

ISSN 2063-5346



# INSULIN INFUSION SYSTEM (IIS) FOR TYPE 1 DIABETES PATIENTS DURING POST OPERATION CONDITION USING PID CONTROLLER WITH NEURAL NETWORK TECHNOLOGY

K.SaravanaKumar<sup>1</sup>, Dr.J.Samson Isaac<sup>2</sup>, J.Dhanaselvam<sup>3</sup>, I.U.Perarasi Muthra<sup>4</sup>,  
P.D.Sanchana Sri<sup>5</sup>, D.Vaishnavi Vritika<sup>6</sup>, S.Venkata Prasanna<sup>7</sup>

---

**Article History:** Received: 01.02.2023

Revised: 07.03.2023

Accepted: 10.04.2023

---

## Abstract

Diabetes mellitus is a condition marked by unusually high blood glucose levels brought on by a lack of insulin. For patients with diabetes mellitus, the use of a continuous glucose monitor, insulin pump, and control algorithm offers an alternative to patient self-management of insulin doses. Automated closed-loop IIS has been studied for a very long time. In closed-loop systems, the control algorithm serves as the main mechanism for precise insulin administration. The primary objective of this project work is to control the blood glucose level of type 1 diabetic patient using a blood glucose level sensor and PID controller based on ANN Technology. The capacity to track a set point (70 mg/dL) from the beginning condition of hyperglycemias as well as in reaction to a meal disruption is suggested based on the result analysis.

**Keywords:** Diabetes, Type 1 Diabetes, Post Operative Management, PID Controller, Artificial Neural Network (ANN).

---

<sup>1,3,4,5,6,7</sup>Department of Instrumentation and Control Engineering, Sri Krishna College of Technology, Coimbatore.

<sup>2</sup>Department of Biomedical Instrumentation Engineering, Karunya Institute of Technology, Coimbatore.

<sup>1</sup>[saravanakumar.k@skct.edu.in](mailto:saravanakumar.k@skct.edu.in) <sup>2</sup>[samsonisaac@karunya.edu](mailto:samsonisaac@karunya.edu) <sup>3</sup>[dhanaselvam.j@skct.edu.in](mailto:dhanaselvam.j@skct.edu.in)

<sup>4</sup>[19tuic021@skct.edu.in](mailto:19tuic021@skct.edu.in)

<sup>5</sup>[19tuic023@skct.edu.in](mailto:19tuic023@skct.edu.in)

<sup>6</sup>[19tuic032@skct.edu.in](mailto:19tuic032@skct.edu.in)

<sup>7</sup>[19tuic033@skct.edu.in](mailto:19tuic033@skct.edu.in)

DOI: 10.31838/ecb/2023.12.s1.063

## 1. INTRODUCTION

Diabetes is an endocrine metabolic disorder that is deadly. Numerous serious diabetes-related side effects, including peripheral neuropathy, nephropathy, peripheral neuropathy, blindness and retinopathy, have an impact on millions of individuals worldwide [1]. In 2014, the International Diabetes Federation predicted that 387 million people worldwide had diabetes, and that number will rise to 592 million by the year 2035 [2]. Thus, it is essential for diabetics to maintain normal blood glucose levels.

### 1.1 T1D mellitus (Type 1 Diabetes)

T1D, an autoimmune disease, results in the pancreatic islets producing no insulin or little. The anabolic polypeptide hormone insulin controls how much blood sugar is in circulation and how carbohydrates are metabolized. T1D is typically seen among members of the family with a record of such disorder, despite the fact that its cause is unknown [26]. The World Health Organization (WHO) has established various diagnostic criteria that may be used to determine if a person has T1D [27]. To maintain blood sugar levels, patients with this type of diabetes require external insulin therapy, often in the form of subcutaneous injections. The four kinds of injectable acting insulin are short, rapid, long, and intermediate. Traditionally, a doctor will decide how much insulin to give a patient depending on the patient's characteristics and medical history.

The inability of the pancreatic beta cell to release insulin is the primary cause of T1D. Their blood sugar levels are managed by exogenous insulin. A continuous subcutaneous insulin infusion (CSII) or an insulin pump is being used to control type 1 diabetes in patients [3]. Due to the growing degree of dietary and physical activity, convenience, and accuracy flexibility, the CSII showed real benefits than the MDI approach [4]. There are several open-loop insulin pumps available that can be set up to provide the correct amount of insulin. It can provide patients with the appropriate quantities of insulin without using a human [5]. The closed-loop system is composed primarily of three components: an intelligent controller, an insulin pump, and continuous glucose monitoring (CGM).

### 1.2 Post-Operative Management

Reviewing the intra-operative hyperglycemia treatment in the post-anesthesia care unit (PACU) is crucial, as is maintaining strict glucose control with either intravenous or subcutaneous insulin.

### A. Ambulatory

Patients who underwent ambulatory surgery and were stable and able to tolerate oral intake after their recovery in the PACU might be sent home with the same anti-hyperglycemic medication.

### B. Non-critically Ill

Subcutaneous (SC) insulin is administered to non-critically unwell patients who need to be admitted from the PACU to the surgical/medical ward. Basal with correctional insulin is preferable when oral intake is inadequate or absent.

### C. Critically Ill

A medical or surgical intensive care unit should manage critically ill patients with continuous insulin infusion (CII), with regular insulin and blood sugar testing every one to two hours, under institutional procedure.

The bolus insulin doses for open-loop insulin pumps, which can help diabetics manage their postprandial blood glucose levels, are calculated using a bolus calculator. It includes a variety of elements, such as the correction factor (CF), insulin sensitivity, carbohydrate ratio (I: C), current blood glucose, goal blood glucose, and the number of consumed carbs [4]. In the control algorithm, high degrees of reliability and robustness are required. A few examples of various control systems are PID control [6], sliding mode control, optimal control [9], model predictive control (MPC) [7, 8], and adaptive control [10] [11]. The PID controller is one of the control algorithms that is frequently utilized in industrial control systems. Because of its advantages of simple implementation, significant adaptability, resilience, and a basic structure with few parameters, the PID controller is appealing for controlling blood sugar levels.

## 2. RELATED WORK

For AP systems on commercially accessible devices, contemporary PID and MPC-based control algorithms have been created [6, 11, 12, 14, 15]. The hybrid closed-loop systems that PID and MPC controllers frequently operate call for notifications of the number of carbohydrates in meals and the level of exercise [7]. The Metronics 770G and 670G with PID and Tandem Control-IQ with MPC are two profitable, FDA-approved systems [6]. The majority of commercial PID and MPC solutions employ Predictive Low Glucose Suspend (PLGS) to prevent hypoglycemia overnight [37]. Before hypoglycemia sets in, the PLGS technology predicts changes in

glucose concentration and cuts off insulin delivery. Although a PID controller is straightforward, it has trouble adjusting to food control [6, 7].

A recent study specifically addresses T1DM regulation and covers the majority of the methods applied thus far [5]. This work almost entirely reveals the specification of the action and state space, class of employed RL algorithms, and successful learning experience elements, also referred to as the strategies and the diversity of options used in them. While glucose models are simplified in both situations, strong solutions are shown. In contrast, the simulator we utilize in this research is more realistic and typically calls for DRL to simulate the value function.

In two recent articles [7, 20], Fox et al. take a similar stance as in this study. The value function was approximated using three straightforward DNN architectures, although the gains over the PID baseline were barely perceptible. The SAC approach is used in their second research [7]. When action phase is persistent as well as the state vector also includes the most recent CGM and insulin data from the previous four hours. Furthermore, each situation has different incentive mechanisms. In contrast, we only use the most recent CGM data in this study, employ a relatively lengthy delay between observations and actions (between 30 and 60 minutes), and create a simplified reward function. Yamagata et al. [13] describe a hybrid model-based strategy that combines a distinct action space with a meal announcement. The controller uses a PID-controlled DRL SAC agent as a starting policy, and it also extends the observation state using predictions from a dual attention network. Lin et al [21] 's most recent recommendation for this set of machine learning tactics for managing BGs. Controlling the behaviors is also a safe and adaptive exercise. In the Discussion section, the outcomes of last three strategies [7, 13, 21] mentioned above are contrasted with our own.

Several studies have examined the use of PID controllers with ANNs in insulin infusion systems for type I diabetes patients during post-operation conditions. One such study, published in the Journal of Medical Systems in 2019, developed a PID-ANN controller that could adjust the insulin infusion rate based on the patient's blood glucose level and predicted future blood glucose levels. The study found that the proposed controller was effective in regulating blood glucose levels during post-operation.

### 3. SYSTEM METHODOLOGY

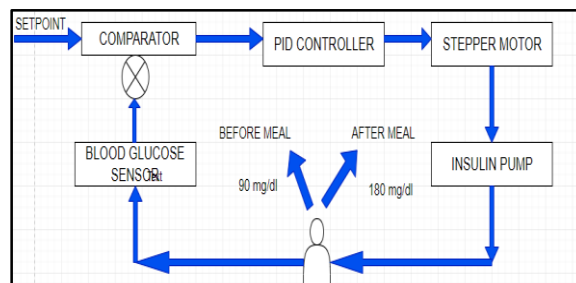


Figure 1 Block Diagram

#### 3.1 Blood Glucose Sensors

One of the simplest and widely popular methods of checking your blood sugar levels is by using a blood glucose meter. The devices employ enzyme-coated test strips, that can only respond through one blood specimen. This test strip production uses a certain enzyme concentration. Since test strips are intended to be utilized once, they cannot be reused. The test strip is attached to the blood glucose meter after being injected and collecting a blood sample. After computing the blood glucose level, the meter shows the results on the screen. Test strips and blood glucose meters are frequently less expensive than equipment for continuous glucose monitoring. Since meters don't have to be worn on the human body, they also allow for more discreet and irregular testing.

#### 3.2 Insulin Pumps

Insulin pump users with diabetes can easily manage their blood sugar levels. At specified times, these small devices provide insulin amounts. Many patients consider insulin pumps to be a more adaptable substitute for insulin pen injections. You can switch to a different insulin-control method at any time. so insulin pumps don't have to be a lifelong commitment. A tiny technological device known as an insulin pump. It disperses insulin through a tiny tube that is put under your skin. They resemble little mobile phones because they are so small. Medication dosages are delivered by insulin pumps in accordance with a set schedule. Your hormone insulin regulates your blood sugar levels.

#### 3.3 Stepper motor

Step motor and stepping motor are other names for a stepper motor. The motor shaft's ability to revolve in steps or by a predefined amount of degrees is the fundamental property of an electric motor known as a stepper motor. This feature, which is made feasible by the internal structure of the motor, allows for the simple counting of steps to determine the exact angular position of the shaft.

### 3.4 Design of PID Controller with ANN

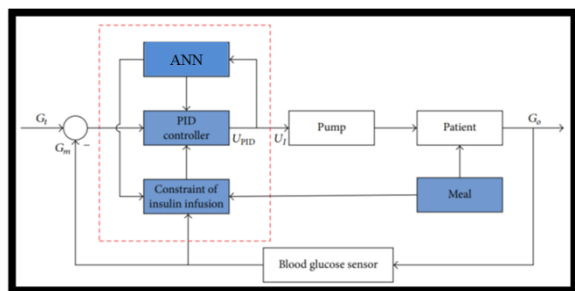


Figure 2 Architecture for the improved PID controller with ANN

#### 3.4.1 PID Controller

Figure 2 demonstrates the PID controller's structure using an ANN approximation, where  $G_o$  stands for the actual blood glucose level of the diabetic patient,  $G_t$  stands for the goal blood glucose level,  $G_m$  for the blood glucose level as determined by a glucose sensor, and  $U_I$  for the maximum IIS rate. The control law  $U_{PID}$  is as follows:

$$U_{PID} = U_0 + k_c [(G_m - G_t) + I \int_0^t (G_m - G_t) dt + \tau_D \frac{d(G_m - G_t)}{dt}] \quad (1)$$

where  $U_{PID}$  is the output of the closed-loop control. The difference between the goal blood glucose and the actual blood glucose is quantified as  $G_m - G_t$ . The rate of basal insulin infusion is  $U_0$ . The three variables that may be changed are:  $K_c$  referred as proportional gain,  $I$  defines integral time, and  $D$  refers derivative. Utilizing the requirement output of insulin infusion and the ANN, the control output of insulin infusion rate  $U_I$  is produced. The internal workings of the control algorithm are shown in Figure 3. The controller's result is

$$U_I = K U_{PID} \quad (2)$$

When the value is set to 0  $k=1$ , the gain  $k$  is achieved as the average value of, and the upper constraint output of the PID controller is taken into consideration in this research. The top constraint has been determined using the ANN with evaluation, correction factor, and  $I:C$  ratio. The highest restriction is there to prevent excessive insulin infusion. What to do is determined by the ensuing circumstance.

$$\text{If } I_{CHO} + I_G > I_{OB}, \quad (3)$$

$$U_{max} = I_{CHO} + I_G - I_{OB}, \quad (4)$$

$$\text{Else } U_{max} = I_{CHO} \quad (5)$$

where  $I_{CHO}$  is the amount of insulin necessitated to make for a specific meal and  $U_{max}$  seems to be the highest constraint output of the IIS rate.

$$I_{CHO} = D \cdot (I:C) \quad (6)$$

where  $D$  refers the meal's weight and  $I:C$  is the ratio of the quantity of  $CHO$  that one unit of insulin can eat.  $I_G$ , which is defined by the following circumstance, is the quantity of insulin required to compensate for a rise over the desired blood sugar level:

$$\text{If } G_m - G_t > 0 \quad (7)$$

$$I_G = (G_m - G_t) \cdot CF, \quad (8)$$

$$\text{Else } I_G = 0, \quad (9)$$

where the matching measured and desired blood glucose levels are denoted by the letters  $G_m$  and  $G_t$ . The correction factor is  $CF$ .

#### 3.4.2 Artificial Neural Network (ANN)

Artificial neural networks are used for data-driven learning since it was found that human brains are highly good at digesting vast amounts of incoming data from many sources. When the output does not match the predicted one, neural networks use back propagation, which pushes the networks to modify their unseen neuron layers. Before it can comprehend the process, the input layer of a multi-layer network must choose unique features. ANN models find relationships and use those correlations to create rules by examining a large number of input and output examples. An artificial neural network with three layers of feed-forward computation is used in the study being reported. It has eight nodes in the first layer of the input layer, three hidden nodes ( $h_1$ ,  $h_2$ , and  $h_3$ ) in the hidden layer, one output node ( $O_i$ ) in the output layer. The input layer uses the following 8 inputs: area ratio, irregularity index ( $I$ ) ( $AR$ ),  $L$  length of the vector, angle  $\alpha$ , angle  $\beta$ ,  $R_{red}$  (relative chromaticity in red),  $R_{green}$  (relative chromaticity in green), and  $R_{blue}$  (relative chromaticity in blue) will all be used to determine if a diabetic is present ('1' or '0'). Back-propagation is used to train the network.

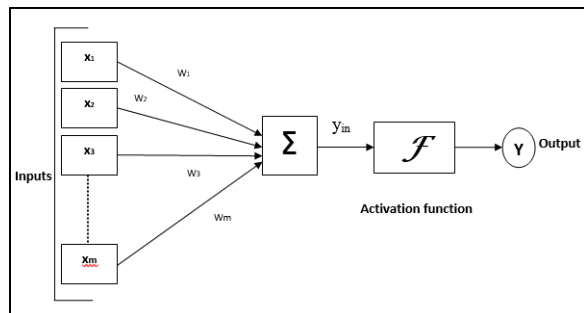


Figure 3 Three layered feed forward neural network architecture

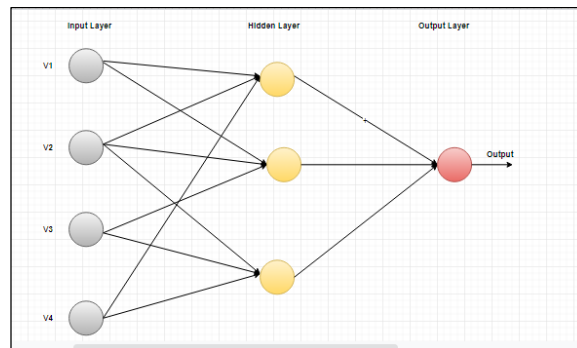


Figure 4 Structure of Feed Forward Neural Network

#### 4. EXPERIMENTAL RESULTS

The success of glucose management for a virtual individual is summarized using Feed Forward Neural Network Algorithm, which evaluates the advised control method. A feed-forward neural network (FFNN), also known as a multilayer perceptron (MLP), is a type of artificial neural network in which information flows only in the forward direction, from the input layer through the hidden layers to the output layer. The network consists of an input layer, one or more hidden layers, and an output layer. Each layer is composed of a set of neurons, which perform a weighted sum of their inputs, followed by the application of an activation function. The activation function introduces non-linearity into the network, allowing it to model complex relationships between inputs and outputs.

To train the FFNN, a set of input-output pairs is used to adjust the weights of the connections between neurons. This is done by forward propagating the input through the network to obtain an output, comparing the output to the desired output, and then back propagating the error through the network to adjust the weights using a gradient descent algorithm. The process of forward propagation followed by back propagation is repeated for multiple epochs until the network converges to a satisfactory level of performance.

The FFNN can be used for a wide range of tasks, including classification, regression, and prediction. It has been applied to a variety of domains, such as image recognition, speech recognition, natural language processing, and finance. The architecture of the network, the activation function used, and the optimization algorithm employed are some of the hyper parameters that can be tuned to achieve better performance. In this paper we are using FFNN to provide accurate results of Blood glucose level monitoring and controlling.

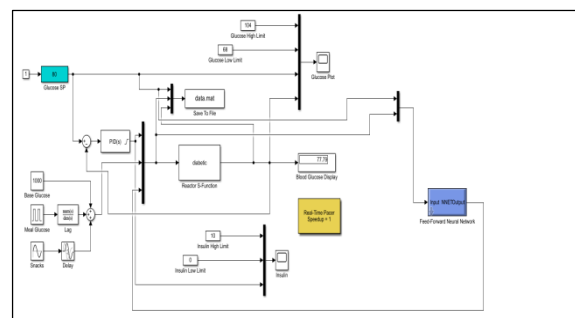


Figure 5 Simulation Design for Type 1 Diabetes with Artificial Neural Networks

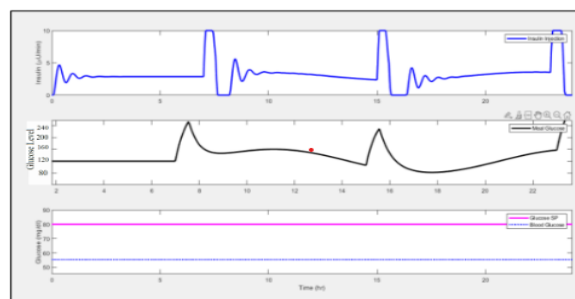


Figure 6 Simulation results for blood glucose level and insulin infusion level

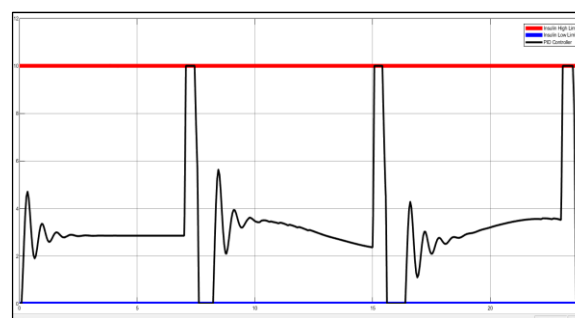


Fig 7: Insulin variation using PID Controller Graph



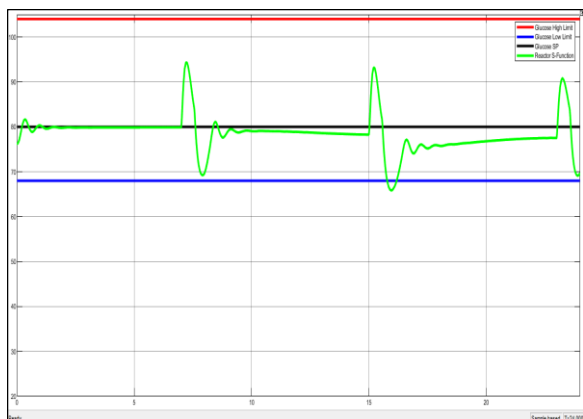


Fig 8: Glucose level plot

Set Point (mg/dl)	BGL Low Limit (mg/dl)	BGL High Limit (mg/dl)	Insulin Infusion (Units)
120 mg/dl	80 mg/dl	240 mg/dl	0-10 Units

Table 1: Reference Values in data.mat

The results demonstrate the effectiveness and dependability of the PID controller with ANN. More precisely than the conventional PID controller, blood glucose may be controlled.

The simulation design of Feed Forward Neural Network starts from the patient's mealtime (breakfast, lunch, and dinner), the glucose level before the meal and the glucose level after the meal. The set point is basically 80-120 mg/dl. The input is given to the PID controller. PID controller analyses the blood glucose level after meal and sends it to the feed forward control neural network and the insulin infusion pump to infuse the required quantity of insulin. The data is collected, and the plot is shown in Figure 7, the increases and normalization of blood

glucose levels are plotted. And the blood glucose display is implemented to display blood glucose levels after the infusion of insulin. The insulin level is basically set between 1-10. If it goes beyond 10, it may lead to severe health problem.

Patient's Name & Age	Time (App)	Before Meal	After Meal	Insulin
Sharanya 45	7:15 AM	90.56 mg/dl	187.2 mg/dl	7.2 Units
	1:30 PM	126.7 mg/dl	165.6 mg/dl	6.8 Units
	8:00 PM	117.86 mg/dl	195 mg/dl	7.1 Units
Ayyappan 62	7:30 AM	100.8 mg/dl	190.2 mg/dl	9.4 Units
	1:00 PM	86 mg/dl	147.1 mg/dl	8.8 Units
	7:55 PM	138.7 mg/dl	176 mg/dl	9.09 Units

Table 2: Type 1 Diabetes Patient's data and units of insulin required to normalize their BGL after meal (consultation from clinic)

## 5. CONCLUSIONS

Based on all the results discussed, it is found that in order to retrieve a satisfactory glucose regulation through the Proportional-Integrated-Derivative (PID) control, the parameter settings towards closed loops responses of a short rise time, steady-state error elimination and, overshoot and setting time decrement are required. The performance of PID controller which controls the optimum tuning response to maintain the blood glucose level of Type-1 Diabetic Mellitus (T1DM) Patient. And the implementation of Feed Forward Neural Network gives us more accuracy, easy to use, rapid results and parallel processing Therefore the blood of the patient can be monitored and controlled.

## References

- [1] J. Li, Y. Kuang, and C. C. Mason, "Modeling the glucose-insulin regulatory system and ultradian insulin secretory oscillations with two explicit time delays," *Journal of Theoretical Biology*, vol. 242, no. 3, pp. 722–735, 2006.
- [2] G. Marchetti, M. Barolo, L. Jovanovic, H. Zisser, and D. E. Seborg, "An improved PID switching control strategy for type 1 diabetes," *IEEE Transactions on Biomedical Engineering*, vol. 55, no. 3, pp. 857–865, 2008.
- [3] H. Zisser, L. Robinson, W. Bevier et al., "Bolus calculator: a review of four 'smart' insulin pumps," *Diabetes Technology and Therapeutics*, vol. 10, no. 6, pp. 441–444, 2008.
- [4] K. Mythreyi, S. C. Subramanian, and R. Krishna Kumar, "Non-linear glucose-insulin control considering delays-Part II: control algorithm," *Control Engineering Practice*, vol. 28, no. 1, pp. 26–33, 2014.
- [5] E. M. Watson, M. J. Chappell, F. Ducrozet, S. M. Poucher, and J. W. T. Yates, "A new general glucose homeostatic model using a proportional-integral-derivative controller," *Computer Methods and Programs in Biomedicine*, vol. 102, no. 2, pp. 119–129, 2011.
- [6] H. Lee and B. W. Bequette, "A closed-loop artificial pancreas based on model predictive control: human-friendly identification and automatic meal disturbance rejection," *Biomedical Signal Processing and Control*, vol. 4, no. 4, pp. 347–354, 2009.
- [7] L. Magni, D. M. Raimondo, C. Dalla Man, G. De Nicolao, B. Kovatchev, and C. Cobelli, "Model predictive control of glucose concentration in type I diabetic patients: an in silico trial," *Biomedical Signal Processing and Control*, vol. 4, no. 4, pp. 338–346, 2009.
- [8] I. Y. S. Cha'vez, R. Morales-Mene'ndez, and S. O. M. Chapa, "Glucose optimal control system in diabetes treatment," *Applied Mathematics and Computation*, vol. 209, no. 1, pp. 19–30, 2009.
- [9] M. Ottaviano, M. Barolo, H. Zisser, E. Dassau, and D. E. Seborg, "Adaptive blood glucose control for intensive care applications," *Computer Methods and Programs in Biomedicine*, vol. 109, no. 2, pp. 144–156, 2013.
- [10] A. G. Gallardo Hern'andez, L. Fridman, A. Levant et al., "High-order sliding-mode control for blood glucose: practical relative degree approach," *Control Engineering Practice*, vol. 21, no. 5, pp. 747–758, 2013.
- [11] E. Ackerman, L. C. Gatewood, J. W. Rosevear, and G. D. Molnar, "Model studies of blood-glucose regulation," *The Bulletin of Mathematical Biophysics*, vol. 27, no. 1, pp. 21–37, 1965.
- [12] R. N. Bergman, L. S. Phillips, and C. Cobelli, "Physiologic evaluation of factors controlling glucose tolerance in man. Measurement of insulin sensitivity and  $\beta$ -cell glucose sensitivity from the response to intravenous glucose," *Journal of Clinical Investigation*, vol. 68, no. 6, pp. 1456–1467, 1981.
- [13] C. Cobelli and A. Mari, "Validation of mathematical models of complex endocrine-metabolic systems. A case study on a model of glucose regulation," *Medical and Biological Engineering and Computing*, vol. 21, no. 4, pp. 390–399, 1983.
- [14] R. Hovorka, V. Canonico, L. J. Chassin et al., "Nonlinear model predictive control of glucose concentration in subjects with type 1 diabetes," *Physiological Measurement*, vol. 25, no. 4, pp. 905–920, 2004.
- [15] International Diabetes Federation Diabetes Atlas, 9th edition; 2019. Available from: <https://www.diabetesatlas.org>.
- [16] Bequette BW, Cameron F, Buckingham BA, Maahs DM, Lum J. Overnight Hypoglycemia and Hyperglycemia Mitigation for Individuals with Type 1 Diabetes: How Risks Can Be Reduced. *IEEE Control Systems Magazine*. 2018; 38(1):125–134. <https://doi.org/10.1109/MCS.2017.2767119>
- [17] Khodakaramzadeh S, Batmani Y, Meskin N. Automatic blood glucose control for type 1 diabetes: A trade-off between postprandial hyperglycemia and hypoglycemia. *Biomedical Signal Processing and Control*. 2019; 54:101603. <https://doi.org/10.1016/j.bspc.2019.101603>
- [18] Bekiari E, Kitsios K, Thabit H, Tauschmann M, Athanasiadou E, Karagiannis T, et al. Artificial pancreas treatment for outpatients with type 1 diabetes: systematic review and meta-analysis. *BMJ (Clinical research ed)*. 2018. <https://doi.org/10.1136/bmj.k1310> PMID: 29669716
- [19] Tejedor M, Woldaregay AZ, Godtliebsen F. Reinforcement learning application in diabetes blood glucose control: A systematic review. *Artificial Intelligence in Medicine*. 2020; 104:101836. <https://doi.org/10.1016/j.artmed.2020.101836> PMID: 32499004
- [20] Bothe MK, Dickens L, Reichel K, Tellmann A, Ellger B, Westphal M, et al. The use of reinforcement learning algorithms to meet the challenges of an artificial pancreas. *Expert Review of Medical Devices*. 2013; 10(5):661–673. <https://doi.org/10.1586/17434440.2013.827515> PMID: 23972072
- [21] Fox I, Lee J, Pop-Busui R, Wiens J. Deep reinforcement learning for closed-loop blood glucose control. In: *Machine Learning for Healthcare Conference*. PMLR; 2020. p. 508–536.
- [22] Renard E, Place J, Cantwell M, Chevassus H, Palerm CC. Closed-loop insulin delivery using a

- subcutaneous glucose sensor and intraperitoneal insulin delivery: feasibility study testing a new model for the artificial pancreas. *Diabetes care*. 2010; 33(1):121–127. <https://doi.org/10.2337/dc09-1080> PMID: 19846796
- [23] Magni L, Raimondo DM, Bossi L, Man CD, Nicolao GD, Kovatchev B, et al. Model Predictive Control of Type 1 Diabetes: An in Silico Trial. *Journal of Diabetes Science and Technology*. 2007; 1(6):804–812. <https://doi.org/10.1177/193229680700100603> PMID: 198851
- [24] C. Dalla Man, M. Camilleri, and C. Cobelli, “A system model of oral glucose absorption validation on gold standard data,” *IEEE Transactions on Biomedical Engineering*, vol. 53, no. 12, pp. 2472–2478, 2006.
- [25] X. Gao, H. Ning, and Y. Wang, “Systematically in silico comparison of unihormonal and bihormonal artificial pancreas systems,” *Computational and Mathematical Methods in Medicine*, vol. 2013, Article ID 712496, 10 pages, 2013.
- [26] C. Ellingsen, E. Dassau, H. Zisser et al., “Safety constraints in an artificial pancreatic  $\beta$  cell: an implementation of model predictive control with insulin on board,” *Journal of Diabetes Science and Technology*, vol. 3, no. 3, pp. 536–544, 2009.
- [27] F. León-Vargas, F. Garelli, H. De Battista, and J. Vehí, “Postprandial blood glucose control using a hybrid adaptive PD controller with insulin-on-board limitation,” *Biomedical Signal Processing and Control*, vol. 8, no. 6, pp. 724–732, 2013.
- [28] B. P. Kovatchev, W. L. Clarke, M. Breton, K. Brayman, and A. McCall, “Quantifying temporal glucose variability in diabetes via continuous glucose monitoring: mathematical methods and clinical application,” *Diabetes Technology & Therapeutics*, vol. 7, no. 6, pp. 849–862, 2005.
- [29] L. Magni, D. M. Raimondo, C. Dalla Man et al., “Evaluating the efficacy of closed-loop glucose regulation via control-variability grid analysis,” *Journal of Diabetes Science and Technology*, vol. 2, no. 4, pp. 630–635, 2008.
- [30] Yamagata T, Ayobi A, O’Kane A, Katz D, Stawarz K, Marshall P, et al. Model-Based Reinforcement Learning for Type 1 Diabetes Blood Glucose Control. In: *Singular Problems for Healthcare Workshop at ECAI 2020*; Conference date: 29-08-2020 Through 08-09-2020; 2020. p. 1–14.
- [31] Ferdinando MD, Pepe P, Gennaro SD, Palumbo P. Sampled-Data Static Output Feedback Control of the Glucose-Insulin System. *IFAC-PapersOnLine*. 2020; 53(2):3626–3631. <https://doi.org/10.1016/j.ifacol.2020.12.2044>
- [32] Borri A, Pola G, Pepe P, Benedetto MDD, Palumbo P. Symbolic Control Design of an Artificial Pancreas for Type-2 Diabetes. *IEEE Transactions on Control Systems Technology*. 2021; p. 1–16.
- [33] Ngo PD, Wei S, Holubova A, Muzik J, Godtliessen F. Control of Blood Glucose for Type-1 Diabetes by Using Reinforcement Learning with Feedforward Algorithm. *Computational and Mathematical Methods in Medicine*. 2018; 2018:1–8. <https://doi.org/10.1155/2018/4091497> PMID: 30693047
- [34] Robertson G, Lehmann ED, Sandham W, Hamilton D. Blood Glucose Prediction Using Artificial Neural Networks Trained with the AIDA Diabetes Simulator: A Proof-of-Concept Pilot Study. *Journal of Electrical and Computer Engineering*. 2011; 2011:1–11. <https://doi.org/10.1155/2011/681786>