

# Predicting Future Type 2 Diabetes through Machine Learning

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**Abstract**—We present a prediction model that assesses the future risk of developing type 2 diabetes mellitus (T2DM). We use the oral glucose tolerance test (OGTT) data collected from a group of 1,551 healthy subjects to construct a machine learning model employing the support vector machines. We trained and validated the models on the data obtained from the second cohort of the San Antonio Heart Study, using a set of four features derived from the glucose measurements in the OGTT. The results of the proposed scheme show an average validation accuracy of 97.23% and recall of 77.27%. The results also show that the plasma glucose based features are the strongest predictors of the future development of T2DM.

**Index Terms**—Type 2 Diabetes prediction, machine learning, disease risk assessment, San Antonio heart study.

## I. INTRODUCTION

THE global incidence of diabetes was estimated at 422 million in the year 2014 and its prevalence among the adult population has seen an increase from 4.7% in the year 1980 to 8.5% in 2014 [1]. In 2015 alone, an estimated 1.6 million deaths worldwide were attributed to diabetes. In addition, a diabetic patient is at a greater risk of developing cardiovascular diseases, visual impairment and limb amputations, as compared to a non-diabetic person. Due to the substantial socio-economic burdens that are associated with diabetes, its early detection, intervention and prevention has become a worldwide top-level health concern.

Impaired glucose tolerance (IGT), defined by World Health Organization (WHO) [2] and the American Diabetes Association (ADA) [3], that is used to detect diabetes in its early stage, known as pre-diabetes, which identifies the impaired insulin response. Glucose clamp techniques can quantify the IGT. However, such techniques are labor-intensive and complicated for clinical practice or large epidemiological studies. A less invasive technique to quantify IGT involves an oral glucose tolerance test (OGTT) that samples the blood concentration of glucose and insulin over 2 h after a standardized glucose dose [4]. However, the studies have shown that only 50% of

such cases actually develop diabetes within a span of 10 years [5], [6]. Moreover, 40% diabetic subjects do not show any IGT in the initial screening. Previous studies have shown that extended OGTT, that assesses the blood glucose and insulin in the period prior to 2 h limit, can predict diabetes onset more reliably [7].

In this paper, we revisit the data generated by a population-based, epidemiological study, the San Antonio Heart Study [8], [9], and use a machine learning model to predict the onset of diabetes by using predefined OGTT features used earlier in the literature. On top of a range of glucose and insulin concentrations and their derivatives, our approach also takes into account physiological factors such as age, ethnicity, and body mass index (BMI).

Does it improve the prediction performance over other models such as SADPM that do not require any invasive procedure. SADPM is based on demographics data and fasting plasma glucose.

## II. RELATED WORK

1. Abdul-Ghanis work on diabetes prediction model using statistical tools 2. Machine learning approaches primarily work on the aspects of diagnosis rather than prediction. BARAKAT rule based diagnosis 3. Ensemble based approach on diabetes diagnosis models

1. BARAKAT 2. ABDUL-GHANI 3. SAn Antonio Diabetes Prediction Model 4. Chinese paper using SVMS 5. Ensemble based approach for T2DM prediction

## III. MATERIALS AND METHODS

### A. San Antonio Heart Study

We developed the diabetes prediction models using the data extracted from a population-based epidemiological study, the San Antonio Heart Study (SAHS). The aim of the SAHS was to assess the risk factors of diabetes and cardiovascular diseases [8], [9], for which 5,158 men and non-pregnant women of Mexican-American and non-Hispanic white residents of San Antonio, Texas were recruited. The age of the subjects at the time of recruitment was between 25 and 64 years. As a part of the data collection, the blood glucose and insulin levels were recorded during an oral glucose tolerance test (OGTT), which measures the subject's body response to a standard 75 g dose of glucose after fasting overnight. The OGTT was performed both at the baseline and follow-up phases of the study, which had an average span of 7.5 years. The SAHS subjects were recruited in 2 cohorts, the first during the period 1979 to 1982,

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and the second from 1984 to 1988 [10]. The reassessment during the follow-up period took place during the years 1987 to 1990 for the first cohort, and 1991 to 1996 for the second cohort. For the future T2DM prediction problem, we construct the machine learning model using the data from the second cohort, in which the plasma glucose and insulin levels of 1,496 of healthy subjects were recorded during the OGTT at times 0, 30, 60 and 120 minutes in the baseline evaluation. During the course of the study, a total of 171 subjects developed T2DM within which 10 subjects also reported of at least one cardiovascular event such as a heart attack, stroke or angina.

At the follow-up assessment, the participants were classified as having type 2 diabetes (T2D), cardiovascular disease (CVD) or normal. For T2D diagnosis, the WHO criteria, defining fasting glucose level  $\geq 126$  mg/dL or 2-hour glucose level  $\geq 200$  mg/dL was followed [11]. Any participant reportedly taking anti-diabetic medications was also classified as diabetic. For CVD classification, any cardiovascular event such as a heart attack, stroke or angina reported by the participant, was considered as an identifier. Table I outlines the distribution of patient classification used in this study. In order to construct a binary classifier for this study, the subjects categorized under the DMI and DMI+CVD were encoded as the positive class whereas the Healthy labels were the negative class. We restricted the classification to only two classes and the samples with the label CVD were ignored.

TABLE I: The classification of the 1,496 subjects used in this study

Healthy	DMI	CVD	DMI+CVD
1.281	161	44	10
85.63 %	10.76 %	2.94 %	0.67 %

### B. Preparation of the Data

The dataset included the glucose and insulin values recorded at the baseline, 30, 60 and 120 minute intervals, and a distribution of these values marked by the follow-up labels of healthy and diabetic is shown in Fig. 1. Moreover, the socio-demographic information such as age, ethnicity and body-mass index (BMI) was also part of the dataset. From the glucose and insulin measurements, we computed the slope and area under the curve between all the possible combinations of a pair of readings. In addition, we also calculated parameters such as the insulinogenic (ratio of insulin and glucose slopes between any two time intervals) and Matsuda indices, as defined in [12], [13]. These variables have shown a good efficacy of diabetes prediction in previous studies [7], [13], since they are used to quantify the amount of insulin required by the body to maintain healthy glucose levels. In total we prepared 68 features for the classification problem and removed the rows that had missing entries or contained zero or infinite values. The dataset was then partitioned into training and validation sets. As can be observed from the Table I, the SAHS dataset is intrinsically imbalanced with the class distribution skewed toward the majority class with a ratio of 7.5:1. Considering

the Therefore, we took two approaches for the training set, one in which the dataset was balanced by a randomized undersampling of the majority class, and second in which we persisted with natural class distribution. In both the cases, the validation set had the same class distribution representative of the original dataset. A total of 1360 samples were used for training that accounted for 91 % of the dataset, and 99 samples, consisting of 11 diabetic and 83 healthy subjects were reserved for the validation of the trained prediction models.

### C. Machine Learning Framework

We developed a supervised learning scheme in which the classifier output labels were obtained from the follow-up data, and the support vector machine (SVM) technique was used to construct the future diabetes prediction framework. The SVM works on the principle of *structural risk minimization* (SRM) in which the goal is to develop a model from the given training data such that it generalizes well to new datasets and minimizes the empirical risk associated with misclassification of samples in the training set [14], [15]. For a binary classification problem, the model constructed by the SVM finds a decision boundary or a separating hyperplane which aims to minimize the overlapping between the two classes in the training set. For problems that may not be amenable to linear separation between the two classes, the SVM technique is very attractive due to fact that the input feature space is first transformed to a higher dimension and then a linear boundary is determined, which generally gives better training performance [16]. Let us consider a training data  $(x_1, y_1), (x_2, y_2), \dots, (x_k, y_k)$  of  $k$  pairs containing  $x_i \in \mathbb{R}^N$  features and the binary classes  $y_i \in -1, 1$ . The SVM approach transforms the input features using a nonlinear mapping  $\Phi : x \mapsto \phi(x)$  into a higher dimension space  $\mathbb{R}^P$ , where in general  $P \gg N$ . Due to the transformation, the classes can then be separated using a linear decision boundary in the enlarged space. The non-linear SVM classifier F is expressed in terms of the higher dimensional hyperplane,

$$F = \text{sign} \left( \phi(x)^T \beta + \beta_0 \right). \quad (1)$$

When the classes may not be completely separable, introducing a slack variable  $\zeta$  in the higher dimension space  $\mathbb{R}^P$  is a common practice which allows for the classifier output in (1) to be on the incorrect side of the margin. Therefore, in order to find the optimal separating hyperplane that maximizes the distance  $M$  from the boundary for all the points, and bounds the value of  $\sum_i \zeta_i$  and in turn misclassification rate, we introduce the convex optimization problem,

$$\min_{\beta, \beta_0} \frac{1}{2} \|\beta\|^2 + C \sum_{i=1}^P \zeta_i, \quad (2)$$

with the nonlinear constraints  $y_i(\phi(x_i)^T \beta + \beta_0) \geq 1 - \zeta_i \quad \forall i$  and  $\zeta_i \geq 0$ , and the coefficient  $C$  is termed as the cost parameter which decides the rigidity of the margin of the classifier. The

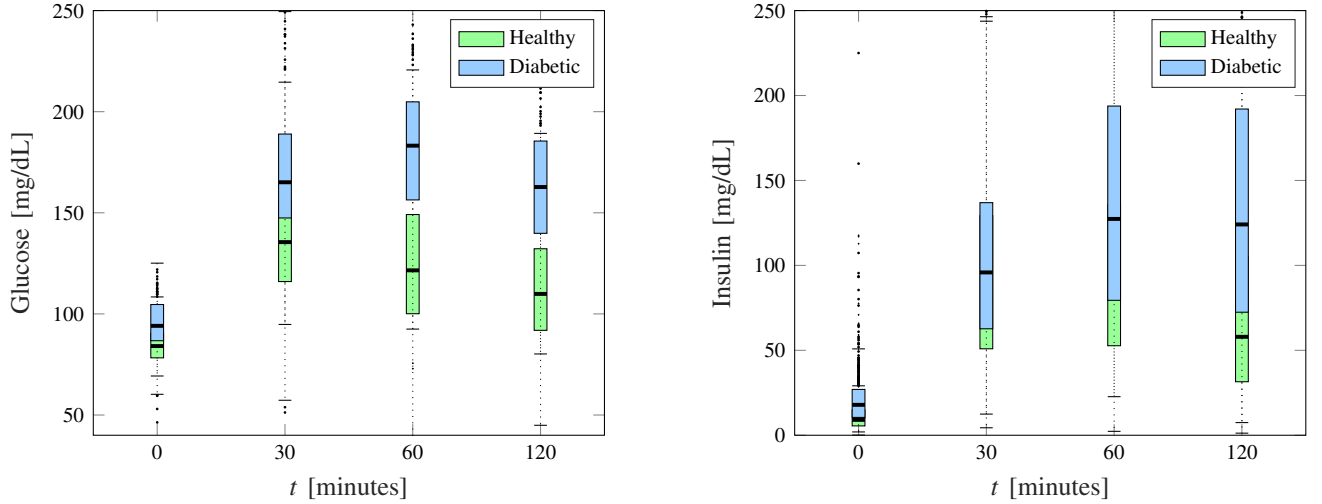


Fig. 1: Box plots of glucose and insulin measurements for healthy and diabetic subjects.

solution of (2) can be computed using the Lagrange primal objective function [16],

$$L_p = \frac{1}{2} \|\beta\|^2 + C \sum_{i=1}^P (1 - \mu_i) \zeta_i - \sum_{i=1}^P \alpha_i \left[ y_i \left( \phi(x_i)^T \beta + \beta_0 \right) - (1 - \zeta_i) \right]. \quad (3)$$

By minimizing  $L_{\text{primal}}$  with respect to  $\beta$ ,  $\beta_0$ , and  $\zeta_i$ , we get the corresponding dual form of the Lagrange function,

$$L_{\text{dual}} = \sum_{i=1}^P \alpha_i - \frac{1}{2} \sum_{i=1}^P \sum_{i'=1}^P \alpha_i \alpha_{i'} y_i y_{i'} \langle \phi(x_i), \phi(x_{i'}) \rangle \quad (4)$$

subject to  $0 \leq \alpha_i \leq C$  and  $\sum_i \alpha_i y_i = 0$  and the constraints,  $\zeta_i, \mu_i \geq 0 \forall i$ . The nonzero coefficients  $\alpha_i$  and  $\beta_0$  are determined using (1). As the dimension of the input feature space goes up, the computation of the mapping  $\Phi$  gets excessive in complexity. With the introduction of a kernel,

$$k(x, x') = \langle \phi(x), \phi(x') \rangle, \quad (5)$$

we can compute the inner product on (4) without computing the mapping  $\Phi$  [17], which becomes computationally expensive as the dimension of the input feature space increased. In this paper, we used the Gaussian radial basis function,

$$K(x, x') = \exp \left( -\frac{\|x - x'\|^2}{2\sigma^2} \right) \quad (6)$$

as the kernel where  $\sigma$  is a free parameter. During the training, we tuned the values of the parameters  $C$  and  $\gamma$  through a grid search to obtain the optimal performance of the SVM.

#### D. Feature Selection

Before constructing the SVM model to predict the future risk of diabetes, we aim to find the most effective subset of the features in terms of the relevance to the classifier output. This process greatly reduces the computational cost

during the model development by reducing the feature space dimension and also dispense useful scientific insight in to the classification problem. We performed a two-step filter selection, first of which was the *filter* method in which ten features that correlated the most to the classifier target class were shortlisted. In order to define the relevance between the feature and the class labels, consider a feature  $\mathbf{X}$  from a feature set  $\mathcal{X}$  as a continuous random variable and the class label  $\mathbf{Y}$  as a discrete random variable. Their relationship can be described in terms of the mutual information,  $I$  defined as [19]:

$$I(\mathbf{X}, \mathbf{Y}) = - \int p_i \ln p_i - \sum_j p_j \ln p_j + \sum_j \int p_{ij} \ln p_{ij}, \quad (7)$$

where  $p_i$  is the probability of a random variable  $\mathbf{X}$  taking a particular value  $x_i$  and so forth, and  $p_{ij}$  denotes the joint probability  $P\{\mathbf{X} = x_i, \mathbf{Y} = y_j\}$ . The three terms in (11) are the continuous, discrete and joint entropies of the random variables. The features that are most relevant to the class label are the ones that individually yield the maximum  $I$ . However, a drawback of pursuing this approach is that the selected features may be mutually correlated, and having a redundant list of shortlisted features only adds to the computational cost of the classifier without necessarily improving its performance. Even more so, the addition of extra features commonly result in the deterioration of the classifier performance [20]. Therefore, an instinctive way forward is to keep only one feature from a correlated set of features that provide similar relevance information, and discard the remaining features from the set  $\mathcal{X}$ . We follow the minimal-redundancy-maximal-relevance () algorithm [21], that selects the features, that not only yield the maximal mutual information (11) with respect to the class label, but minimizes the mutual correlation among the features expressed in terms of redundancy  $R$  as:

$$R(\mathcal{X}) = \sum_{\mathbf{X}_i, \mathbf{X}_j \in \mathcal{X}} I(\mathbf{X}_i, \mathbf{X}_j). \quad (8)$$

where  $I$  is defined in (11). By minimizing  $R$ , the mRMR framework selects a set of mutually exclusive features that

are most relevant to the class label. In this paper, we shortlist a set of ten features that are strong predictors of the future development of type 2 diabetes. With the application of the mRMR algorithm, Table II shows the list of the ten features ranked in order of their relevance to the class label, where the prefixes *au* and *sl* denote the area under the curve and slope respectively and the time interval is shown in the subscripts. In the second phase, we further pruned the number

TABLE II: List of ten most relevant features ranked by the mRMR algorithm

Rank	Feature
1	AuC-Glu <sub>0-120</sub>
2	Sl-Glu <sub>120-0</sub>
3	Sl-Glu <sub>120-60</sub>
4	Sl-Glu <sub>60-0</sub>
5	Sl-Glu <sub>30-0</sub>
6	AuC-Glu <sub>60-120</sub>
7	PG <sub>0</sub>
8	PG <sub>120</sub>
9	PG <sub>60</sub>
10	AuC-Glu <sub>0-30</sub>

of features to four only by selecting the ones that provided the best performance in terms of validation accuracy using the SVM classification scheme. Table III shows the four best features obtained by averaging the validation accuracy over 100 iterations of the classification scheme.

TABLE III: Validation Performance of individual features in 100 iterations of running a SVM model with RBF kernel.

Features	Mean Accuracy (Standard Deviation)
AuC-Glu <sub>60-120</sub>	0.973 (0.013)
PG <sub>120</sub>	0.971 (0.015)
PG <sub>60</sub>	0.967 (0.022)
AuC-Glu <sub>0-120</sub>	0.958 (0.019)
AuC-Glu <sub>30-120</sub>	0.950 (0.018)
Sl-Glu <sub>60-0</sub>	0.946 (0.025)
Sl-Glu <sub>120-0</sub>	0.931 (0.026)

#### IV. EXPERIMENTS

1. Balanced Training -> Unbalanced Validation 2. Unbalanced Training -> Balanced Validation

$$I(\mathbf{x}) = \text{sign} \sum_{i=1}^N (c_i \mathbf{z}_i \cdot \mathbf{x} + b_0). \quad (9)$$

In this study, we employed the linear SVM kernel by utilizing the Matlab's `svmtrain` function. The training data was first scaled to have a unit standard deviation. The misclassification cost was configured by setting the value of the `boxconstraint` parameter to a high value of 100, which would cause a stricter partitioning of the data with respect to the class labels.

To predict the future risk of type 2 diabetes, we defined a positive class (occurrence of diabetes at the follow-up) and a negative class (healthy). As illustrated in Table I, the OGTT data used in this study is heavily unbalanced. With 171 positive class instances as compared to 1281 that of the negative

class, the size of class labels is unbalanced with the ratio of positive-to-negative instances of 1:8. To avoid the problem of overfitting to the majority class during the learning phase of the technique, we under-sampled the majority class (healthy) to the size of the minority class (diabetic) by a randomly selecting equal number of samples. During the prediction model generation, we employed 10-fold cross-validation framework in which 90 % of the training data, consisting of 360 samples was used for training and the remaining 10 % was used to test the model. To validate the trained models, we used a holdout data set with the same unbalanced ratio of negative-to-positive classes in the original data, i.e., 11 samples of the positive class, and 88 samples of the negative class. We started our experiments using one feature at a time, and then more number of features were incrementally added. This exercise assists in discovering any feature dependencies. In total, we performed 1,023 classification experiments. Each of these experiments was trained as a 10-fold cross-validation (CV) and, to minimize the effect of random selection of samples from the majority class, 100 iterations were performed for each experiment. Owing to the small sample size of the holdout dataset, this strategy ensures the unbiased reporting of the classifier performance. To maximize reliability of the model to predict diabetes events, we maximized the recall metric during the training phase, which is defined as,

$$\text{Recall} = \frac{\text{TP}}{\text{TP} + \text{FN}}, \quad (10)$$

where TP and FN are the true-positives and false-negatives respectively. During the validation phase, we tracked the confusion matrices for all the models yielding the maximum training recall for all the feature combinations.

##### A. Feature Selection

Before constructing the future diabetes prediction model based on the support vector machines, we aim to find the most effective subset of the features in terms of the relevance to the classifier output. This process greatly reduces the computational cost during the model development by reducing the feature space dimension and also dispense useful scientific insight in to the classification problem. We performed a two-step filter selection, first of which was the `emphfilter` method in which ten features that correlated the most to the classifier target class were shortlisted. In order to define the relevance between the feature and the class labels, consider a feature  $\mathbf{X}$  from a feature set  $\mathcal{X}$  as a continuous random variable and the class label  $\mathbf{Y}$  as a discrete random variable. Their relationship can be described in terms of the mutual information,  $I$  defined as [19]:

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drawback of pursuing this approach is that the selected features may be mutually correlated, and having a redundant list of shortlisted features only adds to the computational cost of the classifier without necessarily improving its performance. Even more so, the addition of extra features commonly result in the deterioration of the classifier performance [20]. Therefore, an instinctive way forward is to keep only one feature from a correlated set of features that provide similar relevance information, and discard the remaining features from the set  $\mathcal{X}$ . We follow the minimal-redundancy-maximal-relevance () algorithm [21], that selects the features, that not only yield the maximal mutual information (11) with respect to the class label, but minimizes the mutual correlation among the features expressed in terms of redundancy  $R$  as:

$$R(\mathcal{X}) = \sum_{\mathbf{X}_i, \mathbf{X}_j \in \mathcal{X}} I(\mathbf{X}_i, \mathbf{X}_j). \quad (12)$$

where  $I$  is defined in (11). By minimizing  $R$ , the mRMR framework selects a set of mutually exclusive features that are most relevant to the class label. In this paper, we shortlist a set of ten features that are strong predictors of the future development of type 2 diabetes. With the application of the mRMR algorithm, Table II shows the list of the ten features ranked in order of their relevance to the class label, where the prefixes *au* and *sl* denote the area under the curve and slope respectively and the time interval is shown in the subscripts. In the second phase, we further pruned the number of features to four with the evaluation criteria of mean classification accuracy on the validation set. For this purpose, we ran the only by selecting the ones that provided the best performance in terms of validation accuracy using the SVM classification scheme. Table sdf shows the four best features obtained by averaging the validation accuracy over 100 iterations of the classification scheme.

$$x = \sum_{i=0}^z 2^i Q \quad (13)$$

## V. CONCLUSION

The conclusion goes here.

## ACKNOWLEDGMENT

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**Jane Doe** Biography text here.