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IMPLEMENTATION OF PID CONTROL STRATEGIES ON BERGMAN MODEL REPRESENTING TYPE 1 DIABETES-T1D

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Abstract. In this work, we address Type 1 diabetes (T1D), a chronic autoimmune condition characterized by elevated glucose levels in patient's bloodstream. We propose a robust approach for regulating blood glucose (BG) levels in individuals with T1D by utilizing a proportional-integral-derivative (PID) control method. The minimal Bergman model is utilized to represent the dynamics of glucose-insulin in the blood plasma. The proposed control strategy integrates the PID controller as a core element for BG regulation. Through simulations, our findings demonstrate the efficacy of the proposed controller in maintaining BG levels close to a target value of 80 mg/dL, starting from a state of hyperglycemia, even amidst various perturbations associated with meal intake.

Keywords: PID-control; type-1 diabetes; blood-glucose regulation; Bergman model.

2020 AMS Subject Classification: 93C10, 92C60.

1. INTRODUCTION

The pancreas plays a pivotal role in regulating macronutrient digestion and, therefore, metabolism and energy homeostasis through the release of various digestive enzymes and pancreatic hormones [1]. Positioned behind the stomach in the left upper abdominal cavity, it is anatomically divided into the head, body, and tail. Predominantly composed of acinar or exocrine

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cells, this secretory organ secretes pancreatic juice laden with digestive enzymes like amylase, pancreatic lipase, and trypsinogen into the ducts, including the main pancreatic and the accessory pancreatic duct. Conversely, pancreatic hormones are discharged in an endocrine manner, directly into the bloodstream. These endocrine cells cluster to form the islets of Langerhans, small, island-like structures within the exocrine pancreatic tissue, representing only 1–2% of the entire organ (see Figure 1). Within these islets, five distinct cell types release various hormones: glucagon-producing α-cells, representing 15–20% of the total islet cells; amylin-, C-peptide-, and insulin-producing β-cells [2], accounting for 65–80%; pancreatic polypeptide (PP)-producing γ-cells [3], comprising 3–5% ; somatostatin-producing δ-cells, constituting 3–10% ; and ghrelin-producing ε-cells [4], which make up less than 1% of the total islet cells. Each hormone has distinct functions: glucagon elevates blood glucose levels, while insulin lowers them [5]. Somatostatin inhibits both glucagon and insulin release [6], whereas PP regulates the exocrine and endocrine secretion activities of the pancreas [7]. Together, these hormones intricately regulate glucose homeostasis in vertebrates. Although the cellular composition is similar among species like humans, rats, and mice, their islet cytoarchitecture varies significantly. Rodent islets are predominantly composed of centrally situated β-cells with other cell types in the periphery, whereas human islets exhibit interconnected α- and β-cells [8].

The pancreas plays a crucial role in maintaining blood glucose levels within the tightly regulated range of $4-6$ mM through the orchestrated actions of various hormones, notably glucagon and insulin. This process is known as glucose homeostasis. During periods of low blood glucose, such as during sleep or between meals, α-cells release glucagon, which triggers hepatic glycogenolysis and stimulates hepatic and renal gluconeogenesis, thereby raising endogenous blood glucose during extended fasting [10]. Conversely, when blood glucose levels rise, particularly after a meal, β-cells are stimulated to secrete insulin [11]. Upon binding to its receptor on muscle and adipose tissue, insulin facilitates the uptake of glucose into these tissues, consequently reducing blood glucose levels by clearing exogenous glucose from the bloodstream (SEE Figure 2) [12]. Additionally, insulin promotes glycogenesis, lipogenesis, and the incorporation of amino acids into proteins, exhibiting its anabolic properties in contrast to the catabolic effects of glucagon [13] - [15].

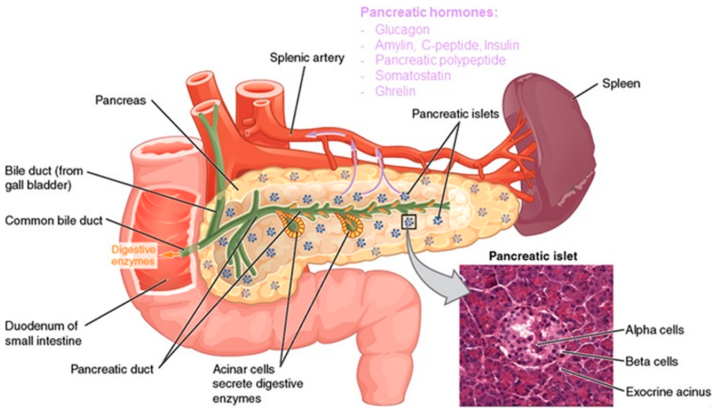

FIGURE 1. Anatomical organization of the pancreas. The exocrine function of the pancreas is mediated by acinar cells that secrete digestive enzymes into the upper small intestine via the pancreatic duct. Its endocrine function involves the secretion of various hormones from different cell types within the pancreatic islets of Langerhans. The micrograph shows the pancreatic islets. Adapted from Human Anatomy and Physiology, an OpenStax College resource [9]

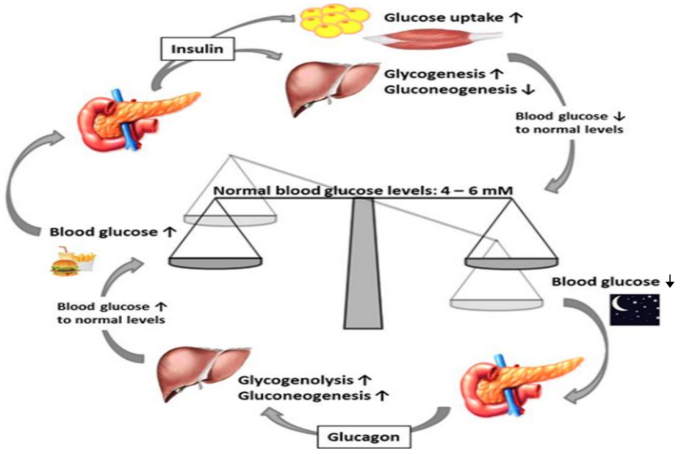

FIGURE 2. Maintenance of blood glucose levels by glucagon and insulin. When blood glucose levels are low, the pancreas secretes glucagon, which increases endogenous blood glucose levels through glycogenolysis. After a meal, when exogenous blood glucose levels are high, insulin is released to trigger glucose uptake into insulin-dependent muscle and adipose tissues as well as to promote glycogenesis [12]

Diabetes, a growing health concern, occurs when the body either fails to produce enough insulin or cannot use it effectively. This disrupts how sugar (glucose) is processed for energy, leading to high blood sugar levels and potential complications. There are two main types: Type 1 and Type 2 [16], [17].

- **Type 1 diabetes**, formerly known as juvenile diabetes, results from the immune system attacking insulin-producing cells. It requires daily insulin injections for management, and its underlying cause remains unclear. By 2021, it was estimated that approximately 1.2 million individuals under the age of 20 were living with type 1 diabetes worldwide.
- **Type 2 diabetes**, the more common form, develops when the body becomes resistant to the effects of insulin. Over time, it can damage nerves and blood vessels. In 2021, 537 million adults worldwide were living with diabetes, which represented 10.5% of the global adult population. Projections indicate that this figure will increase to 643 million (11.3%) by 2030 and 783 million (12.2%) by 2045.

Additionally, diabetes was responsible for around 6.7 million deaths in 2021, with nearly half occurring in individuals under the age of 70. Notably, the mortality rate due to diabetes has seen a significant rise, particularly in countries with lower-middle incomes.

Revolutionary closed-loop systems combine smart insulin pumps with continuous glucose monitors. These systems function like an artificial pancreas, continuously monitoring blood sugar and automatically adjusting insulin levels for optimal control. This approach reduces blood sugar fluctuations, lowers the risk of complications, and improves the quality of life for people with diabetes. Unlike simpler systems, closed-loop systems adapt in real-time, maintaining more stable blood sugar levels even in the face of changing conditions.

The use of closed-loop control in blood glucose prediction models plays a critical role in anticipating and predicting fluctuations in glucose and insulin levels in the body. While devices can measure the current blood glucose levels, utilizing predictions based on these models offers several significant advantages [18]. Firstly, it helps compensate for the inherent delay in direct glucose measurement, which is crucial for making appropriate insulin dosing decisions. Moreover, the ability of these models to anticipate future glucose variations enables a proactive response from the artificial pancreas, preventing significant glucose fluctuations before they

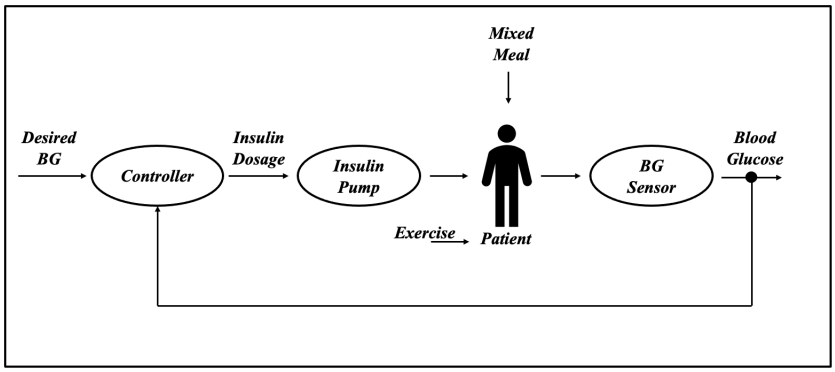

FIGURE 3. Closed loop control for diabetes

even occur. Additionally, these models facilitate insulin dosing optimization by adjusting more precisely based on the system dynamics, contributing to better glycemic control and avoiding both hyperglycemia and hypoglycemia. Finally, these models can be leveraged to anticipate the effects of meals on blood glucose, providing proactive insulin dosing management in response of postprandial glucose increases.

Recent years have seen significant growth and diversification in the literature related to this area. In 2014, N. Tadrisi Parsa, A. R. Vali, and R. Ghasemi [19] identified diabetes as a growing global health issue, with particular emphasis on the need for strict glycemic control in patients with Type 1 diabetes due to their deficiency in insulin production. Their paper proposed a method to regulate blood glucose levels using a mathematical body model, specifically the Bergman minimal model, to develop a nonlinear controller. They introduced a novel backstepping-based sliding mode control (B-SMC) strategy to ensure practical tracking of desired glucose concentrations. In 2016, J. Yadav et al. [20] presented a Fuzzy-PID (FPID) control scheme for managing blood glucose levels in Type 1 diabetic patients. They utilized the metaheuristic Cuckoo Search Algorithm (CSA) to optimize the gains of the FPID controller, which provides fast convergence and efficient handling of global optimization in continuous nonlinear systems. This controller combines fuzzy logic and optimization to efficiently address complex problems such as blood glucose regulation, aiming to maintain normal glucose levels rapidly with minimal insulin doses. The PID and FPID controllers were tuned using Genetic Algorithm and CSA for comparative analysis and were tested on the Bergman minimal model, taking into account parameter uncertainties, meal disturbances, and sensor noise. In 2022, E.

Matamoros-Alcivar et al. [21] highlighted that Type 1 Diabetes Mellitus (T1DM) patients require lifelong insulin replacement. They discussed closed-loop therapies, or artificial pancreas systems, which include a continuous subcutaneous insulin infusion pump, a continuous glucose monitoring sensor, and a control algorithm that automatically adjusts insulin infusion in real time. These systems function similarly to a healthy pancreas, regulating glucose levels with minimal user input. The control algorithms commonly used in the development of artificial pancreas systems, such as Model Predictive Control (MPC) and Proportional-Integral-Derivative (PID), are adapted to help T1DM patients regulate their blood glucose levels.

There are multiple versions of the Bergman model, each with specific features adapted to various situations. In this article, a specific version of the Bergman model was chosen, and the PID (Proportional-Integral-Derivative) control was applied in different contexts. These contexts include normal individuals as well as Type 1 diabetic individuals, both in fasting states and in the presence of meals. This application will be integrated into the artificial pancreas due to its predictive capabilities. Although this device can identify blood glucose levels, using a predictive model helps avoid critical states and maintain glucose levels within the normal range. Other studies in this field have used different models or types of equations with various choices of control parameters, but the results obtained are almost similar, demonstrating the effectiveness of this control for blood glucose regulation.

The current investigation is structured as follows: Firstly, we introduce a minimal Bergman model. Next, in section 3, we define the PID control. Lastly, in section 4, we present numerical simulations of the theoretical results obtained.

2. MINIMAL BERGMAN MODEL

At the heart of understanding blood sugar regulation lies the minimal Bergman model. Developed by physiologist Richard N. Bergman, this model acts as a simplified map of the intricate dance between glucose and insulin in our bloodstream. While the actual system is incredibly complex, the Bergman model captures the key elements with a set of differential equations. These equations represent fundamental biological processes:

- **Glucose absorption:** how quickly sugar enters the bloodstream after a meal.

- **Insulin secretion:** how the pancreas releases insulin in response to rising glucose levels.
- **Tissue insulin sensitivity:** how effectively cells throughout the body utilize insulin to absorb glucose.

By simulating these processes, the Bergman model allows scientists to analyze the dynamic behavior of the glucose-insulin system. This provides valuable insights into:

- **Physiological mechanisms:** how our bodies naturally regulate blood sugar.
- **Glycemic control strategies:** development of effective methods to manage blood sugar levels, particularly for diabetic patients.

The mathematical details of this model are described as follows

$$\begin{cases} \dot{G} = -p_1 [G(t) - G_b] - X(t)G(t) + M(t) \\ \dot{X} = -p_2 X(t) + p_3 [I(t) - I_b] \\ \dot{I} = -n[I(t) - I_b] + \gamma(I(t) - h) \end{cases} \tag{1}$$

The definitions of the parameters used in the model are listed in the following table. Imagine

Parameter	**Symbol**	**Units**
Plasma glucose level	$G(t)$	mg/dL
Remote insulin	$X(t)$	mU/L
Plasma insulin level	$I_{(t)}$	mU/dL
Glucose base level before injection	G_{b}	mg/dL
Insulin base level before injection	I_{b}	μU/ml
Input (insulin)	u(t)	mU/min
Glucose absorption rate to blood via food	M(t)	-
Insulin independent constant	p_1	1 / min
Decrease rate of tissue's glucose up taking	p_2	1 / min
Enhanced glucose up taking capability (insulin	(μU / ml) / min^2	
Plasma insulin decay rate	n	1 / min
Insulin secretion of β cells	γ	μmg / dL

TABLE 1. The meaning of parameters

your body as a system managing sugar (glucose). Bergman's minimal model simplifies this system into three key parts:

(1) **Blood Sugar Level** (G): This represents the amount of glucose circulating in the bloodstream.
(2) **Insulin Action** (X): Insulin acts as a key that allows cells to absorb sugar. X reflects how effectively insulin is working at the tissue level, though we can't directly measure it.
(3) **Circulating Insulin** (I): This refers to the amount of insulin currently present in your blood.

The model also considers disruptions caused by eating, represented by $M(t)$. In healthy individuals, the body has a built-in mechanism for regulating blood sugar (represented by $\gamma(I(t)-h)$). However, in diabetic patients, this internal control system weakens. Bergman's model cleverly simplifies things by neglecting this term for diabetics. This allows scientists to focus on the altered metabolic processes in diabetes, making it easier to understand the disease and develop better treatments and management strategies.

While Bergman's minimal model is a great starting point, it doesn't account for how we treat diabetes. That's where the concept of a control variable comes in. Imagine a dial ($u(t)$) that represents the amount of insulin injected into a diabetic patient's bloodstream. By adjusting this dial, doctors and patients can directly control insulin levels (I) based on blood sugar readings (G). The objective is to maintain blood sugar within a healthy range, similar to a thermostat regulating room temperature. This approach, known as glycemic control, is crucial for managing diabetes and preventing complications. By incorporating this control variable into the Bergman model, we obtain a more powerful tool. This modified model allows researchers to simulate and analyze different insulin delivery strategies, paving the way for the development of more effective diabetes treatment plans. Then, we obtain the following system:

$$\begin{cases} \dot{G} = -p_1\left[G(t)-G_b\right] - X(t)G(t) + M(t) \\ \dot{X} = -p_2 X(t) + p_3\left[I(t)-I_b\right] \\ \dot{I} = -n\left[I(t)-I_b\right] + u(t) \end{cases} \tag{2}$$

The minimal Bergman model in the presence of control in patients can be represented by the following schema, which integrates the main metabolic parameters.

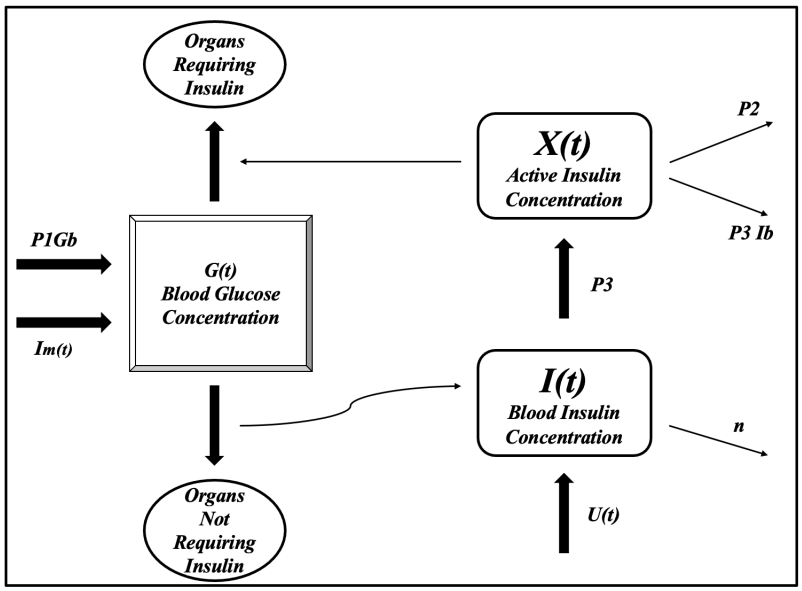

FIGURE 4. Diagram of Blood Glucose and Insulin Dynamics

3. PID CONTROL

To achieve tighter control of blood glucose, we can enhance model (1) by introducing a control signal, $u(t)$. This signal acts as the conductor of an insulin delivery system, implemented using a PID (Proportional-Integral-Derivative) controller. The PID controller analyzes the difference between the desired and actual blood sugar levels [22]. It then fine-tunes the insulin dosage dynamically in three ways:

- **Proportionally:** responds immediately to the current difference between target and actual glucose. A higher difference triggers a larger insulin correction.
- **Integrally:** considers the history of these differences. If blood sugar consistently runs high or low, the controller gradually adjusts insulin delivery to compensate for this trend.
- **Derivatively:** anticipates future changes by analyzing the rate of change in glucose levels. This proactive approach helps prevent large glucose swings by adjusting insulin in advance

Through these combined actions, the PID controller optimizes the system's response, aiming for a stable blood sugar balance. This approach provides a precise and responsive strategy for regulating blood glucose. The specific control scheme is illustrated in the following diagram

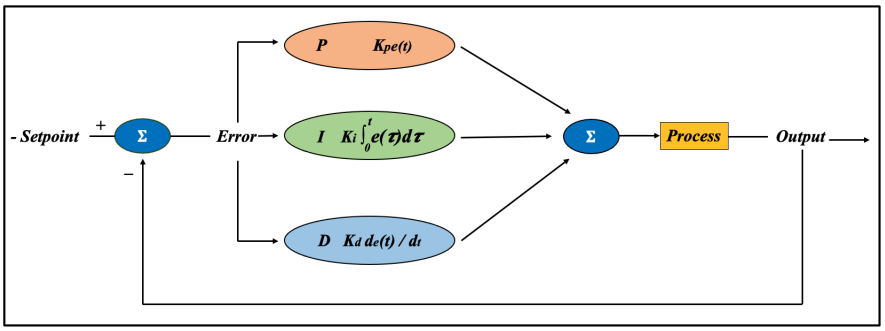

FIGURE 5. Functional Diagram of a PID Controller

- The proportional term (P) reacts proportionally to the current error, i.e., the difference between the setpoint and the measured value of the process. It acts to reduce this error based on its magnitude.
- The integral term (I) takes into account the cumulative integral of the error over time. It acts to eliminate persistent long-term errors by accumulating a correction proportional to the duration for which the error persists.
- The derivative term (D) is proportional to the derivative of the error with respect to time. It anticipates error variations by calculating the trend of change in the error over time. It acts to attenuate oscillations and stabilize the system by preventing rapid variations in the error.

This control can be mathematically expressed by the following formulation:

$$u(t) = K_p e(t) + K_i \int_0^t e(\tau)d\tau + K_d \frac{de(t)}{dt}$$

Where

- $e(t) =$ desired value $- G(t)$: The error between the desired output and the actual output of the system at a given moment.
- K_p, K_i and K_d : the proportional, integral, and derivative gain coefficients.

For diabetic patients, the Bergman model with PID (Proportional-Integral-Derivative) control offers a sophisticated approach to managing blood glucose levels through insulin delivery. This control system acts like a conductor for insulin, fine-tuning the amount based on current and anticipated glucose fluctuations. The proportional term reacts immediately to the current difference between measured glucose and the target level. If glucose levels are high, it increases the insulin dose to bring them down. The integral term addresses long-term trends by accumulating past deviations from the target and gradually adjusting insulin delivery to counteract persistent imbalances. The derivative term focuses on the rate of change in glucose levels. By anticipating future variations based on the current slope, it proactively adjusts insulin to prevent large swings. PID control refines the insulin dosage, without altering the injection method. This dose can be delivered through traditional subcutaneous injections or via a continuous pump that provides a steady stream of insulin.

4. Simulations and Discussion

This section explores the use of the Bergman model to predict blood glucose levels. Through numerical simulations, we will compare the glucose response of two individuals: a healthy person and someone with diabetes. We will analyze both fasting and meal scenarios to understand how their bodies react. For the diabetic individual, we will introduce a PID (Proportional-Integral-Derivative) control mechanism to investigate its effectiveness in regulating blood sugar levels. The simulations use parameter values provided in the table below.

Figure 6 illustrates the simulated blood glucose concentration during a fasting period (without a meal) for two individuals, representing a baseline state. Both individuals begin with an initial glucose level of 200. In healthy individuals, glucose levels rapidly return to the normal range 70–100 mg/dL, eventually stabilizing around 80 mg/dL. This demonstrates their body's effective ability to regulate blood sugar. In stark contrast, the diabetic individual's glucose concentration remains persistently elevated, exceeding the normal range. This highlights the impaired ability of a diabetic person to maintain healthy blood sugar levels, even in a fasting state.

Parameter	**Normal**	**Patient**
p_1	0.031	0
p_2	0.012	0.011
p_3	4.92^{-6}	5.3^{-6}
V	0.0039	0.0042
n	0.265	0.26
h	79.035	80.2
G_b	70	70
I_b	7	7
G_0	220	220
I_0	364.8	50

TABLE 2. parameters values.

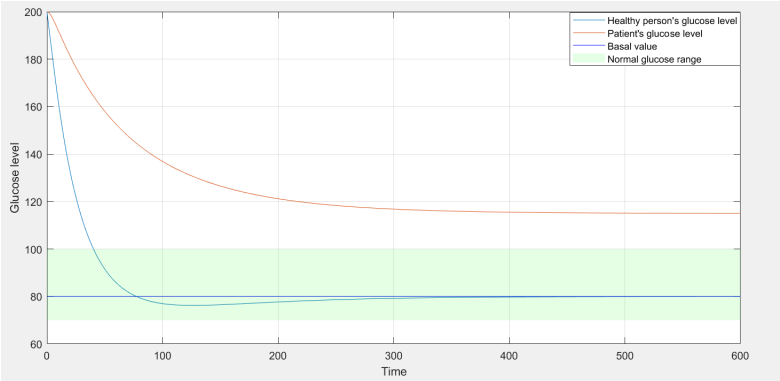

FIGURE 6. Comparative Blood Glucose Levels of Healthy and Diabetic Individuals

Figure 7 simulates the blood sugar response of a healthy person following a meal. The initial glucose level is 200. At time t=300, the meal introduction triggers a rapid rise in blood sugar, exceeding 160. This postprandial surge is transient, however, as the body's insulin response effectively regulates glucose levels. Blood sugar swiftly returns to normal values (between 70 and 100) and eventually stabilizes around 80. This figure exemplifies a healthy body's remarkable ability to maintain blood sugar control after eating. Even though a temporary increase occurs

following the meal, the body efficiently restores glucose homeostasis, achieving long-term stability.

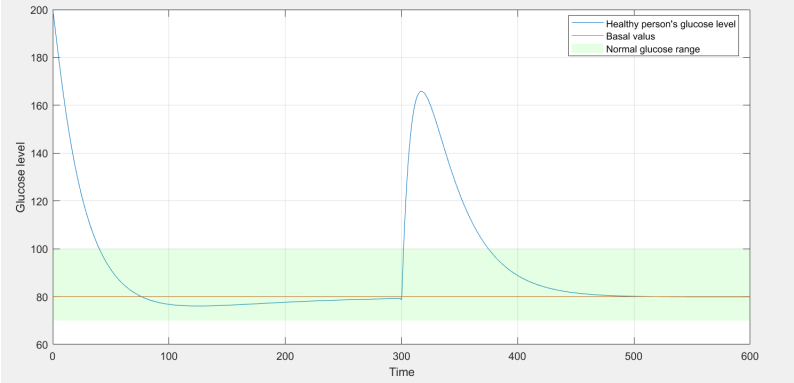

FIGURE 7. Blood glucose levels of normal person under meal disturbance.

Figure 8 illustrates the concerning blood sugar response of a diabetic individual following a meal. While the initial glucose level is similar to the healthy case (200), the patient struggles to regulate blood sugar after the meal is introduced at $t = 400$. Unlike the healthy person, glucose levels experience a dramatic rise, reaching dangerously high values. This uncontrolled hyperglycemia poses a significant health risk, highlighting the critical challenge diabetics face in managing blood sugar spikes after meals. Such uncontrolled spikes can lead to severe long-term complications if not properly managed.

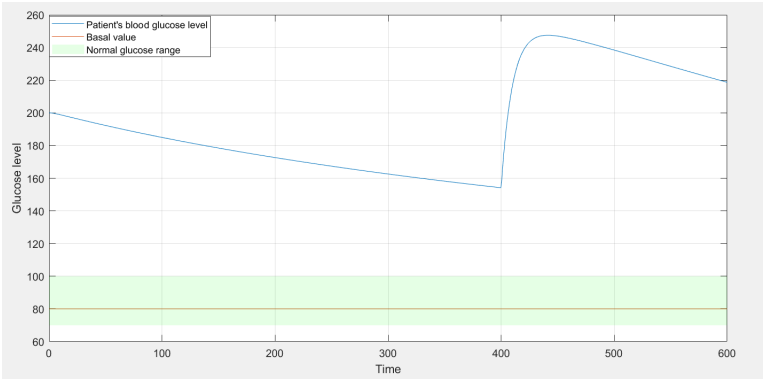

FIGURE 8. Blood glucose levels of Patient under meal disturbance.

Figure 9 showcases the promising impact of automatic insulin injection with PID control on a diabetic patient's blood sugar levels. Similar to the previous simulations, the initial glucose level is set at 200. This control system demonstrates remarkable effectiveness. It rapidly normalizes blood sugar, bringing it back within the healthy range $(70-100)$ and converging towards the desired target of 80. Notably, even after introducing meals at $t = 150$ and $t = 400$, glucose levels rapidly return to normal. This rapid response suggests that PID-controlled automatic insulin injection can significantly improve diabetic patients' quality of life. By efficiently managing blood sugar fluctuations, even after meals, this system offers a potential path towards a more normal and worry-free lifestyle.

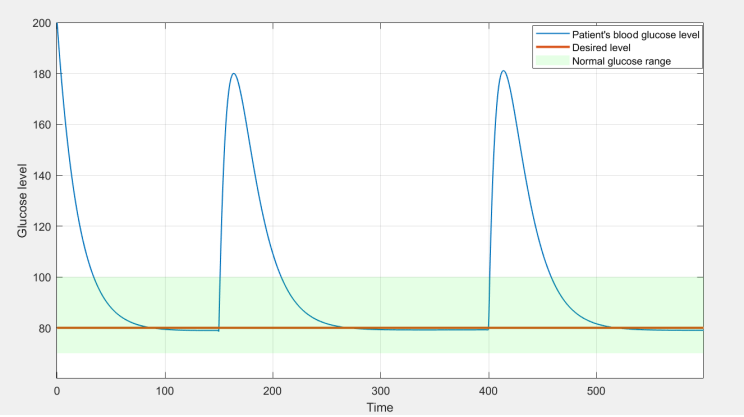

FIGURE 9. Blood glucose levels of the patient during meal disturbance with PID control.

To conclude, the findings depicted in the four figures offer a thorough understanding of blood glucose dynamics across various contexts. The initial figure starkly contrasts the fasting blood glucose levels of healthy individuals with those of diabetic patients, emphasizing the ongoing struggle with glucose regulation in diabetes. Following this, the second figure illustrates the prompt post-meal glucose regulation observed in healthy individuals, highlighting their efficient metabolic response. Conversely, the third figure illuminates the challenges diabetic patients encounter in regulating their blood glucose levels post-meal, indicating potential health hazards. Lastly, the fourth figure showcases a promising approach: automatic insulin injection with PID control. This method demonstrates fast glucose normalization even after meals, indicating its potential for effective glycemic management and improved quality of life in diabetic patients.

The numerical simulations build upon these findings by illustrating the potential of PID control in stabilizing blood glucose levels in individuals with Type 1 diabetes, particularly during meal disturbances. However, it is important to note that these simulations are conducted under idealized conditions, such as perfect sensor accuracy and constant insulin sensitivity, which do not fully capture the complexities of real-life diabetes management. In reality, factors such as delayed insulin action, daily variations in insulin sensitivity, and external influences like physical activity, stress, and inconsistent food intake can significantly affect glycemic control. To ensure that PID control systems are truly reliable, safe, and effective in everyday scenarios, future research should aim to integrate these variables into more dynamic and realistic models. This would allow for better testing of how PID systems perform under varying conditions, leading to more robust and adaptive control strategies for real-world diabetes management.

5. CONCLUSION

In this study, we have examined the complex realm of blood glucose regulation, particularly focusing on individuals with Type 1 diabetes (T1D). Using the minimal Bergman model and applying PID (Proportional-Integral-Derivative) control strategies, we have explored new approaches for robust blood glucose (BG) management. Our investigation commenced with a comprehensive overview of pancreatic physiology, elucidating the crucial roles of various pancreatic hormones, notably insulin and glucagon, in orchestrating glucose homeostasis. We highlighted the disparity in metabolic capabilities between healthy individuals and those with diabetes, emphasizing the urgent need for effective management strategies. Central to our study was the utilization of the minimal Bergman model, a powerful tool that encapsulates the dynamic interplay between glucose and insulin in the bloodstream. Leveraging this model, we elucidated the fundamental principles underlying blood glucose regulation, laying the groundwork for our subsequent analyses. Introducing the concept of PID control, we embarked on a journey to refine BG regulation in diabetic individuals. Through meticulous simulations, we demonstrated the efficacy of PID-controlled automatic insulin injection systems in swiftly normalizing BG levels, even amidst perturbations induced by meal intake. Our findings highlight the potential of integrating advanced control strategies, such as PID, into the management

protocols for T1D. By offering real-time insulin dosage adjustments, these systems could revolutionize glycemic control, reduce the risks of hyperglycemia, and improve the quality of life for people with diabetes.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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