A DEEP LEARNING BASED APPROACH FOR PREDICTING HYPOGLYCEMIA IN TYPE-1 DIABETIC PATIENTS USING RECURRENT NEURAL NETWORKS

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Abstract

Hypoglycemia is a dangerous scenario arises in the case of patients with Diabetic Meletus, when the blood glucose level falls below a threshold level (70 mg/dL or 3.9 mmol). This is very common among Type-1 diabetic patients. This may cause a lot of negative implications in the affected patient's body, such as cognitive disabilities, seizures, and in the extreme case, death of the patient. We can make use the huge amount data available with new generation diabetic health care instruments like continuous glucose monitors (CGMs) and insulin pumps to predict future events of hypoglycemia, thereby saving the life of a patient. Our paper recommends a deep learning model to predict the upcoming hypoglycemic events using Recurrent Neural Networks (RNN).

Keywords: Diabetes Meletus, Hypoglycemia, Prediction, Deep Learning, Recurrent Neural Networks (RNN)

I INTRODUCTION

Diabetes Meletus is a group of decease conditions which happens due to the poor digestion of carbohydrates in human body. In normal cases, the processed carbohydrates are converted to glucose, which provides energy to our body. But the standard value of blood sugar in human body should be within 70 mg/dL (3.9mmol/L) and 100 mg/dL (5.6 mmol/L). If the sugar level in blood exceeds this range, the state is known as hyper glycemia and when it falls below the range, it is known as hypoglycaemia [1].

Hypoglycemia is a very dangerous condition and if not treated early enough, it may disrupt the cognitive progressions of the human body leading to seizures and eventually death of the patient. Early prediction of risk of hypoglycemia may help to deliver proper medical assistance to the patient and thereby save a life [2].

The impact of digital technology in medical science has improved the treatment methodologies for diabetes a lot. Modern electronic equipment such as Continuous Glucose Monitor (CGM) and insulin pump helps the patients to record their blood glucose values and administrate proper amount of insulin without painful needle pricks [3]. The CGM measures the blood glucose of a patient once in every five minutes and almost all CGMs continuously works for 14 days. Also, an insulin pump can provide with a sequence of dosage of administrated insulin. We can make use of this data for predicting the future glucose level as well as risk of events like hypo or hyper glycemia [4].

The proposed model is based on Deep Leaning techniques to forecast the future hypoglycemic events by making use of the features of Recurrent Neural Networks. The data used in this model is the CGM data and insulin dosage of 4000+ subjects donated in the Tidepool Big Data donation data set. After pre-processing of the row data, the RNN predicted the occurrence of hypoglycemia with an accuracy of 94.68% within a prediction horizon of 30 minutes.

II RELATED WORKS

In 1999, Bremer and Gough [4] predicted upcoming glucose levels using prior glucose values. From there onwards, many researchers have laid out models for hypoglycemia anticipating utilizing factual and AI methods. There are only a few works for predicting hypoglycemia

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using deep learning techniques. Most of the works concentrate on predicting future blood glucose level, when the current value is given as input.

Mujahid O, Contreras I and Vehi J (2021) conducted a review on machine learning techniques for early hypoglycemia prediction [5]. This study comprises 13 different models which follows different ML architectural styles, which include LDA: Linear Discriminant Analysis; PLSR: Partial Least Square Regression; IR: Infra-Red; ANN (Artificial Neural Network) CNN (Convolutional Neural Network), LSVM (Linear Support Vector Machine), LR (Logistic Regression), RF (Random Forest), SVM (Support Vector Machine), DT (Decision Tree), KNN (K Nearest Neighbour) etc.,

Another study by Sudharsan B, Peeples M and Shomali (2014) was based on Machine Learning to predict hypoglycemia in Type-2 diabetic patients [6]. After training a probabilistic model with Machine Learning algorithms they have self-monitored blood glucose values from different patients. The model was analysed using different sets of data and also a second model was also tested by given medicine dose as additional input. The model showed a sensitivity of 92% for predicting a hypoglycemia in the next 24 hours and the specificity was 70%. When medicine information is incorporated, the specificity improved to 90% [6].

Yue Ruan, Alexis Bellot, Zuzana Moysoya, Garry D. Tam, Alistair Lumb, Jim Davies, Mihaela van der Schaar and Rustan Rea(2020) have forecasted the chance of hypoglycemia in patients with diabetes admitted to a large hospital using machine learning technique [7]. They used four years of data containing electronic health reports, laboratory results, administrated medicines, physiological features of the patients, and various procedures that the patient has undergone during the admission period. From their study, it was observed that the XGBoost model (AUROC 0.96) was the machine learning model with the best performance. This outstripped the LR model, for which the AUROC was 0.75 for the assessment of the stake of clinical hypoglycemia [7].

Seo, W., Lee, YB., Lee, S. (2019), proposed an ML model for predicting post prandial hypoglycemia [8]. They used CGM datasets of 104 patients for whom there occurred at least one hypoglycemia during three-days. The model was based on ML models like K-nearest neighbour, and a logistic regression. The performance of each model was evaluated using 5-fold cross-subject validation. Within a prediction horizon of 30 min the model showed an average AUC ,0.966, the average sensitivity 89.6%, the average specificity of 91.3%, and the average F1 score of 0.543[8].

In the paper titled, “Precision Medicine and Artificial Intelligence: A Pilot Study on Deep Learning for Hypoglycemic Events Detection based on ECG” (2020), Mihaela Porumb, Saverio Stranges, Antonio Pescapè and Leandro Pecchia made use of AI to detect mid-night hypoglycemia using heartbeats of patients taken from ECG signal recorded with wearable devices, in healthy people, observed 24 hours for 14 successive days [9]. In addition to this, they have presented a visualization technique to depict which part of the ECG is associated with the nocturnal hypoglycemic event. The prescribed model used a combination of CNN and RNN for the classification of ECG signals.

This model is a RNN based model for predicting the manifestation of hypoglycemia in Type-1 diabetic patients, given the previous blood glucose values and dosage of medicine administration as input.

III METHODS AND MATERIALS

The prescribed model is systematized in two phases, pre-processing of data and construction of RNN model. This section describes the working of each section in detail.

3.1. Data Pre-Processing

3.1.1 Data Set

In this model we used a small part from the Tidepool Data Set (Tidepool, Palo Alto, CA) which comprises more than 4000 subjects. The data set contains more than 27000 days and 22,000 nights of CGM data and insulin dose given to 124 Type-1 diabetic patients of various age groups ranging from 12 to 50 years. All these were multi-vendor insulin pump users. The data set also describes the occurrence of hypoglycaemic events too. CGM readings were gotten each 5 min. The collected data covered more than 17,000 nights when no hypoglycemia was observed and 5600 nights when hypoglycemia was noticed. Tidepool does not provide any personal data regarding the patients other than their age [10]. In order to avoid overfitting of data, 65% of the data have been used for training the model and remaining 35% for testing purpose.

3.2 Interpolation

The Figure 1 shows the CGM data of a Type-1 diabetic patient observed on a single day. It can be observed that the data sequence contains missing data at some points.

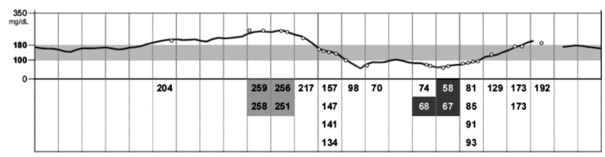

Figure 1: CGM data of a Type -1 Diabetic Patient observed on a single day[11,12]

As the result of our model highly rely on the difference between current and future data points it is inappropriate to have missing data points in the training as well as testing data. [13]

In this model, the method of linear interpolation is used to fill up the missing points. According to this method we can find the missing points by using the following equation.

$$\text{Linear Interpolation}(y)=y1+(x-x1)\,(y2-y1)/x2-x1) \quad [2]$$

where (x1, y1) is the primary point, (x2, y2) is the subsequent point and (x, y) is the missing one which is to be calculated.

3.3 Filtering

After interpolation, the data sequence is found to have unexpected spikes at some points. To remove these spikes, we use the median filter [14], in which the unfitted values are replaced with the median of the nearby points. In our model, the window size for median filtering is selected as 5. The median filtering is only applied on the training data. After interpolation and filtering, the data appears to be as given in Figure 2.

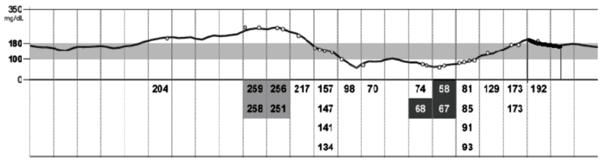

Fig.2. Big Data Characteristics

RNN has an input layer, hidden layers and one output layer. In the case of RNN, the output of each layer will become the input to the next layer. While considering the independent input to each step, it takes the results of previous stage also into consideration. Also, the hidden states have the ability to remember certain details about the sequence. Generally, we can consider RNN as a sequence of neural networks which can be trained one after the other with back propagation. Figure 3 shows the basic structure of RNN [10] [11].

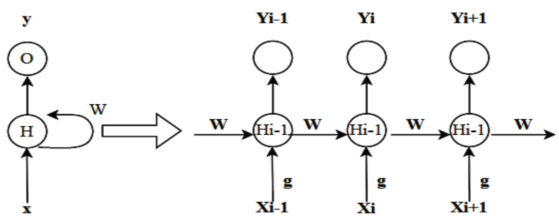

Figure 3: Basic structure of RNN

The first layer is the input layer The subsequent layer is known as the hidden layer which is answerable for weight assignment, where we applied the tangent sigmoid function. $\tanh(x)=2g(2x)-1$.

Each layer has a bias which is created from its previous layer. The training algorithm of Levenberg-Marquardt [3] is used to randomly adjust and update weights and biases. Through back propagation, the weights are optimized. [14]

The input contains two neurons for inputting the CGM data as well as the insulin dosage, and the hidden layer contains three neurons. In this model, we try to anticipate the stake of hypoglycemic occasions in 30 minutes, 45 minutes and 60 minutes of prediction horizons respectively.

V RESULTS AND DISCUSSION

With this model we have predicted the occurrence of hypoglycemia. Table1 shows a subsection of the result set.

Trials	*Predicted Hypoglycaemia*	*Actual Result*	*Remarks*
1	Yes	Yes	Real Positive
2	No	No	Real Negative
3	No	Yes	Fake Negative
4	No	No	Real Negative
5	Yes	Yes	Real Positive
6	Yes	No	Fake Positive
7	No	No	Real Negative
8	No	No	Real Negative
9	Yes	Yes	Real Positive
10	Yes	Yes	Real Positive
11	Yes	No	Fake Positive
12	Yes	No	Real Positive

Table 1: Subset of Results After Prediction

Using these results, the accuracy of the prescribed model can be calculated as: -

Accuracy = (RP+RN)/(RP+FP+FN+RN)

RP- Number of Real Positives

RN-Number of Real Negatives

FP- Number of Fake Positives

FN-Number of Fake Negatives

The analysis of overall results is summarised in Table 2.

	PH	**> 30 min**	**>45 min**	**> 60 min**
Predicted Hypoglycemic	**TP**	14502	9504	22687
	FP	2462	3621	6345
Predicted Non-Hypoglycemic	**TN**	45709	54328	56304
	FN	924	1287	1008
Accuracy		0.9467585	0.9286005	0.914841

Table 2: Analysis of Prediction Result

From the result we can observe that for shorter PH the model shows high accuracy. As the Prediction Horizon increases the accuracy slightly decreases. For PH of 30 min, the prescribed model shows the highest accuracy rate of 94.68%.

VI CONCLUSION AND FUTURE ENHANCEMENTS

Hypoglycemia is a life-threatening condition affection diabetic patient, especially Type-1 diabetic patients. Early prediction of risk of hypoglycemia may save the life of a human being. Through our study, we describe a deep learning-based model for early forecasting the presence of hypoglycemia in Type-1 diabetic patients. We used RNN for the prediction and the prescribed model showed 94.68% accuracy rate as per our findings.

The overall architecture of our model is summarised in Figure 4.

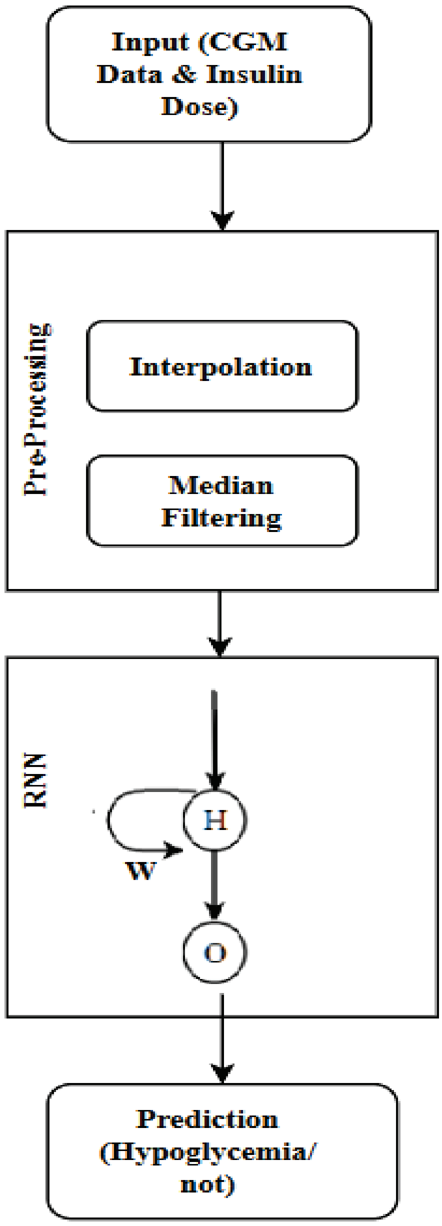

Figure 4: Overall Architecture of Proposed Model

In this study, we have used the CGM data and insulin dosage as inputs to the Deep Learning network. But for a Type-1 diabetic patient, the previous blood glucose reading and insulin intake will not be sufficient to predict the future glucose level or occurrence of events such as hypo or hyper glycemia. There are a lot of other factors which may affect the decision in predicting whether there will be hypoglycemia or not.

The blood glucose curve may rise abruptly at the time of meal events and it may fall when the patient undergoes excessive physical activities. So, this model could show better accuracy if the total carbs intake (food) and amount of physical activity (in terms of carbs burn) are also considered along with the previous blood glucose value and insulin intake.

While pre-processing of data we used the method of interpolation for filling up the missing data. When the entire data set is considered, missing data may appear frequently. Only shorter intervals of missing data can be effectively filled by using interpolation. The CGM will normally reads blood glucose level once in every five minutes. So, it is unlikely to have larger time intervals of missing data in the data input series. In the proposed model, there is no way to compensate if longer contiguous intervals appear. In this case we could divide the long missing intervals into discrete small intervals and interpolate the missing values for each smaller part separately.

REFERENCES

[1] Mosquera-Lopez, Clara et al. "Predicting and Preventing Nocturnal Hypoglycemia in Type 1 Diabetes Using Big Data Analytics and Decision Theoretic Analysis." Diabetes technology & therapeutics vol. 22,11 (2020): 801-811. doi:10.1089/dia.2019.0458.

[2] Linear Interpolation Formula - Derivation, Formulas, Examples (cuemath.com)

[3] A. D. Association. Standards of medical care in diabetes – 2017. Diabetes Care, vol. 40, no. 1, pp. S1–S135, 2018.

[4] Bremer T, Gough DA. Is blood glucose predictable from previous values? A solicitation for data. Diabetes. 1999;48(3): 445-451.

[5] Mujahid O, Contreras I, Vehi J. Machine Learning Techniques for Hypoglycemia Prediction: Trends and Challenges. Sensors. 2021; 21(2):546. https://doi.org/10.3390/s21020546

[6] Sudharsan B, Peeples M, Shomali M. Hypoglycemia Prediction Using Machine Learning Models for Patients With Type 2 Diabetes. Journal of Diabetes Science and Technology. 2015;9(1):86-90. doi:10.1177/1932296814554260

[7] Yue Ruan, Alexis Bellot, Zuzana Moysova, Garry D. Tan, Alistair Lumb, Jim Davies, Mihaela van der Schaar, Rustam Rea; Predicting the Risk of Inpatient Hypoglycemia With Machine Learning Using Electronic Health Records. Diabetes Care 1 July 2020; 43 (7): 1504–1511. https://doi.org/10.2337/dc19-1743

[8] Seo, W., Lee, YB., Lee, S. et al. A machine-learning approach to predict postprandial hypoglycemia. BMC Med Inform Decis Mak 19, 210 (2019). https://doi.org/10.1186/s12911-019-0943-4

[9] Porumb, M., Stranges, S., Pescapè, A. et al. Precision Medicine and Artificial Intelligence: A Pilot Study on Deep Learning for Hypoglycemic Events Detection based on ECG. Sci Rep 10, 170 (2020). https://doi.org/10.1038/s41598-019-56927-5.

[10] L. Iliadis and C. Jayne (Eds.): "A Recurrent Neural Network Approach for Predicting Glucose Concentration in Type-1 Diabetic Patients", EANN/AIAI 2011, Part I, IFIP AICT 363, pp. 254–259, 2011. © IFIP International Federation for Information Processing 2011

[11] Dae-Yeon Kim 1, Dong-Sik Choi 2 , Jaeyun Kim 3, Sung Wan Chun 1, Hyo-Wook Gil 1, Nam-Jun Cho 1, Ah Reum Kang 4,* and Jiyoung Woo 3,* , "Developing an Individual Glucose Prediction Model Using Recurrent Neural Network", Sensors 2020, 20, 6460; doi:10.3390/s20226460

[12] Muhammad Asad, Usman Qamar, Babar Zeb, Aimal Khan, Younas Khan, "Blood Glucose Level Prediction with Minimal Inputs Using Feedforward Neural Network for Diabetic Type 1 Patients", ACM ISBN 978-1-4503-6600-7/19/02…$15.00 DOI: https://doi.org/10.1145/3318299.3318354.

[13] Taiyu Zhu, Kezhi Li, Pau Herrero, Jianwei Chen, Pantelis Georgiou, "A Deep Learning Algorithm For Personalized Blood Glucose Prediction", submitted to the Blood Glucose Level Prediction Challenge, the 27th International Joint Conference on Artificial Intelligence and the 23rd European Conference on Artificial Intelligence (IJCAI-ECAI 2018), International Workshop on Knowledge Discovery in Healthcare Data.

[14] Zhu T, Li K, Chen J, Herrero P, Georgiou P. Dilated Recurrent Neural Networks for Glucose Forecasting in Type 1 Diabetes. J Healthc Inform Res. 2020 Apr 12;4(3):308-324. doi: 10.1007/s41666-020-00068-2. PMID: 35415447; PMCID: PMC8982716.