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TOWARDS MODELING HUMAN BODY RESPONSIVENESS TO GLUCOSE INTAKE AND INSULIN INJECTION BASED ON ARTIFICIAL NEURAL NETWORKS

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ABSTRACT

Diabetes is one of the most widespread diseases around the world, especially in the western world where non-healthy and fast foods are widely used. Many types of research have been conducted for developing methods for predicting, diagnosing and treating diabetes. One of the tools used for this purpose is mathematical modelling, which is used for developing models of blood glucose and insulin intake. In this paper, a model to determine the proper insulin dose for diabetic inpatients was implemented using Artificial Neural Network (ANN). The model is developed by taking into consideration ten different parameters (Patient's Gender, Patient's Age, Body Mass Index for Patient, Disease History, Total Daily Insulin Doses, Diabetes Type, Smoking Factor, Genetic Factor, Creatinine Clearance and Accumulative Glucose), in addition to real-time blood glucose readings. The model is developed based on a dataset from 159 inpatients from three different hospitals. It was found that the model with the best performance was based on one hidden layer with six neurons and seven inputs. The significant inputs were glucose readouts, glucose difference, normal range, accumulative glucose, history of the disease, total insulin dose and the patient's gender. The MSE of the best model was 5.413 and the correlation was 0.9315 with negligible training time.

KEYWORDS

Neural networks, Insulin dose, Glucose level, Modelling.

1. INTRODUCTION

In the recent decades, improvement in engineering techniques and their applications in different fields in the daily life has been noticed. Today, we can see their applications almost everywhere. The medical field is one of the widest and most important fields in engineering applications. We can see devices or equipment developed using different technologies in every hospital room, so that any medicine doctor can't do his work without using these devices [1]. During recent decades, humanity developed many devices which are used to help doctors in diagnosis and treatment, as well as in overcoming illness, body's organ insufficiency, diseases, accidents and congenital malformations. In ancient times, these devices were simple and primitive. However, mankind instinct has made it vital to be discovered [2].

One of the common diseases in current decades is diabetes, which is mainly a result of the modern life style. Diabetes has two main types; type one and type two. It infects all ages and both genders [1]-[2]. Therefore, researchers focused on using the engineering science and its applications or technologies to contribute to diabetes diagnosis and therapy. The therapy of diabetic disease involves life style change, weight loss and oral medications; but mostly it depends on insulin injection based on the readings of blood glucose monitoring devices which determine the amount of glucose in the patient's blood [2]-[4].

Diabetes mellitus is one of the most popular diseases around the world with around three hundred forty seven million people worldwide having this illness [1]. It occurs when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin produced, where this will cause what is called hyperglycemia. Hyperglycemia can be interpreted as an increment in the blood glucose level above the normal rate. There are two main types of diabetes: Type 1 and Type 2 diabetes. Type 1 diabetes usually appears in childhood age and the patients require a lifetime insulin injection. Type 2 diabetes usually develops in adulthood and mid-age. This is the most common type, representing over 90% of

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diabetes cases worldwide [2]-[4]. The treatment of this type may involve life style change, weight loss, oral medications or insulin injection [2]. Diabetes represents a major challenge for human health in the 21st century; so, there are many studies trying to provide medical solutions to this disease [3]. For patients who depend on insulin injection, the proper insulin dose is a very important issue, where determining this dose is a diabetes consultant matter. Such consultant is not always available; so, the patient must determine the dose by himself/herself, depending on his/her experience with the behavior of his/her body, which is medically unsafe.

This problem becomes more complicated by time, because diabetics mostly suffer from a slow damage of their sensitive organs, like vision problems and decline in sight intensity; so, the ability to see the injection shot's gauge becomes difficult and patients need external help for this task which is not always available [4]-[5]. Figure 1 shows a block diagram for the blood glucose track in human body by insulin interactive role to exchange glucose to energy. The digestive track breaks down the carbohydrate in the food into glucose and glucose is stored in the liver as glycogen. If the blood glucose drops under a certain threshold, the liver releases stored glucose. In order to extract glucose from the body, the liver needs insulin, which suppresses the inverse process. Most cells need insulin to consume the necessary glucose, like muscles which produce energy. If the glucose level increases in blood above the renal threshold, the body gets rid of this glucose by urine [5].

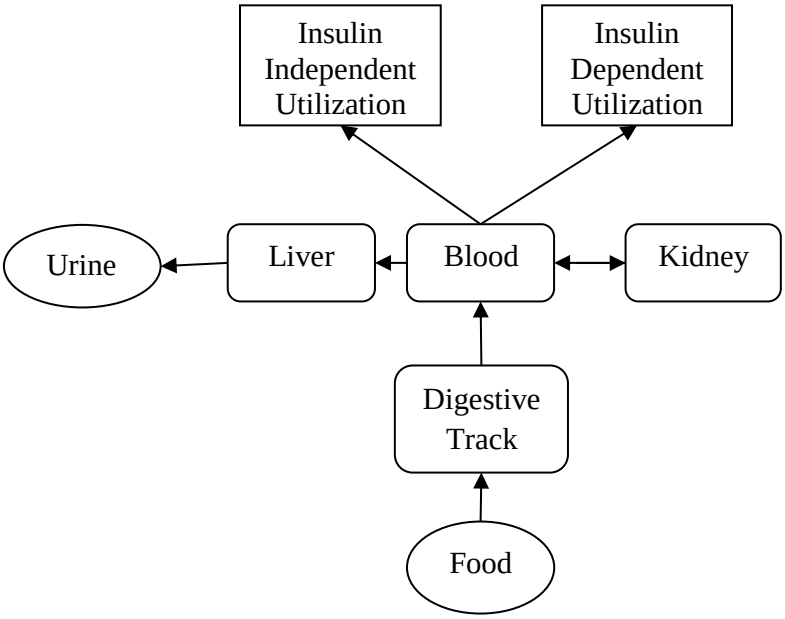

Figure 1. Glucose track in the human body, which is promoted and inhibited by insulin in the blood [5].

As research brought new renaissance in the world of manufacturing, the so-called information revolution resulted in new machines and devices. These machines and devices have artificial intelligence systems that allow to receive data and make decisions. As a result, smart devices have invaded various fields including the field of medicine and health care, providing higher accuracy in testing, measuring, supervising, controlling, organizing, alarming and achieving higher efficiency in the treatment of problems. One of the most important things that smart devices improved was the time needed to perform tasks; some testing that needed a day or even more can now be done in a few seconds. For example, blood analysis, which causes a lot of pain and suffering, is now carried out saving effort and cost and above all saving lives. Currently, there are many automatic medical devices used to monitor or treat diabetes disease. The most famous of these devices are:

1.1 Blood Glucose Monitoring Devices (BGMDs)

Blood glucose monitoring devices are considered very important for diabetic patients to monitor and manage their cases. These devices are widely used and easy to use, with both high accuracy and low

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cost [6]-[7]. BGM strips are used to withdraw the blood sample which is tested to measure the blood sugar ratio.

1.2 Insulin Pumps

An insulin pump is a small device which is controlled by a programmed microcontroller to deliver insulin doses to diabetic patients. These doses are delivered by a catheter, which is a flexible plastic tube. This catheter is inserted through the skin and placed into fatty tissues [8].

There are many advantages of using insulin pumps, like reducing unnecessary insulin doses. Insulin is delivered more accurately than by injection, resulting in fewer large swings in the blood sugar level, which makes the delivery of insulin easier, makes the food regime more comfortable, reduces sharp, low blood glucose level and eliminates unpredictable effects of intermediate or long acting insulin [9].

As glucose level increases in the patient's blood, the pancreas responds to this increase by producing an appropriate amount of insulin to consume glucose in the blood and reduce it to the normal level [5]. This process can be modelled and simulated if we develop a formula that can determine the relationship between real-time glucose level and insulin dose. To achieve this goal, different parameters in the human body should be considered.

This paper proposes a new methodology for modeling human body responsiveness to glucose intake and insulin injection using artificial neural networks (ANNs). The paper shows a neural network-based model that determines the relation between different human factors, the level of blood sugar and the appropriate insulin dose needed. In this paper, ten parameters (patient's gender, patient's age, body mass index, previous total daily insulin dose, history of the disease, smoking factor, family history, diabetic type, creatinine clearance and accumulative glucose test) are taken into consideration to investigate the relationship between them and the glucose and insulin levels.

2. PREVIOUS WORK

Many researchers have worked in this field. Here, we overview some research papers that have discussed the blood glucose control process in order to predict the right amount of insulin dose. In [9], the researchers have aimed mainly at determining the appropriate insulin dose for diabetic patients automatically based on patient's historical data in real time. A Markov process was used for modeling blood sugar level, which can be used to determine the future value for a random variable depending on its history through the current observation. An experiment was conducted in Jordanian hospitals. Four factors were taken into consideration; the body weight, the amount of carbohydrate in the breakfast meal, the amount of carbohydrate in the lunch meal and the amount of carbohydrate in the dinner meal. For the body weight, three weights were considered; 100 lb, 200 lb and 300 lb. One patient was chosen for each category and for 27 days, the amount of carbohydrate in the breakfast and dinner was changed in three levels; 30, 60 and 120 grams, while the amount of carbohydrate in the lunch meal was changed in three levels; 60, 120 and 180 grams. The problem of this method is that the prediction of blood sugar values is depending on a few factors, which are the amount of carbohydrate and the body weight, which will not give an accurate prediction, because there are other factors that must be considered.

In [10], researchers developed a neural network algorithm to adjust the appropriate next insulin dose based on the history of blood-glucose measurement and insulin dose setting. 25000 data recorded from 747 insulin-pump users were used to achieve a generalization. An insulin pump device was designed and controlled by a neural network. The researchers used the neural network technology to predict the insulin dose which we will use for the same goal, but in their model, they depended on the history of blood-glucose measurement, while our model will take other parameters as well as the future value of blood-glucose measurement into account.

In [11], the researchers presented a self-tuning algorithm to adjust an on-line insulin dosage in Type 1 diabetic patients. This dosage doesn't need information about insulin-glucose dynamics. In this model, three daily doses were programmed, where two types of insulin were used: rapid and slow. The results of a closed loop simulation were illustrated by a nonlinear model of the subcutaneous insulin-glucose dynamics with meal intake in diabetes Type 1 patients. This model is not safe and doesn't give true results, because it predicts the value of the insulin dose depending on a nonlinear insulin-glucose model which is totally dependent on the meal.

In [12], a microcomputer program was developed to use educated and assisted information whenever diabetes patients needed to make a decision in conjunction with self-monitoring of blood glucose. This information consists of the amount of optimum insulin dosage and the time at which this dosage should be taken. This information was useful and objective according to the researchers' opinion because it can be obtained from insulin sensitivity and is mathematically substantiated, in addition to that good control of blood glucose was achieved.

In [13], the researchers studied the application of neural networks for modeling glucose level in diabetic patients' blood. Recurrent neural network and time neural network were compared to linear model and nonlinear compartment model. The experiment showed that taking the proper error in consideration improved the results. A powerful model was achieved by combination of linear error model and recurrent neural network and gave the best results for blood glucose prediction.

In [5], blood glucose metabolism was studied to predict the glucose concentration using offline training for artificial neural network model. The prediction was based on accessible information, like physical effort of the patients, food intake and blood glucose readouts. The study performed online prediction using a special particle filter. This study discussed the level of glucose in the blood. The difference between this study and our model is that our model uses more factors and predicts and determines more accurately the proper insulin dose for the patient in addition to the glucose value.

In [24], the study proposed a Type 1 diabetes glucose-insulin regulator using an artificial high-order recurrent neural network. Using this network, a nonlinear system will be identified and controlled in order to represent the pancreas behavior for diabetic patients. This model uses Kalman filter algorithm to get a quick conversance and uses safety block between the output control system and the patients. This model uses a feed forward neural network to control the glucose values in Type 1 diabetic patients' blood. It doesn't consider any parameters related to the patient or to the disease, except the glucose readouts. Further, it doesn't include Type 2 diabetics in the study and the insulin dose is not considered.

In [25], the paper presented two models to simulate the glucose-insulin interaction for Type 1 diabetes children only. The models were based on a combination of Compartmental Models (CMs) and artificial Neural Networks (NNs). The database used consists of a continuous glucose monitoring, insulin dosages and food intake. The system provided short-term prediction of glucose values. The paper presents a prediction system for glucose-insulin metabolism for children with Type 1 diabetes. It takes only three parameters into account and doesn't determine the proper insulin dose for the prediction of glucose values. Although it uses continuous data about glucose-insulin readouts, it doesn't predict any insulin dosages. In [14], the researchers presented an automatic blood glucose classifier to help the specialist provide a better interpretation for blood glucose readouts in case of gestational diabetes. Their paper compared six different feature selection methods for two learning methods; decision tree and neural networks. Three searching algorithms (Genetic, Greedy and Beat First) were companied with two evaluators (Wrapper and CSF). The best results were obtained when the model consists of decision tree with a feature set selection with Wrapper evaluator and Best First search algorithm. In spite of the results, the goal was to provide a classification system and not to predict a future value or determine insulin dosages.

In addition to the mentioned previous work, literature has many other contributors in this filed. Some other relevant publications can be found in [26]-[30]. In [26]-[28], blood glucose was predicted using artificial neural networks trained with the AIDA diabetes simulator. In [29], the goal was to find technological solutions to manage and treat diabetes. In [30], a neuro-fuzzy system was studied in order to improve diabetes therapy.

3. METHODOLOGY

3.1 Data Collection

In this paper, data and parameters were collected from 149 patients who have diabetes mellitus in normal conditions and are experiencing normal diet. These patients were using sliding a scale system to measure their sugar level. A medical record was created for every case of them. Some information was taken from the patient's file in the hospital, while other information was taken from the patient himself. The 149 patients who were taking insulin injection in the abdomen area. were previewed starting from May

to September 2104 in Jordanian hospitals. These hospitals are: Princess Basma Teaching Hospital, King Abdullah University Hospital and Jordan University Hospital. Table 1 shows the parameters collected from the patients and used in this study.

Table 1. Parameters used in the study.

#	Name	Description
1	Patient's gender	Determines whether the patient is male or female.
2	Patient's age	Determines the age of the patient.
3	Body mass index (BMI)	Calculated by the formula (M/L^2); where M is the mass in kg and L is the height in meters; the normal range for body mass index is 18-24.
4	Previous total daily insulin dose (TDID)	It is the total insulin dose that patient used to take at home throughout the day.
5	The history of the disease	How long the patient had diabetes.
6	Smoking factor	Determines whether the patient is a smoker or a non-smoker.
7	Family history (genetic factor)	Determines whether the genetic factor exists or not.
8	Diabetic type	Determines whether the patient suffers from Type 1 or Type 2 diabetes.
9	Creatinine Clearance (CC)	It is a sign of efficiency of the kidney work, calculated from age, gender, weight and creatinine value in the blood.
10	Accumulative glucose test (HbA1C)	It is a test to determine the glucose accumulative average in the blood within the last three months.

3.2 Neural Network

In this paper, different neural network architectures have been implemented and studied to decide which one is the best. The parameters which were previously explained will be normalized and used as inputs to the network together with the blood sugar level of the patient. The desired output is the insulin dose ranging from 140 to 180 mg/dL [10]-[11]. The network uses the relation between all the inputs and the target to determine and adjust the weights of the connections to get a zero difference between the actual and the desired output in the training phase. The data is divided into three parts; training data (70%), testing data (15%) and validation data (15%) [12]-[15].

Considering the parameters which have been previously explained and in order to create a trained neural network, we need to provide the network with maximum number of diabetes patients' information. Figure 2 shows a basic block diagram for the neural network that is going to be used to determine the proper insulin doses based on the patients' data. The input to the neural network is the medical profile for the patient which was previously created and prepared. Because of the nature of the input data, it needs to be prepared before being used in the network [15]-[16].

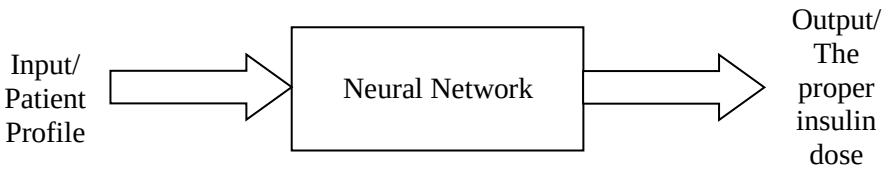

Figure 2. Neural network block diagram.

This preparation process includes several operations for every parameter, which will be explained later. Figure 3 shows the steps of modeling the neural network. First step is to arrange the input with its corresponding output. Then, the input profiles are prepared (quantification, normalization).

The data of the patient will be divided based on the level of glucose respective to insulin dose reduction. For this goal, a new indicator will be added to show whether the current insulin dose reduces the glucose to normal level or not. The input data doses that reduce the glucose to normal level are also divided into two parts; the first part used to training and the second part used in testing. The doses that didn't reduce the glucose to the normal level are assumed to be improper doses and will be used in the validation part to get actual outputs that represent the proper doses for the used inputs [17]-[22].

3.3 Parameters' Correlation

In this paper, the correlation between the patient input parameters and the glucose level is calculated. The correlation indicates the effect of the parameters on the diabetes mellitus. The correlation between the input parameters and the insulin doses is calculated as well. It shows the effect of the input parameters on the insulin doses. Table 2 shows the average glucose and insulin dose for both genders in the cases under consideration. The table shows an increase in both averages in the males' cases. Table 3 shows the average glucose and insulin doses for both smokers' and non-smokers' cases. It is clear that both averages are higher in the smokers' cases. Table 4 shows the average glucose and insulin doses for genetic and non-genetic cases. It is clear that both averages are higher in the genetic cases. Table 5 shows the average glucose and insulin doses for both genders for Type 1 and Type 2 diabetes. It is clear that the averages are higher in the Type 1 cases.

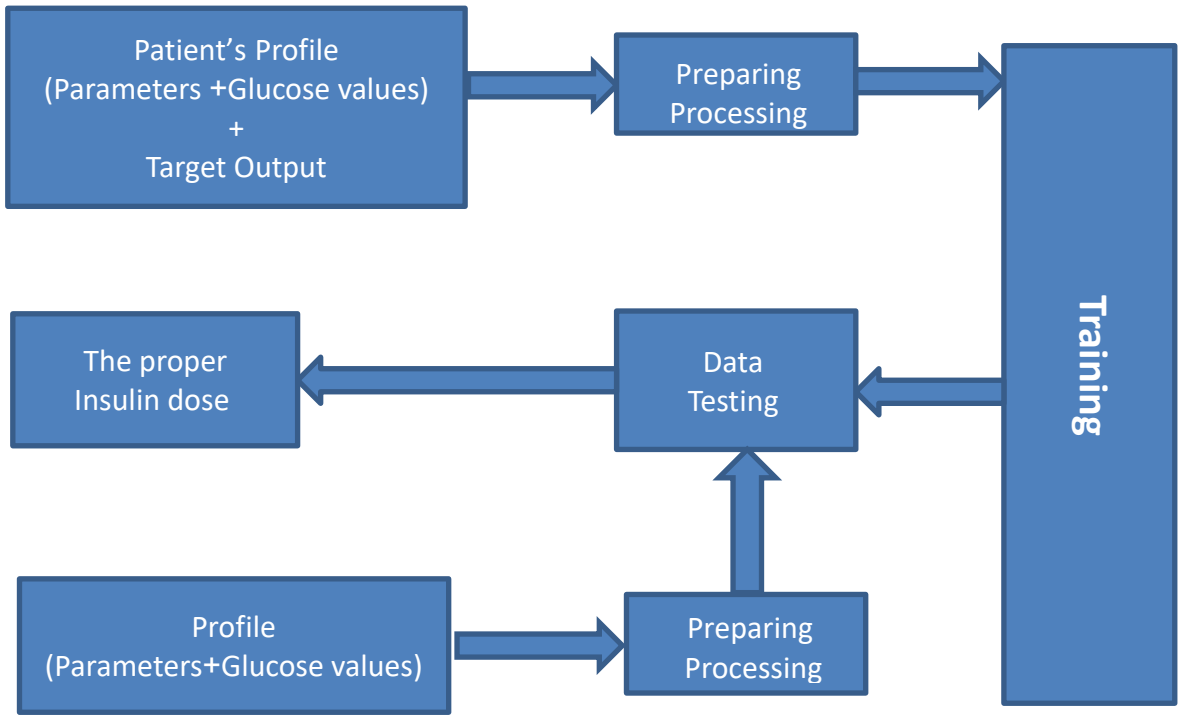

Figure 3. Block diagram for creating the neural network model [23].

Table 2. Average glucose/insulin for males and females [23].

Gender Parameter	Males	Females
Average Glucose (mg/dL)	214.8	264.9
Average Insulin (unit)	5.4	10

Table 3. Average glucose/insulin for smokers and non-smokers [23].

Smoking Factor	Smokers (50 Cases)	Non-smokers (85 Cases)
Average Glucose (mg/dL)	243.9	226
Average Insulin (unit)	7.9	6.5

The correlation factor can be calculated using the following equation [19]-[20]:

$$Corr = \frac{\frac{1}{n}\sum_{i=1}^{n}((Y_i - \mu_Y)(T_i - \mu_T))}{\sigma_Y \sigma_T} \quad (1)$$

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where, Corr: correlation factor, n: number of samples, Y: the predicted values, T: the actual values
μ_Y , μ_T : the mean value of predicted values and actual values, respectively.
σ_Y, σ_T: the standard deviation of predicted values and actual values, respectively, which can be calculated using:

$$\sigma_Y = \sqrt{\frac{(Y-Y')^2}{n}}, \sigma_T = \sqrt{\frac{(T-T')^2}{n}} \quad (2)$$

Table 4. Average glucose/insulin for genetic and non-genetic cases [23].

Genetic Factor	Genetic (69 Cases)	Non-genetic (55 Cases)
Average Glucose (mg/dL)	247	223.5
Average Insulin (unit)	7.5	7.2

Table 5. Average glucose/insulin for Type 1 and Type 2 diabetes [23].

Diabetes type Parameter	Type 1 (20 Cases)	Type 2 (109 Cases)
Average Glucose (mg/dL)	262.3	232.3
Average Insulin (unit)	8.6	7.1

Table 6 shows the correlation of each parameter with the insulin dose in descending order. From the table, we can see that accumulative glucose (HbA1C) has the highest correlation, which comes from the fact that the insulin intake is highly correlated to the glucose level (correlation= 0.84877), which is in turn related to the accumulative glucose. The HbA1C parameter is considered one of the most important parameters to determine the insulin dose.

Table 6. Correlation between patient profile parameters and insulin [23].

Parameter	Correlation
HbA1C	0.6102
TDID	0.3167
Gender	-0.3109
History	0.2478
Smoking Factor	0.0963
Type	-0.0658
Age	-0.0400
Genesis	0.0204
CC	-0.0086
BMI	-0.0041

Table 7 shows the correlation of each parameter with the glucose level in descending order. From the table, we can see that accumulative glucose (HbA1C) has the highest correlation as well, which comes from same reason that the accumulative glucose is related to the glucose level in the blood.

3.4 Neural Network Inputs

The inputs for the neural network are the parameters that were previously discussed, in addition to glucose readouts and a matrix called (**Per**) containing four sub-matrices, (**P1**, **P2**, **P3** and **P4**), where:

- **P1**= all insulin-glucose readouts for all patients given at 5:00 am.

Table 7. Correlation between patient profile parameters and glucose [23].

Parameter	Correlation
HbA1C	0.6995
TDID	0.3274
History	0.2440
Gender	0.2242
Genetic Factor	-0.1069
Type	0.0859
Smoking Factor	0.0803
Age	-0.0465
CC	-0.0259
BMI	-0.0075

- **P2**= all insulin-glucose readouts for all patients given at 11:00 am.
- **P3**= all insulin-glucose readouts for all patients given at 5:00 pm.
- **P4**= all insulin-glucose readouts for all patients given at 11:00 pm.

Each sub-matrix contains 5 columns (variables) as follows:

- Column number 1: contains all the glucose readouts for all the patients which were taken in that period.
- Column number 2: corresponding insulin doses (the target).
- Column number 3: the difference between the glucose current readout and the next readout to distinguish whether the dose is correctly working or not.
- Column number 4: contains a factor to determine whether or not the patient goes to the healthy glucose level after he was given an insulin dose. If the insulin dose reduces the glucose to the normal level, the factor is (+1), while if it failed to reduce the glucose to the normal level, then it is (-1).
- Column number 5: period indicator, to determine the time for this dose.

First, periods were independently discussed to distinguish whether the time of the insulin dose is an effective parameter or not. The patient's response to insulin doses was taken into consideration to find out whether or not it could be changed according to the dose time. To determine the period's effect, the correlation between the glucose and the insulin doses in each period was measured in normal cases (in which insulin doses reduce the glucose to the normal level). Table 8 shows the correlation between the glucose values and the insulin doses in each time period and the number of samples in each period.

Because there are no obvious differences between period correlations and because the number of samples is small, time factor was not considered as a parameter. Figure 4 shows the architecture of the neural network with its all inputs. Inputs from 4 to 13 were arranged based on Table 6 and Table 7. The inputs of the neural network are:

- Input number 1: glucose readouts; included in the **Per** matrix.
- Input number 2: glucose difference between current and next readouts; included in the **Per** matrix.
- Input number 3: normal or abnormal glucose range; included in the **Per** matrix.
- Input number 4: HbA1C, referred to as **O_Mat**.
- Input number 5: TDID, referred to as **F_Mat**.
- Input number 6: History, referred to as **H_Mat**.
- Input number 7: Gender, referred to as **A_Mat**.
- Input number 8: Genetic Factor, referred to as **J_Mat**.

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- Input number 9: Type, referred to as **K_Mat**.
- Input number 10: Smoking Factor, referred to as **I_Mat**.
- Input number 11: CC, referred to as **L_Mat**.
- Input number 12: Age, referred to as **B_Mat**.
- Input number 13: BMI, referred to as **E_Mat**.

Table 8. Correlation and number of normal samples in each time periods [23].

Periods	Insulin-glucose correlation	Number of samples
All periods	0.85	228
P1 (5:00 am)	0.82	61
P2 (11:00 am)	0.82	62
P3 (5:00 pm)	0.87	62
P4 (11:00 pm)	0.92	43

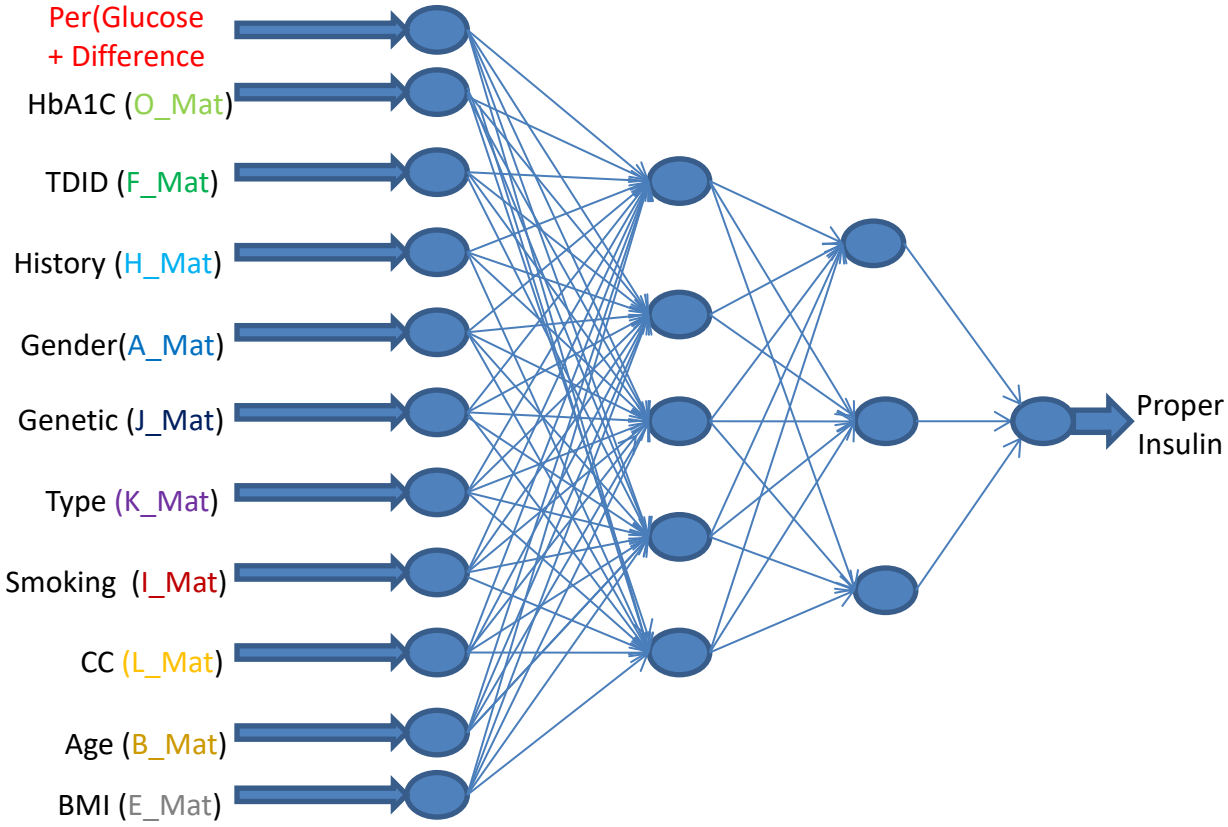

Figure 4. Data presentation in the neural network [23].

4. Results and Discussion

In this paper, several scenarios of different neural network models have been implemented and tested with different combinations of inputs. The main goal was to find the best model/input combination that would give the best insulin dose. In order to achieve our goal, one hidden layer and two hidden layer architectures will be investigated. The number of hidden layers will be referred to as HL. The number of neurons in each hidden layer will be varied and referred to as NN. This factor will be changed; the initial value of this factor will be (2) and it will be increased until it becomes equal to the number of inputs (which will be referred to as N). In the case of one hidden layer, the number of neurons for this hidden layer will be equal to NN, while in the case of two hidden layers, the number of neurons of the first hidden layer will be equal to 2*NN, while the number of neurons of the second hidden layer will be NN. Different neural network combinations and scenarios will be investigated using Matlab in order

to determine the best model that has the best overall results. The mean factor to compare the scenarios is the Mean Square Error (MSE), which can be calculated by [19]:

$$MSE = \frac{1}{n}\sum_{i=1}^{n}(Y_i - T_i)^2 \quad (3)$$

4.1 One Hidden Layer-Architecture Results

In this part, a one hidden layer neural network has been implemented. The input size (N) was changed from 4 to 13. In the case when the input size was four, the four inputs were (Input number 1 to Input number 4). In the case when the input size was five, the five inputs were (Input number 1 to Input number 5),… and so on until we reach the input size of 13, where all inputs from Input number 1 to Input number 13 have been used. For every input case, the number of neurons (NN) in the hidden layer was changed from 2 to N. This will lead to 75 scenarios of different input sizes and different numbers of neurons in the hidden layer. The scenarios were labeled as SN, as shown in Table 9. Table 9 shows the results of one hidden layer neural network. Scenario number 29 was the best among all the scenarios. The input size (N) was 7 and the number of neurons (NN) was 6. The table shows the results of the

Table 9. Results for *one* hidden layer, NN= 2 to N (normal cases) [23].

SN	N	NN	Corr.	MSE	Training Time (s)	SN	N	NN	Corr.	MSE	Training Time (s)
1	4	2	0.8562	8.4683	1.99	72	10	7	0.8657	12.7573	5.47
2	4	3	0.8558	8.4847	2.11	73	10	8	0.8286	16.1753	2.51
3	4	4	0.8557	8.4858	2.36	74	10	9	0.7983	15.3577	3.27
7	5	2	0.9094	6.9048	1.57	75	10	10	0.8456	15.8539	4.02
8	5	3	0.9077	7.005	2.59	85	11	2	0.8342	9.5567	2
9	5	4	0.9032	6.9725	2.61	86	11	3	0.8333	10.9242	1.9
10	5	5	0.9035	7.2051	3.03	87	11	4	0.8328	12.6808	2.48
15	6	2	0.8969	8.0996	2.08	88	11	5	0.5431	23.5971	3.4
16	6	3	0.8818	9.5068	2.43	89	11	6	0.6105	26.0511	8.25
17	6	4	0.8983	7.6662	3.6	90	11	7	0.4476	33.071	3.42
18	6	5	0.781	16.4711	2.37	91	11	8	0.4719	29.3541	3.89
19	6	6	0.7424	20.8346	3.83	92	11	9	0.5803	21.3855	5.26
25	7	2	0.8809	9.4062	2.74	93	11	10	0.4521	51.2194	5.73
26	7	3	0.9097	7.2851	2.04	94	11	11	0.4987	33.1392	7.25
27	7	4	0.8629	12.2306	2.6	105	12	2	0.8157	10.7657	1.83
28	7	5	0.8864	9.5751	3.25	106	12	3	0.8116	12.1597	3.01
29	**7**	**6**	**0.9315**	**5.4135**	**2.75**	107	12	4	0.83	14.1061	1.94
30	7	7	0.9217	5.9918	3.69	108	12	5	0.7931	13.4011	6.36
37	8	2	0.9223	5.953	1.97	109	12	6	0.5103	23.909	3.83
38	8	3	0.891	8.2438	2.16	110	12	7	0.4282	32.1775	3.7
39	8	4	0.8674	10.1898	3.59	111	12	8	0.4243	30.5901	4.86
40	8	5	0.8804	9.4356	2.83	112	12	9	0.635	21.3933	4.75
41	8	6	0.8745	11.5904	2.71	113	12	10	0.48	32.069	6.75
42	8	7	0.9079	6.9399	3.22	114	12	11	0.502	32.6276	9.07
43	8	8	0.8231	19.9454	2.82	115	12	12	0.5226	38.6858	12.41
51	9	2	0.9083	7.1136	2.23	127	13	2	0.8508	8.1012	3.08
52	9	3	0.8896	8.5694	2.08	128	13	3	0.8203	15.2744	2.58
53	9	4	0.8961	8.0417	3.04	129	13	4	0.5097	29.1451	2.46
54	9	5	0.8604	13.1336	3.65	130	13	5	0.5334	22.8252	3.43
55	9	6	0.8929	9.1926	3.59	131	13	6	0.515	24.146	2.96
56	9	7	0.8817	10.0915	3.09	132	13	7	0.4636	34.2889	3.77
57	9	8	0.822	12.8006	5.02	133	13	8	0.4926	30.04	3.7
58	9	9	0.823	12.8966	3.71	134	13	9	0.513	30.7419	8.26
67	10	2	0.8832	9.4369	2.48	135	13	10	0.5221	34.7157	11.34
68	10	3	0.8605	11.3827	3.07	136	13	11	0.5204	32.9236	9.23
69	10	4	0.8439	15.12	2.14	137	13	12	0.5328	28.7386	10.66
70	10	5	0.8934	8.6533	2.16	138	13	13	0.5085	28.2032	10.84
71	10	6	0.8672	13.011	9.29						

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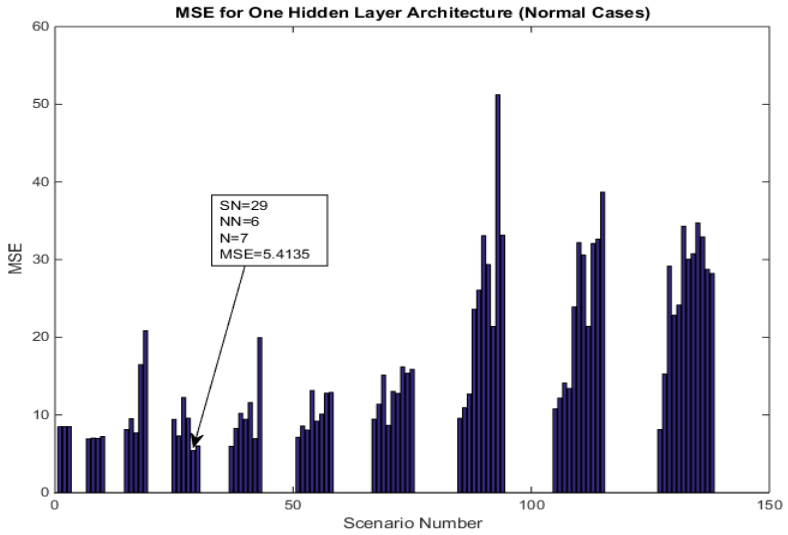

Figure 5. One hidden layer scenarios *vs.* MSE (normal cases) [23].

Table 10. Results for *one* hidden layer, NN= 2 to N (abnormal cases) [23].

SN	N	NN	Corr	MSE	SN	N	NN	Corr	MSE
1	4	2	-0.7011	415.055	72	10	7	-0.2038	130.412
2	4	3	-0.7088	249.964	73	10	8	-0.1083	279.252
3	4	4	-0.7114	214.299	74	10	9	-0.3052	466.544
7	5	2	-0.0173	127.864	75	10	10	0.0618	214.826
8	5	3	-0.023	128.49	85	11	2	0.5667	270.886
9	5	4	-0.1774	138.771	86	11	3	0.5024	127.568
10	5	5	-0.1504	131.275	87	11	4	0.0392	252.909
15	6	2	-0.1663	129.429	88	11	5	-0.243	352.265
16	6	3	-0.0343	127.966	89	11	6	0.1349	299.206
17	6	4	-0.2809	372.335	90	11	7	0.232	3230.6
18	6	5	0.3146	1738.44	91	11	8	0.1042	1397.1
19	6	6	0.3502	2129.36	92	11	9	-0.0332	780.922
25	7	2	0.08091	663.815	93	11	10	0.1356	425.308
26	7	3	-0.2346	165.87	94	11	11	0.4511	364.769
27	7	4	-0.1129	467.074	105	12	2	0.2111	301.557
28	7	5	-0.2888	293.282	106	12	3	0.3227	118.661
29	7	6	-0.5796	311.631	107	12	4	0.2158	193.543
30	7	7	-0.2927	230.686	108	12	5	-0.4071	169.868
37	8	2	0.1638	269.832	109	12	6	-0.2415	255.226
38	8	3	-0.3729	133.849	110	12	7	0.036	287.44
39	8	4	-0.3006	603.954	111	12	8	-0.2248	325.014
40	8	5	-0.0467	149.393	112	12	9	0.0259	1788.97
41	8	6	-0.2008	196.793	113	12	10	0.0185	186.216
42	8	7	0.0521	111.905	114	12	11	-0.2651	174.921
43	8	8	0.2686	344.154	115	12	12	0.2148	165.216
51	9	2	0.5682	87.2875	127	13	2	0.6198	75.1694
52	9	3	-0.066	129.276	128	13	3	0.0798	211.182
53	9	4	-0.0909	130.158	129	13	4	0.5105	723.819
54	9	5	-0.1384	258.689	130	13	5	0.0748	111.795
55	9	6	-0.2429	239.904	131	13	6	0.1437	355.578
56	9	7	0.1439	369.6	132	13	7	-0.0059	800.93
57	9	8	-0.2437	668.028	133	13	8	0.0092	371.203
58	9	9	0.6097	607.261	134	13	9	0.1511	179.785
67	10	2	-0.2459	130.456	135	13	10	0.0482	230.17
68	10	3	-0.2401	129.275	136	13	11	0.0887	125.798
69	10	4	-0.2342	136.658	137	13	12	-0.0971	173.311
70	10	5	-0.195	170.287	138	13	13	-0.014	200.059
71	10	6	-0.2566	190.287					

normal cases, where the insulin dose that was given to the patient reduced the glucose level to the normal range. The table shows that the results of this scenario have high correlation between the estimated insulin dose and the actual insulin dose that was given to the patient. The table shows that the training time was very small in scenario 29 and in the other scenarios as well. Figure 5 shows the MSE results indicating the best scenario (SN=29) as well.

In Table 10, the results were presented for the abnormal cases, where the insulin dose that was given to the patient did not reduce the glucose level to the normal range. The table shows very high MSE and very low correlation values between our estimated insulin dose and the insulin dose that was given to the patient. This result was expected, because the insulin dose that was given to the patient was inaccurate and far from truth and our estimated insulin doses should not agree with it.

4.2 Two Hidden Layer-Architecture Results

In this part, a two hidden layer neural network has been implemented. The input size (N) was changed from 4 to 13. In the case when the input size was four, the four inputs were (Input number 1 to Input number 4). In the case when the input size was five, the five inputs were (Input number 1 to Input number 5),… and so on until we reach the input size of 13, where all inputs from Input number 1 to Input number 13 have been used. For every input case, the number of neurons (NN) in the hidden layer was changed from 2 to N. The number of neurons in the first hidden layer was 2N, while the number of neurons in the second hidden layer was N. This will lead to 75 scenarios of different input sizes and different numbers of neurons in the hidden layers. The scenarios were labeled as SN, as shown in Table 11. Table 11 shows the results of two hidden layer neural network. Scenario number 31 was the best among all the scenarios. The input size (N) was 7 (same as in scenario 29) and the number of neurons (NN) was 4 in the first hidden layer and 2 in the second hidden layer, totaling 6 neurons (same as in scenario 29). The table shows the results of the normal cases, where the insulin dose that was given to the patient reduced the glucose level to the normal range. The table shows that the results of this scenario have high correlation between the estimated insulin dose and the actual insulin dose that was given to the patient. The table shows that the training time was very small in scenario 31 and in the other scenarios as well. Figure 6 shows the MSE results indicating the best scenario (SN=31) as well. Figure 7 shows the MSE results of all the 150 scenarios.

In Table 12, the results were presented for the abnormal cases, where the insulin dose that was given to the patient did not reduce the glucose level to the normal range. The table shows very high MSE and very low correlation values between our estimated insulin dose and the insulin dose that was given to the patient. This result was expected, because the insulin dose that was given to the patient was inaccurate and far from truth and our estimated insulin dose should not agree with it. Figure 8 shows the MSE results of all the 150 scenarios.

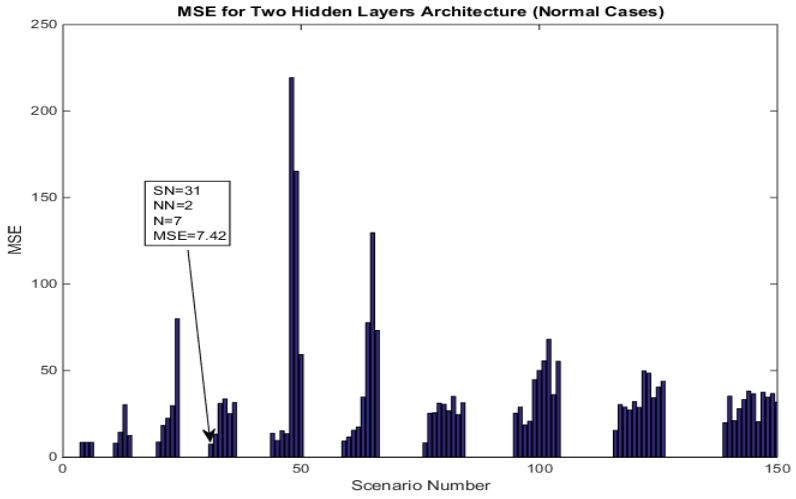

Figure 6. Two hidden layer scenarios *vs.* MSE (normal cases) [23].

Table 11. Results for *two* hidden layers, NN=2 to N (normal cases) [23].

SN	N	NN	Corr	MSE	Training Time	SN	N	NN	Corr	MSE	Training Time
4	4	2	0.857	8.4385	98.94	81	10	7	0.6958	26.7493	39.54
5	4	3	0.857	8.4376	139.48	82	10	8	0.634	35.0497	78.02
6	4	4	0.857	8.4371	94.11	83	10	9	0.7159	24.5227	108.71
11	5	2	0.8885	7.9654	3.6	84	10	10	0.6653	31.3797	126.58
12	5	3	0.7824	14.3083	5.78	95	11	2	0.6388	25.3486	2.82
13	5	4	0.6557	30.2161	10.68	96	11	3	0.6103	28.8664	3.09
14	5	5	0.8169	12.4147	11.8	97	11	4	0.763	18.5614	9.06
20	6	2	0.8885	8.6562	3.4	98	11	5	0.7239	20.6724	10.89
21	6	3	0.7806	18.259	4.58	99	11	6	0.3986	44.6389	37.18
22	6	4	0.732	22.425	7.18	100	11	7	0.5592	50.0105	49.95
23	6	5	0.6866	29.64	7.18	101	11	8	0.4823	55.6072	243.68
24	6	6	0.5938	79.912	23.53	102	11	9	0.5352	68.0122	74.95
31	**7**	**2**	**0.9077**	**7.42**	**3.11**	103	11	10	0.5769	36.0068	348.79
32	7	3	0.8604	13.2376	4.94	104	11	11	0.4616	55.3296	289.85
33	7	4	0.7024	31.0033	5.57	116	12	2	0.7575	15.3573	4.86
34	7	5	0.7548	33.5846	8.34	117	12	3	0.5743	30.3351	5.72
35	7	6	0.68	25.0394	16.99	118	12	4	0.5817	28.8664	5.62
36	7	7	0.6833	31.5006	25.24	119	12	5	0.5998	27.1308	15.21
44	8	2	0.8616	13.7006	2.43	120	12	6	0.589	32.0639	27.25
45	8	3	0.8912	9.5164	5.05	121	12	7	0.5796	28.6148	58.11
46	8	4	0.8481	15.1299	5.78	122	12	8	0.4509	49.7981	62.25
47	8	5	0.8543	13.4325	6.82	123	12	9	0.5171	48.4747	127.88
48	8	6	0.4644	219.2823	21.43	124	12	10	0.4706	34.2603	173.52
49	8	7	0.7182	165.1854	40.43	125	12	11	0.4928	40.4477	171.63
50	8	8	0.6936	59.254	64.49	126	12	12	0.5319	43.7363	153.93
59	9	2	0.8769	9.2321	3.2	139	13	2	0.7443	19.7896	2.73
60	9	3	0.858	11.5581	4.92	140	13	3	0.456	35.19	4.73
61	9	4	0.8613	15.3942	9.41	141	13	4	0.7469	20.9884	6.8
62	9	5	0.7575	17.368	15.49	142	13	5	0.7292	27.9412	26.23
63	9	6	0.7316	34.6058	14.04	143	13	6	0.7634	33.1865	21.69
64	9	7	0.569	77.6212	45.5	144	13	7	0.4733	38.0705	111.03
65	9	8	0.6752	129.6203	69.8	145	13	8	0.4926	36.5358	43.86
66	9	9	0.5392	73.1059	94.44	146	13	9	0.6869	20.3738	210.67
76	10	2	0.8998	8.1551	3.35	147	13	10	0.5859	37.4392	178.57
77	10	3	0.8318	25.2445	3.46	148	13	11	0.5532	34.5468	175.65
78	10	4	0.7051	25.569	8.66	149	13	12	0.5023	36.6599	114.03
79	10	5	0.7487	31.1132	7.49	150	13	13	0.485	31.7137	399.4
80	10	6	0.6379	30.4688	19.63						

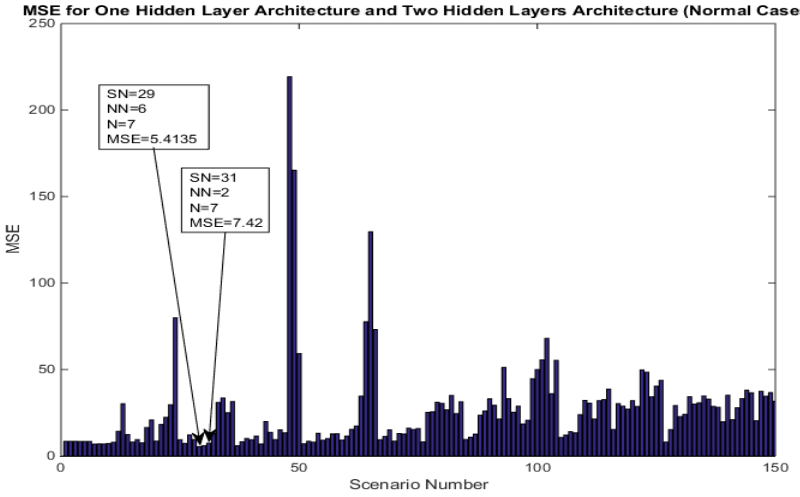

Figure 7. All scenarios *vs.* MSE (normal cases) [23].

"Towards Modeling Human Body Responsiveness to Glucose Intake and Insulin Injection Based on Artificial Neural Networks", A. Alqudah, A. Bani Younes and A. M. Alqudah.

Table 12. Results for *two* hidden layers, NN=2 to N (abnormal cases) [23].

SN	N	NN	Corr	MSE	SN	N	NN	Corr	MSE
4	4	2	0.7736	137.908	81	10	7	-0.0951	303.386
5	4	3	0.7668	145.385	82	10	8	0.3492	261.933
6	4	4	0.7627	149.726	83	10	9	0.1155	794.418
11	5	2	-0.0439	128.76	84	10	10	0.419	988.89
12	5	3	0.5536	1209.45	95	11	2	0.5643	73.2999
13	5	4	-0.3063	2628.33	96	11	3	0.5231	87.7208
14	5	5	0.1386	170.128	97	11	4	0.2985	1261.97
20	6	2	-0.1232	128.855	98	11	5	-0.138	1002.16
21	6	3	-0.0264	128.428	99	11	6	0.0628	327.401
22	6	4	0.5232	58.3101	100	11	7	0.0956	336.302
23	6	5	0.6149	3386.87	101	11	8	0.2405	259.946
24	6	6	-0.4645	12271.5	102	11	9	0.4853	361.524
31	7	2	0.219	250.472	103	11	10	0.1099	221.032
32	7	3	-0.2211	366.505	104	11	11	0.1657	441.659
33	7	4	0.0254	550.042	116	12	2	-0.0627	164.374
34	7	5	0.4985	715.249	117	12	3	0.2321	206.586
35	7	6	0.1834	797.093	118	12	4	0.4231	87.7208
36	7	7	-0.0719	147.863	119	12	5	0.1802	395.365
44	8	2	0.6417	209.077	120	12	6	0.3635	437.953
45	8	3	-0.4245	708.868	121	12	7	0.3707	158.253
46	8	4	-0.0693	469.126	122	12	8	0.0129	139.908
47	8	5	0.2435	398.054	123	12	9	0.1484	114.586
48	8	6	-0.2242	6194.88	124	12	10	0.1274	259.738
49	8	7	-0.1899	648.739	125	12	11	0.3391	167.358
50	8	8	0.1758	2159.4	126	12	12	0.281	141.162
59	9	2	-0.3566	288.816	139	13	2	0.1254	176.047
60	9	3	0.0608	3243.18	140	13	3	-0.4203	500.726
61	9	4	0.2364	117.433	141	13	4	0.411	2092.45
62	9	5	0.4535	96.9451	142	13	5	0.094	803.296
63	9	6	0.1131	4479.02	143	13	6	0.1014	256.486
64	9	7	-0.1486	653.451	144	13	7	0.0351	175.18
65	9	8	0.1135	3768.88	145	13	8	-0.03	146.857
66	9	9	0.6558	1395.86	146	13	9	0.3455	482.715
76	10	2	0.1486	105.647	147	13	10	0.6095	85.7366
77	10	3	0.2631	193.772	148	13	11	0.4303	87.258
78	10	4	0.105	550.041	149	13	12	0.1839	204.988
79	10	5	0.4139	258.184	150	13	13	0.42	157.063
80	10	6	0.1884	1759.14					

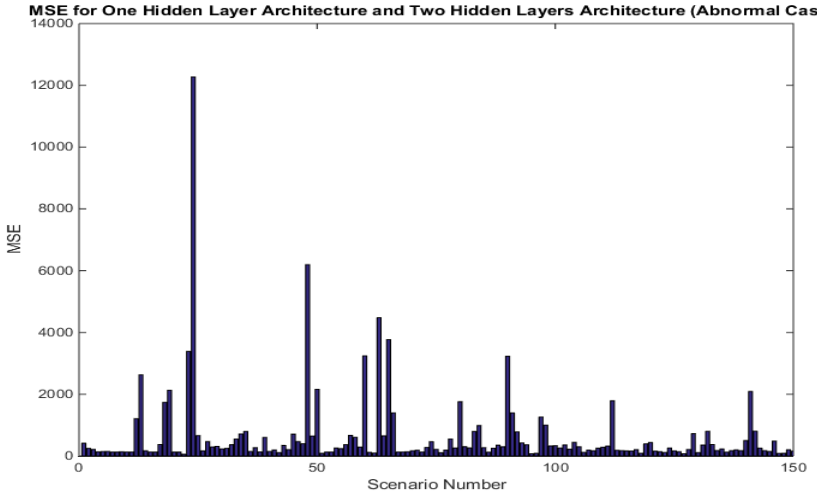

Figure 8. All scenarios *vs.* MSE (abnormal cases) [23].

Table 13. A comparison between proposed system and systems in literature.

Reference	Method	Number of Factors (Inputs)	RMSE (mg/dL)
[31]	Artificial Neural Networks (ANNs)	1	10, 18, 27
[32]	Recurrent Neural Networks (RNNs)	12	19.04
[33]	Convolutional Neural Networks (CNNs)	6	19.31, 29.3
Proposed	Artificial Neural Networks (ANNs)	11	2.3265

5. SUMMARY AND CONCLUSION

This paper aimed to discuss the effect of certain parameters on diabetes mellitus and on the insulin dose for diabetes patients, in order to determine the proper insulin dose for diabetic patients based on medical profiles based on neural networks. To determine the proper insulin dose, a neural network was modeled using glucose-insulin continuous readouts for in-hospital diabetic patients as input for our model, in addition to other parameters.

The parameters that were discussed in this paper are: patient's gender, patient's age, body mass index, previous total daily insulin dose, patient's nutrition status, history of the disease, smoking factor, family history, diabetic type, creatinine clearance and accumulative glucose test. The used samples were taken from three Jordanian hospitals, Princess Basma Teaching Hospital, King Abdullah University Hospital and Jordan University Hospital, from May to September 2014. The results show that the most effective parameter was the accumulative glucose, while the least effective parameter was the body mass index.

The results also show that the best architecture for our model was obtained when we used an architecture with one hidden layer, six neurons and seven inputs. The significant inputs were glucose readouts, glucose difference, normal range, accumulative glucose, history of the disease, total insulin dose and patient's gender. The MSE of the best model was 5.413 and the correlation was 0.9315 with negligible training time. Table 13 provides a comparison between our proposed methodology and other methods presented in literature [31]-[33]. It is clear that our proposed method has better performance in terms of RMSE. The RMSE of our proposed method was 2.3265, being larger than those for the other methods.

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ملخص البحث:

يعدّ مرض السكري أحد أكثر الأمراض انتشاراً على مستوى العالم، وبخاصة في العالم الغربي حيث يكثر تناول الأطعمة السريعة وغير الصحية. وقد أجريت أبحاث متعددة لإيجاد طرق لتوقع مرض السكري وتشخيصه وعلاجه. ومن بين الطرق المستخدمة لهذا الغرض النمذجة الرياضية التي تستخدم لتطوير نماذج لجلكوز الدم وامتصاص الإنسولين.

في هذه الورقة، تم تطوير نموذج لتحديد جرعة الإنسولين المناسبة لمرضى السكري باستخدام شبكة عصبية اصطناعية. وقد تم تطوير النموذج مع أخذ عشرة متغيرات بعين الاعتبار (جنس المريض؛ عمر المريض؛ مؤشر كتلة جسم المريض؛ التاريخ المرضيّ؛ إجمالي جرعات الإنسولين اليومية؛ نوع مرض السكري؛ عامل التدخين؛ العامل الوراثي؛ تصفية الكرياتنين؛ الجلكوز التراكمي)، إضافة الى قراءات الجلكوز في الدم في الزمن الحقيقي. وجرى تطوير النموذج بناءً على مجموعة بيانات تعود الى 159 من مرضى السكري من 3 مستشفيات مختلفة.

وُجد أنّ أفضل النماذج من حيث الأداء هو ذلك النموذج المبني على طبقة مخفيّة واحدة مع ستّة عصبونات وسبعة مداخل. وكانت المداخل المهمة: قراءات الجلكوز؛ فرْق الجلكوز؛المدى الطبيعي؛ الجلكوز التراكمي؛ تاريخ المرض، الجرعة الكلية للإنسولين؛ عمر المريض. وبلغ متوسط مربع الخطأ للنموذج الأفضل (5.413)، بينما بلغ معامل الارتباط (0.9315) مع زمن تدريب يمكن إهماله.