CZU: 616.379-008.64:004.032.26 **https://doi.org/10.59295/sum6(176)2024_20**

DEVELOPMENT OF A NEURAL NETWORK MODEL ARCHITECTURE FOR PERSONALIZED INSULIN DOSAGE CALCULATION IN TYPE I DIABETES

Ghenadie USIC, Aurelia PROFIR,
Moldova State University

Type I diabetes is a chronic autoimmune disease characterized by insulin hormone deficiency in the body, requiring patients to rely on external administration of this hormone for survival. Additionally, blood glucose monitoring and precise insulin dose calculation are essential aspects in managing this disease. The current research proposes an approach that uses machine learning techniques to optimize and personalize insulin dose calculations for patients with type I diabetes. The developed model is based on neural networks and has been trained using pharmacodynamic profiles and a simulated dataset. The research was conducted over a period of two months, focusing on adapting the algorithm to individual patient characteristics to improve blood glucose level management.
Keywords: *artificial neural network, machine learning, type 1 diabetes management, predictive model, glycemic control, insulin dosage, real-time analysi.*

DEZVOLTAREA UNEI ARHITECTURI DE MODEL BAZAT PE REȚELE NEURONALE PENTRU CALCULUL PERSONALIZAT AL DOZELOR DE INSULINĂ ÎN DIABETUL ZAHARAT DE TIP I

Diabetul zaharat de tip I este o boală cronică autoimună, caracterizat*ă* prin deficienţa hormonului insulin in organism, astfel că pacienții au nevoie de administrare externă a acestui hormon pentru a supraviețui. Totodată, monitorizarea nivelului glicemiei și calcularea precisă a dozelor de insulină sunt aspecte esențiale *în* gestionarea acestei boli. Cercetarea actuală propune o abordare, care folosește tehnici de învățare automatizată pentru a optimiza și personaliza calculul dozelor de insulinâ la pacienți cu diabet zaharat tip I. Modelul elaborat se bazează pe rețele neuronale și a fost instruit utilizând profilurile farmacodinamice și un set de date simulate. Cercetarea s-a desfăşurat pe o perioadă de două luni, urmărind adaptarea algoritmului la caracteristicile individuale ale pacienților pentru *îmbunătățirea* gestionării nivelului glicemiei.
Cuvinte-cheie: *rețea neuronală artificială, învățare automată, management diabet tip 1, model predictive, control glicemic, dozare insulină, analiză timp-real.*

Introduction

Management of diabetes type I requires individuals to follow a strict daily regimen involving careful monitoring of multiple factors such as dietary intake, physical activity, and medication administration to achieve optimal blood sugar control. Recent studies have emphasized the importance of rigorous glucose level management in preventing or reducing the progression of diabetes-associated complications [1].

Accurate determination of insulin doses is a detailed and complex process. Previous studies have identified several essential factors that must be considered in this complex evaluation: blood sugar levels before main daily meals, carbohydrate intake estimation, individual insulin sensitivity, and the insulin-to-carbohydrate ratio [2]. These elements generate an intricate decision matrix that patients must manage multiple times throughout the day.

Clinical studies highlight significant problems encountered in the manual calculation of insulin doses by patients with Type I diabetes. One study found that approximately 63% of patients with Type I diabetes made errors in calculating their manually determined insulin doses [4]. Subsequent research has shown that the introduction of automatic insulin dose calculators has led to a significant decrease in both hypoglycemic and hyperglycemic episodes [5]. Additionally, patient satisfaction studies have shown that people clearly prefer automated calculation methods over traditional manual approaches [6].

Unfortunately, current insulin dose calculation systems rely primarily on generic mathematical models that are not personalized to individual patient characteristics. While limited research has been conducted regarding the development of automatic insulin dose calculators [5, 7], there remains a significant gap in personalized approaches.

This research attempts to overcome this limitation by proposing a model that calculates insulin doses using advanced machine learning techniques, specifically artificial neural networks. The main goal is to develop a personalized insulin dose calculator that adjusts to individual patient characteristics, thereby improving glycemic control.

Methods and materials

The standard formulas of calculating insulin dosages

According to DAFNE, the insulin in patients with T1D is administrated, as follows [5]: „Most people need approximately 0.5 to 0.8 units of insulin per kilogram (Kg) of body weight each day. Roughly, half of this daily dose is taken as long acting (background insulin) and this is usually divided into two injections. The remainder of the total daily dose is taken at meal times, matched to carbohydrate. This needs use of quick acting (QA) insulin.”

Calculations of insulin doses for meals are dependent on the insulin-carbs ratio, it shows how much QA insulin is needed to cover one Carbohydrate Portion (1 CP = 10g). According to DAFNE, „1 CP is covered by 1 – 3 units of QA at breakfast and 1 – 2 units of QA insulin at other meals”. The QA bolus for meals is typically calculated from:

$QA\ bolus = Correction + Carbs\ coverage$

The correction dosage specifies the amount of insulin to correct a blood glucose level above the patient's target range, it depends on each patient's insulin sensitivity factor (ISF), it can be found out by a special medical test. The correction dosage is calculated as following:

$Correction = (C_{BG} - T_{BG}) / ISR$

Where is current blood glucose amount and is the target blood glucose amount after the meal intake.

Adjustment of the standard formulas

Several studies, specifically, the methods of Scheiner [8] and Pettus and Edelman [9] have proposed to correct the insulin amount computed in (1) as:

$B = (CHO / CR) + ((G_c + f(\cdot)) - G_T) / CF) - IOB$

Where:

1. B [U] is the recommended dose of insulin
2. CHO [g] is the estimated amount of carbohydrate intake
3. CR is the insulin-to-carbohydrate ratio [g/U]
4. CF is the correction factor [mg/dL/U]
5. G_c [mg/dL] is the measured BG level
6. G_T [mg/dL] is the target BG concentration
7. $f(\cdot)$ is a deterministic function, with a -100 mg/dL to 100 mg/dL range
8. IOB [U] is the insulin-on-board, i.e. an estimate of the amount of insulin previously injected in the body not assimilated by the organism yet

Personalizing bolus insulin calculations using ANNs

In this study a model of 2 ANNs modules is proposed to personalize IOB and $f(\cdot)$ values, the general outline is shown in Fig. 1.

Fig. 1. Outline of the IOB and Optimal Bolus Insulin ANNs Structure of the Insulin-on-board (IOB) Neural Network.

The Insulin-on-board (IOB) NN structure has been adopted from [5] and follows a feed-forward multi-perceptron neural network architecture that consists of:

- An input layer of 1 neuron, which represent last QA insulin injection time.
- A hidden layer of 8 neurons each with hyperbolic tangent activation functions:

tanh = $(e^{2x} - 1) / (e^{2x} + 1)$

- An output layer of one neuron which uses a sigmoid activation function:

$S(x) = 1 / (1 + e^{x-1})$

The network output result represents the amount of free IOB.

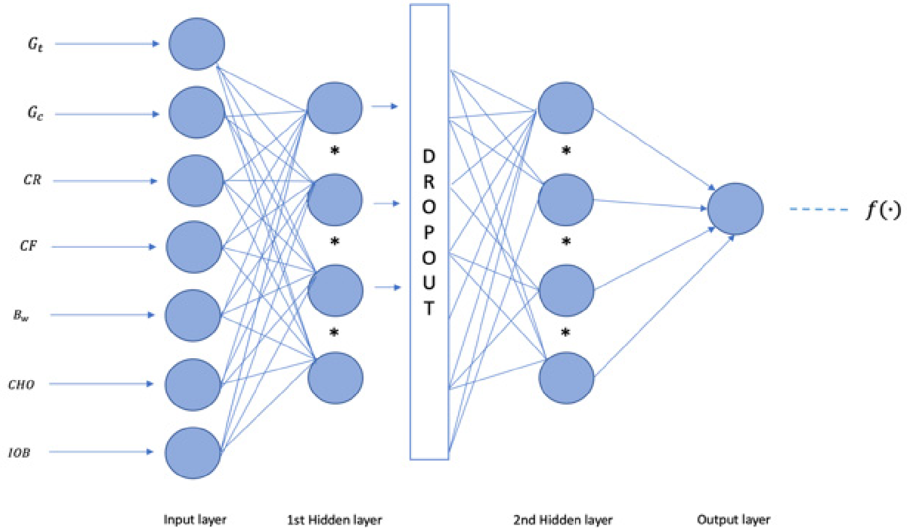
Created ANN was pre-trained using pharmacodynamics profiles adapted from [10]. The Levenberg-Marquardt algorithm [11] that combines the benefits of both the gradient descent algorithm and the Gauss-Newton method was used to train the ANN. The profile data was distributed as following: training data (70%), validation (15%), test (15%).

Structure of the Optimal Bolus Insulin Neural Network

The Optimal Bolus Insulin neural network structure, presented in Fig. 2, has been adopted from [12] and follows a feed-forward fully-connected neural network architecture. It consists of two hidden layers with 200 neurons each and one dropout layer between each hidden layer to prevent overfitting and improve generalization efficiency.

The NN inputs are 7 characteristics: IOB, generated by the Insulin-on-board NN, patient's pre-status G_c, patient's therapy parameters: *CR, CF*, and G_T, body weight B_w and the carbohydrates intake *CHO*.

Fig. 2. Structure of the proposed neural network



The optimal insulin bolus amount $f(\cdot)$ calculation methodology has been taken from [13] and obtained by first symmetrizing the glucose scale as:

$f(BG) = 1.509[log(BG)^{1.084} - 5.381]$

Where is the blood glucose measurement and then calculating it's value as:

$f(\cdot) = \sum_{k=1}^{N} f(BG_k)^2$

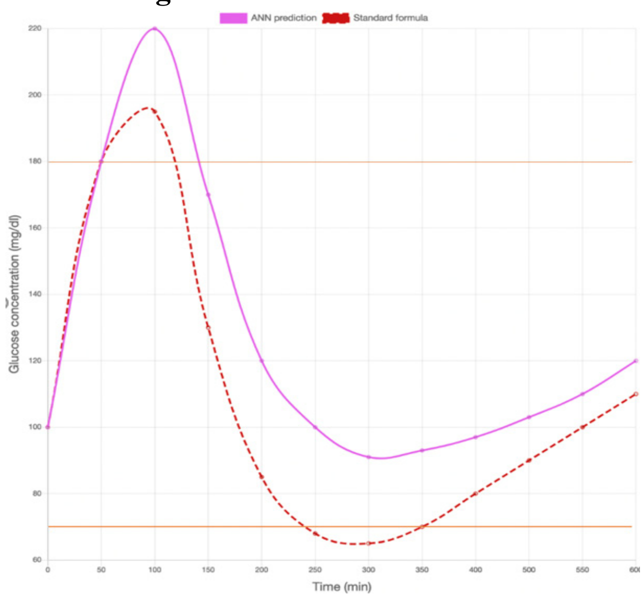
The virtual dataset for the NN consisted of 200 virtual items generated using the UVa/Padova T1D Simulator [13]. Training was performed through the RMSprop training algorithm. The profile data was distributed as following: training data (70%), validation (15%), test (15%).

Obtained results and discussions

Fig. 3 shows blood glucose concentrations obtained using standard formula calculations and those predicted by the ANN module for a patient with G_c = 100 mg/dL and a meal intake *CHO* of 70 g.

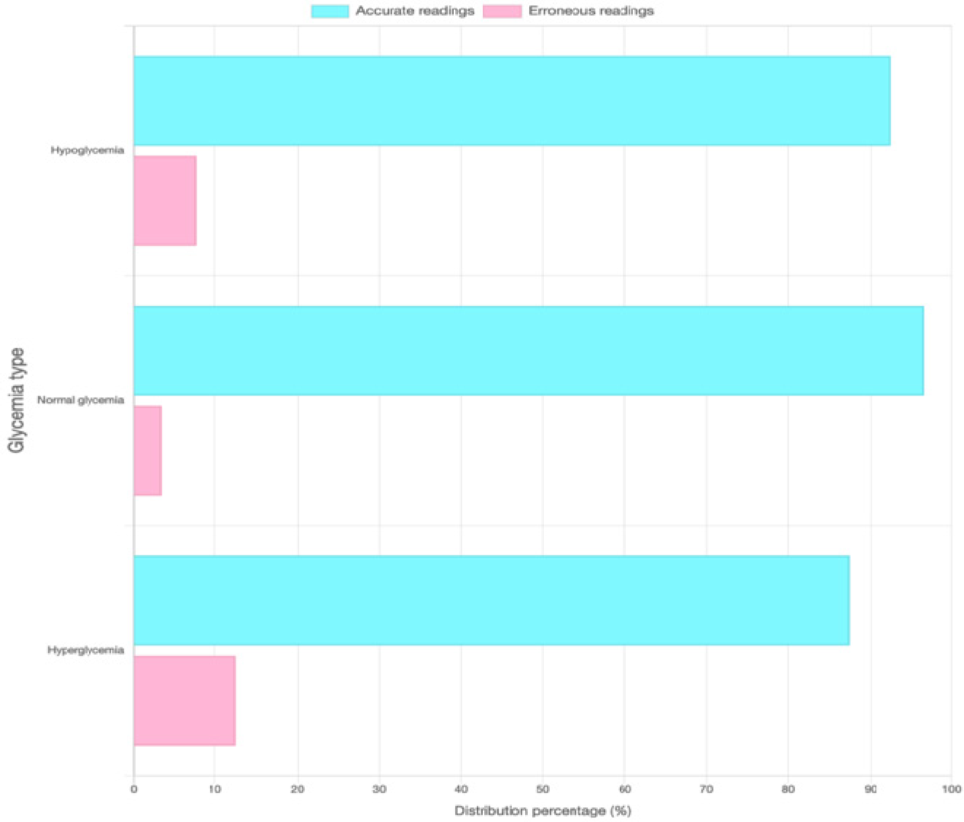
The obtained prediction results are pretty close to the standard formula calculations, besides that ANN predictions helped to avoid hypoglycemia, keeping blood glucose level higher than 70 mg/dL.

Fig. 3. Example of ANN predictions vs Standard formula calculations for a patient with G_c = 100 mg/dL and a meal intake *CHO* of 70 g.



The error distribution grid is presented in Fig. 4.

Fig. 4. Continuous error distribution by glycemia types.



Conclusions

This study represents an attempt to use machine learning techniques to personalize and optimize the insulin dosage calculations for patients with T1D. In particularity a model of two ANNs to predict optimal bolus insulin dosages using patient's pre-prandial data, therapy parameters and physical characteristics has been presented. Created ANNs were trained using pharmacodynamics profiles and a virtual dataset. The study lasted for 2 months. Obtained results have shown that the use of the proposed modeling technique can help to decrease risks of hypoglycemia and to possibly reduce insulin administration excesses. The created ANN is planned to be tested using simulator of Vettoretti et al. [14], besides that, to get better results, this study requires bigger training datasets and a longer period of trial testing.

References:

1. INTERNATIONAL DIABETES FEDERATION, International Diabetes Federation, *IDF Diabetes Atlas*, 9th Edition, 2019, p. 111, ISBN: 978-2-930229-87-4.
2. C. G. PARKIN and J. A. DAVIDSON, *Value of Self-Monitoring Blood Glucose Pattern Analysis in Improving Diabetes Outcomes, J. Diabetes Science and Technology,* vol. 3(3), 2009, p. 500-508.
3. J. D. SORKIN, D. C. MULLER, J. L. FLEG and R. ANDRES, *„The Relation of Fasting and 2-h Post Challenge Plasma Glucose Concentrations to Mortality: Data from the Baltimore Longitudinal Study of Aging with a Critical Review of the Literature," J. Diabetes Care*, vol. 28(11), 2005, p. 2626-2632.
4. A. SUSSMAN, E. J. TAYLOR, M. PATEL, J. WARD, S. ALVA, A. LAWRENCE et al., *Performance of a Glucose Meter with a Built-in Automated Bolus Calculator versus Manual Bolus Calculation in Insulin - Using Subjects, J. Diabetes Science and Technology*, vol. 6(2), 2012, p. 339-344.
5. AL-TAEE, M. A., AL-NUAIMY, W., MUHSIN, Z. J. et al., *Smart Bolus Estimation Taking into Account the Amount of Insulin on Board*, IEEE International Conference on Computer and Information Technology, 2015, p. 1051-1056.

6. T. M. GROSS, D. KAYNE, A. KING, C. ROTHER, S. JUTH, *A Bolus Calculator is an Effective Means of Controlling Postprandial Glycemia in Patients on Insulin Pump Therapy, J. Diabetes Technology and Therapeutics*, vol. 5(3), 2003, p. 365-369.
7. TILMAN UTZ, MATTHIAS BRAUN, KNUT GRAICHEN, GUIDO FRECKMANN, *Model of the glucose-insulin system of type-1 diabetics and optimization-based bolus calculation*, UKACC International Conference on Control, 2014, p. 579-584.
8. G. SCHEINER, *Practical CGM: improving patient outcomes through continuous glucose monitoring*, American Diabetes Association, 2015. ISBN: 1580406033.
9. J. PETTUS, S.V. EDELMAN, *Recommendations for using real-time continuous glucose monitoring (rtCGM) data for insulin adjustments in type 1 diabetes, J. Diabetes Sci. Technol*., vol. 11, 2017, p. 138-147.
10. P. D. HOME, *The Pharmacokinetics and Pharmacodynamics of Rapid-Acting Insulin Analogues and Their Clinical Consequences, J. Diabetes, Obesity and Metabolism,* vol. 14(9), 2012, pp. 780-788.
11. R. MATIGNON, *Neural Network Modeling Using SAS Enterprise Miner,* AuthorHouse, 2005. ISBN: 978-1418423414.
12. GIACOMO CAPPON et al., *Optimal Insulin Bolus Dosing in Type 1 Diabetes Management: Neural Network Approach Exploiting CGM Sensor Information*, 40th International Conference of IEEE Engineering in Medicine and Biology Society, 2018, p. 340-343.
13. C. DALLA MAN et al., *The UVa/Padova type 1 diabetes simulator: new features, J. Diabetes Sci. Technol.,* vol. 8, 2014, p. 26-34.
14. M. VETTORETTI et al., *Type 1 diabetes patient decision simulator for in silico testing safety and effectiveness of insulin treatments*, IEEE Transactions on Biomedical Engineering, 2017, p. 1-11.

Date about authors:
Ghenadie USIC**,** PhD student, Moldova State University.
ORCID: 0009-0003-8423-0443
E-mail: ghenvl@gmail.com

Aurelia PROFIR, Moldova State University.
ORCID: 0009-0003-7535-8816
E-mail: aureliaprofir@yahoo.com

Presented on 30.09.2024