



Multi-Parametric Glucose Prediction Using Multi-Layer LSTM

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Abstract

Diabetes causes irregular glucose levels, such as hyperglycemia (high glucose) and hypoglycemia (low glucose), which affect the quality of life of diabetes patients. Early detection of hyperglycemia and hypoglycemia is important for effective management of the disease. In recent years, progress has been made in the development of artificial intelligence-based tools for effective diabetes management. These tools aim to predict glucose levels before they reach critical levels, enabling people with diabetes to take proactive measures to keep their glucose levels within a healthy range. However, most of these tools use single-layer architectures and rely only on glucose measurement as a predictive parameter, thus resulting in low predictive accuracy. Here, this paper proposes a multi-layer Long-Short Term Memory (LSTM)-based model for glucose prediction. The proposed model was tested on the OhioT1DM dataset and the lowest Root Mean Square Error value was obtained as 14.364 mg/dL for glucose prediction over a 30-min prediction horizon. The results demonstrate the performance of the proposed system, which uses a multi-layer LSTM algorithm to overcome the complex memory operations associated with multi-parameter prediction.

Keywords: Artificial Intelligence, LSTM, Diabetes, Glucose Prediction.

Çok Katmanlı LSTM Kullanarak Çok Parametrelilikli Glikoz Tahmini

Öz

Diyabet, hastaların yaşam kalitesini etkileyen hiperglisemi (yüksek glikoz) ve hipoglisemi (düşük glikoz) gibi düzensiz glikoz seviyelerine neden olmaktadır. Hiperglisemi ve hipogliseminin erken teşhisi bu hastalığın etkin yönetimi için önemlidir. Son yıllarda, etkili diyabet yönetimi için yapay zeka tabanlı araçların geliştirilmesinde ilerleme kaydedilmiştir. Bu araçlar, glikoz seviyelerini kritik seviyelere ulaşmadan önce tahmin etmeyi ve diyabetli kişilerin glikoz seviyelerini sağlıklı bir aralıkta tutmak için proaktif önlemler almalarını sağlamayı amaçlamaktadır. Ancak, bu araçların çoğu tek katmanlı mimariler kullanmakta ve tahmin parametresi olarak yalnızca glikoz ölçümüne dayanmakta, dolayısıyla düşük tahmin doğruluğu ile sonuçlanmaktadır. Bu makalede, glikoz tahmini için çok katmanlı Uzun-Kısa Süreli Bellek (LSTM) tabanlı bir model önerilmektedir. Önerilen model OhioT1DM veri kümesi üzerinde test edilmiş ve 30 dakikalık bir tahmin ufku boyunca glikoz tahmini için en düşük Kök Ortalama Kare Hata değeri 14.364 mg/dL olarak elde edilmiştir. Sonuçlar, çok parametrelilikli tahminle ilişkili karmaşık bellek işlemlerinin üstesinden gelmek için çok katmanlı bir LSTM algoritması kullanan önerilen sistemin performansını göstermektedir.

Anahtar Kelimeler: Yapay Zeka, LSTM, Diyabet, Glikoz Tahmini.

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1. Introduction

Diabetes is a persistent metabolic condition characterized by reduced insulin production, leading to fluctuations in blood glucose levels that deviate from the norm (Palaz et al., 2021). These fluctuations in blood glucose levels, which affect human well-being, are divided into hyperglycemia, characterized by high blood glucose levels, and hypoglycemia, characterized by low blood glucose levels (Kılıç, 2021). In this context, continuous glucose monitoring (CGM) devices have been developed to improve diabetes management through monitoring the regularity of glucose level (Mercan et al., 2020; Mercan & Kılıç, 2020). However, these devices provide instantaneous warnings and metabolism is affected until patients take the necessary precautions. Therefore, there has been increasing interest in recent years for the development of sophisticated artificial intelligence (AI)-based systems to predict glucose levels in diabetes patients. These systems aim to take the necessary precautions and improve diabetes management through predicting future glucose levels (Kılıç et al., 2022; Strollo et al., 2021). Machine learning and deep learning algorithms, which are subfields of artificial intelligence, are used in AI-based systems for glucose prediction (Akosman et al., 2021; Sayraci et al., 2023; Şen et al., 2022). Machine learning algorithms are designed to learn from historical and current glucose data, making predictions about future glucose levels (Çaylı et al., 2021; Doğan et al., 2022). These algorithms analyze patterns in the data to identify correlations and make accurate predictions. However, with machine learning algorithms, feature extraction is performed manually, which introduces the risk of missing important patterns or relationships that the algorithm could have captured. On the other hand, deep learning algorithms extract features autonomously, resulting in more robust predictions (Çaylı et al., 2023).

Alberti et al. (2019) presented an approach to glucose prediction using a nonlinear autoregressive neural network and Long-Short-Term Memory (LSTM) models (Aliberti et al., 2019). The results clearly show that the nonlinear autoregressive neural network gives promising results for prediction. Wang et al. proposed a new approach, VMD-IPSO-LSTM, which combines Variable Modal Decomposition (VMD) and advanced particle swarm optimization (IPSO) algorithm to optimize the LSTM model. The results of the study indicate that the VMD-IPSO-LSTM method outperformed the other methods in terms of achieving lower Root Mean Squared (RMSE) values (Wang et al., 2020). Li et al. introduced the Convolutional Recurrent Neural Network (CRNN) model, which is a combination of LSTM and Convolutional Neural Network (CNN) layers. They showed that the CRNN model outperformed the traditional Recurrent Neural Network (RNN) and CNN models for predicting glucose levels (Li, Daniels, et al., 2019). Song et al. presented an approach combining Empirical Mode Decomposition (EMD) and LSTM for glucose prediction (Song et al., 2019). Their study showed that the combination of EMD and LSTM outperformed other approaches for short-term predictions. Zhu et al. introduced a deep learning model based on the Extended Recurrent Neural Network architecture, called DRNN (Deep Recurrent Neural Network) (Zhu et al., 2020). The DRNN model uses expansion to capture long-term dependencies and has a larger receptive field in terms of neurons. The study presented the success of the DRNN model in capturing long-term dependencies. Li et al. presented GluNet, which uses a personalized neural network to predict the probabilistic distribution of CGM measurements (Li, Liu, et al., 2019). Results showed improvements over existing methods in terms of RMSE for different prediction horizons (PH). Bhimireddy et al. developed a prediction model using methods such as Bidirectional LSTM, BiLSTM, CNN, and Convolutional LSTM (Bhimireddy et al., 2020). The results showed that BiLSTM outperformed the compared models. Zhang et al. used methods such as array-to-array LSTM, multiple linear regression, bidirectional reservoir calculation, and Dilated CNN for blood glucose prediction. The results showed that the model they proposed provided a practical solution while minimizing computational effort (Zhang et al., 2021).

The aforementioned studies use algorithms in the traditional single-layer framework, which limits the prediction accuracy. To overcome this limitation and further improve the accuracy of glucose prediction, more sophisticated approaches are required. In this paper, we introduce a novel prediction model for glucose prediction that leverages a multi-layer LSTM algorithm. The ability to learn and extract detailed contextual information from sequential data is improved through increasing the number of layers in a neural network structure (Fetiler et al., 2021). In addition, the accuracy of glucose prediction is related to the number of parameters used in the prediction process. The proposed model includes additional parameters such as glucose level, bolus insulin, basal insulin and carbohydrate amount, allowing it to include a wider range of factors affecting glucose levels and provide more robust predictions.

The rest of this paper is structured as follows: Section 2 provides a detailed description of the proposed model. Section 3 presents the dataset and the experimental results. Finally, Section 4 concludes the paper with a brief summary.

2. Methods

This section presents a comprehensive analysis of the RNN-based algorithms and data preprocessing steps that are the key components of the proposed model.

2.1. Recurrent Neural Network

An RNN is built with recurrent connections that facilitate the flow of information from one time step to another, allowing the network to capture temporal dependencies and process sequences of different lengths. The basic framework of an RNN encapsulates a hidden state that is constantly changing and self-improving with each temporal increment that combines the current input with the previous input. This hidden state acts as a memory that holds information about past inputs, allowing the network to make predictions or generate outputs from the context of the sequence (Graves et al., 2013). RNNs are flexible and can handle sequences of different lengths. However, they suffer from some limitations, such as difficulties in capturing long-range dependencies (vanishing and exploding gradients) and computational inefficiency. As a result, more advanced RNN variants, such as LSTM and Gated Recurrent Unit (GRU), have been developed to address these issues and improve the modeling of sequential data (Chen, 2016; Çaylı et al., 2022).

2.2. Long-Short Term Memory

LSTM is a specialized RNN model designed to overcome the vanishing gradient problem and provide superior learning of long-term dependencies. The LSTM architecture consists of memory cells connected by a series of gates, including an input gate, a forget gate, and an output gate, which control the flow of information within the network, allowing it to selectively remember or forget information at each time step. This gating mechanism enables LSTMs to capture and retain relevant information over long sequences, making them suitable for tasks that require modeling long-range dependencies. The input gate helps to regulate the flow of new information to be stored in the memory cell, while the forget gate determines how much of the past memory is retained. The output gate is designed to modulate the amount of information transferred from the memory cell to the next time step.

2.3. Gated Recurrent Unit

GRU is a specialized RNN architecture designed for the purpose of handling and representing sequential data. The GRU architecture consists of a gating mechanism that allows the network to selectively update and reset its hidden state at each time step (Keskin et al., 2021). This gating mechanism helps the network retain relevant information and discard irrelevant information, allowing it to capture long-term dependencies. GRU combines the forget and input gates into a single update gate, simplifying the architecture and reducing the number of gates (Aydın et al., 2022; Betül et al., 2022). An advantage of GRU networks is their computational efficiency compared to LSTM networks, as they have a simpler architecture with fewer parameters. This makes GRU networks faster to train and more suitable for applications with limited computational resources.

2.4. Data Preprocessing

Data preprocessing is the steps taken to prepare and cleanse raw data before it can be used for analysis or modeling purposes. It involves transforming the data into a format suitable for the task, such as filling in missing values, normalizing or scaling variables, and selecting features.

Missing values, a common problem in data analysis, often result from incomplete or unrecorded parameters. Missing values in time series data are a challenge because they can affect the accuracy of learning and prediction processes. Linear interpolation is a widely used method that estimates missing values by filling them with values that lie on a straight line between two neighboring observed values. This method assumes a linear relationship between the observed values to predict the missing values.

On the other hand, data normalization is a preprocessing technique used to transform data into a standard format that allows fair comparisons and analyses between different variables or datasets. It involves adjusting the values of variables to a common scale while preserving the original distribution or without losing important information. Standard scaling, one of the most common data normalization techniques, is used to transform numerical data into a standard distribution characterized by zero mean and one standard deviation. The purpose of standard scaling is to put all variables on a common scale, which is particularly useful when variables have different units or scales.

Feature Selection is used to select a subset of features that can represent the data and improve the performance of predictive models. In feature selection, correlation heatmaps are commonly used to visually explore the relationships between features in a dataset. Correlation heatmaps are a type of graph used to visualize relationships between numerical variables. A correlation heatmap is a graphical representation used to illustrate relationships between numerical variables. In this visual representation, numerical variables are organized as columns and the rows represent the associations between each possible pair of variables. The values within the heatmap cells convey the degree of association, with positive values indicating positive correlations and negative values indicating negative correlations, as shown in Figure 1.



Figure 1. Correlation heatmap: 1-Glucose, 2-Basal insulin, 3-Bolus insulin, 4-meal, 5- Basis GSR, 6- Basis skin temperature, 7- Acceleration

3. Experimental Evaluations

3.1. Dataset

The OhioT1DM dataset includes an eight-week data collection period for each of the twelve individuals diagnosed with type 1 diabetes, uniquely identified by randomly assigned ID numbers: 540, 544, 552, 559, 563, 567, 570, 575, 584, 588, 591 and 596. Insulin pump therapy with CGM was employed by all patients, and their life event data were reported through a custom smartphone app. Additionally, physiological data from a fitness band was provided by them. The first cohort of six patients wore the Basis Peak, while the second cohort of six patients wore the Empatica Embrace fitness bands. In 2018, data from the first cohort of the Blood Glucose Level Prediction Trial (BGLP) were published. Two years later, in 2020, the second cohort of the BGLP follow-up will publish its data set. This comprehensive dataset includes a range of information, including CGM readings taken at five-minute intervals, finger-stick glucose readings, detailed records of both bolus and basal insulin doses, and self-reported meal entries with associated carbohydrate estimates. It also includes time stamps for exercise sessions, sleep periods, work-related activities, stress states, and periods of illness. Adding to the richness of the dataset, data collected from fitness bands, particularly the Basis Peak band, provides additional information. This additional information consists of statistics collected at five-min intervals for heart rate, galvanic skin response, skin temperature, air temperature, and step count (Marling & Bunescu, 2020).

3.2. Evaluation Metrics

In this paper, we evaluate the performance of the model using 4 widely known statistical measures: RMSE, Mean Absolute Error (MAE), Mean Absolute Percentage Error (MAPE), and R^2 . These metrics are widely used in various systems to measure the accuracy of predictions compared to the actual values of users. In addition, the study included an assessment of the robustness and accuracy of the model through the incorporation of a clinical metric, the Surveillance Error Grid (SEG). RMSE measures the square root of the mean squared difference between predicted and actual values, providing an overall measure of the magnitude of errors. On the other hand, MAE is a metric used to quantify the average size of errors or deviations between predicted and actual values. MAPE is a metric used to measure the percentage difference between predicted and actual values. The R^2 metric is a statistical measure used to assess the quality of fit of a regression model. The formulas for RMSE, MAE, MAPE, and R^2 can be expressed as follows:

$$\text{RMSE} = \sqrt{\frac{1}{n} \sum_{i=1}^n (y_i - \hat{y}_i)^2} \quad (1)$$

$$\text{MAE} = \frac{1}{n} \sum_{i=1}^n |y_i - \hat{y}_i| \quad (2)$$

$$\text{MAPE} = \frac{1}{n} \sum_{i=1}^n \left| \frac{y_i - \hat{y}_i}{y_i} \right| \times 100 \quad (3)$$

$$R^2 = 1 - \frac{\sum_{i=1}^n (y_i - \hat{y}_i)^2}{\sum_{i=1}^n (y_i - \bar{y})^2} \quad (4)$$

where i represents the index of each observation, m represents the total number of observations, y_i denotes the actual values, \hat{y}_i represents the predicted values, and \bar{y} represents the mean of the actual values.

SEG metric is a tool used to assess the accuracy and robustness of glucose monitoring systems. The SEG metric assesses the clinical impact of glucose measurement errors and categorizes them into different zones based on their potential to affect patients.

Table 1. Performance comparison of RNN-based architectures according to the number of layers

Model	2-layer	4-layer	6-layer	8-layer	10-layer
ML RNN	15.112	15.398	15.087	15.013	14.789
ML LSTM	14.787	14.364	14.734	14.930	15.747
ML GRU	14.867	14.435	14.547	14.725	14.788

3.2. Results and Discussion

In this study, the OhioT1DM dataset was used to train the RNN, LSTM, and GRU algorithms. Prior to training, a careful selection of hyperparameters was made to optimize the performance of the models. The hyperparameter values that gave the least error during testing were selected for training. The models were trained for 200 epochs with a learning rate of 0.0001, a batch size of 32, and the RMSprop optimizer. In order to study the performance of the multi-layer versions of the algorithms on a 30-min PH, experiments were performed with 2, 4, 6, 8, and 10 layers, as shown in Table 1. A comprehensive evaluation was carried out to assess the performance of these architectures using data from a sample of twelve patients. Based on the analysis of the results, increasing the number of layers has a positive effect on the models. The results also show that the 4-layer LSTM model outperforms the other models in terms of predictive ability.

Detailed results of the proposed multi-layer LSTM prediction model by patients are shown in Table 2. Patient 544 had the lowest RMSE value of 11.382 mg/dL among the twelve patients. To demonstrate the reliability and robustness of the proposed model, an SEG analysis was performed on patient 544, as shown in Figure 2. This analysis aimed to evaluate the performance and accuracy of the model by comparing its predictions with the actual values. The results of the SEG analysis showed a high level of agreement between the predicted results produced by the proposed method and the actual values. Table 3 provides a comprehensive comparison of the proposed prediction model with existing studies using the OhioT1DM dataset. The results clearly show that the proposed model outperforms the state-of-the-art studies in terms of prediction accuracy. Among the existing studies, the closest to the proposed model is the study by (Zhu et al., 2020) which achieved a prediction error of 18.90 mg/dL. In contrast, the proposed model achieves a lower prediction error of 14.364 mg/dL. The relatively poor performance of existing studies can be attributed to the use of simple architectures such as single-layer neural networks. In addition, existing studies depend on only glucose as a parameter for prediction. This limited feature set may not fully capture the multifaceted nature of glucose dynamics.

Table 2. Statistical evaluation of the proposed prediction model for each patient

Patients	RMSE	MAE	MAPE	R^2
540	16.328	10.840	7.860	0.940
544	11.382	7.574	5.070	0.956
552	12.810	8.193	6.270	0.942
559	14.241	8.645	5.490	0.956
563	14.944	9.012	5.650	0.894
567	15.230	9.754	6.960	0.920
570	12.096	7.840	4.070	0.967
575	17.943	9.925	6.970	0.910
584	16.307	10.540	6.990	0.928
588	13.072	8.700	5.320	0.928
591	15.683	10.069	7.660	0.903
596	12.326	7.939	5.920	0.941
Average	14.364	9.086	6.186	0.9321

Table 3. Comparison of state-of-the-art studies and proposed model

	Method	RMSE (mg/dl)
(Zhu et al., 2020)	DRNN	18.90
(Bhimireddy et al., 2020)	BiLSTM	20.60
(Zhang et al., 2021)	Seq-to-Seq LSTM	20.17
(Aliberti et al., 2019)	LSTM	19.47
(Li, Liu, et al., 2019)	GluNet	19.28
Proposed System	Multi-layer LSTM	14.364

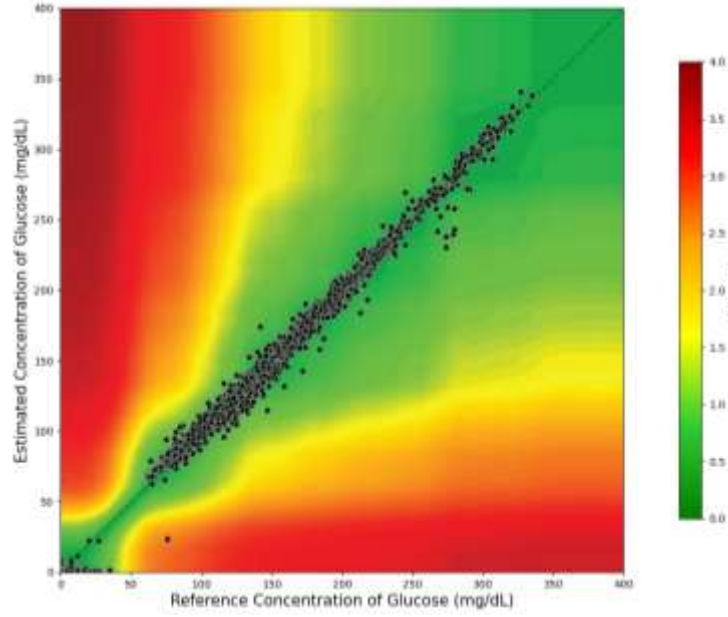


Figure 2. SEG of patient 544

4. Conclusion

This paper introduces an innovative glucose prediction model based on multi-layer LSTM networks, which aims to mitigate the risk of complications arising from fluctuations in glucose levels. In the proposed model, the use of multi-layer structures addresses the complex memory challenges associated with predicting glucose levels involving multiple parameters. As a result of evaluations using the OhioT1DM dataset, the proposed model shows promising results with an RMSE of 14.364 mg/dL, MAE of 9.086 mg/dL, and MAPE of %6.186 with a value of 0.9321 R^2 for 30-min PH. The results clearly show that the proposed model has superior performance compared to other studies. In addition, the SEG of patient 544 shows that the glucose predictions obtained are within acceptable limits, demonstrating the robustness and reliability of the proposed method. Our future work will focus on integrating the developed predictive model into an Android application. This integration aims to provide users with a user-friendly platform to access and use the predictive capabilities of our model. Through this integration, individuals will be empowered to make informed decisions regarding their dietary choices, physical activity regimes, and overall health management.

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