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Comparative Analysis of the Performance of Four Learning Models for Predicting Blood Glucose Levels in Type 1 Diabetic Patients Based on Blood Glucose Measurements

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Abstract:

Type 1 diabetes requires strict blood glucose management to maintain normal levels and prevent complications. Predicting future blood glucose levels is essential for effective management. This study compares four learning models to assess their effectiveness in predicting blood glucose based on current measurements. The literature review focused on articles exploring blood glucose prediction in type 1 diabetes with minimal human intervention. The selection criteria considered the reliability and accuracy of approaches in predicting blood glucose. Performance evaluation involved measures such as root mean square error, mean absolute percentage error, coefficient of determination, relative error analysis, and sum of squares of glucose prediction errors. The datasets consisted primarily of patients with type 1 diabetes. Preliminary results showed that some approaches performed well in the short term, indicating their ability to accurately predict future blood glucose levels. Other approaches demonstrated good long-term results, highlighting the need for extended evaluation in diabetes management. Understanding the strengths and weaknesses of each approach is crucial to guide future research. This comparison underscores the importance of developing robust prediction methods tailored to clinical needs to improve the management of type 1 diabetes and prevent complications. Further research is needed to explore the most promising approaches and adapt them to the individual needs of patients.

1. Introduction :

Type 1 diabetes is a chronic disease caused by the autoimmune destruction of beta cells in the pancreas responsible for insulin production [1]. This results in insulin deficiency and the subsequent chronic increase in blood glucose levels known as hyperglycemia [2]. The International Diabetes Federation (IDF) Diabetes Atlas report in 2021 [3] revealed a continuous global rise in diabetes prevalence, with an estimated 537 million adults aged 20 to 79 living with diabetes, representing approximately 1 in 10 individuals in this age group. Projections indicate that this number will reach 643 million by 2030 and 783 million by 2045 [3]. Understanding blood glucose levels and their related conditions, hypoglycemia, and hyperglycemia, is essential for preventing complications. Hypoglycemia occurs when blood glucose levels drop abnormally low, usually below 70 mg/dL [4], leading to severe consequences if left untreated, such as seizures, loss of consciousness, and even coma. Conversely, hyperglycemia is characterized by excessively high blood glucose levels, often associated with fasting plasma glucose above 126 mg/dL or random plasma glucose above 200 mg/dL in the context of diabetes [4]. Poorly controlled chronic hyperglycemia can result in long-term complications affecting blood vessels, nerves, kidneys, eyes, and increasing the risk of cardiovascular diseases, strokes, and circulatory problems [5] [6]. The primary treatment for these conditions involves regulating blood glucose levels through insulin administration. Individuals with type 1 diabetes typically require insulin injections to compensate for insufficient insulin production by the pancreas. Achieving optimal glycemic control through precise insulin dosing is crucial for the best healthcare outcomes. Continuous glucose monitoring (CGM) systems offer a promising solution for improving glycemic regulation [7]. CGM devices allow real-time glucose monitoring throughout the day and night, offering an alternative to traditional self-monitoring of blood glucose (SMBG). Integrating intelligent prediction and control algorithms into CGM systems can generate alerts for hypoglycemia or hyperglycemia risks, further enhancing diabetes management.

This study compares four learning approaches for predicting future blood glucose levels in type 1 diabetes patients, focusing solely on blood glucose measurements. While other algorithms use various inputs like diet, emotions, activities, and stress, and other factors. our study concentrates on glycemic measurements. By reviewing existing literature, we evaluate the performance, advantages, and limitations of these approaches, shedding light on applied techniques, data, results, and challenges. This analysis unveils strengths and weaknesses in a clinical context, identifying accurate and reliable methods for glycemic prediction. Ultimately, these findings will enhance type 1 diabetes management, offering tailored decision support tools to cater to patient needs.

The remainder of this article is organized as follows: Section 2 will present the specific learning approaches used in the comparison, explaining their basic principles, operation, and application for glycemic prediction, as well as the evaluation metrics used to assess their performance. Section 3 will provide the results and discussion of the performance of the different blood glucose prediction algorithms based on the

literature. In Section 4, we will present the conclusion and explore the future work possibilities to enhance diabetes management through predictive models.

2. Methodology

2.1. Description of Dataset

Continuous glucose monitoring (CGM) is a crucial technology providing real-time measurements of blood glucose levels for modeling and prediction. A comparative study analyzed algorithms using the OhioT1DM dataset, constructed from CGM values of 12 type 1 diabetes patients. The dataset includes glucose measurements, insulin doses, and other relevant physiological sensor data. OhioT1DM was chosen for its representativeness and availability as a CGM data source for in-depth analysis of blood glucose prediction approaches.

2.2. Presentation of learning models

2.2.1. Vector regression based on the differential evolution algorithm

Hamdi et al. [8] used support vector regression (SVR) with the differential evolution (DE) algorithm [8] to predict future blood glucose levels. SVR is a robust predictive analysis technique commonly applied in diverse domains [9]. It focuses on structural risk minimization, estimating a function by minimizing the generalization error's upper bound [10]. Mathematically, SVR maximizes the hyperplane margin to minimize error tolerance and predicts blood glucose at time t+PH using the current time t and prediction horizon PH.

$$y_{t+PH} = f(x_t) = \langle \omega, \phi(x_t) \rangle + b \quad (1)$$

Here, x_t represents the past glucose measurements, ϕ is a fixed transformation of the feature space, ω is the weighting matrix, and b is the bias. The SVR algorithm aims to solve a non-linear regression problem by projecting the training data x_i (where i=1,...,N and N is the size of the training dataset) into a new feature space called ϕ, where the relationship between x_i and y_i becomes linear. For this purpose, an ϵ-insensitive loss function is used, where the error is tolerated up to a certain value ϵ. The SVR model parameters (C, ϵ, γ) are estimated using the differential evolution (DE) algorithm, which optimizes these parameters to improve the accuracy of predictions. In this context, the SVR algorithm solves the following optimization problem:

Minimize :

$$\frac{1}{2}\|w\|_+^2 C * \sum_{i=1}^{N}(\varepsilon + \varepsilon_i^*) \quad (2)$$

Subject to constraints:

$$y_i - \langle w, \varphi(x_i) \rangle - b \leq \varepsilon + \varepsilon_i \quad (3)$$
$$\langle w, \varphi(x_i) \rangle + b - y_i \leq \varepsilon + \varepsilon_i^* \quad (4)$$
$$\varepsilon_i, \varepsilon_i^* \geq 0 \text{ For i} = 1,\ldots, \text{N} \quad (5)$$

The constant C determines the trade-off between the smoothness of the SVR function f(x) and the tolerance for deviations larger than ϵ. In this work, the radial basis function (RBF) was used as the kernel function, defined by a specific equation where γ is a kernel parameter. The proposed approach was applied to blood glucose prediction using data from diabetic patients. Prediction performance was evaluated using statistical measures such as:

Root Mean Squared Error (RMSE):

$$RMSE = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(y_i - \hat{y}_i)^2} \quad (6)$$

Mean Absolute Percentage Error (MAPE):

$$MAPE = \frac{1}{n}\sum_{i=1}^{n}\left|\frac{y_i - \hat{y}_i}{y_i}\right| \times 100\% \quad (7)$$

Coefficient of Determination (R2):

$$R_2 = 1 - \frac{\sum_{i=1}^{n}(y_i - \hat{y}_i)^2}{\sum_{i=1}^{n}(y_i - \bar{y})^2} \quad (8)$$

Where n is the number of samples, y_i is the actual blood glucose value, $\hat{y}_i$ is the predicted blood glucose value, and $\bar{y}$ is the average of the actual blood glucose values. The results demonstrated that the DE-SVR approach was accurate, with an average RMSE of 9.44 mg/dL, an average MAPE of 3.74%, and an average R2 of 0.971 for a prediction horizon of 15 minutes. The performance was also evaluated for different prediction horizons, showing an increase in RMSE with increasing horizon [8]. The DE-SVR approach proves effective for biomedical prediction tasks and time series forecasting.

2.2.2. Artificial Neural Networks (ANNs)

Ben Ali et al. [11] propose an approach for blood glucose prediction using Artificial Neural Networks (ANNs) based on previous measurements. The ANN architecture includes an input layer with Nbin neurons, a hidden layer with Nbhid neurons, and an output layer with a single neuron. The prediction utilizes a sliding window of length Nbin, incorporating past glucose measurements and predictions to forecast future values and exploit temporal relationships for enhanced accuracy. The Levenberg-Marquardt algorithm [12] is employed to train the ANN, adjusting weights and biases to minimize the error between predicted and actual glucose values [13].

The prediction formula is expressed as :

$$\boldsymbol{G_{pred}} = f(G(t\text{-}Nbin+1), G(t\text{-}Nbin+2), \ldots, G(t\text{-}1)) \quad (9)$$

In this formula, $\boldsymbol{G_{pred}}$ represents the predicted blood glucose value at time t, and G(t-Nbin+1) to G(t-1) represent the previous glucose measurements. To determine the optimal structure of the ANN, a specific algorithm is used. In this

algorithm, the number of neurons in the hidden layer (Nbhid) is fixed, while the number of neurons in the input layer (Nbin) is gradually increased. At each step, the Root Mean Squared Error (RMSE) is calculated to evaluate the prediction performance of the ANN. The algorithm stops when the predefined minimum error (min_RMSE) is reached or when the maximum number of allowed neurons in the input layer is reached [11].

The study involves 12 patients with type 1 diabetes, using FreeStyle Libre data divided into training (70%) and test (30%) sets [14]. Each patient's ANN is trained, and prediction performance is evaluated with RMSE, MAPE, R2, REA, and SSGPE statistical measures.

The expression for Relative Error Analysis (REA) is:

$$\boldsymbol{REA} = \frac{\mathbf{100}}{\boldsymbol{n}} * \sum_{\boldsymbol{i=1}}^{\boldsymbol{n}} \left(\left| \frac{G_{pred\,(i)} - G_{actual(i)}}{G_{actual(i)}} \right| \right) \quad (10)$$

The expression for Sum of Squared Glucose Prediction Errors (SSGPE) is defined as:

$$\boldsymbol{SSGPE} = \sum_{\boldsymbol{i=1}}^{\boldsymbol{n}} \left(\boldsymbol{G_{pred(i)}} - \boldsymbol{G_{actual(i)}} \right)^2 \quad (11)$$

The mathematical formulas used for evaluation demonstrate the quantitative performance of the ANN proposed by Ben Ali et al. [11]. The results indicate that the approach exhibits good blood glucose prediction, with RMSE values ranging from 1.14 to 8.83, MAPE values ranging from 0.56% to 5.83%, and R2 values ranging from 0.974 to 0.995, showing accurate predictions of glucose levels. However, challenges persist due to variations caused by external and internal factors, impacting prediction accuracy. Generalizing results to different patient populations is crucial. Nevertheless, the ANN approach holds promise for blood glucose prediction, inspiring potential applications in various forecasting tasks [11].

2.2.3. Artificial Neural Networks with Temporal Features

As part of the methodology used by Ganjar Alfian et al. [15], CGM devices were used by type 1 diabetic patients to collect their real-time glucose data. The real-time glucose data was used to train a prediction model using a machine learning algorithm. To predict glucose levels, a Multilayer Perceptron (MLP) model was utilized. The methodology by Ganjar Alfian et al. [15] includes the following steps:

2.2.3.1. Data preparation

The collected CGM glucose data underwent a filtering process to remove noise, represented mathematically as:

$$Preprocessed\ data = Filtering\ (Raw\ data) \quad (12)$$

The data was then divided into training and testing sets using the split function.

$$Training\ set, Testing\ set = split\ (Preprocessed\ data) \quad (13)$$

To transform the glucose data into a suitable format for learning, the sliding window approach was used. This involves creating windows of size "n" from previous data, where "n" represents the number of data points used for prediction. Mathematically, this can be represented as:

$$Window = Preprocessed\ data\ [t-n:\ t-1] \quad (14)$$

In this formula, "t" represents the current time, and "t-n:t-1" indicates the indices of previous data points to include in the window. The glucose values for the next "h" minutes were used as the desired output vector for each input window. This can be expressed mathematically as:

$$Output\ vector = Preprocessed\ data\ [t:\ t+h-1] \quad (15)$$

Here, "t+h-1" represents the index corresponding to the end of the prediction period.

Finally, the constructed input and output datasets were split into distinct sets for training and testing, as mentioned earlier.

2.2.3.2. Temporal Domain Functionality and proposed Prediction Model

To improve the prediction of future blood glucose levels, statistical attributes of the temporal domain, such as minimum, maximum, mean, and standard deviation, were used as additional features for the previous blood glucose values. These statistical features were combined with the previous values to create an input matrix. A Multilayer Perceptron (MLP) model was used to predict future blood glucose levels, with the backpropagation algorithm used to train the MLP by minimizing the RMSE between the predictions and the actual values.

The MLP model had two hidden layers with 100 neurons each, utilizing the ReLU activation function and the Adam solver for weight optimization. A regularization parameter of 0.0001, learning rate of 0.001, and maximum of 1000 iterations were set [15]. The grid search algorithm was employed to determine the optimal parameters, as presented in Table 1 [15].

Number of layers	Number of neurons	Activation function	Solver for weight optimization	Regulation parameter (alpha)	Learning rate	Maximum number of iterations
2	100	Relu	Adam	0,0001	0,001	1000

Table 1: MLP model parameters for predicting future blood glucose levels

The proposed model was evaluated using the DirecNet CGM dataset, which included data from 12 patients with type 1 diabetes. The model's performance was measured in terms of RMSE, MAPE, and R_2, according to equations 6, 7, and 8, respectively. Additionally, the glucose-specific metric, gMSE, was used to evaluate the model's performance. The formula for gMSE is given by:

$$gMSE = \frac{1}{N}\Sigma_t(y - \hat{y}_t)^2 Pen(y, \hat{y}_t) \quad (16)$$

Ganjar Alfian et al. [15] employed the grid search algorithm to evaluate parameter combinations, selecting the ones that achieved minimal prediction error and improved glucose prediction accuracy. It's important to note that these parameters may vary depending on the data and model requirements, but they demonstrate the adjustability of parameters through grid search to enhance MLP model performance.

2.2.4. A Deep Neural Network Fusion Approach for Predicting Glucose Levels in Diabetes Management

In their study, Hatice Vildan et al. [16] developed an innovative approach for diabetes management and glucose level prediction. They employed three deep neural networks (LSTM, GRU, and WaveNet) and utilized a 30-minute history of blood glucose for training. The networks were used to predict glucose levels in advance for 30, 45, and 60-minute periods. Hyperparameters were optimized by testing various combinations for each network. The study utilized the OhioT1DM dataset, consisting of glucose measurements, insulin amounts, and physiological sensor data, from 12 patients with type 1 diabetes.

2.2.4.1. LSTM (Long Short-Term Memory)

LSTM is a specialized recurrent neural network that captures long-term dependencies in sequence data, making it ideal for processing word sequences in text or time series data [17] .

The prediction formula of an LSTM utilizes the output from the previous cell, h(t-1), to predict the current output, h(t). Here is the corresponding mathematical formula:

$$h(t) = LSTM(x(t), h(t-1)) \quad (17)$$

In this formula, x(t) represents the input at time step t, and h(t-1) is the previous hidden state. This formula computes the current output by utilizing the current input and the previous hidden state. This enables the LSTM to incorporate information from the past when predicting future values.

2.2.4.2. GRU (Gated Recurrent Unit)

The Gated Recurrent Unit (GRU) is a simpler version of LSTM used for modeling sequence data, with two main gates: the reset gate and the update gate [18]. These gates control the flow of information and the impact of past data on future data.

The mathematical formula to compute the output of a GRU is as follows:

$$h(t) = GRU(x(t), h(t-1)) \quad (18)$$

In this formula, x(t) represents the input at time step t, h(t-1) is the previous hidden state, and h(t) is the current output. Computing the output of the GRU involves several steps, governed by the reset and update gates. The reset gate determines which part of the previous state should be forgotten and which part of the current input should be considered. The formula for the reset gate is typically defined as follows:

$$r(t) = sigmoid\ (Wr * [h(t-1), x(t)]) \quad (19)$$

The forget gate controls the update of the previous hidden state using the current input and the previous state. The formula of the forget gate is typically defined as follows:

$$z(t) = sigmoid\ (Wz * [h(t-1), x(t)]) \quad (20)$$

Then, the candidate state is calculated using the current input and the previous hidden state, along with the reset gate:

$$h'(t) = tanh(W * [r(t) * h(t-1), x(t)]) \quad (21)$$

Finally, the current hidden state is calculated by combining the previous state weighted by the forget gate and the candidate state:

$$h(t) = (1 - z(t)) * h(t-1) + z(t) * h'(t) \quad (22)$$

This formula updates the hidden state by utilizing information from the previous state, the current input, and the reset and forget gates.

2.2.4.3. WaveNet

WaveNet, a deep neural network for modeling and generating sequential data like audio signals, distinguishes itself from traditional recurrent neural networks through the use of dilated convolutions, capturing patterns at different time scales [16] [10]. These dilated convolutions enable the model to consider samples at varying distances, allowing it to capture long-term relationships within the sequence [10].

The general formula for WaveNet is given as:

$$y(t) = \text{WaveNet}(x(t), h(t)) \quad (23)$$

In this formula, x(t) represents the input at time step t, h(t) is the hidden state, and y(t) is the current prediction or output. The WaveNet function takes into account both the current input and the hidden state to generate the prediction. WaveNet's distinctive feature is the utilization of dilated convolutions, employing filters with varying distances between their values. This technique widens the model's receptive field, enabling it to capture patterns across different

time scales. The specific formula for dilated convolution in WaveNet depends on model parameters like the number of filters, filter sizes, and dilation rates, which are selected based on the task's specific characteristics and requirements.

2.2.4.4. Fusion Performance of LSTM, GRU, and WaveNet Networks for Predicting Glucose Levels in Type 1 Diabetes

The trained models underwent separate data testing to assess their glucose level prediction performance. Predictions from LSTM, GRU, and WaveNet were fused using specific rules, resulting in seven distinct outcomes per patient [16]. This fusion aimed to capitalize on the strengths of different neural network architectures for varying glucose levels. The Surveillance Error Grid (SEG) was employed to determine the relative performance of the three networks at different glucose levels [16]. A decision-level fusion mechanism was proposed, assigning weights to the networks based on their performance in high-risk regions.

In cases where both networks made identical predictions, their results were combined for fusion. However, if this rule couldn't be applied, a weighted sum was calculated based on each network's accuracy in glucose prediction. The fusion result was then determined by considering the weighted sum of the three networks, with LSTM, WaveNet, and GRU networks having fixed weighting coefficients of 0.4, 0.2, and 0.4, respectively, based on the analysis of their performances for different prediction durations.

To select hyperparameters for LSTM, WaveNet, and GRU networks, a grid search method was employed. This involved defining a grid of possible hyperparameter combinations, such as hidden layer size and learning rate, and evaluating the model's performance for each combination. Various evaluation metrics, including RMSE, MAE, RMSPE, MAPE, and SEG. The calculations for these numerical evaluation metrics were provided in equations (6), (7), (10), (24). A visualization of a simple SEG figure is shown in Figure 1.

$$RMSPE = \sqrt{\frac{1}{n}\Sigma_{i=1}^{n}\left(\frac{predictedi - measuredi}{measuredi}\right)^2} \quad (24)$$

A grid search was performed to select hyperparameters for LSTM, WaveNet, and GRU neural networks. It systematically explored various combinations in the hyperparameter space, using values commonly employed in the literature to ensure established knowledge and best practices. The grid search identified the optimal hyperparameter combinations for LSTM, WaveNet, and GRU based on their glucose level prediction performance. These optimal values were utilized in training the models and presenting the study's results.

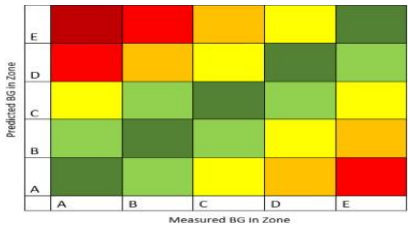

Figure 2: Displaying the SEG regions visually [16].

The evaluations demonstrate that the fusion method of LSTM, GRU, WaveNet networks yielded the most effective performance in terms of blood glucose prediction. This approach achieved the lowest RMSE values, namely 21.90 mg/dL, 29.12 mg/dL, and 31.10 mg/dL for prediction periods of 30, 45, and 60 minutes respectively [16]. These results indicate a relatively high accuracy in glucose level prediction.

3. Results and Discussion

The performance of different blood glucose prediction algorithms based on the literature is summarized in table 2, and table 3.

Métrique	RMSE (mg/dl)	MAE	MAPE (%)	RMSPE
30 min	21.90	15.87	10.96	25.89
45 min	29.12	21.52	14.93	20.86
60 min	31.10	26.41	18.53	15.40

Table 2: Performance of Vildan Duduku et al.'s algorithm for RMSE, MAE, MAPE, and RMSPE metrics.

	Metric / PH	RMSE (mg/dl)	MAPE (%)	R2
Takoua Hamdi el al. [17]	15 min	9.44	3.74	0.971
	30 min	10.78		
	45 min	11.78		
	60 min	12.95		
Ben Ali et al. [18]	15 min	6.43	3.87	0.986
	30 min	7.45		
	45 min	8.13		
	60 min	9.03		
Ganjar et al [19]	15 min	2.82	1.52	0.99
	30 min	6.31	3.46	0.97
	45 min	10.65	5.89	0.91
	60 min	15.33	8.68	0.82

Table 3: Comparison of the Performance of Various Learning Models for Blood Glucose Prediction

The study compared various models for predicting blood glucose levels in patients with type 1 diabetes. Takoua Hamdi et al. [8] and Ben Ali et al. [11] provided RMSE metrics for all prediction periods (15, 30, 45, and 60

minutes), but only calculated MAPE and R2 metrics for the 15-minute prediction period. In contrast, Ganjar et al. [15] and Vildan Duduku et al. [16] presented comprehensive results across all prediction periods. The results indicated that Ganjar Alfian et al.'s algorithm [15] outperformed others in terms of RMSE, MAPE, and R2 for 15 and 30-minute predictions. Ben Ali et al.'s algorithm [11] demonstrated higher RMSE performance for 45 and 60-minute predictions, suggesting its effectiveness for long-term forecasting. Takoua Hamdi et al.'s algorithm [8] showed comparable performance to Ben Ali et al.'s [11] but slightly lower. Vildan Duduku et al.'s algorithm [16] displayed higher RMSE and MAPE values, indicating lower accuracy compared to the other algorithms. These discrepancies in performance can be attributed to differences in techniques, approaches, datasets, features, parameters, and metrics used in each study. Ganjar Alfian et al.'s algorithm [15] was found to provide the best short-term predictions, while Ben Ali et al.'s [11] performed better for long-term predictions, utilizing custom feature input and a "recursive strategy" for multi-step time series prediction. In contrast, Ganjar Alfian et al.'s study [15] used a "direct strategy".

The findings suggested that machine learning algorithms have the potential to predict future blood glucose levels effectively, facilitating improved diabetes management by offering accurate predictions for patients to take appropriate measures. Ganjar Alfian et al.'s algorithm showed promising results, indicating its potential as a solution for future blood glucose prediction.

4. Conclusion

In conclusion, this comparative review highlights the importance of learning algorithms in predicting future blood glucose levels in individuals with type 1 diabetes, while also emphasizing opportunities for improvement and suggesting promising research directions. These findings contribute to a better understanding of the performances of different algorithms, particularly when compared to other approaches that utilize factors such as sports and diet, States of emotions, activities, stress, emotional strain, along with glycemic measurements and other factors. It is essential to note that the algorithms examined in this study focused on glucose predictions without human intervention, making glycemic devices smarter by automatically detecting hypoglycemia and hyperglycemia. Ganjar Alfian's algorithm demonstrated better short-term performance, whereas Jaouher Ben Ali's showed superior long-term results, illustrating the respective advantages of direct and recursive strategies. Moreover, artificial neural networks were identified as providing the best results among the evaluated approaches. These conclusions underscore the significance of further research to validate and improve these algorithms using larger and more diverse datasets, aiming to enhance their effectiveness for broader clinical use and improve the management of type 1 diabetes. The results of this study deepen our understanding of the predictive capabilities of these algorithms and pave the way for potential advancements in the field of diabetes management.

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