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Context-aware system for glycemic control in diabetic patients using neural networks

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Abstract: Diabetic patients are quite hesitant in engaging in normal physiological activities due to difficulties associated with diabetes management. Over the last few decades, there have been advancements in the computational power of embedded systems and glucose sensing technologies. These advancements have attracted the attention of researchers around the globe developing automatic insulin delivery systems. In this paper, a method of closed-loop control of diabetes based on neural networks is proposed. These neural networks are used for making predictions based on the clinical data of a patient. A neural network feedback controller is also designed to provide a glycemic response by regulating the insulin infusion rate. An activity recognition model based on convolutional neural networks is also proposed for predicting the patient's current physical activity. Predictions from this model are transformed into a six-level code and are fed as input to the neural network glucose prediction model. Experimental results of the proposed system show good performance in keeping blood glucose levels in the nondiabetic range.

Key words: Neural networks, diabetes, closed-loop control, insulin, convolutional neural networks

1. Introduction

Type 1 diabetes, also called diabetes mellitus, is a condition in which the body fails to keep the blood glucose levels within the euglycemic range. Blood glucose (BG) increases (hyperglycemia) for a longer duration of time can increase the risk of kidney failure, heart attack, blindness, etc. In normal or healthy individuals these levels are maintained within normal limits ($<$154 mg/dL) [1] by insulin secretions from the pancreas. Type 1 diabetes (T1D) usually develops in children and adults due to the destruction of beta cells resulting in insulin deficiency [2, 3]. People with type 1 diabetes require lifelong insulin injections to prevent hyperglycemia for survival. Type 2 diabetes is characterized by hyperglycemia due to insulin resistance, which is believed to occur due to increased weight, stress, and lack of exercise [4, 5]. The most frequently used methods for T1D management are multiple daily injections and insulin delivery via an insulin pump [6–8]. In the last few decades, both glucose sensing capabilities and insulin delivery methods have greatly improved. These technological advancements, along with advancement in computer control systems, have led to the development of a closed-loop insulin delivery system also called an artificial pancreas [9–12]. An artificial pancreas is a system consisting of a continuous glucose monitor (CGM), insulin pump, and control algorithm as shown in Figure 1.

In the literature, many control algorithms have been proposed for the closed-loop control of diabetes [9, 13]. The authors in [14] developed a closed-loop control system that uses continuous glucose measurements and a pump that can deliver both insulin and glucagon. A computer algorithm decides the amount of insulin or glucagon to be delivered based on the blood glucose measurements of a patient. The 27-h experiment conducted

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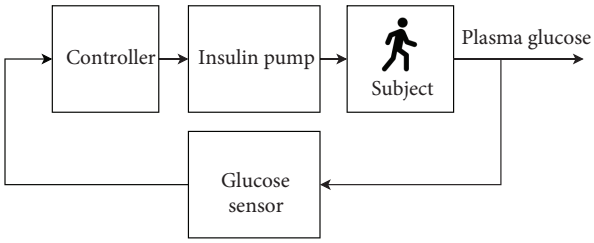

Figure 1. Closed-loop feedback controller.

with 11 subjects with announced carbohydrate meals revealed that the closed-loop system achieved a mean BG concentration of 140 mg/dL in six subjects and none of the subjects experienced hypoglycemic events requiring treatment during the experiment. Another study involving closed-loop glucose regulation via an adaptable control algorithm was presented in [15]. The algorithm uses two modules, a range correction module and safety supervisor module. Both of these modules interact with each other to avoid glucose increases in a predefined range.

Meals of varied types and sizes have direct impacts on the glucose levels of an individual. For any treatment considering diabetes management, meal detection is a must. In [16] the authors developed a meal-detection algorithm where meals are detected based on rate of appearance of glucose estimations provided by the CGM. Estimations from the algorithm are given to the multivariable adaptive control system, which prevents after-meal hyperglycemia. The authors used a modified version of Bergman's minimal model and an unscented Kalman filter (UKF) to calculate the glucose dynamics and estimation of states and parameters, respectively. Like meal disturbances, physical activities of different intensities are also known to affect the glucose levels of an individual. Any physical work of high intensity can lead to hyperglycemia in the case of a diabetic patient. The work presented in [17] discussed how patients with diabetes (type 1) are exposed to hypoglycemia when they are engaged in some physical activities (running, exercise, etc.), especially in the afternoon or evening. The authors also highlighted the importance of integrating different sensing technologies, similar to smart calculators (glucose, insulin, exercise calculators, etc.) and control algorithms, so that real-time data like heart rate, movement, and blood lactate levels during a workout can be used to manage blood glucose levels with minimal or no user input. The authors in [18] used heart rate signals as markers of physical activity. This information is used by the control algorithm to minimize hypoglycemia. The study included subjects without any cardiovascular complications. Moreover, subjects taking medication known to affect the heart rate were not considered in this study. There was no method considered in this study to differentiate between increased heart rate due to physical activity and some other significant factors like stress, medicine, etc. The work presented in [19] used a predictive low glucose suspend (PLGS) algorithm to avoid physical activity associated hypoglycemia. Data from eighteen subjects were manually fed to an algorithm, which indicates hypoglycemic events, and based on these data, basal insulin infusion is suspended by the supervising staff. The authors in [20] developed a multivariate adaptive artificial pancreas (MAAP) system integrated with an early hypoglycemia alarm system. In the closed-loop setup, blood glucose measurements and physical activity information is manually fed to the control system every 10 min. An insulin bolus calculated by the control algorithm is then supplied through the pump manually. In [19, 20], the authors suggested to increase the clinical sample data for better statistical analysis and least manual intervention to make the system more robust and less prone to human bias and errors. Furthermore, in [20], average physical activity was estimated by the supervising staff over the period of 5 min and this estimate was less reliable than automated activity recognition systems.

Due to the nonlinear nature of biological systems, researchers have used artificial neural networks (ANNs) in diabetes control. ANNs are widely applied in problems of nonlinear nature. The work presented in [21–23] used ANNs for making nonlinear glucose predictions and in some studies these networks were used in feedback control algorithms [23–25]. Other authors [26] presented a system comprising a neural network and compartmental model (CM). The CM provides an estimation of insulin bolus and also takes absorption delay into consideration. The neural network predicts the glucose levels based on the estimations provided by the CM and the values provided by the CGM.

These studies suggest that by using ANNs it is possible to obtain a glucose prediction model for a diabetic person based on his clinical data. However, few of these studies incorporate physical activity as a part of closed-loop control in T1D; most of the studies use Bergman's model to represent the glucose-insulin dynamics of an individual, which sometimes fails to mimic nonlinear behavior, resulting in less efficient treatment.

In this article, a neural network (NN)-based glucose prediction model is proposed, which provides glucose-insulin dynamics for each patient with T1D. Furthermore, an activity recognition algorithm based on convolutional neural networks (CNNs) is also proposed. The developed CNN model recognizes the patient's current physical activity; this information along with values from the CGM and an already known dietary schedule is supplied as input to the NN-based glucose predictor. An optimized NN-based feedback controller is designed to keep the blood glucose levels within the euglycemic range by regulating the insulin infusion rate. The experimental results obtained show good glycemic control and the developed model is more accurate than the Zone-MPC (model predictive controller) developed by Grosman et al. [27].

2. Methodology

A CNN-based human activity/context recognition classification algorithm is proposed to identify six different human activities $a(t)$ that have an effect on the glucose dynamics of T1D patients. The recognized activity $a(t)$ is supplied as one of the inputs to the glucose prediction model. The glucose prediction model, in addition to $a(t)$, receives predefined food intake $f(t)$ and past glucose readings $g_m(t)$ using a feedback loop as inputs. Based on the input, the glucose prediction model employs a NN to predict blood glucose levels $g_{pred}(t+15)$ at time t with prediction horizon of 15 min. Finally, a feedback controller is used to calculate the insulin bolus $i(t)$. The controller uses a feedback loop to receive $i(t)$ as one input and glucose prediction error g_e, calculated using $g_{pred}(t+15)$ and glucose settling point, as the other. The complete model is shown in Figure 2.

2.1. Proposed activity recognition model

The activity recognition model is a classification algorithm based on CNNs, which we train to classify six basic human activities (jogging, walking, moving upstairs, moving downstairs, sitting, and standing) using a publicly available dataset.[1] The data were collected using smartphone accelerometers and data distribution with respect to various activities as given in Figure 3.

A CNN is a special kind of feedforward NN that significantly reduces the number of parameters in a deep neural network with many units, without losing too much in the quality of the model. CNNs have found applications in image and text processing where they outperform many previously established benchmarks. The architecture of the CNN used for activity recognition is shown in Figure 4.

[1] AIM '94 (1994). Diabetes Data Set [online]. Website https://archive.ics.uci.edu/ml/datasets/Diabetes [accessed 23 August 2019].

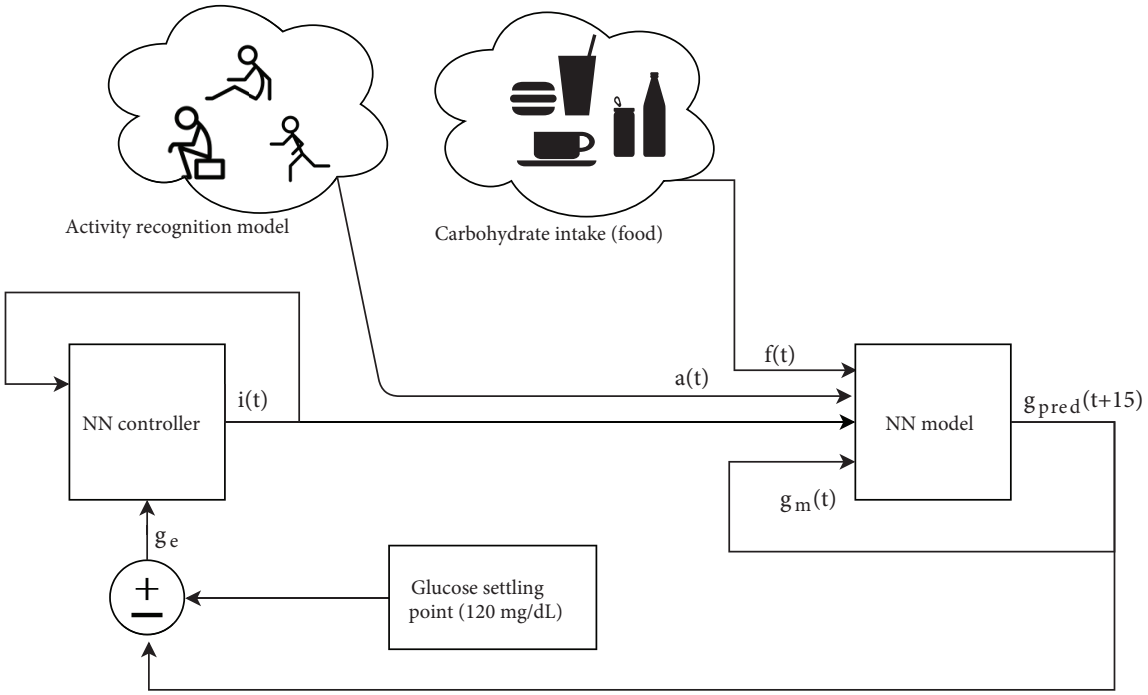

Figure 2. Feedback controller.

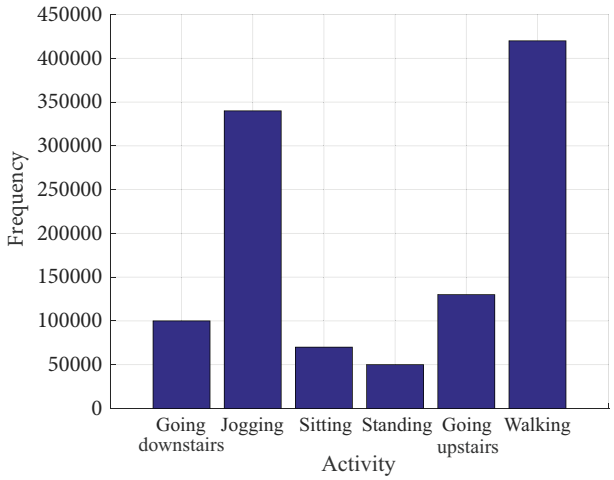

Figure 3. Physical activity data distribution.

Data from the smartphone sensors need to be transformed and segmented so that features can be easily drawn from them. The continuous stream of data can be segmented using a sliding window of fixed or varied length. In this study, input data from the 3 channels (x-axis, y-axis, z-axis) were prepared by dividing the raw data signal into fixed sized segments. These segments were stacked along a vertical dimension so that the input would be of the form (input width, input height, and number of channels). The segmentation window consists of 90 data points (4.5 s of data) with 50% data overlap. Windows from three channels were stacked to perform the one-dimensional convolution over the input signal. Acceleration values were normalized to have zero mean

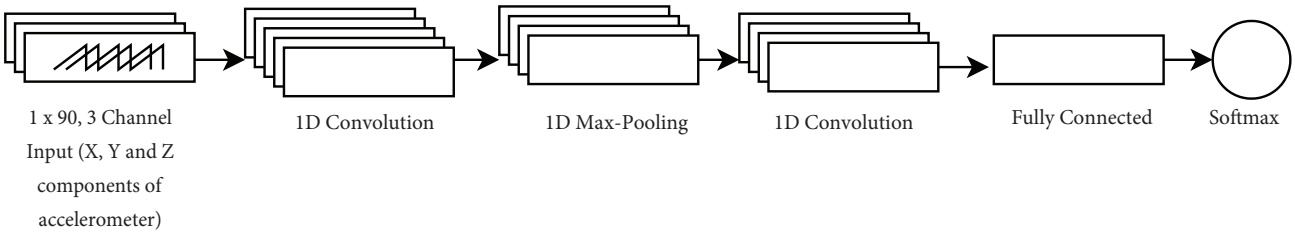

Figure 4. CNN architecture.

and unit standard variance. The NN uses backpropagation to compute the gradients and parameters were optimized using the gradient descent algorithm. The model shown in Figure 4 consists of a max pooling layer separating the two convolution layers. The convolution layer is followed by a fully connected layer, which is further connected to a softmax layer. Both max pool and convolution layers are temporal or 1-dimensional. The first convolutional layer has a filter size and depth of 60 (number of channels, as output from the convolutional layer), and after performing the 1D convolution over the input channel data, output is passed through the ReLU activation function. Training hidden layers with the ReLU has been thoroughly discussed in the literature, and it is significant to avoid the vanishing gradient problem. The pooling layer has a filter size of 20 with a stride of 2. The convolutional layer at the top takes an input from the max-pooling layer, applying the filter size of 6 and having a tenth of the depth of the max pooling layer. The output is flattened for the fully connected layer, which consists of 1000 neurons. It uses the $tanh(.)$ function as defined by Eq. (1) for nonlinearity. Finally, the softmax layer is defined by Eq. (2) to output the probabilities of class labels.

$$u_{ij}^{x} = tanh(b_{ij} + \Sigma_m \Sigma_{p=0}^{pi-1} w_{ijm}^{p} u_{(i-1)m}^{x+p}) \tag{1}$$

Here, $tanh(.)$ is the tangent function, m is the index over the set of feature maps in the (i - 1)th layer connected to the current feature map, b_{ij} is the bias for this feature map, w_{ijm}^{p} is the value at position p of the convolutional kernel, and P_i is the length of convolutional kernel. For the jth feature map in the ith layer of the CNN, the value in the xth row is denoted as u_{ij}^{x}. The softmax function is defined as follows:

$$u_{ij} = \frac{exp(u_{(i-1)j})}{\Sigma_{j=1}^{c} exp(u_{(i-1)j})} \tag{2}$$

Here, C is the number of output classes. Table 1 shows the confusion matrix for our CNN model.

Table 1. Confusion matrix for proposed CNN.

	Downstairs	Jogging	Sitting	Standing	Upstairs	Walking
Downstairs	618	19	12	0	22	30
Jogging	36	1825	0	0	103	36
Sitting	3	0	357	21	1	11
Standing	1	0	2	275	6	4
Upstairs	38	21	0	0	648	81
Walking	17	62	0	1	133	2488

The model was trained on a desktop machine with a Core i5 processor with 6 GB of RAM and 2 GB NVIDIA graphics card. Table 2 shows the experimental setup of the CNN.

Table 2. Experimental setup.

Parameter	Input height	Input vector size	Number of channels	Learning rate	Batch size	Hidden neurons	Kernel size	Depth
Value	1	90	3	0.0001–0.001	10–15	1000	60	60

2.2. Neural network-based glucose prediction model

Neural networks are interconnected networks of nonlinear elements with adjustable weights. Much like biological neurons in the human brain, these nonlinear elements have as their inputs a weighted sum of the outputs of other elements. These networks are mostly used now for providing a nonlinear mapping between input and output. An artificial neural network changes its structure based on data provided during the training phase, and once the training is complete, verification is done by testing the performance of the trained model with data that were left out during the training. A neural network is a mathematical function of the following form:

$$y = f_N N(x) = f_l(z) \tag{3}$$

$$f_l(z) = g_l(W_l z + b_l) \tag{4}$$

Here, l is a layer number and can vary from 1 to the number of layers in a network, g_l is an activation function, and W_l and b_l are the weighted matrix and bias calculated during optimization.

In this study, a NN model is trained for each patient using his or her clinical data. The dataset is distributed as follows: 60 data instances are used for training the network and the remaining 10 data instances are used for testing the accuracy of the model. The NN model shown in Figure 5 is a fully connected feedforward network with a three-layer structure. The input layer consists of twelve neurons, which are fully connected with the five neurons of the hidden layer. An output layer has a single neuron predicting the glucose output of a patient. These predictions are made 15 min ahead of the present time to deal with uncertain disturbances. Both input as well as the hidden layer use a hyperbolic tangent function as their transfer function. For the outer layer a simple linear transfer function is used to make the predictions.

The proposed glucose prediction model in Table 3 is trained on a publicly available dataset[2] containing data from 70 patients collected over several weeks to months. A patient (#2) is randomly selected among 70 patients and his clinical data are shown in Figure 6. The data shown in Figure 6 constitute a 24-h profile of a patient, where insulin and blood glucose measurements were taken every 5 min (1853 samples in a day). It should be noted that the data are collected after the predefined dietary schedule where fixed amounts and times were assigned to breakfast (08:00), lunch (12:00), dinner (18:00), and bedtime (22:00). Table 3 shows the mean glucose levels, standard deviation, minimum and maximum values of insulin bolus, and measured plasma glucose levels.

The glucose prediction model shown in Figure 5 was trained individually for each patient with glucose level gm measured at a particular time t, insulin infusion rate $i(t)$, physical activity of a patient $a(t)$, and carbohydrate (food) intake $f(t)$ as inputs and the predicted level of glucose $g_{pred}(t+t_1)$ as output. The input

[2]AIM '94 (1994). Diabetes Data Set [online]. Website https://archive.ics.uci.edu/ml/datasets/Diabetes [accessed 23 August 2019].

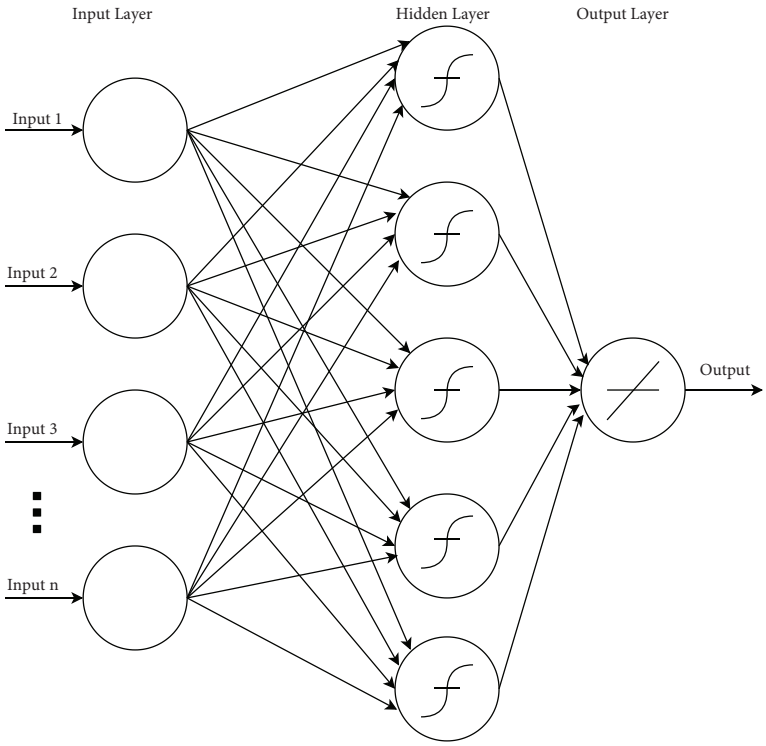

Figure 5. Neural network architecture.

Table 3. Glucose prediction model setup.

Model inputs	Model structure	Activations	Accuracy (average RMSE)
Activity $a(t)$, food intake $f(t)$, measured glucose $g_m(t)$, insulin bolus $i(t)$	Single input layer, 2 hidden layers, single output unit	Hyperbolic tangent, linear	5.84

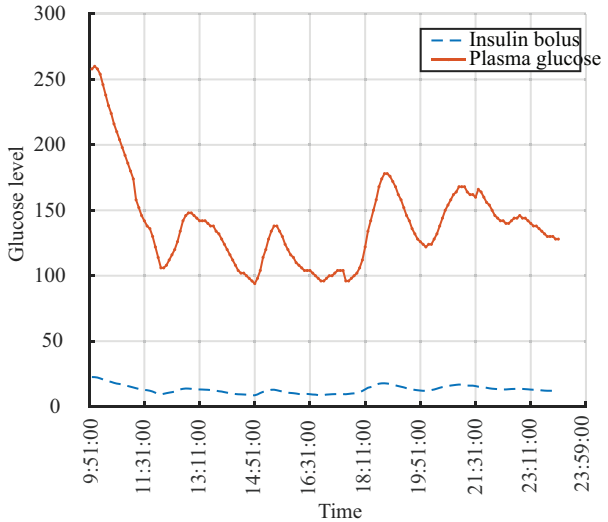

Figure 6. Patient Clinical data.

vector is of the form of Eq. (5).

$$g_{pred}(t+t_1) = Layer1(g_m(t), i(t), a(t), f(t)) \tag{5}$$

To accommodate for the carbohydrate consumption rate, the authors have built a mathematical function that considers the calorie consumption rate of a patient as described in [28]. Devices like continuous glucose monitors (CGMs) are also subject to some inherent delay [29], and while making glucose predictions this subcutaneous delay is also taken into account. Similarly, there is also some delay associated with the absorption rate of carbohydrates, which is usually calculated as glucose response during fasting. Keeping in view the difficulty of calculating this parameter, this parameter was determined using the values provided in [30].

Another vital parameter that serves as input to the proposed model and has an effect on the glucose dynamics of a patient is the patient's current activity. The proposed activity recognition model in Figure 4 predicts a patient's activity based on his data with an accuracy of 90 percent. Outputs from the activity recognition model shown in Figure 4 were turned into a six-level code ranging from 0 to 5 (0 (sitting), 1 (walking), 2 (jogging), 3 (standing), 4 (moving upstairs), 5 (moving downstairs)) and fed as input to the NN-based glucose prediction model based on the activity a user is performing. Table 4 shows part of the input profile of a patient for a single day.

Table 4. Plasma parameters of patients

Parameter	Glucose (mg/dL)	Insulin (mU/min)
Mean	132.771	12.767
SD	36.284	3.823
Minimum	52	5.49
Maximum	260	26.15

Weights of the neural network are started from small random values initially and are updated using a backpropagation algorithm. Because of the simple architecture of the proposed NN model, the model is trained using a damped least-squares optimization technique [31]. This technique is proven to converge faster when the size of the network is not very large [31]. The optimization algorithm is applied in batch mode where changes are accumulated over all patterns and are done after a complete pass (epoch) over the whole training set is made. Finally, the NN model response is validated with 10 test data instances in the dataset.

2.3. Neural network feedback controller

The NN-based feedback controller in Figure 2 is designed for the calculation of optimal insulin infusion, delivered via an insulin pump. Glucose predictions from the model discussed in the above section are used to calculate the error g_e between measured glucose g_m and glucose settling point g_{sp} (120 mg/dL). g_e calculated along with past insulin intake $i(t-t_1)$ serves as input to the controller while the amount of insulin $i(t)$ to be given in order to bring g_e close to g_{sp} is taken as output (Eq. 6).

$$i(t) = (g_e(t), i(t-t_1)) \tag{6}$$

An optimal three-layered NN structure was obtained with 3 units in the input layer and a single neuron in the output layer. The hidden layer contains an adequate number of neurons, which is considered to be

patient-specific. The control parameter was adjusted using the backpropagation of g_e and the network was trained in a similar way as discussed in the above section with the same least-square optimization technique, also called the Levenberg–Marquardt method [31, 32].

3. Results and discussion

In order to evaluate the performance of the glucose prediction model, the measured and predicted glucose levels of a patient were plotted as in Figure 7 and the root mean square (RMS) error was calculated. Table 5 shows the RMS error values and correlation coefficient of 10 randomly selected patients among a group of a total of 70 patients in the dataset.

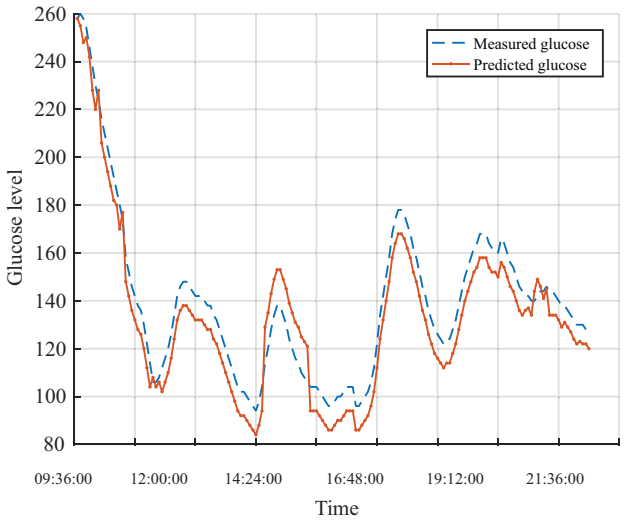

Figure 7. Glucose Prediction Model.

Table 5. Input profile of a patient.

Glucose level	258	116	112	146	128	114
Insulin inf. rate	22.59	10.3	11.99	13.53	11.96	10.58
Activity	1	1	2	4	0	0
Carbohydrate intake	0	0	82	54	0	0
Time	10:01	14:01	18:01	22:01	0:01	04:01

Glucose: mg/dL Insulin inf. rate: mU/min Carbohydrate intake: g

Figure 8 shows the performance of a NN-based feedback controller for a patient (#2). In order to bring the glucose levels close to the settling point (120 mg/dL), as shown in Figure 8a, the control algorithm, based on the predictions made by the glucose prediction model, manipulates the control variable (insulin bolus), as shown in Figure 8b. Table 6 shows the hyper- and hypoglycemic events for the same 10 subjects whose RMSE values are shown in Table 5.

The proposed NN model showed good prediction capability (Figure 7) during nominal meal conditions for each patient. There were very few hyper- and hypoglycemic events in the original dataset because the dataset includes data from diabetic patients who were under treatment. The predicted glucose levels from the model showed the acceptable average RMS percentage value (5.84) calculated from Table 5.

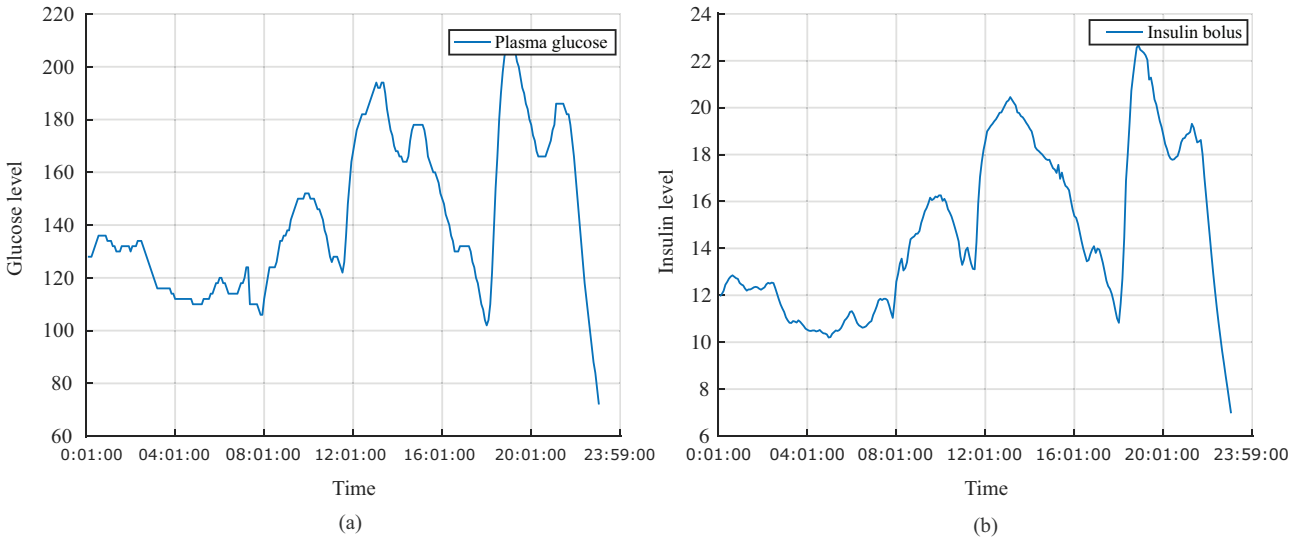

Figure 8. Controller performance, (a) Glucose Level maintained, (b) Insulin bolus calculated.

Table 6. NN controller performance.

Patient	Median	>180 mg/dL (%)	<70 mg/dL (%)	70–180 mg/dL (%)
1	132.8	6.6	0	93.4
2	153.2	9.7	3.2	87.1
3	143.1	7.4	0	92.6
4	148.3	7.6	2.1	90.3
5	134.6	5.3	0	94.7
6	138.3	3.9	0	96.1
7	143.7	4.4	1.8	93.8
8	135.9	5.8	0	94.2
9	141.6	8.4	0	91.6
10	133.6	7.6	0	92.4

The proposed feedback controller was successful in providing tight control of the glucose levels. Data from Table 6 reveal that the controller adjusted well to the activity and meal disturbances by keeping the subcutaneous glucose levels within the normal glycemic range. There were very few hypoglycemic events (Table 5) during the control and the average euglycemic rate was 92.62%. Table 7 provides the comparison of the proposed technique with other existing techniques used in the literature [27] in terms of average RMS error and percentage of values in the nondiabetic range. The glucose prediction technique used in the MPC (model predictive control) of [27, 33] is based on regression (ARX models), which uses a cost function to minimize the error between actual and predicted output. The system is modeled using the minimal Bergman model composed of 3 equations to represent the dynamic human glucose insulin behavior.

$$dG/dt = -P_1 - X(G + G_b) + D(t) \tag{7}$$

$$dX/dt = -P_2X + P_3I \tag{8}$$

$$dI/dt = -n(I + I_b) + U(t)/V_1 \tag{9}$$

Here, G is plasma glucose conc. (mmol/L) above basal value, X is proportional to I in remote compartment (mU/L), I is plasma insulin conc. (mU/L) above basal value, D(t) is meal glucose disturbance, U(t) is manipulated insulin infusion rate (mU/min), and G_b and I_b are basal values of glucose and insulin conc. (4.5 mmol/L, 15 mU/L). The initial model parameters are shown in Table 8. After the prediction is made, the MPC controller is engaged to manipulate the control variable (insulin infusion rate) in order to keep the blood glucose levels in a nondiabetic range for a fixed prediction horizon. The work described in [27] also provides control for a zone instead of control for a fixed settling point, which helps in minimizing the frequent controller adjustments. Proportional, integral, and derivative (PID) controllers were one of the early approaches used in closed-loop insulin delivery systems [33]. PID controllers have also shown good control in insulin regulation but issues like increased controller tuning, computational delays, signal conditioning, and noise cancellation need to be addressed more rigorously while implementing PIDs on digital hardware.

Table 7. Performance comparison of different techniques.

	Average RMSE (%)	Average 70–180 (%)
Zone-MPC	8.75	89.71
PID-controller	11.58	85.69
Proposed technique	5.84	92.62

All the simulations were done in the MATLAB programming environment. Both the neural network glucose prediction model and feedback controller were trained on a Core i5 processor with 6 GB of RAM and 2 GB NVIDIA graphics card.

Table 8. Initial model configuration.

$P_1 = 0\ min^{-1}$	$P_2 = 0.025\ min^{-1}$	
$P_3 = 0.000013$ mU/L	$V_1 = 12$ L	n = $5/54\ min^{-1}$

4. Conclusion

In this study, an optimized closed-loop insulin delivery system based on neural networks for model identification and control of diabetes mellitus is proposed. Convolutional neural networks are employed to recognize the physical activity of the subject and the recognized activity is incorporated into the model using a code to improve the glucose predictions. Experimental results reveal that the NN-based model performed well with an acceptable value of RMS error. Use of the NN-based feedback controller as a design choice for closed-loop control of diabetes proved to be a good choice. The controller performed well in keeping the blood glucose levels in a euglycemic range with accuracy of more than 90 percent. Several other factors, other than those discussed in this article, that affect blood glucose levels in an individual are stress, unpredicted meals, complex activities, etc. Consideration of these factors to further enhance the efficiency of the proposed model provides scope for future research. Further studies will also consider the use of hybrid models (i.e. recurrent NNs and CNNs) in modeling and experimentation with feedback controllers for improved control of the disease.

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Author disclosure statement

The authors have no conflicts of interest.

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