Personalized Deep Glucose Level Prediction For Type 1 Diabetic Patients

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I. Introduction

In modern life, there is a possibility for at least one member in the family suffering from diabetes. It is a type of disease that occurs when the person's body has insufficient insulin production or ineffective insulin use. It occurs mostly when the body is unable to produce enough insulin or it doesn't effectively utilize the insulin. Insulin is a hormone produced by pancreas, works in regulating blood glucose levels. It helps to absorb glucose from the bloodstream to utilize energy for later use. If the person's body fails in generating the insulin properly, then the diabetes will become too high, leading to severe health problems. Diabetes are of three types, They are Type1 diabetes, Type 2 diabetes and Gestational diabetes. Patients suffering from Type 1 diabetes should need daily insulin injections to manage their glucose levels. It occurs at any age. It is caused where the body immune system attacks the insulin producing cells in pancreas. Type 2 Diabetes occur when the body fails to produce enough insulin to manage the glucose levels. It occurs because of obesity, lack of exercise etc. Gestational diabetes occurs mostly during pregnancy time and it results in the possibility of producing Type 2 diabetes for both mother and a child. Here we consider only Type 1 diabetes for predicting the Blood glucose levels.

To overcome this Type 1 diabetes, accurate glucose level prediction is important. The earlier approach follows the physiological process models, which provides the better understanding of the approach but lacks in flexibility and also it's accuracy is very low, whereas the black box model can be able to identify and learn the patterns from historical data, but it doesn't interpret the data properly, which results in difficulty of understanding the decision- making process [1].

This research aims to develop an accurate blood glucose level prediction by using physiological white box model along with the black box models for overcoming these limitations and improving the accuracy.The data can either been taken from Patient as real time data by using the CGM Monitoring devices or we can simply use the Real Time data simulator, which can be used for retrieving the best features by simulation, which is as similar to as the data retrieved from the patient in real time.

Physiological model is inspired by UVA/Padova T1D Simulator and the methodology used here is particle filter, which consists of three subsystems [1]. Then the result of this white box model is sent to black box models (as Addl input) such as LSTM, GRU, Non parametric models and finally predict the glucose level [8]. The Ultimate goal is to predict the blood glucose level in an optimal approach.

II. Related Works

This section discusses some of the relevant works carried out for Predicting Blood Glucose level.

Giacomo Cappon *et.al.* (2023) performed a study which describes the comparative evaluation of the glucose prediction models for Type 1 Diabetes (T1D). It compares the Physiological white box model with Black box model and evaluates which is better one for predicting the glucose level based on the features.The main drawback in this research is the black box models are not interpretable enough, eventhough they give good predictions, whereas the white box models had worse performance in making predictions especially in real-time predictions. So we have extended this by making this as a base for our research by taking important features from both the models and developed a hybrid approach utilized both black box and white box models efficiently. [1]

Cindy Marling[1] & Razvan Bunescu performed a study on the research done by collecting the data from 12 individuals over an 8 week period and continuously monitoring the glucose level and tracking their usage of insulin. For Physiological model, they had monitored the patients wearing the fitness bands for heart rate and their physical activity. They also used their smartphone app to track their routine life events like meals, exercise etc. that could impact their glucose levels. It includes comprehensive data collection and limits generalizability. [2]

Mario Munoz-Organero (2020) performed a study on the research which unites the physiological data by developing a deep learning model to predict a glucose level in Type 1 diabetes patients. It models the complex physiological interactions by utilizing deep neural networks. It improves the accuracy of prediction for T1DM patients through advanced modelling techniques. Here deep learning model can be complex and may face some challenges across diverse patient populations. [3].

Ganjar Alfian *et.al.* (2021) performed a study on the research which has been done by collecting the real world glucose data from T1DM Patients. Time domain features includes glucose trends and pattern over time were extracted for Model development. The Artificial Neural Network based model is used to accurately predict the blood glucose level and these performance were evaluated by performance metrics such as Mean Absolute Error(MSE) and Root Mean Squared Error(RMSE). ANN Model perform a robust performance in prediction , at the same time it is more complex and resource extensive. [4].

Jobeda Jamal Khanam & Simon Y. Foo (2021) conducted a study on the research which has been done by comparing various machine learning algorithms for predicting diabetes and the performance is evaluated in each algorithm using standard metrics like accuracy, precision and recall. It provides a comparison of different machine learning algorithm for predicting diabetes and helps in identifying the most efficient algorithm. Here the performance can vary depending on the quality and content of dataset. For evaluating multiple algorithms , it requires substantial computational resources. [5].

Wonju Seoa *et.al.* (2021) performed a study on the research which has been done by collecting the real world CGM(Continuous Glucose Monitoring) data like meal intake, Physical activity etc... The model is developed by initial training on a generic CGM dataset using regression models and neural networks. To adapt the model for individual glucose response , it transfers learning for personalization, custom loss function for glucose response variability. The performances are evaluated by Mean Absolute Error(MSE) and Root Mean Squared Error(RMSE) metrics. Here Prediction accuracy is improved through Personalized fine-tuning. Advance Machine learning techniques lead to the complexity of model and it is not efficient without sufficient patient data. [6].

Hatice Vildan Dudukcu *et.al.* (2021) performed a study on the research, in which blood glucose levels are predicted by utilizing deep neural networks combined with weight decision level fusion. Also multiple prediction models and applied fusion techniques were integrated to improve accuracy and robustness performance. Deep neural networks effectively capture complex patterns in glucose data. For training and fusion process it requires significant computational resources and the performance heavily depends on the weight of fusion and the quality of input data. [7].

The authors Shahid Mohammad Ganie & Majid Bashir Malik (2022) performed a study on the research which has been done by applying an ensembled Machine learning using lifecycle activities such as diet, exercise etc. for predicting type 1 diabetes. It improves the accuracy of prediction and robustness performance. It utilizes an ensembled approach to reduce overfitting as well as to enchance prediction accuracy. Performance may vary based on the quality and relevance of lifestyle data. [8].

Yang Guanci *et.al.* (2023) performed a study to predict the short-term blood glucose level by implementing a temporal multi head attention mechanism. To enchance the prediction accuracy it utilizes various historical glucose data and attention mechanisms. It is crucial for timely diabetes management as it focusses more on short term glucose level predictions. It effectively captures the temporal glucose data. The performances can vary depending on the different type of glucose monitoring devices. [9].

Gangani Dharmarathne *et.al.* (2024) performed a study on the research which focuses more on Interpretability so they have developed a machine learning model for diabetes diagnosis. It provides transparent and understandable predictions by implementing a Self explainable interface. With advanced machine learning techniques it potentially improves diagnostic accuracy. It give clear explanations of diagnosis decisions and may be limited by the quality and representiveness of training data. [10].

Sean Pikulin *et.al.* (2024) performed a study on the research which has been done by collecting the physiological data using smart watch sensors. Based on the smart watch data , they had developed a predictive model. using physiological data it provides real time glucose predictions. Accuracy may vary depend upon the quality and type of data taken from smartwatch and alsoit has the issues with data privacy and security. [11].

Deepjyoti Kalita *et.al.* performed a study on the research which uses GAN architecture which leads to better glucose forecasting using high-fidelity data, which will lead a better clinical outcomes. It uses both real and synthetic data for improving the accuracy of the glucose forecasting model, by achieving lower RMSE than previous methods,but it's architecture has increased computational complexity. [12]

FEDERICO D'ANTON[I] *et.al.* performed a study on the research which effectively improves the performance by training only the meta -learner with limited amount of data, but including additional parameters beyond CGM did not significantly improves the performance. [13]

Zhendong Wang *et.al.* performed a study on the research which proposes a generalized multivariate forecasting for predicting the glucose levels, utilizing the method called "COMET", which has three domain-specific constraints for diabetic patients, but it can't incorporate the clinical experts in assessing the effectiveness and relevance in glucose forecasting. [14]

Sadegh Mirshekarian *et.al.* proposed a study on the research which uses LSTM networks for predicting the blood glucose levels, as it is good for time series data. Since it can learn from multiple variables, it addresses the vanishing gradients, but it needs a large datasets for accurate prediction, which is not always available. [15]

Sadegh Mirshekarian *et.al.* proposed a study on the research which effectively compares the LSTM and attention-based neural networks for predicting the BG levels for T!D patients using real and synthetic datasets, while attention mechanisms provides improved accuracy, it requires more time and may not generalize the data for predicting the blood glucose levels. [16]

Roberto Visentin *et.al.* proposed a study on a computational tool, which is specifically designed for identifying the Type 1 diaetes patients. If provides a cost-effective and time saving methodology for clinical trials, but the mathematical models used here is very difficult to understand. [17]

Giacomo Cappon *et.al.* proposed a study on the research which represents a bayesian framework for estimating the parameters of Type 1 diabets using the available patient data. It addresses the issues by incorporating the Bayesian estimation with Markov chain Monto Carlo to provide better estimation of parameters and interval, however this methodology is best suitable for synthetic data, not on real data. [18]

John Daniels *et.al.* proposed a study on the research which improves the blood glucose predictions by utilizing the data from multiple subjects, which enhances the model using limited specific data features. It performs better than traditional methd, but the training complexity is very difficult, and also it requires a careful training to avoid the overfitting. [19]

Giulia Noaro *et.al.* proposed a study on the research which provides an effective and safe rule for the composition of mealtime insulin dosage in T1D management. They have proposed an ensemble method for mealtime insulin bolus, which combines the two models. It has been trained using a synthetic data of 100 virtual mealtime objects, but id doesn't provides multiple sources such as CGM, CHO,, and also it doesn't use the real data by leveraging the proposed in-silico framework for addressing the T1D management. [20]

III. Proposed Methodology

Our Methodology predicts the blood glucose levels using an hybrid layered approach that combines the benefits from physiological (white-box) models with deep learning models such as LSTM, GRU, TCN and Non Parametric Models. This hybrid model provides better understanding of glucose levels by utilizing the best features of deep learning techniques to accurately predict the glucose levels, particularly for patients with Type 1 Diabetes Mellitus (T1DM).

A. Data Collection and Description

Data which has been used here was taken from the Ohio Type 1 Diabetes Mellitus(T1DM) dataset, which can be accessible from [2]. It consists of atmost 20 features taken from Patients over the period of 8 weeks with the difference of every 5 mins.Out of which this model has taken only few features which are most important for predicting the blood glucose level, which has been explained in the corresponding sections. It consists of 8 patient's data. Out of which 6 patient's data has been utilized for effective training of this model, whereas the remaining 2 patient's data has been utilized for testing and validating the prediction accuracy of this model.

For accurately predicting the glucose levels, this model utilized the data that influence glucose features. In this work, the following data features are utilized:

- **Continuous Glucose Monitoring (CGM) Data**: CGM devices provide real-time measurements of interstitial glucose concentrations at regular intervals (e.g., every 5 minutes). This data captures the sudden changes/deviations in glucose levels, acting as a neccessary input for prediction.
- **Insulin Intake**: Information about insulin intake, insulin dosage and time at which the Insulin intake by the person is neccessary, as excess insulin intake will seriously affect glucose levels. Data on both basal (long-acting) and bolus (rapid-acting) insulin dosage are collected.
- **Meal Intake Data**: Carbohydrate intake, meal intake, and time stamps are needed to model glucose absorption system from meals. This includes data from the glycemic level of foods, which influences the speed of glucose absorption.

B. Data Preprocessing

The raw data collected from various sources is then sent for preprocessing to ensure flexibility and reliability for better glucose level predictions. The steps involved include:

- **Time Series Data and its Alignment**: Since the data has been collected from different sources with varying sampling rates, all time-series are aligned to a common time field for easy interaction and prediction. Techniques like interpolation are used to align the time series data to consistent intervals (e.g., every 5 minutes), ensuring order alignment of time stamps across the features.
- **Handling Missing Values**: Since this model used the real world data, which is often incomplete. Missing glucose readings are replaced using some common methods, while missing meal or insulin records has been replaced by nearest-neighbor data.
- **Normalization and Standardization**: To perform model training, all numerical features are normalized to a standard level (e.g., Min-Max Normalization).
- **Feature Engineering**: The raw data has been finally converted to identify important features such as moving averages, rates of change, and lagged values, which has been described elaborately in corresponding sections.

C. Feature Extraction

To improve the accuracy of the model for better prediction, various features has been extracted from the preprocessed data, which involves creating new features for identifying meaningful patterns and temporal relations from the data:

- **Moving Averages** : The moving average of glucose readings is described over different time windows (e.g., 15, 30, and 60 minutes) which helps in determining the longer trends in glucose dynamics.

D. White-Box Physiological Modeling

White box models are implemented by a nonlinear physiological model , it is a benchmark for comparison against blackbox model by simulating glucose-insulin dynamics. Here, physiological equations are used to describe glucose insulin interactions , biologically based predictions etc.. There are two algorithms used here ,they are Bayesian Estimation and Particle filter. In Bayesian Estimation, Markov Chain Rule

Monte Carlo (MCMC) has been used to estimate the individual parameter,which uses Single Component Metropolis-Hastings(SCMH). Whereas in Particle Filter(PF), State Estimation(SE) method is used, which handles the non linearity and allows real time glucose prediction. Using these algorithm, we can derive three subsystems which is used for predicting the glucose level. They are Insulin Absorption Subsystem, Oral Glucose Absorption Subsystem and Glucose-Insulin Kinetics Subsystem The three Subsystems involved are explained as follows:

- **Subcutaneous Insulin Absorption Subsystem**: Looking onto the Insulin absorption subsystem, which models the movement of insulin through the body after it's injected. It tracks the absorption of insulin accounting for injected insulin entering into the bloodstream. It utilizes different compartments for absorption of insulin such as monomeric and non monomeric form.
  Here the equations for diffusion and absorption to predict plasma insulin level.

$$I_{sc1}(t) = -k_d \cdot I_{sc1}(t) + I(t-\beta)/V_I \tag{1}$$

$$I_{sc2}(t) = k_d \cdot I_{sc1}(t) - k_{a2} \cdot I_{sc2}(t) \tag{2}$$

$$I_p(t) = k_{a2} \cdot I_{sc2}(t) - k_e \cdot I_p(t) \tag{3}$$

  where,
  - $I_{sc1}(t)$:represents insulin which has been available in the first compartment as non-monomeric form. (before it starts to become active). t
  - $I_{sc2}(t)$: represents insulin that has been transformed to a monomeric state (ready for absorption into the bloodstream).
  - $I_p(t)$: is the plasma insulin concentration.
  - k_d : is the rate at which insulin transforms from a non-monomeric state to a monomeric state.
  - k_{a2} :is the absorption rate from the monomeric form into the plasma.
  - k_e : is the clearance rate, which indicates how quickly insulin is removed from the plasma.
  - $I(t-\beta)$: represents the insulin injected at time $(t-\beta)$, with a delay β
  - V_I : is the volume of insulin distribution in the body.
- **Oral Glucose Absorption Subsystem**: Next we look onto the Oral Glucose Absorption System , which models the absorption of glucose from carbohydrates consumed during meals, focusing on how glucose moves through different compartments. The techniques used here describes the glucose absorption in a two compartment system (ie.) stomach, Intestine. Glucose moves through two storage compartments where it can be absorbed into the bloodstream before reaching the gut. This model briefly elaborate the effects of carbohydrate intake, gastric emptying, and absorption rates with different parameters for gastric emptying and absorption of intestinal using differential equations which is represented by the below formula:

$$\dot{Q}_{sto1}(t) = -k_{gri} \cdot Q_{sto1}(t) + CHO(t) \tag{4}$$

$$\dot{Q}_{sto2}(t) = k_{gri} \cdot Q_{sto1}(t) - k_{empt} \cdot Q_{sto2}(t) \tag{5}$$

$$\dot{Q}_{gut}(t) = k_{empt} \cdot Q_{sto2}(t) - k_{abs} \cdot Q_{gut}(t) \tag{6}$$

$$R_a(t) = f \cdot k_{abs} \cdot Q_{gut}(t) \tag{7}$$

  where,
  - $Q_{sto1}(t)$: is the amount of glucose in the solid state in the stomach.
  - $Q_{sto2}(t)$: is the glucose in the liquid state after being broken down in the stomach.
  - $Q_{gut}(t)$:represents the glucose in the intestines which is ready for absorption into the bloodstream.
  - k_{gri} : is the rate constant of grinding.
  - k_{empt} :is the gastric emptying rate, determining how quickly glucose moves from the stomach to the intestines.
  - k_{abs} : is the rate of glucose absorption from the intestines into the bloodstream.
  - $CHO(t)$: represents the carbohydrate intake (in mg/kg/min) at time t.
  - $R_a(t)$:is the rate at which glucose enters the bloodstream
  - f : is a constant representing the fraction of glucose absorbed.
- **Glucose-Insulin Kinetics Subsystem**:This subsystem represents interation between both the glucose and insulin for predicting the glucose transport and utilization in the body. It focuses mainly on how glucose levels change in response to insulin and how insulin sensitivity may vary over time. It describes how plasma glucose levels change due to insulin's effects and elaborate the dynamic nature of the insulin sensitivity. The three compartment model used here is explained using differential equations, it is represented by the formula:

$$\dot{G}(t) = -\left[SG + \rho(G)X(t)\right] \cdot G(t) + \frac{SG \cdot G_b + Ra(t)}{V_G} \tag{8}$$

$$\dot{X}(t) = -p_2 \cdot \left[X(t) - SI \cdot (I_p(t) - I_{pb})\right] \tag{9}$$

$$\dot{I_G}(t) = -\frac{1}{\alpha}\left(I_G(t) - G(t)\right) \tag{10}$$

  where,

- $G(t)$: represents the plasma glucose concentration.
- SG : which represents the body's ability for disposing the glucose.
- $\rho(G)$: is a function that increases insulin action when glucose levels are low.
- $X(t)$: is the insulin action on glucose, which represents how quickly insulin reduces blood glucose.
- G_b : is the basal glucose level.
- $Ra(t)$: Rate of appearance of glucose at time t.
- V_G: is the volume of glucose distribution in the body.
- p_2 : is a rate constant which is related to insulin action dynamics.
- SI : is the insulin sensitivity, which indicates how responsive, the body is to insulin.
- $I_p(t)$: Plasma insulin concentration at time t.
- I_{pb} : is the basal (normal) insulin level in the plasma.
- $I_G(t)$: is the interstitial glucose concentration, which is measured by CGM devices.
- α : is the delay factor between plasma glucose and interstitial glucose.

E. Black-Box Deep Learning Models

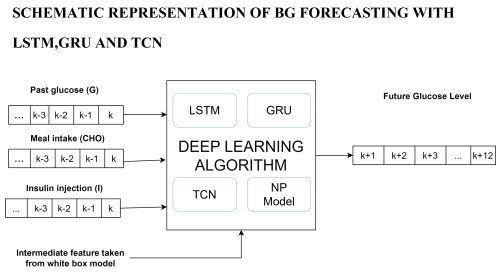

Fig. 1. Schematic Representation of BG Forecasting.

The deep learning models (black-box) uses deep techniques to capture complex relations in time-series data:

- **Long Short-Term Memory (LSTM) Networks**: LSTM networks are designed to overcome the vanishing gradient problem by using memory cells that maintain information over long sequences. This makes LSTMs suitable for capturing long term level of insulin or meals.
- **Gated Recurrent Units (GRU)**: GRUs simplify the architecture of LSTMs by using fewer gating mechanisms with effective modeling in predicting the glucose levels.
- **Temporal Convolutional Networks (TCN)**: TCNs used for handlling sequential data, utilizing convolutional layers.
- **Non Parametric Models**: NP models extend traditional neural networks by providing estimates of the uncertainty in the predictions. It's capability is more useful for real-world applications for better predictions.

F. Hybrid Model Integration

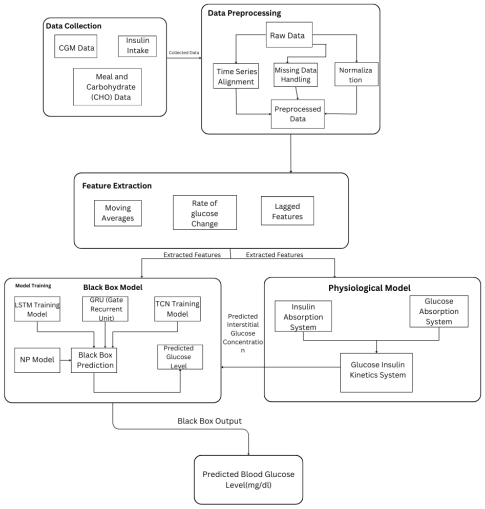

Fig. 2. System Diagram of the Proposed Approach

The hybrid modeling framework integrates the outputs of the physiological model with deep learning models:

- **Physiological Model Outputs**: The outputs from the white-box model, such as predicted glucose levels and insulin intake, has been provided as additional inputs to the black-box model, which allows the deep learning models for predicting the final glucose levels for Type 1 diabetic patients with better insights and accuracy.

G. Model Training and Evaluation

The training process involves better prediction of the model parameters and evaluating performance of the model using specific metrics:

- **Data Partitioning**: The data is divided into training, validation, and test sets utilizing for better training of the model.
- **Evaluation Metrics**: Accuracy and Performance of the developed model has been identified using metrics such as Mean Absolute Error (MAE), Root Mean Squared Error (RMSE) and Time Gain(TG).

H. Prediction Output

The final output consists of the predicted glucose levels for different time horizons such as 30 mins, 45 mins, 60mins:

- **Prediction Horizon**: The model is designed to predict glucose levels over a specified time horizons such as 30mins, 60mins etc..

Thus our proposed methodology describes an hybrid approach by combining both physiological modeling(three subsystems) and deep learning techniques for blood glucose prediction, which provides more accurate and personalized prediction model for predicting the Glucose levels accurately.

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