Unraveling the Potential of Heart Rate Variability for Type 1 Diabetes Prediction

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***Abstract*—Type 1 diabetes (T1D) is an irremediable chronic disease with reduced metabolic functions of pancreatic β-cells, causing insulin diminution and elevated blood glucose concentration. Automatic diagnosis of T1D is crucial in early clinical interventions followed by appropriate management initiatives. This work explores different machine learning (ML) techniques and the ensemble of ML to non-invasively detect T1D patients exploiting the heart rate variability (HRV) captured from ECG. The ensemble classifiers are formed by assigning weights to each ML model, where the area under the receiver operating characteristics curve (AUC) is used as weights, while soft voting generates classification results. An extensive experiment has been carried out to find the appropriate hyperparameters for each ML model through grid search, while AUC is selected as the performance metric due to unbiasedness to class imbalance. A total of 115 ECG recordings (36 diabetics, 79 healthy) from 29 subjects (20 healthy, 9 T1D patients) of the D1NAMO dataset are used in the experiments. The highest classification performance is achieved using the k-nearest neighbor (KNN) classifier achieving an AUC of 0.750 ± 0.090. The outcome of this work will enhance the understanding of distinct HRV features of diabetic and healthy individuals in T1D diagnosis and characterize the impacts of T1D on cardiac asynchrony.**

***Index Terms*—electrocardiogram, heart rate variability, machine learning, non-invasive detection, type 1 diabetes**

I. Introduction

Diabetes indicates an inability to either produce or properly utilize insulin, a peptide hormone regulating glucose metabolism in body cells [1]. Type 1 and 2 are dominant categories of diabetes which can adversely affect major organs with myocardial infarction, kidney failure, retinopathy, leg amputation, etc. [2]. Type 1 diabetes (T1D) mandates synthetic insulin injections for management. While T1D is not primarily characterized by insulin resistance, individuals may experience limited insulin responsiveness. Conversely, prediabetes precedes Type 2 diabetes (T2D), stemming from inadequate insulin production or reduced responsiveness, resulting in elevated blood glucose levels. One of the primary complications of diabetes is atherosclerosis, a condition marked by plaque buildup in blood vessels [3]. This can lead to an increased risk of cardiovascular issues, including heart attacks (myocardial infarctions), due to compromised blood flow to the heart muscle [4]. Accurate and timely diagnosis of diabetes can mitigate many of these complications through early interventions, treatment plans, and appropriate management. With advanced data analytics and machine learning (ML), automatic diabetes detection has gained momentum in recent years [5]–[7].

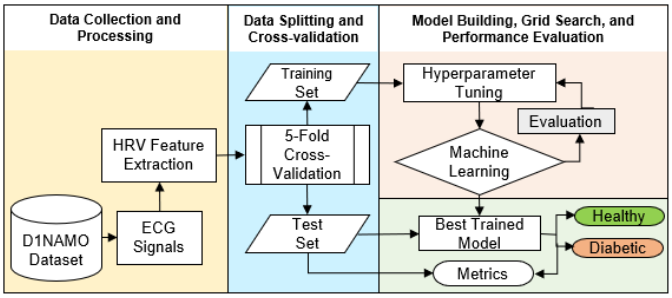

Fig. 1. Overview of type 1 diabetes detection using heart rate variability (HRV) features extracted from ECG signals.

Diabetes negatively impacts the autonomic nervous system (ANS), causing damage to nerve fibers that innervate visceral organs (e.g., the heart) [8]. In addition, it affects coronary arteries, hampering the timely detection and treatment of myocardial infarction. Cardiovascular alterations due to diabetes emerge before the disease appearance, facilitating preclinical assessment investigating heart rate variability (HRV) [9]. Therefore, risk minimization and appropriate management through therapeutic and lifestyle intervention can be facilitated by decoding the connection of diabetes with HRV.

The intrinsic bio-physical mechanism coordinating with the autonomic nervous system (ANS) and endocrine chronotropic control of the heart maintains regular cardiac rhythm [10]. The balanced interaction among these systems modulates the time interval between heartbeats, called heart rate variability (HRV). Ailments in any of the control elements lead to abnormal regulation with minimal adaptive capacity of the cardiovascular system, fluctuating HRV [11]. Diabetes stimulates cardiovascular autonomic neuropathy (CAN), clinically one of the highly relevant complications having life-threatening concerns. HRV is one of the most sensitive parameters that are highly related to CAN, therefore, to the pathogenesis of diabetes. In addition, diabetes-induced glycemic variability causes precapillary impairments affecting the blood circulation in nerves [12]. Other cardiac issues include rapid hardening of arteries (atherosclerosis) and dysfunctional ANS. Therefore, diabetes is highly related to depressed HRV changing the electrocardiogram (ECG) with potential dispersed Q-T, ST-

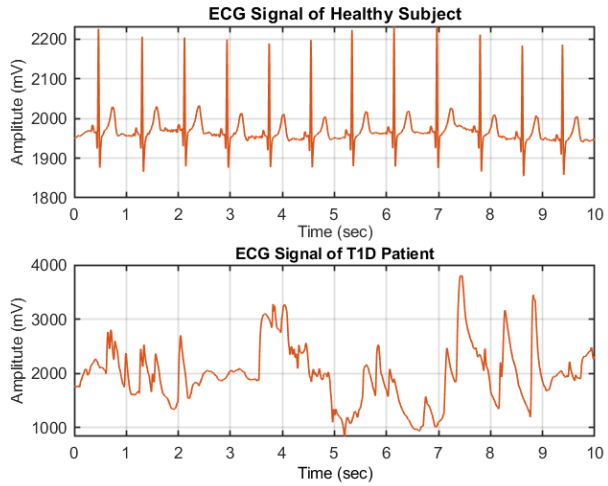

Fig. 2. Distinct ECG morphology of healthy subject and T1D patient.

T alterations, sinus tachycardia, and ventricular hypertrophy [13]. HRV can be measured by analyzing the time alterations in heartbeats (R-R interval) of the electrocardiogram (ECG), which is exploited in this work for T1D diagnosis.

An overview of the T1D detection from HRV features using ML is presented in Fig. 1. ECG signals from the publicly available multi-modal D1NAMO dataset [14] are collected and analyzed for HRV feature calculation. Different ML techniques (AdaBoost (AB), decision tree (DT), k-nearest neighbor (k-NN), naïve Bayes (NB), random forest (RF), XGBoost (XB), and multi-layer perceptron (MLP)) are implemented, and tuned with grid search and five-fold cross-validation [15], in automatically classifying diabetic and healthy subjects from HRV features. In addition, ensemble classifiers are formed and investigated for T1D prediction exploiting area under the receiver operating characteristic curve (AUC) as weights for each model and performing soft voting for generating classification output. The AUC is selected as the performance metric due to class imbalance in the dataset which can affect the accuracy and other related metrics.

The rest of the paper is organized into different sections. In Section II, the dataset and the processing techniques for extracting the HRV features are discussed. Section III describes different ML models employed in this work, as well as the ensemble classifiers that were applied. The analysis of results and the discussion are presented in Section IV. Finally, in Section V, conclusions are drawn.

II. HRV Feature Extraction from ECG

A. D1NAMO Dataset

The publicly available D1NAMO dataset includes breathing, accelerometer, food pictures, and glucose measurements for non-invasive analysis of T1D. The ECG recordings comprise a total of 115 ECG signals (36 T1D, 79 healthy) of 29 subjects (20 healthy and 9 T1D patients) [14]. The D1NAMO is a heterogenous dataset with a healthy subset (4 females and 16 males) of 26-45 years of age, while the T1D patients group (3 females and 6 males) is in a diverse 20-79 age range. The data acquisition was performed in free-living conditions with the wearable ECG sensor patch integrated into Zephyr BioHarness[3] chest-belt system. Two silver-coated nylon electrodes are used to collect the single-lead ECG signal through skin contact at a 250 Hz sampling rate. Fig. 2 illustrates a sample ECG signal from healthy and T1D subsets showing morphological distinction in patterns. The focus of this work is automatically identifying this difference between healthy and T1D patients, aiming for non-invasive T1D prediction from HRV.

TABLE I
HRV Features Calculated from ECG

HRV Features	T1D Patients	Healthy Subjects
	Mean±Std	Mean±Std
Standard deviation of all NN intervals (SDNN)	228.38±201.81	106.61±145.04
Root mean square of successive differences between adjacent RR interval (RMSSD)	380.20±191.07	255.42±147.11
Number of adjacent NN intervals having more than 50 ms difference (NN50)	34.00±15.37	30.15±23.60
Percentage of NN50 count (pNN50)	0.66±0.28	0.46±0.36
Mean heart rate (meanHR)	81.23±15.24	85.13±13.64
Standard deviation of the meanHR (SDHR)	32.53±15.17	22.42±12.80
Mean R-R interval (meanRR)	1.13±0.35	0.87±0.32
Triangular interpolation of NN intervals (TINN)	1699.72±3187.96	1149.03±302.25
R-R triangular index (TI)	124.81±81.54	77.26±78.64

B. HRV Analysis

HRV emerges from intricate heart-brain interactions and dynamic processes inherent in the ANS. HRV metric effectively reflects the regulation of several physiological aspects, including autonomic balance, blood pressure (BP), gas exchange, gut functionality, heart performance, and vascular tone, and potentially extends to encompass dynamics within facial musculature [17]. Nevertheless, it is noteworthy that heightened HRV, stemming from disruptions in cardiac conduction, is robustly associated with elevated mortality risk, particularly among the elderly population; this linkage has

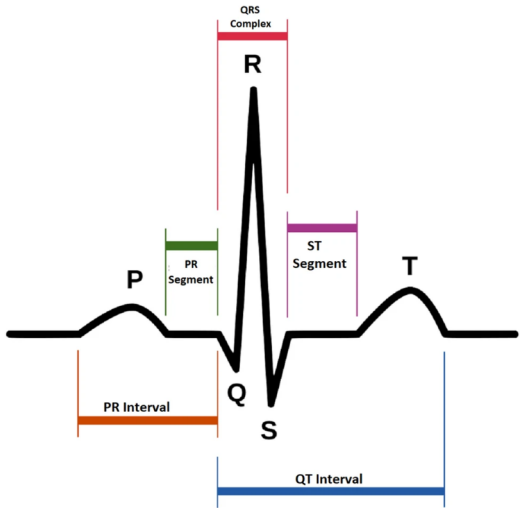

Fig. 3. Peaks and intervals of a normal ECG signal [16].

been well-established. A comprehensive examination of electrocardiogram (ECG) morphologies assumes significance in discerning instances where elevated HRV values may be rooted in conditions like atrial fibrillation [16]. An optimal HRV level is crucial due to its alignment with health, self-regulation, adaptability, and resilience.

With rapid development in sensor technology, ECG measurement technologies have been developed which are non-invasive, offering the analysis of HRV to reveal distinct pathological conditions as a promising early-stage marker [18]. The ECG signal comprises a series of positive and negative deflections, which serve as indicators of cardiac electrical activity [19]. Different fiducial points and regular time intervals are illustrated in Fig. 3. The P wave is a modest positive deflection that signifies the process of atrial depolarization and the T wave indicates ventricular repolarization. The QRS complex is characterized by a minor negative deflection succeeded by a positive peak, which is elicited by the depolarization of the ventricles. The interval between the QRS complexes is termed as R-R interval (t_{R-R}), also known as the NN interval. The heart rate ($HR = 60/t_{R-R}$) is calculated as beats per minute (bpm). HRV represents the beat-to-beat variability in heart rate, indicating the sympathetic and vagal elements of ANS in the sinus atria of the heart. Hence, the instantaneous alterations of heart rate and the R-R intervals are both captured in the HRV [20]. In normal resting conditions, the ECG exhibits respiratory sinus arrhythmia with rhythmic change in the R-R interval. With diseases and aging, HRV decreases, indicating ventricular arrhythmia and an obvious connection to diabetes-related CAN [8], [21].

The HRV is quantified using nine time-domain features, as listed in Table I, showing significant statistical variation between the healthy subjects and the T1D patients [20]. SDNN measures variability in normal sinus beat intervals in milliseconds (ms), excluding abnormal beats. Widely regarded as a benchmark for 24-hour cardiac risk assessment, SDNN predicts morbidity and mortality. Values $<$50 ms suggest unhealthy status, 50–100 ms indicate compromised health and $>$100 ms reflect robust health. RMSSD characterizes beat-to-beat variation in HR by calculating the square root of the average of squared successive time differences between normal heartbeats, all measured in ms. Despite the standard minimum recording of 5 minutes, researchers have proposed ultra-short periods of 10 s, 30 s, and 60 s for RMSSD evaluation [20]. As a primary time-domain metric, RMSSD provides insight into vagally mediated changes within HRV. NN50 quantifies the count of consecutive NN intervals exhibiting differences higher than 50 ms. pNN50 calculates the percentage of successive NN intervals with differences surpassing 50 ms. Both NN50 and pNN50 analysis requires a 2-minute epoch for evaluation. MeanHR quantifies the average heart rate over a specific period, providing insight into the overall cardiac activity. SDHR captures the variability in meanHR, shedding light on the fluctuations in heart rate values. MeanRR, on the other hand, represents the average duration between successive R waves in an ECG, offering a crucial perspective on heart rate dynamics. TINN represents the baseline width of an NN interval histogram. Similar to SDNN and RMSSD, even two artifacts within a 5-minute segment can markedly distort its measurement. TI is a geometric metric derived from 24-hour recordings, assessing HRV through the integral of the density of the RR interval histogram divided by its height. Typically evaluated using 5-minute epochs, TI, in conjunction with RMSSD, effectively distinguishes between normal heart rhythms and arrhythmias. A heart rhythm is classified as regular for TI $\leq$ 20.42 and RMSSD $\leq$ 0.068, while an arrhythmic pattern indicates a TI value exceeding 20.42. These features are fed as the input to the ML model providing binary outcomes (1: diabetic, 0: healthy).

TABLE II
OPTIMAL HYPERPARAMETERS FROM GRID SEARCH

ML Models	Optimal Hyperparameters
AdaBoost (AB)	algorithm: SAMME; learning_rate: 0.1; n_estimators: 10
Decision Tree (DT)	criterion: gini; min_samples_leaf: 1; min_samples_split: 0.6; splitter: best
k-Nearest Neighbor (k-NN)	algorithm: brute; n_neighbors: 13, p: 1
Multi-layer perceptron (MLP)	activation: ReLU; batch size: 32; epochs: 200; learning rate: 0.001; dropout rate: 0.3; Init: normal; neurons in layers: 32, 64, 32, 16
Naive Bayes (NB)	var_smoothing: 0.1
Random Forest (RF)	criterion: entropy; n_estimator: 100
XGBoost (XB)	colsample_bytree: 1.0; gamma: 1,max_depth:4; min_child_weight: 1; subsample: 0.5

III. MACHINE LEARNING FOR DIABETES DETECTION

The stratified five-fold cross-validation is used for model building, hyperparameter selection, and evaluation. In each fold, 75% of the data are used for training and validation, and the rest 25% for testing. The stratified cross-validation technique maintains the same percentage of data split as the original, eliminating the negative impact of class imbalance. For hyperparameter tuning, a grid search method is applied to obtain the optimal values as listed in Table II. A total of seven ML models AdaBoost (AB), decision tree (DT), k-nearest neighbor (k-NN), random forest (RF), multi-layer perception (MLP), naive Bayes (NB), and XGBoost (XB) are trained and tested in this work [22]. Adaptive boosting (AB) improves weak learners by amalgamating them into robust learners. During the training process, AB emphasizes misclassified instances and combines the predictions of weak learners through weighted averaging. DT uses feature space partitioning to improve the accuracy using directed trees having root node that represents a decision based on features and internal nodes. The kNN algorithm is a search algorithm that identifies the nearest distance within the training data. XB uses a gradient boosting framework in which each successive model is trained to rectify the inaccuracies of the preceding models, consequently enhancing the overall performance. The NB model is a probabilistic classifier that employs Bayes' theorem to compute the probability of a specific class based on a given set of features. The RF integrates multiple DTs through 'bagging' to mitigate overfitting and enhance the generalization. The MLP model comprises interconnected layers

of nodes, encompassing input, hidden, and output layers [7]. Through iterative training and weight adjustments, the MLP learns intricate relationships present in data. For the MLP, the number of hidden layers, neurons in each layer, activations, batch size, dropout rate, etc. are tuned in grid search to obtain the best predictive model with maximized AUC. In addition, an ensemble of different models is observed in T1D prediction using weighted soft voting using AUC as the weights.

For the performance assessment of different ML techniques, three metrics are used: AUC, accuracy, and precision. The AUC evaluates the ability to accurately distinguish between classes by measuring their separability. A higher AUC indicates better predictive performance in identifying disease and healthy conditions. Accuracy measures the overall correctness of predictions, representing the ratio of correctly predicted instances to the total. Precision focuses on the proportion of correctly identified instances within diabetic cases. These metrics collectively provide valuable insights into the effectiveness of ML models in T1D detection tasks.

IV. Experimental Results

The ML techniques are implemented using Python as the programming language with different TensorFlow, Keras, and sci-kit-learn APIs and packages. The training and the evaluation are carried out on an Intel Xeon CPU with 2 vCPUs@ 2.2GHz and 12GB of RAM. Fig. 4 presents the correlation of different HRV features with the outcome. The RMSSD and meanRR show the highest relation with diabetes, while SDNN, pNN50, SDHR, and TI are significantly related to diabetes. The statistical parameters and probability distribution of HRV features are presented in Fig. 5 demonstrating the differences between the healthy subjects and the T1D patients. Such distinct distribution confirms that HRVs are highly promising in detecting T1D patients. Table III shows the quantitative evaluation of different ML models. The average scores with the associated standard deviation (std) are reported. The highest prediction performance was achieved using the k-NN classifier with an AUC of 0.750±0.090. The random forest algorithm also demonstrates comparable performance with the highest accuracy and precision. While ensembling different models for robust performance, the ensemble classifier with AdaBoost and XGBoost provides the best AUC of 0.718±0.051. However, in the experiments, the k-NN model has demonstrated robust and reliable performance outperforming the ensemble and other ML classifiers for T1D detection from the HRV. In summary, this research confirms the feasibility of using HRV features from the single-lead ECG as a promising tool for the non-invasive detection of T1D.

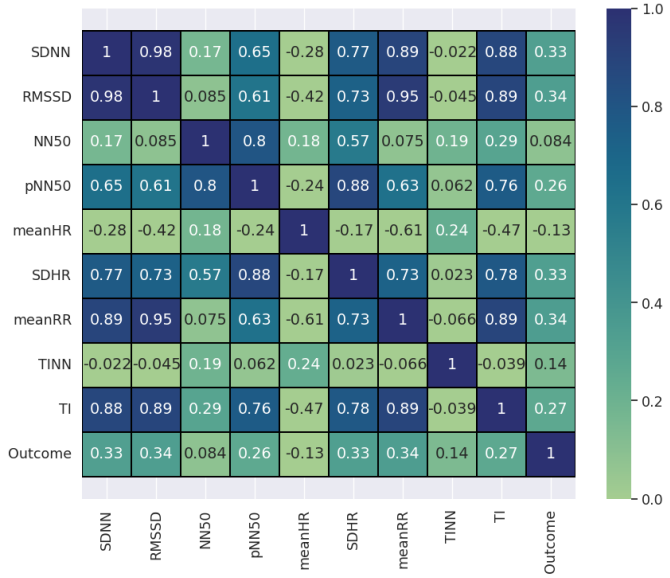

Fig. 4. Correlation matrix of HRV features relating to T1D.

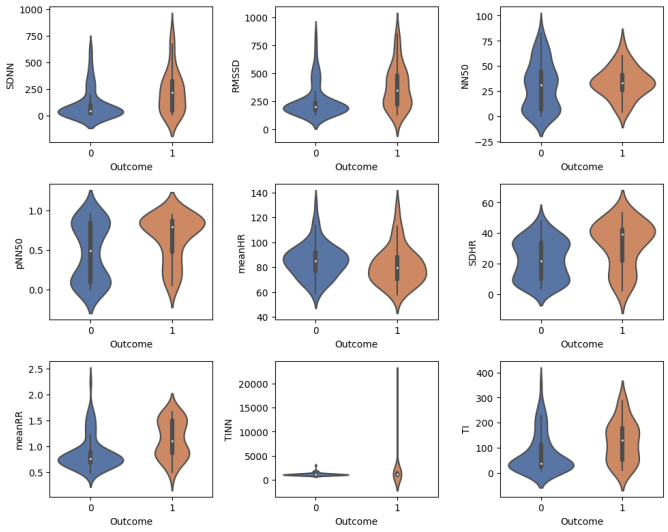

Fig. 5. The statistical analysis and probability distribution of HRV features.

TABLE III
Comparison of Different ML Models for T1D Detection

ML Models	AUC	Accuracy	Precision
XGBoost	0.728 ± 0.039	0.765 ± 0.044	0.798 ± 0.175
AdaBoost	0.688 ± 0.050	0.730 ± 0.051	0.733 ± 0.226
Naive Bayes	0.734 ± 0.058	0.730 ± 0.051	0.800 ± 0.245
Decision Trees	0.643 ± 0.108	0.713 ± 0.052	0.628 ± 0.206
Random Forest	0.700 ± 0.056	**0.791 ± 0.033**	**0.843 ± 0.135**
Multi-layer Perceptron	0.724±0.073	0.730±0.058	0.676±0.130
k-Nearest Neighbor	**0.750 ± 0.090**	0.722 ± 0.044	0.654±0.187

TABLE IV
Performance of Ensemble Classifiers for T1D Prediction

Ensemble Classifiers	AUC	Accuracy	Precision
AB+DT+KNN+NB+RF+XB	0.710 +/- 0.045	**0.765 +/- 0.059**	**0.833 +/- 0.211**
DT+KNN+NB+RF+XB	0.705 +/- 0.049	0.765 +/- 0.059	0.833 +/- 0.211
AB+DT+RF+XB	0.692 +/- 0.035	0.748 +/- 0.058	0.767 +/- 0.200
DT+KNN+XB	0.695 +/- 0.059	0.757 +/- 0.059	0.810 +/- 0.185
AB+XB	**0.718 ± 0.051**	0.748 +/- 0.058	0.814 +/- 0.229

V. Conclusion

The implications of diabetes on overall health, precipitating the onset of concurrent chronic ailments, underscore the

necessity for prompt and precise diagnosis to formulate well-suited treatment regimens. The realm of automated diabetes detection, a focal point of investigation over recent decades, has gained remarkable traction due to the evolution of data-centric machine-learning methodologies. This study delves into the utilization of Heart Rate Variability (HRV) computed from electrocardiography (ECG) for predicting type 1 Diabetes (T1D). Analysis conducted within the temporal domain unveils a noteworthy reduction in HRV among T1D patients than their healthy counterparts. The substantiation through diverse machine learning models affirms the viability of HRV as an avenue for T1D identification, offering a commendable equilibrium between accuracy and precision. Future research endeavors are poised to fortify the system's robustness and dependability. These investigations will span the gamut from empirical evaluations on clinical and non-clinical datasets to the amalgamation of ECG signals harnessed from medical-grade and non-medical wearable sensors. The ultimate aim is the development of a portable diagnostic apparatus for accurate and reliable T1D detection and monitoring.

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