Bio-marker Detection for
Type 1 and Type 2 Diabetes using Deep Learning

Abdul Azeez K, Aravindan M, Adhirai Nandhini A, Tejeswinee K

Abstract— **In developing countries like India, non-communicable diseases such as diabetes have already replaced communicable diseases as the major cause of death. According to data from the International Diabetes Federation(IDF) and 14 cohort studies (representing more than 60 percent of the world population with type 2 diabetes), researchers estimated the burden of type 2 diabetes in 221 countries and territories between 2018 and 2030 and IDF pegs the number of patients with diabetes in India at 65.1 million (it was 50.8 million in 2010) and the number is expected to cross 100 million by 2030 .The number of adults with type 2 diabetes is expected to rise over the next 12 years due to ageing, urbanization, and associated changes in diet and physical activity. In this paper the authors focus on diagnosis of diabetes using the various machine learning techniques of data mining. And, authors have compared various classification techniques such as Naive Bayes, KNN, Adaboost, SVM, Decision tree algorithm J48,Random forest. And three well-performing feature selection algorithms namely, Correlation Feature Subset Selection (CFS), Information Gain(IG) and Gain Ratio (GR) are used to obtain the optimal features contributing to the diabetes disease. Further, Incremental Feature Selection(IFS) techniques are applied to further reduce the feature subset from the optimal feature set.**

Index Terms — **Incremental Feature Selection, Correlation Feature Subset Selection (CFS), Information Gain(IG) , Gain Ratio (GR)**

I. INTRODUCTION

Diabetes mellitus is a complicated illness poignant, causing each tissue and organ system, with metabolic ramifications extending way on the far side impaired aldohexose metabolism. Biomarkers could replicate the presence and severity of hyperglycemia (i.e. polygenic disorder itself), or the presence and severity of the tube-shaped structure complications of polygenic disorder.

Type 1: Type 1 diabetes can occur at any age, but is most commonly diagnosed from infancy to the late 30s. With this type of diabetes, a person's pancreas produces no insulin. It occurs when the body's own defence system (the immune system) attacks and destroys the insulin-producing cells in the pancreas.

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Type 2: Type 2 diabetes is by far the most common type of diabetes - is becoming more common among young people due to lifestyle. People with type 2 diabetes either don't make enough insulin or don't make insulin that the body can use properly. Eventually, the pancreas can wear out from producing extra insulin, and it may start making less and less.

II. LITERATURE SURVEY

Yanqiu Wang; Zhi-Ping Li, proposed a gene coexpression network framework to identify the genes with different coexpression patterns in control and disease. The phenotypic indicators are significantly associated with the outcomes of diabetes and then serve as biomarkers. And they have employed an SVM-based classifier to evaluate the classification of these selected genes for their distinguishing power of classifying different states[1].

Ansam Al-Sabti; Mohamed Zaibi; Sabah Jassim, have used and Integrative Omics approach to identify the sub-network in Diabetes mellitus of Type 2 using a novel network based biomarker identification method to distinguish the disease state from normal state by integrating expression and network datasets. And there proposed approach proves the facility of identifying an accurate biomarker for Type 2 diabetes disorder prognosis due to the including of important topological and network information in scoring the resulting pathways[2].

Azian Azamimi Abdullah ;Nurul Sakinah Fadil ; Wan Khairunizam, have developed a Fuzzy expert system for diagnosis of Diabetes by simple GUI layout design, where user enters his data such as Name, Age, Height, Weight, WC (Waist Circumfernce), WHR (Waist to Hip Ratio) for both men and women[3].

Neeru Lalka; Sushma Jain used same approach as [3] and they proposed a method of Insulin Dosage Control (IDC) which enables capturing accurate precison level of probability to recommend the usage of IDC to Type 1 diabetes.And the probability or severity of diabetes in person, lies between 0 and 1[4].

K. Zarkogianni, E. Litsa, K. Mitsis, P. Wu, C. D. Kaddi, C. Cheng, M.D. Wang; and K.S. Nikita have discussed a review of emerging technologies for management of diabetes. They have founded some existing technologies such as Google Smart Lens, iQuickIt Saliva Analyzer, and Abbott developed Freestyle. And they have concluded there review as, Enhanced integration of patient data through the development of multiscale and multilevel physiological models can generate new clinical knowledge and contribute to a more effective personalized diabetes care approach[5].

Sidong Wei; Xuejiao Zhao; Chunyan Miao in there papers they have used Machine Learning Techniques such as Deep Neural Network, Support Vector Machine (SVM) etc. to identify diabetes and they have used Pima Indian Diabetes data set[6].

Many nice results are created using numerous algorithms. For example, **Asha** and her colleagues used a hybrid model of Genetic algorithmic program and Back Propagation Network to identifiy polygenic disorder [7]. They particularly targeted on adopting the rule on some specific input data and reached 84.7% on the known inputs. **Kayaer's** team used GRNN technique [9] to spot polygenic disorder. They mentioned a way to build the network and had a similar result as **Gail A. Carpenter** and his cluster has created, which used a really difficult ARTMAP-IC network [8]. The technique Kayaer used was abundant simplified compared to Gail's, however it absolutely was still a posh one relevance the dimensions of the data set. From all those researches we will see that all of them explored diabetes identification through one specific methodology, and modified and improved it to its best or approximate best.

III. PROPOSED COMPUTATIONAL FRAMEWORK

Fig. 1

A. Dataset Generation

The dataset consists of structural and physicochemical properties of proteins related to the genes of type1 and type2 diabetes. It is in the form of CSV(Comma standard value) shown in Fig. 2 .The dataset contains 43 gene sample for Type 1, 47 gene sample for Type 2 Diabetes and 2 gene samples are common to both Type 1 and 2.

Fig. 2

B. Feature Selection

All the genes have 1437 protein properties each. The properties are broadly classified as G1 to G9 feature descriptors, Fig. 5.1, 5.2 and 5.3 show the parameter for each feature group. To find the specific genes that are most contributing to Type 1 and Type 2 diabetes, feature selection methodologies were investigated. Three mechanisms were applied to find the optimal feature set- Correlation Feature Subset Selection (CFS), Information Gain (IG) and Gain Ratio(GR).
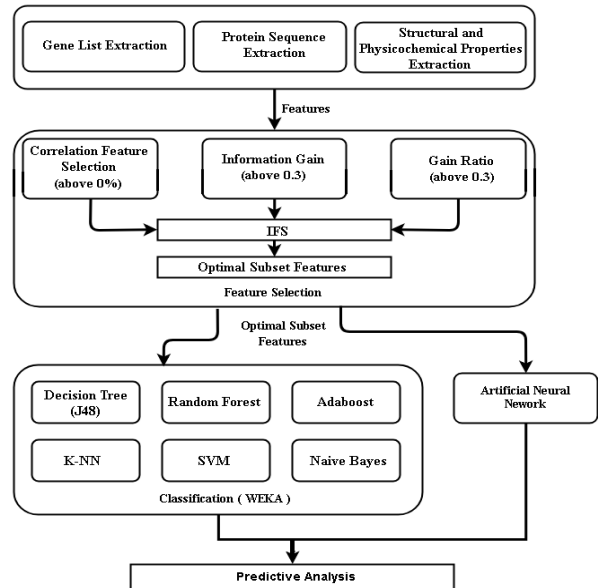

Fig. 3

The feature subsets obtained post feature selection were fed as input to the classification phase wherein classifiers viz, Support Vector Machine (SVM), Random Forest, Decision Tree (J48), Naive Bayes, Adaboost, k-NN were employed and their accuracy in predicting the correct diagnostic class was measured. Fig. 3 shows the proposed framework for feature selection while Fig. 4 depicts the various data mining algorithms that were investigated on the extracted feature subset.
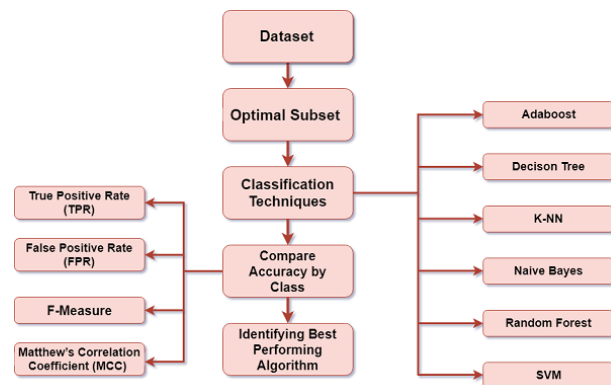

Fig. 4

The accuracy of each class Type 1 and Type 2 diabetes is measured by True Positive Rate (TPR), False Positive Rate (FPR), F-Measure and Mathew's Correlation Coefficient (MCC).

Fig. 5.1

Fig 5.2

Fig. 5.3

IV. EXPERIMENTAL RESULTS

The investigation of existing techniques revealed the importance of selecting important features for classification. 10-fold cross validation was employed to measure the performance of the data mining algorithms. Two performance parameters were identified to rank the algorithms.

A. **Accuracy**

The degree to which the result of a measurement, calculation, or specification conforms to the correct value or a standard.

$$Recall = \frac{tp}{tp + fn}$$

$$Precision = \frac{tp}{tp + fp}$$

$$Accuracy = \frac{tp + tn}{tp + tn + fp + fn}$$

F-measure

$$F = 2 \cdot \frac{precision \cdot recall}{precision + recall}$$

This is also known as the F_1 measure, because recall and precision are evenly weighted.

B. Matthews' Correlation Co-efficient (MCC)

It's the measure of the quality of binary (two-class) classifications. It takes into account true and false positives and negatives .

$$MCC = \frac{(TP \times TN) - (FP \times FN)}{\sqrt{(TP + FN) \times (TN + FP) \times (TP + FP) \times (TN + FN)}}$$

TP = true positives: number of examples predicted positive that are actually positive; FP = false positives: number of examples predicted positive that are actually negative; TN = true negatives: number of examples predicted negative that are actually negative; FN = false negatives: number of examples predicted negative that are actually positive.

Mean absolute error (MAE) : MAE measures the average magnitude of the errors in a set of forecasts, without considering their direction. It measures accuracy for continuous variables. The MAE is the average over the verification sample of the absolute values of the differences between forecast and the corresponding observation. The MAE is a linear score which means that all the individual differences are weighted equally in the average;

Root mean squared error (RMSE) : RMSE is a quadratic scoring rule which measures the average magnitude of the error. The difference between forecast and corresponding observed values are each squared and then averaged over the sample. Finally, the square root of the average is taken. Since the errors are squared before they are averaged, the RMSE gives a relatively high weight to large errors. This means the RMSE is most useful when large errors are particularly undesirable.

Kappa statistic 0.9403 <- agreement of prediction with true class. Mean absolute error 0.0309 <- not squared before

averaging. Root mean squared error 0.1493 <- squared before averaging, so large errors have more influence. Relative absolute error 6.9047 % <- Relative values are ratios, and have no units.

Before feature selection, the dataset consisted of 1437 attributes and by extracting the gene set using GSEC we get 90 attributes of datasets. (43gene sample of type1 and 47 gene sample of type2).

Investigation was carried out using WEKA 3.4 tool open source data mining suite. Once the dataset was pre-processed, feature selection techniques were explored.

A threshold greater than or equal to 0.3 was chosen for Information Gain (IG) and greater than or equal to 0.3 was chosen for Gain Ratio (GR) and 0% above for Correlation Feature Subset Se. Correlated Feature Subset Selection (CFS) is an automated method that uses Best-First Search strategy to identify and narrow down to the optimal feature subset. The CFS subset evaluation algorithm extracted a subset containing 153 attributes. The output generated three subsets, one for each of the above mentioned mechanisms.

All the six classification algorithms were implemented and their accuracy was measured. Their results are shown below.

Adaboost

```
Correctly Classified Instances       79       87.7778 %
Incorrectly Classified Instances     11       12.2222 %
Kappa statistic                      0.7548
Mean absolute error                  0.1352
Root mean squared error              0.3273
Relative absolute error              27.0601 %
Root relative squared error          65.4517 %
Total Number of Instances            90

          === Detailed Accuracy By Class ===
```

	TP Rate	FP Rate	F-Measure	MCC	Class
	0.860	0.106	0.871	0.755	Type 1
	0.894	0.140	0.884	0.755	Type 2
Weighted Avg.	0.878	0.124	0.878	0.755	

Decision Tree (J48)

```
Correctly Classified Instances       77       85.5556 %
Incorrectly Classified Instances     13       14.4444 %
Kappa statistic                      0.7114
Mean absolute error                  0.1578
Root mean squared error              0.3756
Relative absolute error              31.5886 %
Root relative squared error          75.1083 %
Total Number of Instances            90

          === Detailed Accuracy By Class ===
```

	TP Rate	FP Rate	F-Measure	MCC	Class
	0.884	0.170	0.854	0.713	Type 1
	0.830	0.116	0.857	0.713	Type 2
Weighted Avg.	0.856	0.142	0.856	0.713	

K-NN

```
Correctly Classified Instances       72       80       %
Incorrectly Classified Instances     18       20       %
Kappa statistic                      0.5952
Mean absolute error                  0.2072
Root mean squared error              0.442
Relative absolute error              41.4791 %
Root relative squared error          88.3738 %
Total Number of Instances            90

          === Detailed Accuracy By Class ===
```

	TP Rate	FP Rate	F-Measure	MCC	Class
	0.674	0.085	0.763	0.611	Type 1
	0.915	0.326	0.827	0.611	Type 2
Weighted Avg.	0.800	0.211	0.796	0.611	

Naive Bayes

```
Correctly Classified Instances       80       88.8889 %
Incorrectly Classified Instances     10       11.1111 %
Kappa statistic                      0.7778
Mean absolute error                  0.1111
Root mean squared error              0.3333
Relative absolute error              22.2401 %
Root relative squared error          66.6534 %
Total Number of Instances            90

          === Detailed Accuracy By Class ===
```

	TP Rate	FP Rate	F-Measure	MCC	Class
	0.907	0.128	0.886	0.779	Type 1
	0.872	0.093	0.891	0.779	Type 2
Weighted Avg.	0.889	0.110	0.889	0.779	

Random Forest

```
Correctly Classified Instances       72       80       %
Incorrectly Classified Instances     18       20       %
Kappa statistic                      0.5992
Mean absolute error                  0.2799
Root mean squared error              0.3475
Relative absolute error              56.0299 %
Root relative squared error          69.4925 %
Total Number of Instances            90

          === Detailed Accuracy By Class ===
```

	TP Rate	FP Rate	F-Measure	MCC	Class
	0.791	0.191	0.791	0.599	Type 1
	0.809	0.209	0.809	0.599	Type 2
Weighted Avg.	0.800	0.201	0.800	0.599	

Support Vector Machine (SVM)

```
Correctly Classified Instances       81       90       %
Incorrectly Classified Instances     9        10       %
Kappa statistic                      0.7998
Mean absolute error                  0.1
Root mean squared error              0.3162
Relative absolute error              20.0161 %
Root relative squared error          63.233  %
Total Number of Instances            90

          === Detailed Accuracy By Class ===
```

	TP Rate	FP Rate	F-Measure	MCC	Class
	0.907	0.106	0.897	0.800	Type 1
	0.894	0.093	0.903	0.800	Type 2
Weighted Avg.	0.900	0.099	0.900	0.800	

The result of each algorithm is tabulated in Table 1 for full Dataset and the subset for each CFS, IG, GR are tabulated Table 2, Table 3 and Table 4 respectively. And it is visually represented in the form of Bar Chart as Chart 1 for Pre-feature selection and Chart 2 for Post-feature selection (CFS), Chart 3 for Post-feature Selection(IG) and Chart 4 for Post-feature selection(GR).

Algorithm/Accuracy	TP Rate	FP Rate	F-Measure	MCC
NaiveBayes	0.889	0.110	0.889	0.779
J48	0.856	0.142	0.856	0.713
IBk	0.800	0.211	0.796	0.611
RandomForest	0.800	0.201	0.800	0.599
AdaBoostM1	0.878	0.124	0.878	0.755
SMO	0.900	0.099	0.900	0.800

Table 1

Algorithm/Accuracy	TP Rate	FP Rate	F-Measure	MCC
NaiveBayes	0.944	0.055	0.944	0.889
J48	0.844	0.162	0.843	0.693
IBk	0.867	0.142	0.865	0.743
RandomForest	0.933	0.067	0.933	0.866
AdaBoostM1	0.911	0.091	0.911	0.822
SMO	0.956	0.045	0.956	0.911

Table 2

Algorithm/Accuracy	TP Rate	FP Rate	F-Measure	MCC
NaiveBayes	0.900	0.101	0.900	0.800
J48	0.878	0.118	0.878	0.761
IBk	0.822	0.182	0.822	0.645
RandomForest	0.889	0.106	0.889	0.786
AdaBoostM1	0.900	0.097	0.900	0.802
SMO	0.900	0.101	0.900	0.800

Table 3

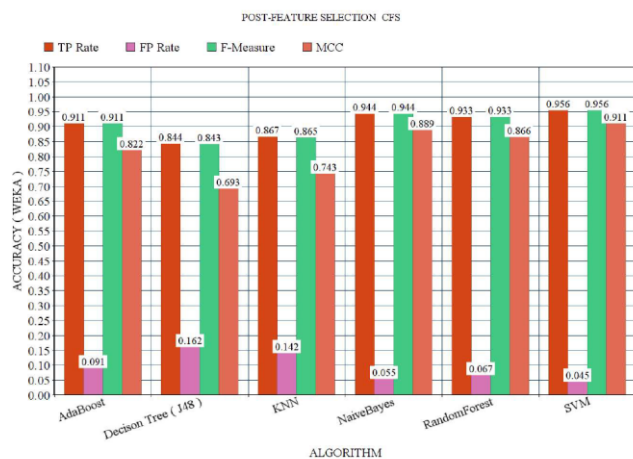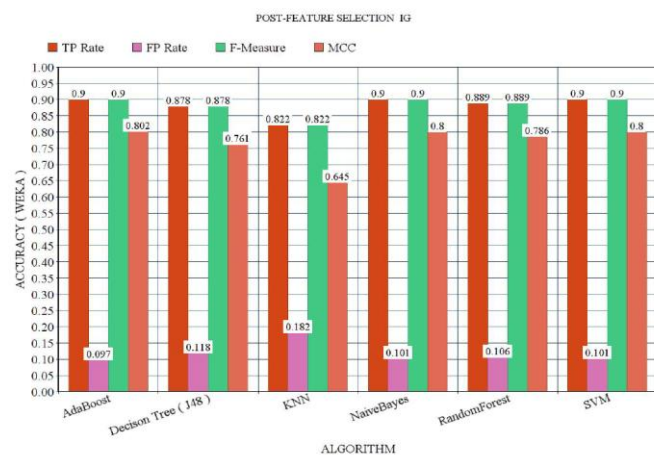| Algorithm/ Accuracy	TP Rate	FP Rate	F-Measure	MCC
NaiveBayes	0.922	0.079	0.922	0.844
J48	0.867	0.134	0.867	0.733
IBk	0.856	0.150	0.855	0.714
RandomForest	0.867	0.128	0.866	0.741
AdaBoostM1	0.900	0.097	0.900	0.802
SMO	0.933	0.067	0.933	0.866

Table 4

Chart 1
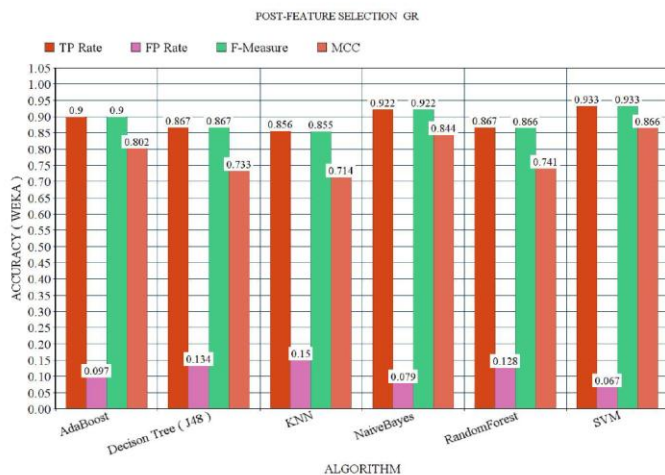

Chart 2

Chart 3

Chart 4

V. RESULTS

The below mention code is used to evaluate the full dataset and the subset data of CFS , IG , GR and another subset of CFS-Naive Bayes, CFS- Adaboost and CFS-SMO, IG-Naive Bayes, IG- Adaboost and IG-SMO and GR-Naive Bayes, GR-Adaboost and GR-SMO.(Code differs for every subset)

```python
import pandas
from keras.models import Sequential
from keras.layers import Dense
import numpy
seed = 10
numpy.random.seed(seed)
dataframe = pandas.read_csv("Datasets/Dataset.csv",header=None,low_memory=False)
dataset = dataframe.values
X = dataset[1:,1:1438].astype(float)
Y = dataset[1:,1438]

model = Sequential()
model.add(Dense(1111, input_dim=1437, activation='relu'))
model.add(Dense(460, activation='softplus'))
model.add(Dense(100, activation='softmax'))
model.add(Dense(1, activation='sigmoid'))

model.compile(loss='binary_crossentropy', optimizer='adam', metrics=['accuracy'])
model.fit(X,Y,epochs = 200,batch_size = 10)

scores = model.evaluate(X,Y)
print("%s: %.2f%%" %(model.metrics_names[1],scores[1]*100))
```

The evaluate method in the above mentioned code gives an accuracy as shown in below Table 5. And the accuracy is pictorically visualized in the Chart 5 for full dataset and pre-feature selection, and Chart 6 for post-feature selection.

DATASET	ACCURACY
Complete Dataset	52.22%
CFS	98.89%
IG	98.89%
GR	91.11%

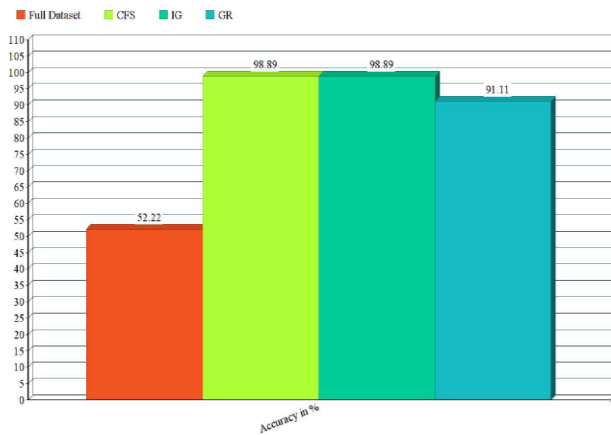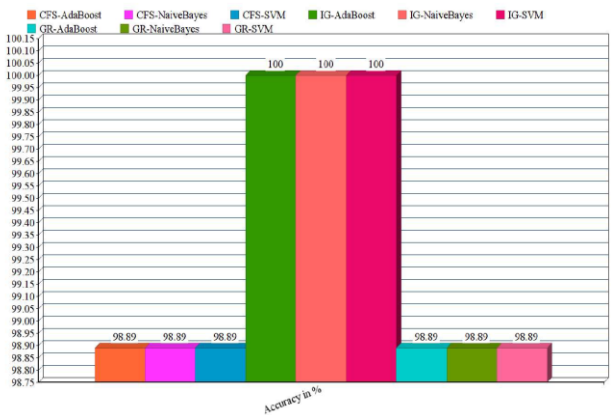|	
CFS-Adaboost	98.89%
CFS-NaiveBayes	98.89%
CFS-SVM	98.89%
IG-Adaboost	100%
IG-NaiveBayes	100%
IG-SVM	100%
GR-Adaboost	98.89%
GR-NaiveBayes	98.89%
GR-SVM	98.89%

Table 5

Chart 5

Chart 6

VI. CONCLUSION

Our case study is able to identify the gene causing Type 1 and Type 2 diabetes. Although in this paper, we have generated a new dataset that consists of genetic information that pertains to theType 1 and Type 2 disease. The dataset, initially extracted from the KEGG database, consisted of 1437 structural and physicochemical protein properties that were extracted from the PROFEAT server. It consisted of 43 gene sample for Type 1, 47 gene sample for Type 2 Diabetes and 2 gene samples are common to both Type 1 and 2.
(1 Missing gene sample in Type 1)

KEGG database, in future has the storage of gene information of all homo-sapiens, which enables to classify the infants having the possibility of diabets in earlier stage itself.

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