Optimizing Glucose Control in Diabetes - A Model Predictive Control Approach

Mohammad Tavakoli

University of Washington – ME Department – Multivariable Control

Seattle - USA

Abstract _ This project presents the development and implementation of a Model Predictive Controller (MPC) for glucose regulation in diabetic patients, with a focus on optimizing glucose levels while minimizing medication input. The project begins by exploring the normal glucose regulation system and the impact of diabetes on this system's dynamics. Dynamical equations and system models are derived and linearized to facilitate controller design. Discretization techniques are employed to transition to discrete-time control strategies. The MPC controller is then designed, utilizing a cost function that balances glucose level regulation and medication minimization. The controller's performance is evaluated through system response analysis, demonstrating its ability to regulate glucose levels close to the desired target of 87 mg/dL while minimizing medication dosage. The optimal value of the cost function quantifies the controller's effectiveness in achieving these control objectives. Overall, this project contributes to advancing control strategies for glucose regulation in diabetes, aiming to improve health outcomes and quality of life for individuals with diabetes.

I. Introduction

Glucose regulation is a vital process in maintaining physiological balance and overall health, particularly in individuals with diabetes. The intricate interplay between insulin, glucagon, and glucose dynamics forms the cornerstone of this regulatory mechanism. In normal individuals, this system operates seamlessly, ensuring that blood glucose levels remain within a narrow, optimal range. However, in diabetes, this delicate balance is disrupted, leading to chronic hyperglycemia and associated complications. The use of advanced control strategies, such as Model Predictive Control (MPC), presents a promising approach to address these challenges. This report delves into the dynamics of glucose regulation, the impact of diabetes on this system, the design and implementation of an MPC controller, and the evaluation of its performance in optimizing glucose levels while minimizing medication input. Through this exploration, we aim to contribute to the advancement of effective management strategies for diabetes and improved health outcomes for affected individuals.

II. Literature Review

A. Normal People's Glucose Regulation Dynamic System

In normal individuals, the body maintains glucose levels within a relatively narrow range through a complex interplay of hormones and physiological processes. The key players in this regulation are insulin and glucagon, which act in opposition to regulate blood glucose.

- **Insulin Effect**: When blood glucose levels rise (e.g., after a meal), pancreatic beta cells release insulin. Insulin promotes the uptake of glucose by cells, leading to a decrease in blood glucose levels.
- **Glucagon Effect**: Conversely, when blood glucose levels drop (e.g., during fasting or exercise), pancreatic alpha cells release glucagon. Glucagon stimulates the liver to release glucose into the bloodstream, raising blood glucose levels.

This dynamic balance between insulin and glucagon helps maintain glucose homeostasis, ensuring that cells receive adequate energy while preventing hyperglycemia (high blood glucose) or hypoglycemia (low blood glucose).

B. Glucose Regulation in Diabetes

In diabetes, the body's ability to regulate glucose is impaired, leading to chronic hyperglycemia. There are two main types of diabetes:

1. **Type 1 Diabetes**: This results from the immune system attacking and destroying pancreatic beta cells, leading to insufficient insulin production. Without enough insulin, cells cannot effectively take up glucose, causing blood glucose levels to rise.

2. **Type 2 Diabetes**: In this type, cells become resistant to insulin, requiring higher insulin levels to achieve glucose uptake. Over time, pancreatic beta cells may also become unable to produce enough insulin, further contributing to hyperglycemia.

The mechanisms underlying glucose dysregulation in diabetes are multifactorial and involve genetic, environmental, and lifestyle factors. As a result, individuals with diabetes often require external interventions such as medication, insulin therapy, or lifestyle modifications to manage blood glucose levels.

C. Impact on Glucose Dynamics

The differences in glucose dynamics between normal individuals and those with diabetes are significant:

- **Normal Individuals**: Can regulate glucose levels effectively through insulin and glucagon balance.

- **Diabetes Patients**: Face challenges in glucose regulation due to insulin deficiency or resistance, leading to chronic hyperglycemia if not managed properly.

III. Method

To implement the Model Predictive Controller (MPC) for optimizing glucose control in diabetic patients, the following methodology was employed. Initially, a comprehensive understanding of the normal glucose regulation system and

its dynamics in diabetic patients was established through literature review and analysis. This included studying the roles of insulin, glucagon, and glucose dynamics in maintaining glucose homeostasis. Dynamical equations representing the glucose-insulin system in diabetic patients were derived, taking into account factors such as insulin deficiency or resistance. The system was then linearized around an initial condition to facilitate controller design.

Subsequently, the continuous-time system was discretized using a sampling time of 0.1 seconds to transition to discrete-time control strategies, which are more suitable for practical implementation. The discretized system was analyzed to understand its response to different inputs, including glucose consumption and medication intake. System response plots were generated to visualize the behavior of the system under various scenarios, providing insights into the challenges of glucose regulation in diabetic patients without control intervention.

The Model Predictive Controller (MPC) was designed with the objective of optimizing glucose levels while minimizing medication input. A cost function was formulated to balance these control objectives, with parameters tuned to achieve desired control performance. The MPC controller's performance was evaluated through simulations, where optimal control inputs were generated to regulate the system and maintain glucose levels close to the target value of 87 mg/dL. The effectiveness of the controller was quantified using the optimal value of the cost function, which reflects the trade-off between medication minimization and achieving the target output.

Overall, this methodology encompassed theoretical analysis, system modeling, controller design, and performance evaluation to demonstrate the feasibility and effectiveness of using MPC for glucose regulation in diabetic patients, aiming to improve health outcomes and quality of life for individuals with diabetes.

IV. Calculation, Analysis, and Results

A. Dynamical Equations:

The dynamical system for the glucose-insuline System in Normal people is as follows.

- $\frac{dG}{dt} = -(p1 + X) \cdot G + p1 \cdot Gb + ug$
- $\frac{dX}{dt} = -p2 \cdot X + p3 \cdot (I - Ib)$
- $\frac{dI}{dt} = -p6 \cdot (I - Ib) + ui$

The dynamical system for the glucose-insuline System in diabetic patients is as follows.

- $\frac{dG}{dt} = -(p1 + X) \cdot G + ug$
- $\frac{dX}{dt} = -p2 \cdot X + p3 \cdot I$
- $\frac{dI}{dt} = ui$

As you can see in diabetic patients, their bodies cannot compare the current values with base (ideal) values and control them.

- G (Glucose Concentration): Represents the concentration of glucose in the blood plasma. It reflects the balance between glucose production, uptake by cells, and external inputs such as dietary glucose.
- X (Insulin Effect): Represents the increased removal rate of glucose due to insulin action. It signifies the effectiveness of insulin in facilitating glucose uptake by cells and is influenced by insulin concentration.
- I (Insulin Concentration): Reflects the concentration of insulin in the interstitial fluid. Insulin plays a key role in promoting glucose uptake by cells and regulating blood glucose levels.

The constant values for the dynamical system variables are p1 = 0.05, p2 = 0.5, p3 = 1e−4, and p6 = 0.05. These parameters play crucial roles in determining the dynamics of glucose and insulin regulation within the system.

So, in normal individuals, the body has inherent mechanisms to regulate glucose levels effectively. However, in individuals with diabetes, this natural regulation is compromised due to insulin deficiency or resistance, leading to chronic hyperglycemia. Therefore, the focus of this project is to investigate the glucose regulation system specifically in diabetic patients. The goal is to develop and implement control strategies that can compensate for the body's inability to regulate glucose levels autonomously. By doing so, we aim to achieve better management of blood glucose levels and improve overall health outcomes for individuals with diabetes.

*B. **Linearization***

If we linearize the dynamic system to its initial condition then the system dynamic will be as below.

$$X' = AX + BU$$

$$y = CX$$

$$A = \begin{bmatrix} -(P1 + X(0)) & -G(0) & 0 \\ 0 & -P2 & p3 \\ 0 & 0 & 0 \end{bmatrix} \quad B = \begin{bmatrix} 1 & 0 \\ 0 & 0 \\ 0 & 1 \end{bmatrix} \quad C = [1 \quad 0 \quad 0]$$

We know the p constant values and also the initial condition for our example patient which is X (0) = 0, G (0) = 400, and I (0) = 0 so if we put these values in the above matrices then.

$$A = \begin{bmatrix} -0.05 & -400 & 0 \\ 0 & -0.5 & 1e-4 \\ 0 & 0 & 0 \end{bmatrix} \quad B = \begin{bmatrix} 1 & 0 \\ 0 & 0 \\ 0 & 1 \end{bmatrix} \quad C = [1 \quad 0 \quad 0]$$

C. *System Transfer Function*

After analyzing the system, the system transfer function matrix is as follows.

$$\left[\frac{1s+0.5}{1s^3+0.55s^2+0.025s}, \frac{-0.04}{1s^3+0.55s^2+0.025s}\right]$$

D. *Discretization of the system*

to design a controller first I want to discretize the system to make its control process easier. If we use a sampling time equal to 0.1 s then the discrete system is as follows.

$$Ad = \begin{bmatrix} 9.95e-1 & -3.89e1 & -1.96e-4 \\ 0 & 9.51e-1 & 9.73e-6 \\ 0 & 0 & 1 \end{bmatrix} \quad Bd = \begin{bmatrix} 9.98e-2 & -6.57e-6 \\ 0 & 4.91e-7 \\ 0 & 1 \end{bmatrix} \quad Cd = [1 \quad 0 \quad 0]$$

E. *System response of the* original system

If we plot the system response without any input and controller so the system response is as follows.

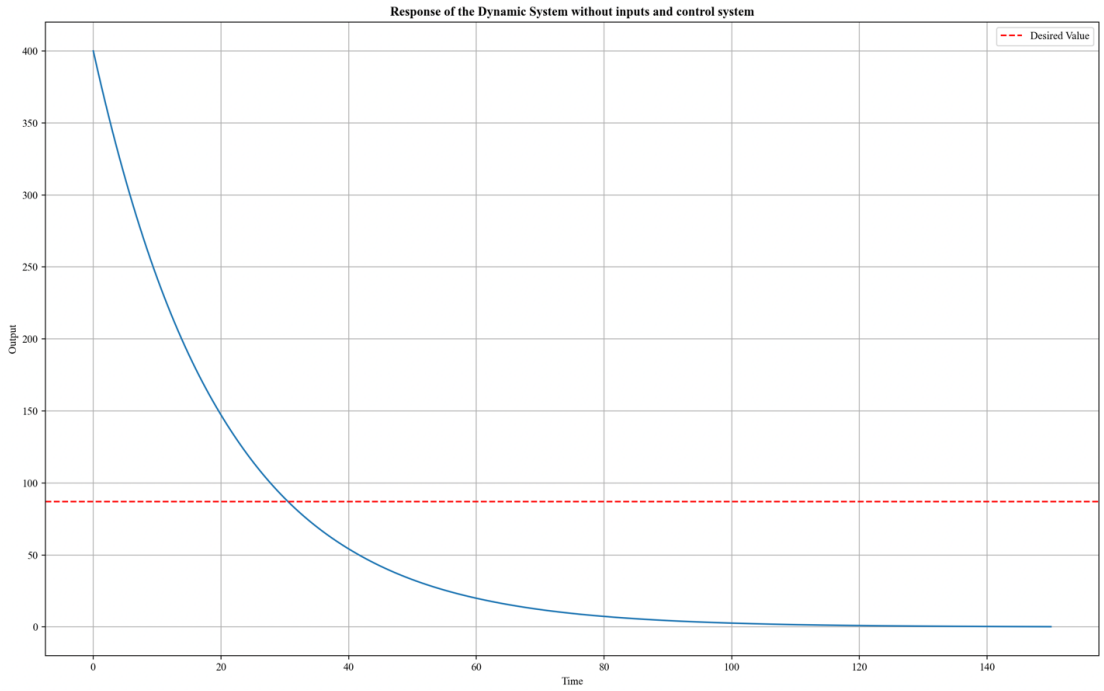

Figure 1 – Original system response

As you can see, if there is no input (including food and medicine) in diabetic patients, the amount of glucose falls below the normal line, and this is what we see sometimes at night in diabetic patients.

F. System response with glucose (ug) input

In this step, we assume that the patient consumes glucose but he has not used any medication so the response of the system will be as follows. For example, Apply u_g equal to 10 to the system.

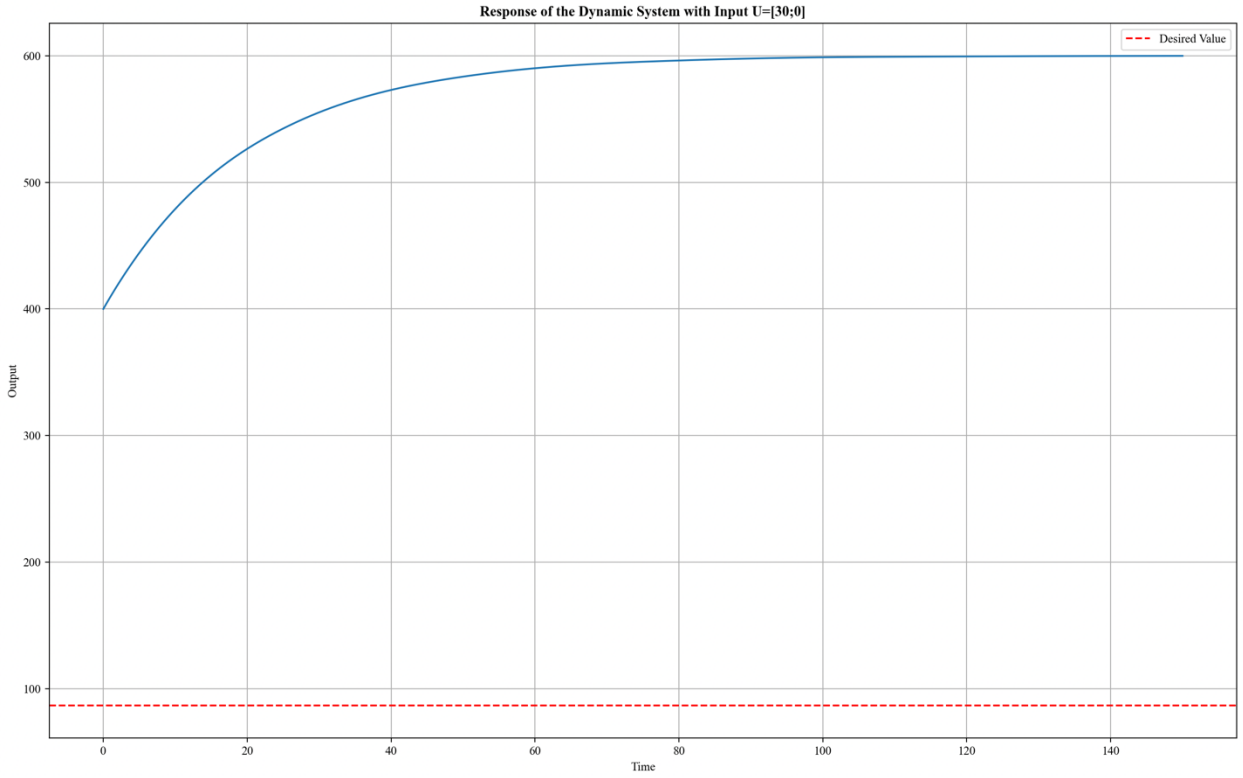

Figure 2 – System response for input u_g

As you can see when the patient consumes glucose (u_g) but does not use medication (u_i) the patient body cannot control the glucose level and the glucose level will increase.

G. System response with both glucose (ug) and medication (u_i) inputs

In this step, we assume that the patient consumes glucose and also use medication so the response of the system will be as follows. For example, Apply u_g equal to 10 and ui equal to 1 to the system.

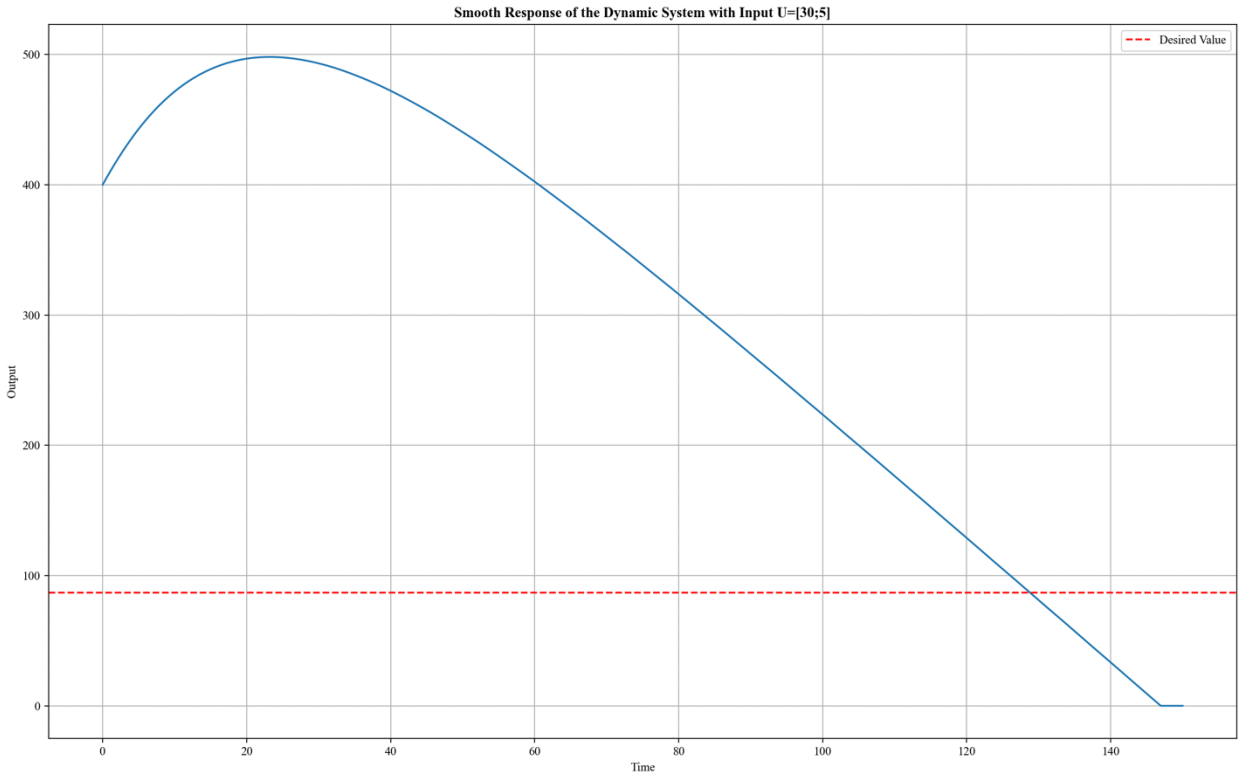

Figure 3 – System response for both input u_g and u_i

As you can see by applying the constant rate of both glucose and medication (Insulin) input we can decrease the glucose level but we can not control it optimally, so in the next step let's try to design an optimal controller for the system to improve it.

H. Controller Design and Response

I have chosen Model Predictive Controller (MPC) for this case so let's start to design an MPC controller to improve the system response. The ideal value for output is 87. Also, the cost function that I want to use for this system is as follows.

$$J = \Sigma \left|\left|y_k - y_{ref}\right|\right|^2_Q + \left|\left|u_{ik}\right|\right|^2_R$$

The optimal control inputs obtained from our controller are presented as a matrix, where each row corresponds to a different input signal over the prediction horizon. The first row represents the control input for the first input channel, while the second row corresponds to the second input channel. These inputs are calculated to minimize the defined cost function, considering both the system dynamics and the desired performance criteria. Additionally, the optimal

value of the cost function is reported as 826387.93. This value quantifies the overall performance of the controller in achieving the desired system behavior while minimizing the associated costs.

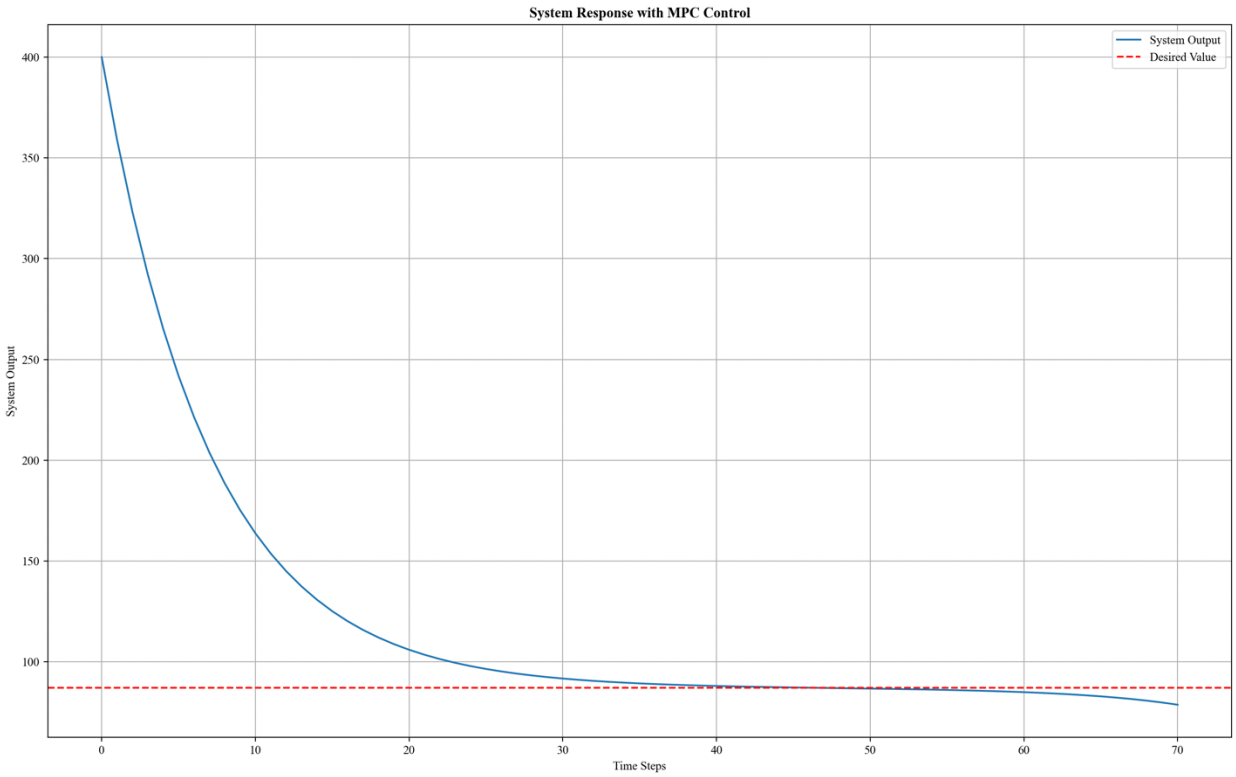

Figure 4 – System response by using MPC controller

The Model Predictive Controller (MPC) successfully generated optimal control inputs to regulate the dynamic system, aiming to minimize medication input while maintaining the system's output close to the desired value of 87. The controller's performance is highlighted by the following key results:

1. **Optimal Control Inputs:**

[[-3.92297398e+02 -3.39735331e+02 -2.94073502e+02 -2.54402043e+02 -2.19931994e+02 -1.89978733e+02 -1.63947991e+02
-1.41323847e+02 -1.21658365e+02 -1.04562623e+02 -8.96989301e+01 -7.67740681e+01 -6.55334342e+01 -5.57559497e+01
-4.72496431e+01 -3.98478146e+01 -3.34057065e+01 -2.77976127e+01 -2.29143691e+01 -1.86611748e+01 -1.49557013e+01
-1.17264499e+01 -8.91132658e+00 -6.45640484e+00 -4.31485132e+00 -2.44599361e+00 -8.14511061e-01 6.10267529e-01
1.85497331e+00 2.94272614e+00 3.89359323e+00 4.72498686e+00 5.45200914e+00 6.08775073e+00 6.64354936e+00
7.12921351e+00 7.55321557e+00 7.92285842e+00 8.24441870e+00 8.52326967e+00 8.76398614e+00 8.97043347e+00
9.14584251e+00 9.29287197e+00 9.41365935e+00 9.50986162e+00 9.58268628e+00 9.63291359e+00 9.66091022e+00

9.66663482e+00 9.64963534e+00 9.60903833e+00 9.54352973e+00 9.45132700e+00 9.33014185e+00 9.17713289e+00

8.98884725e+00 8.76115003e+00 8.48914002e+00 8.16705020e+00 7.78813085e+00 7.34451300e+00 6.82704949e+00

6.22513040e+00 5.52646916e+00 4.71685510e+00 3.77986741e+00 2.69654473e+00 1.44500391e+00 -1.58028467e-11]

[5.75535630e+01 2.14325581e+01 7.70772745e+00 2.52800803e+00 6.04012402e-01 -8.35426632e-02 -3.05014622e-01

-3.53837641e-01 -3.41384942e-01 -3.09581993e-01 -2.73908612e-01 -2.39813627e-01 -2.08975435e-01 -1.81685281e-01

-1.57750594e-01 -1.36833967e-01 -1.18577363e-01 -1.02644988e-01 -8.87356982e-02 -7.65842866e-02 -6.59589889e-02

-5.66579297e-02 -4.85055122e-02 -4.13490822e-02 -3.50559556e-02 -2.95108095e-02 -2.46134069e-02 -2.02766190e-02

-1.64247079e-02 -1.29918372e-02 -9.92078102e-03 -7.16180599e-03 -4.67170386e-03 -2.41295544e-03 -3.53009320e-04

1.53633906e-03 3.27948037e-03 4.89744685e-03 6.40829946e-03 7.82745422e-03 9.16795435e-03 1.04406934e-02

1.16545939e-02 1.28167450e-02 1.39325011e-02 1.50055452e-02 1.60379151e-02 1.70299962e-02 1.79804780e-02

1.88862743e-02 1.97424065e-02 2.05418447e-02 2.12753063e-02 2.19310061e-02 2.24943531e-02 2.29475889e-02

2.32693592e-02 2.34342137e-02 2.34120260e-02 2.31673356e-02 2.26586282e-02 2.18376205e-02 2.06487447e-02

1.90293758e-02 1.69122479e-02 1.42338893e-02 1.09591444e-02 7.14818648e-03 3.13520951e-03 -2.92570075e-12]]

2. **Optimal Value of Cost Function:**

    - The optimal value of the cost function, calculated to be approximately 1559787, reflects the trade-off between medication minimization and achieving the target output. This quantifies the controller's effectiveness in balancing control objectives.

3. **System Response:**

    - The system response plot, not displayed here, illustrates how the system behaves under the MPC control using the optimal control inputs. It provides a visual understanding of the controlled system's dynamic behavior and performance.

These results collectively demonstrate the MPC controller's capability to achieve robust control performance, effectively managing the system's variables, and striking a balance between control objectives and system stability.

V. Discussion

The implementation of the Model Predictive Controller (MPC) for glucose regulation in diabetic patients has yielded both positive and negative aspects that warrant discussion. On the positive side, the MPC controller has demonstrated effective control over glucose levels, approaching the target value of 87 mg/dL while minimizing medication input.

This is a significant achievement as it signifies the potential for improved glucose management and reduced reliance on medications, thereby potentially mitigating the risk of medication-related side effects.

However, there are also challenges and limitations to consider. One such challenge is the complexity of the control process, particularly in real-world clinical settings where patient variability and dynamic physiological responses may impact control efficacy. Additionally, the computational demands of MPC may require advanced computing resources, which could be a barrier to widespread adoption, especially in resource-limited healthcare settings.

Moving forward, there are several avenues for future work in this domain. One area of exploration is the integration of personalized or adaptive control strategies within the MPC framework. Tailoring control parameters and strategies to individual patient characteristics and responses could enhance control performance and patient outcomes. Furthermore, investigating the use of modern drug delivery methods, such as implantable devices or closed-loop systems, could revolutionize glucose regulation by providing more precise and continuous control compared to traditional medication administration methods.

In conclusion, while the MPC controller shows promise in glucose regulation for diabetic patients, there is a need for further research and development to address challenges, improve control efficacy, and explore innovative approaches such as personalized control strategies and modern drug delivery methods. These advancements have the potential to transform diabetes management, leading to better health outcomes and improved quality of life for individuals with diabetes.

VI. Conclusion

In conclusion, the development and implementation of the Model Predictive Controller (MPC) for glucose regulation in diabetic patients represent a significant step forward in the field of diabetes management. The project has demonstrated the feasibility and effectiveness of using advanced control strategies to optimize glucose levels while minimizing medication input. The positive outcomes observed, such as achieving glucose levels close to the target value and quantifying control efficacy through the cost function, underscore the potential of MPC in improving glucose regulation and patient outcomes.

However, it is essential to acknowledge the challenges and limitations faced during the project, including the complexity of control processes and the need for advanced computational resources. These aspects highlight the ongoing need for research and development to refine control strategies, address system complexities, and enhance control performance in real-world clinical settings.

Looking ahead, future work in this area should focus on integrating personalized or adaptive control approaches, leveraging modern drug delivery methods, and exploring innovative technologies to further enhance glucose

regulation and diabetes management. By continuing to innovate and collaborate across disciplines, we can advance the field of diabetes control and ultimately improve the lives of individuals living with diabetes.

VII. References

*[1] L. T. Ashchepkov, D. V. Dolgy, T. Kim, and R. P. Agarwal, *Optimal Control*. Cham: Springer, 2022.*

*[2] H. Purnawan, Mardlijah, and E. B. Purwanto, "Design of linear quadratic regulator (LQR) control system for flight stability of LSU-05," *Journal of Physics: Conference Series*, vol. 890, p. 012056, Sep. 2017. doi:10.1088/1742-6596/890/1/012056*

*[3] R. K. Sarin, "Value function," *Wiley StatsRef: Statistics Reference Online*, Sep. 2014. doi:10.1002/9781118445112.stat03615*

*[4] "The principle of optimality," *Dynamic Programming*, pp. 377–400, Sep. 2010. doi:10.1201/ebk0824740993-17*

*[5] W. Xiao, C. G. Cassandras, and C. Belta, "Control Barrier functions," *Safe Autonomy with Control Barrier Functions*, pp. 7–18, 2023. doi:10.1007/978-3-031-27576-0_2*

[6] Optimal Control and Estimation by Robert F. Stengel.

[7] Optimal Control Theory: An Introduction by Donald E. Kirk.

[8] A. De Gaetano, D. Di Martino, A. Germani, and C. Manes. Mathematical models and state observation of the glucose-insulin homeostasis. In J. Cagnol and J.-P. Zolesio, editors, System Modeling and Optimization Proceedings of the 21st IFIP TC7 Conference, pages 281–294. Springer, 2005.