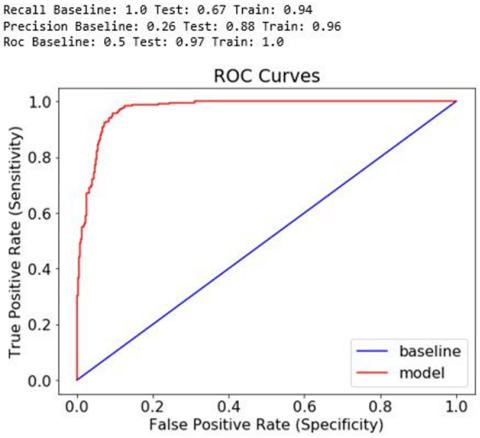


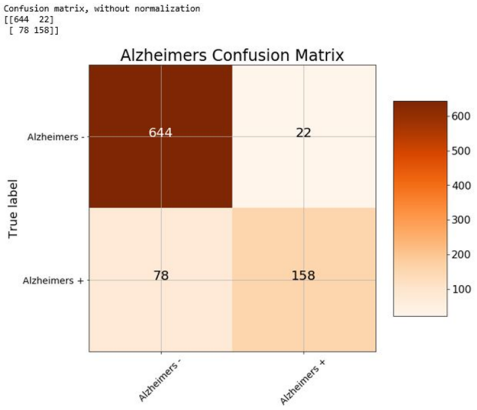
The graph shows the Region of Convergence (ROC) area of the final prediction (model – Random Forest).

We split our data into a training set, valid set and test set. Using the valid set, we tuned the hyper-parameters of the models. Against the test data, Random Forests acquired the highest accuracy score of 88.3% while Neural Networks obtained the highest sensitivity score of 87.2%.

Special focus on Random Forrest ensemble model:
This model uses two key concepts, Random sampling of training data points when building trees and Random subsets of features considered when splitting nodes. Based on the basic decision tree and at each node, the decision tree searches through the features for the value to split on that results in the greatest reduction in Gini Impurity. In our analysis, we didn't set a limit for no. of nodes or maximum depth of a single decision tree. Also, we used 100 trees at a time.

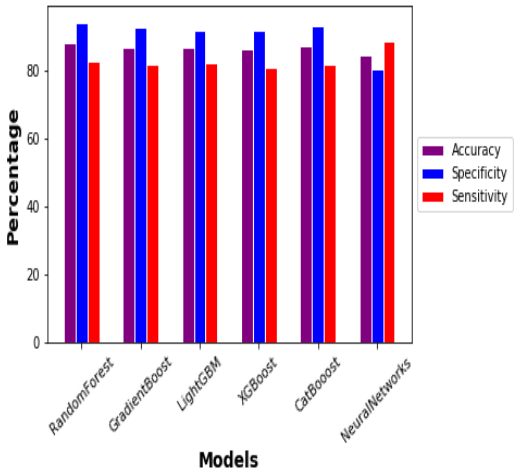






IV. CONCLUSION

Instead of opting for more complex examinations, a few blood tests would reveal the possibility of Alzheimer's with quite a good accuracy. However, there is still an utmost need for identification of relevant attributes for its early detection. It's possible that we are close to the limit of what the random forest and Neural Networks can achieve for this problem. Our future work entails the use of Positron Emission Tomography (PET) scans along with the Blood Biomarkers for classification of Alzheimer's.



The bar plot depicts the performance-comparison of various models.

V. REFERENCES

1. Wu, Y. T., Beiser, A. S., Breteler, M. M., Fratiglioni, L., Helmer, C., Hendrie, H. C., & Matthews, F. E (2017), "The changing prevalence and incidence of dementia over time [mdash] current evidence", Nature Reviews Neurology, 13(6): 327.
2. Jaeger, T.F. (2008), "Categorical Data Analysis: Away from ANOVAs (Transformation or Not) and towards Logit Mixed Models". Journal of Memory and Language, 59, 434-446.
3. Breiman, L. (2001), "Random forests", Machine learning, 45(1): pp. 5-32.
4. Shenghui Yang, Haomin Zhang (2018), "Comparison of Several Data Mining Methods in Credit Card Default Prediction", Intelligent Information Management, pp. 115-122.
5. Anonymous, A Beginner's guide to Neural Networks and Deep Learning.
6. Bhol, Satyabrat, and Bhushan, Abhinav, PhD, "Comparative Analysis for the Detection of Alzheimer's using Multiple Machine Learning Models".
7. Will Koehrsen, Towards Data Science, published in medium.com, May 16, 2018.