On the Control of Glucose Concentration in Diabetic Patients Utilizing the Bergman Model and an Automated Insulin Infusion Pump

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***Abstract*—Biological systems are of special interest in control theory due to the consequences of system failure. In this paper, the group proposes a control system for the regulation of glucose in the body of a diabetic individual. Glucose is controlled through an automated insulin pump that implements the designed control system based on two different variables: deviation of current glucose level from the desired set point, and food intake as glucose over a period of time. The control system modifies the insulin infusion rate of the pump to achieve a steady-state value within the safe range for a diabetic patient. This hybrid feedback-feedforward architecture models food intake as finite duration step pulses of glucose added to the current glucose level present in the body. The group investigates several different design approaches and discusses the results of each. In addition, we examine the robustness of the system such that glucose concentration can be maintained above a specified baseline to avoid potential health conflicts of the patient. Lastly, potential improvements to the model and control system are discussed, as well as potential adjustments necessary for real-world implementation.**

***Index Terms*—control design, diabetes, insulin infusion, feedback, feed-forward, automated insulin pump, biological controls, robust control systems, non-linear controls**

I. Introduction

The body is a complex system containing biochemical sensors with feedback loops and regulators to control countless different parameters at once. While the human body can typically support itself with complex control systems, modern medicine is able to provide auxiliary support the body's effort which can assist and enable abilities to countless people who have biological conditions and disabilities that would otherwise prevent them from such freedoms. This paper discusses how control systems can be designed to help regulate glucose concentration in the blood of individuals who suffer from diabetes. This research will explore the design that provides maximum safety and stability to the users, as well as potential limitations to the systems.

As a patients wellbeing is dependent on the reliability of the controller designed, finding a robust, optimal controller design that ensures patients safety is critical. Based on the works of [1], the infusion rate of an automated insulin pump is the variable being controlled. There are several techniques to accomplish this, however, in this paper, Smith et al. will focus on feedback and hybrid feedback-feedforward control systems. These systems work on the principle of monitoring the patient's current glucose level and attempt to maintain steady levels - with system disturbance being modelled as glucose consumed in meals over a finite time period - within the safe bounds of the system.

II. System Model

To accurately design an insulin infusion controller for a patient, the human body's reaction to glucose concentrations in the blood must be modelled. The Bergman Model is used to represent the relationship between between insulin infusion and blood glucose concentrations [2]. This simple model uses assumed values for blood volume, as well as baseline values for insulin and glucose [1]. The Bergman Model is described in three differential equations listed below:

$$\frac{dG}{dt} = -p_1 G - X(G + G_b) + \frac{G_{meal}}{V_1} \tag{1}$$

$$\frac{dX}{dt} = -p_2 X + p_3 I \tag{2}$$

$$\frac{dX}{dt} = -p_2 X + p_3 I \tag{3}$$

Table 1 below presents the assumed values for blood volume, insulin infusion, and blood glucose in the human body.

TABLE I
Bergman Model Assumed Values

Variable	Description	Value	Unit
G	Deviation in blood glucose	$ControlOutput$	mg/decilitre
G_b	Baseline blood glucose	4.5	mmol/L
G_{meal}	Meal Input	$DisturbanceInput$	mg/decilitre
X	Insulin in "remote" area	$ControlVariable$	mg/decilitre
I	Deviation in insulin	$ControlVariable$	mg/decilitre
I_b	Baseline insulin	4.5	mU/L
p_1, p_2, p_3	Blood volume	$0, 0.0025, 0.000013$	mU/L
n	rate	$5/54$	min^{-1}
V_1	Blood volume	12	L
U	Insulin infusion rate	$ControlInput$	mg/decilitre

Utilizing the assumed values listed in Table 1 above, the system was modelled in the frequency domain as a transfer function, which is simplified and presented below:

$$\frac{G(s)}{I(s)} = -\frac{3.79}{432}\left[\frac{1}{s(s+\frac{1}{10.8})(s+\frac{1}{40})}\right] \tag{4}$$

It should be noted that all units were converted to mg/decilitre. The input disturbance to the system is assumed to be a 50 g glucose meal consumed at a constant rate for 15 minutes, which is represented as a step function for the finite duration [1]. Furthermore, a first order transfer function, presented in Equation 5 below, can be used to represent the absorption of glucose into the bloodstream [1].

$$\frac{G(s)}{I(s)} = \frac{8.334}{s(20s+1)} \tag{5}$$

The previously described transfer functions were modelled in Simulink. The open-loop model for the plant is displayed in Figure 1.

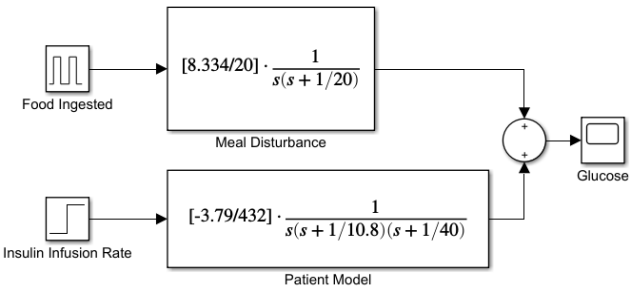

Fig. 1. Open-loop Patient Simulink Model

III. Feedback Control Design

The ideal blood glucose concentration for the average individual with diabetes is 81 mg/decilitre [1]. Moreover, blood glucose levels should not drop below 70 mg/decilitre, and it is not possible to have a negative insulin infusion rate. To maintain healthy blood-glucose levels in a patient with diabetes, a controller in a negative feedback loop can be implemented. A PID controller was designed through an iterative process, beginning with a simple P controller. Values for the proportional, derivative and integral coefficients were adjusted using empirical tuning. The step responses of the system to a minimum of three consecutive meal inputs were analyzed, and adjustments were made to control rise-time, settling time, and overshoot. The closed-loop feedback system, with a saturation term to prevent negative insulin infusion rates is displayed in Figure 2.

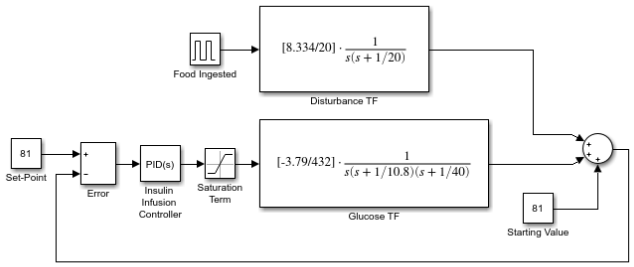

Fig. 2. Closed-loop Feedback Patient Simulink Model

A. Gain Estimation and Tuning Methods

One well known method for finding initial gain values for PID systems is the Ziegler-Nichols method [3]. One issue with this method, however, is the values must be tuned afterwards for optimal gain values as the method is based on linearization and approximation of the plant responses. After rough estimates of the gain values using the Ziegler-Nichols method, the gain values were then empirically tuned with statistical regression to achieve optimal gain values for the system.

B. Proportional Controller

One important factor in the design of the controller is the disturbance term, which is based on glucose consumption in a person. An accurate approximation of food intake is by modelling the glucose consumed as a pulse of 15 minute duration [1]. Unless otherwise stated, the simulations in this paper model the disturbance input as a 50 g glucose ingestion every 4 hours, which lasts for 15 minutes. The lump sum of glucose must be converted into an appropriate amplitude, as the time units are in seconds. This leads to an amplitude of 0.05556 (per s glucose absorption rate) for the pulse.

To begin the control design process, a simple proportional controller was implemented, applying a gain of 1 to the difference between the set-point glucose level and the simulated glucose level. Results are displayed in Figure 3.

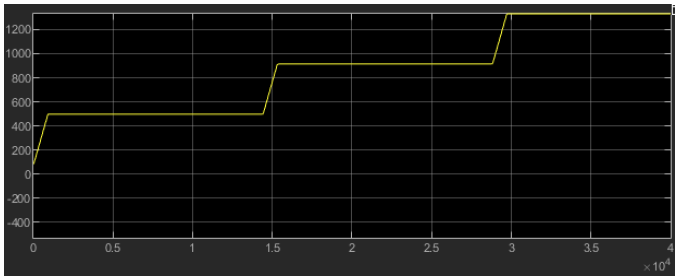

Fig. 3. Glucose Concentration Step-Response with P controller (Gain=1.0) implemented in Feedback System

Evidently, the controller does not perform as desired. Whilst eating, glucose levels rise proportionally and do not change until the next meal, at which point they continue to increase.

This is understood as the error term, which is a negative value when glucose levels are high, is being entered as the insulin infusion rate directly. A negative insulin infusion rate is not possible, and is set to 0 by the saturation block. Thus, the displayed results are comprehensive as no insulin is infused to control the increasing glucose supply. When the error is negative, insulin infusion rate must be positive, and an inverse relationship should be applied. The proportional term was made negative and results were analyzed. The resulting insulin infusion rate and glucose concentration response are displayed in Figure 4 and Figure 5 consecutively.

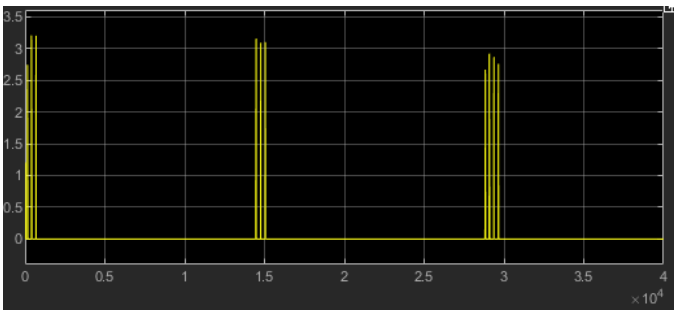

Fig. 4. Insulin Infusion Rate resulting from a P controller (Gain=-1.0) implemented in Feedback System

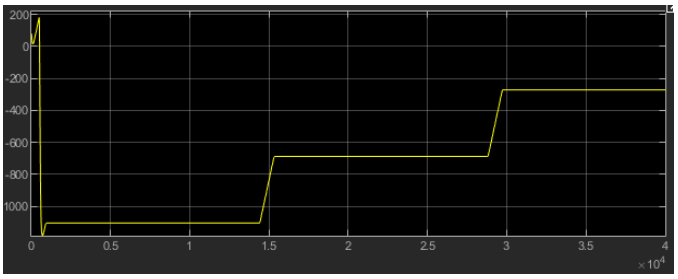

Fig. 5. Glucose Concentration Step-Response with a P controller (Gain=-1.0) implemented in Feedback System

Insulin rate increases proportionally to a high glucose concentration. However, strange oscillation is seen in insulin infusion. Infusion rate spikes and drops dramatically, indicating that the proportional term is likely far to high. The glucose response, seen in Figure 5, drops to below -1000 mg/decilitre after the first meal is completed. This further reinforces that the proportional term is extremely high.

It was found that the ideal P gain value is -0.00631, however, it can be seen that in Figure 6 that the steady-state value of glucose is below 70 mg/decilitre, thus not satisfying the design requirements. Adding a derivative gain to the controller allows for the controller to account for rates of change in error. Knowing if error is increasing or decreasing is essential to maintaining safe glucose levels, thus the group decided to implement a PD controller next.

C. Proportional-Derivative Controller

Although a necessary component, a proportional controller alone cannot achieve successful control over the insulin levels. Rapid fluctuations in insulin levels are detrimental to the health of the patient; as such, it is important to account for the rate of change in glucose level. In addition to this, a proportional controller will treat the patient the same regardless of if there is a steep decline or increase in error, or if the glucose level is stable slightly above or below the desired set point - both being satisfactory states for the system.

To solve this problem, a derivative gain is applied to make a proportional-derivative controller. This allows for the rate of change in glucose level to be included as a factor in the system's decision-making computation. In theory, this solution will cause a reduction in rapid glucose level fluctuations at the expense of altering the steady-state of the signal. To test this hypothesis, the group compares the results of the P and PD controllers in identical conditions.

1) P VS. PD Controller Simulations: The simulation results compare the effectiveness of a tuned P controller to a tuned PD controller for the insulin infusion control variable. The following settings are used to generate the results:

- (P Controller Gain)P: -0.00631
- (PD Controller Gain)P: -0.00629
- (PD Controller Gain)D: -0.60648
- (PD Controller Gain)Filter coefficient: 5.30589
- 50g of glucose is consumed every 4 hours
- Glucose consumed is modelled as a 15 minute pulse with an amplitude of 0.05556 (per second glucose absorption rate)
- Target glucose level is 81 mg/decilitre
- Initial glucose level is 70 mg/decilitre
- Lower bound infusion rate: 0 mg/decilitre
- Upper bound infusion rate: 10 mg/decilitre

Figures 6 and 7 contrast the differences in performance for an identical set-up of glucose concentration between P and PD controllers:

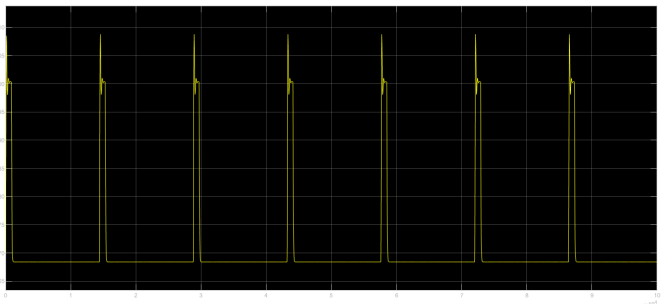

Fig. 6. Glucose Concentration response using optimized P-controller

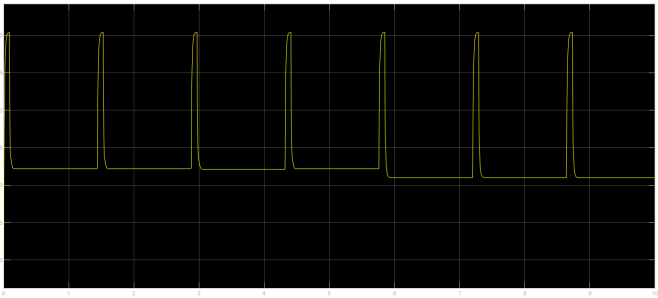

Fig. 7. Glucose Concentration response using optimized PD-controller

2) Simulation Analysis: It is clearly evident that the PD controller is superior to the P controller. In this example, the patient with the P controller will surely parish, as the glucose level drops and stabilizes below the minimum level of 70 mg/decilitre until the next disturbance, meaning it does not meet the control requirements. The PD controller seemed to be effective in this case; it was able to stabilize at a level close to that of the set-point, eventually converging to it.

To further verify the effectiveness of the PD controller, more scenarios must be tested. Figures 8 and 9 are two extreme examples of an initial value and how the system responds using the PD controller:

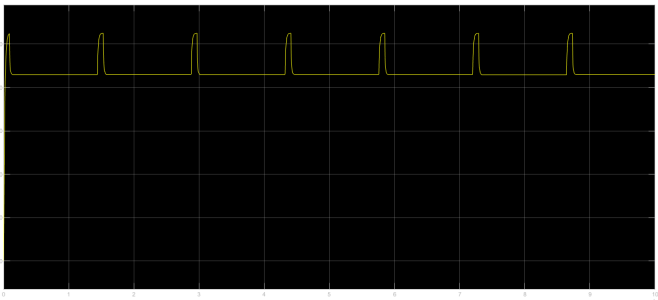

Fig. 8. Glucose Concentration response using optimized PD-controller with initial glucose level of 0 mg/decilitre

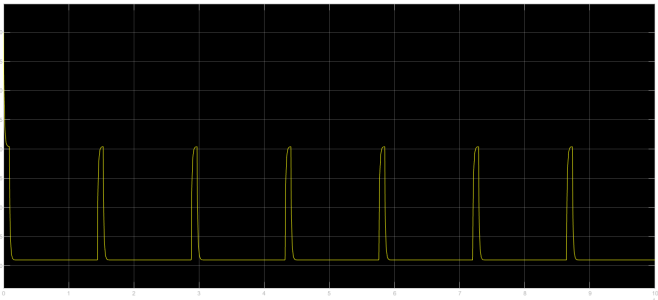

Fig. 9. Glucose Concentration response using optimized PD-controller with initial glucose level of 120 mg/decilitre

These two extreme examples both show promising results. In the case of an initial concentration of 0 mg/decilitre - which is impossible as the patient would surely not survive - the system stabilizes to a value that would sustain life for the patient. In the case of the initial concentration of 120 mg/decilitre, the system was able to stabilize converging on the set-point.

3) Improving Controller: Tuning on the controller design was done with the goal of converging the system to a safe value as rapidly as possible. This, however, leads to several undesirable factors in regards to the controller. One factor that is ignored is the rapid fluctuations when there is a system disturbance. The controller is able to adjust and approach the set-point after a disturbance but has high glucose levels while a disturbance is present. An ideal controller could account for this and maintain a glucose level closer to the set-point.

Another factor this controller does not account for is the possibility of long periods of high or low glucose levels in the body. To account for such periods of extended error, an integral gain term would need to be incorporated into the controller. In the following section, we discuss the viability of this, followed by experimental results of our investigation.

D. Proportional-Integral-Derivative Controller

In an attempt to improve on the design of the tuned PD controller, a PID controller was developed and tuned for the system. After preliminary results, it was concluded that the best results of the PID controller satisfies the control requirements, however, the PD controller performs significantly better in terms of smaller, less rapid fluctuations to glucose concentration. In addition to this, the PID has an increased steady-state error due to the integral term accumulating error over time.

The following settings are used in the simulations:

- P gain: -0.00611
- I gain: -2.652E-06
- D gain: -0.69333
- Filter coefficient: 5.98078548879919
- 50g of glucose is consumed every 4 hours
- Glucose consumed is modelled as a 15 minute pulse with an amplitude of 0.05556
- Target glucose level is 81 mg/decilitre
- Initial glucose levels are 0, 70, 120 mg/decilitre
- Lower bound infusion rate: 0 mg/decilitre
- Upper bound infusion rate: 10 mg/decilitre

Although Figure 12 shows potentially promising results, Figures 10 and 11 highlight the lack of effectiveness of the PID controller.

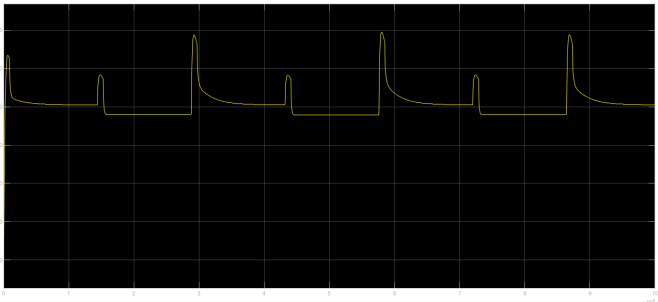

Fig. 10. Glucose Concentration response using optimized PID-controller with initial glucose level of 0 mg/decilitre

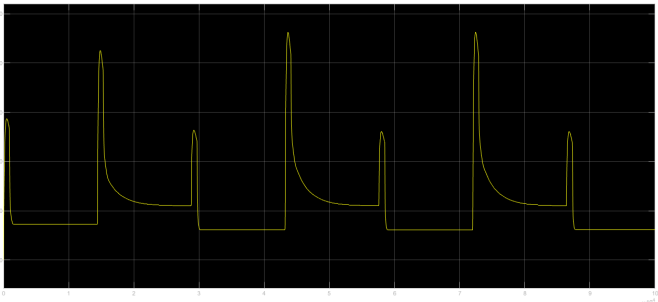

Fig. 11. Glucose Concentration response using optimized PID-controller with initial glucose level of 70 mg/decilitre

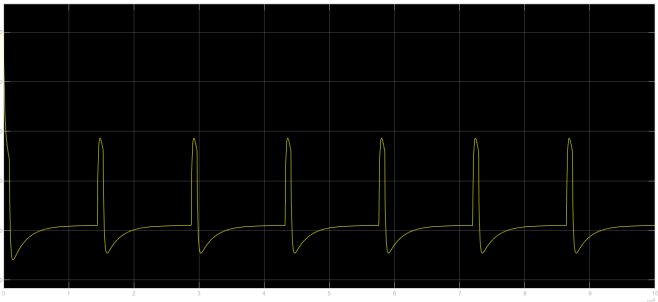

Fig. 12. Glucose Concentration response using optimized PID-controller with initial glucose level of 120 mg/decilitre

E. Feedback Control Conclusions

In regards to feedback control systems, it is clear that the proportional-derivative controller is the best for the proposed scenario. With this conclusion, the group investigates a hybrid feedback-feedforward control system that considers the amount of glucose being consumed by the patient, in which the integral term is incorporated in the feed-forward component.

IV. Robustness of Feedback Control System

To ensure patient safety is not in jeopardy, the system must be resilient to any signals it may encounter.

In previous simulations, the disturbance signal was modelled as the patient consuming 50g of glucose every 4 hours. This lumped sum of glucose was then assumed to be uniformly absorbed over 15 minutes for model simplicity. Although this is satisfactory for typical conditions, the control system must work for all scenarios a patient may encounter. As such, the group will investigate the ability for the controller to maintain a safe glucose level in non-expected scenarios.

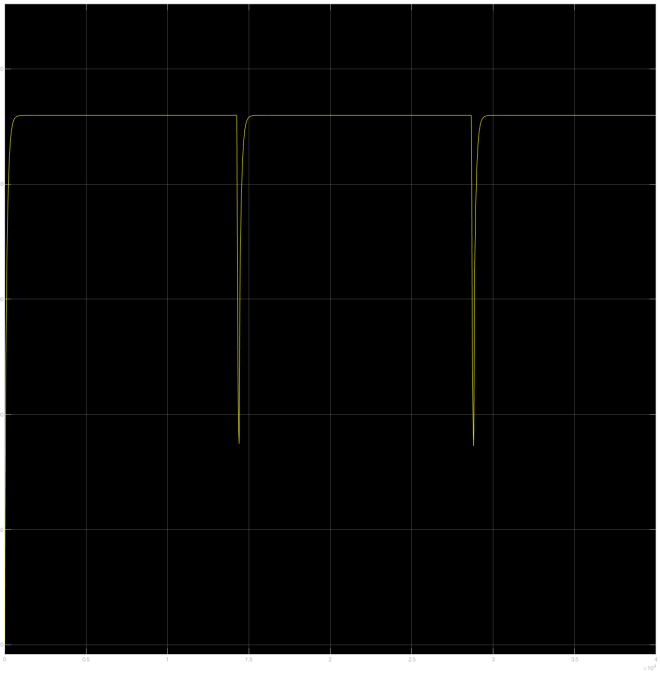

Fig. 13. Glucose Concentration response using optimized PD-controller with initial glucose level of 70 mg/decilitre with large disturbance

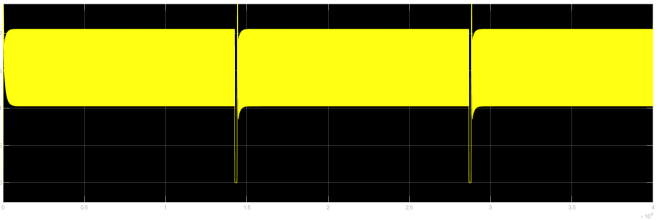

Fig. 14. Glucose Concentration response using optimized PD-controller with initial glucose level of 70 mg/decilitre with large disturbance

Figures 13 and 14 show how the system reacts to an unrealistically high disturbance input. As opposed to having a disturbance of 0.05556 for 15 minutes once every 4 hours, the disturbance was changed to a rate of 0.1 with a pulse width of 99% for a period of 4 hours. This converts to glucose being absorbed at a rate of 0.1 g/s, or 1,425.6 g every 4 hours over a period of 3 hours and 57.6 minutes, followed by 2.4 minutes of not eating. The results show that the system is stable and within the safe bounds, thus, the system is robust for input the patient could realistically consume.

It is important to note that the ability of the controller to tolerate such a unrealistic scenario suggests that this is most likely out of the linear region of the Bergman Model, and as such, the model is no longer valid in this region.

Although mathematically the control system model appears to be capable of robust disturbance rejection, this is likely due to the imperfections of the model.

V. Feed-Forward Control Design

In this scenario with the meal acting as a disturbance on the system there is an opportunity to create a feed-forward design to provide more control and stability to the system. A feed-forward design uses a detection signal of the disturbance occurring and sums it with the proportional derivative controller output. The system controller does not wait for the error to increase to react, but rather adjusts its insulin infusion rate based on the expected disturbance. The feed-forward design implemented can be seen in Figure 15.

- Feedback P gain: -0.008
- Feedback D gain: -0.75
- Feedback Filter coefficient: 6.55780
- Feedforward P gain: 0.0008
- Feedforward I gain: -6E-7
- 50g of glucose is consumed every 4 hours
- Glucose consumed is modelled as a 15 minute pulse with an amplitude of 0.05556
- Target glucose level is 81 mg/decilitre
- Lower bound infusion rate: 0 mg/decilitre
- Upper bound infusion rate: 0.25 mg/decilitre

The controller used for the feed forward was a PI controller due to its capability of ensuring the steady state error is as small as possible. This allows the system to respond faster while staying close enough to the ideal steady state of 81mg/deciliter glucose level. The feed-forward system needed a bit of time delay for the system to initially indicate the start of a meal so the meal timing was shifted by a couple seconds giving time to allow the controller to allow the feed-forward system to act, as can be seen in Figure 16.

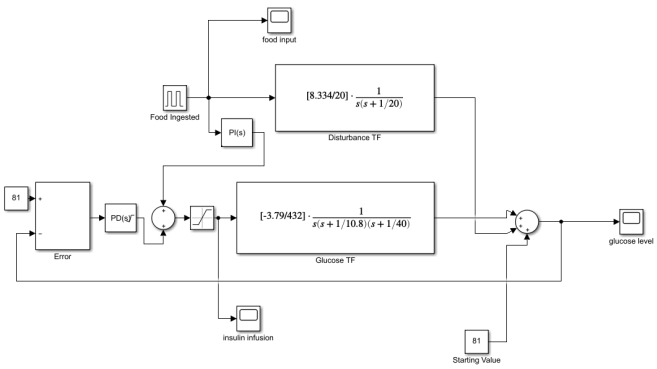

Fig. 15. Simulink Feed-Forward System Design

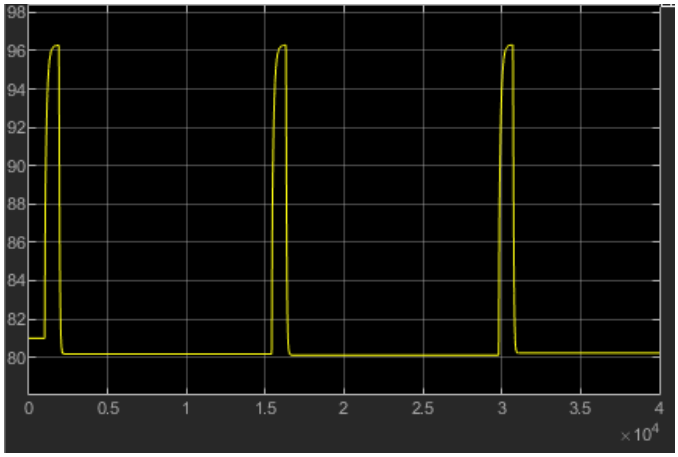

Fig. 16. Glucose Concentration response using tuned PD feedback controller in conjunction with an tuned PI feed-forward controller. Initial glucose level of 81 mg/decilitre

VI. Observations

A. Control Topology and Controller Selection

This process of investigating different control topologies and methods in this experiment provides valuable insight to the feasibility of implementing such controller systems to satisfy the system requirements. A PD feedback controller was ideal for the system model as there was limited undershoot compared to that of the PID feedback controller, while maintaining safe levels of operation unlike the P controller. As there was no firm constraint for upper bound diabetic glucose levels, the PD with occasional overshoot satisfies the systems requirements. Additionally, the PD control system also has a faster settling time than the PID controller. This provides greater overall stability as if meal timing is spaced closer than predicted, the PID system can become uncontrolled. This leads to the conclusion that a PD control system fits the requirements better than the PID system for closed-loop feedback.

B. Ideal VS. Real-World Models

Valuable insight in the limitations of models was also discovered, as the theoretical controller is capable of preserving safe levels even when realistically unsafe levels of glucose are consumed [4]. This highlights the limitations of the control system developed; a controller is only as good as the model used. The model is non-linear, however, can be approximated as linear within certain bounds. Due to the extreme tests conducted and the ability of the controller to maintain theoretically safe glucose levels, the model may not be accurate in such conditions.

Additionally, some controllers and scenarios resulted in rapid fluctuations in infusion rate of the insulin pump. Such rapid changes to the infusion rate may cause the actuator to fail, or not be able to produce the desired output in the time constraint. This would cause discrepancies between the real-world model and the simulated model, thus, the robustness of the real-world controller could not be guaranteed without real-world model validation.

VII. Future Works

Although satisfactory for the selected constraints, there are several potential improvements to the control system designed and implemented in this laboratory experiment.

The first potential improvement would be to add an integration term to the feed-forward proportional-derivative controller, effectively making it a proportional-integral-derivative controller. This was initially decided against due to the accumulation of glucose being consumed in meals over time, as this term would continuously increase instead of stabilizing at 0 as it is not an error, just a signal. To avoid this potential issue, however, an integral reset on rising pulses can be implemented. This would prevent accumulation over long periods of time that would greatly affect our set point and, inevitably, cause fatal injury to the patient by having an unbounded maximum glucose level.

Another factor lacking consideration in the model used is the biological differences between the male and female sexes. Biological differences between genders are often neglected, however, one approach to make the system more resilient would be to account for biologically different groups. This could be implemented using a multi-variable piece-wise function to select pre-tuned gains based on different selected values for sex, weight, and other biological differences [5].

Lastly, a potential improvement to the design would be limiting the rate of change for the automatic insulin pump. This work assumed an ideal actuator capable of rapid insulin infusion rate change. If actually implemented, the system would be limited by the speed which the actuator can adjust the infusion rate, thus, adjustments may be necessary for a real-world implementation of this controller using the Bergman model.

VIII. Conclusions

In conclusion, a PD feedback controller with a PI feed-forward controller was concluded to be the ideal control system for the Bergman Model used in this paper. Although satisfying all design requirements, the theoretical controllers may not necessarily be achievable in reality; limitations due to actuation speed, accuracy of the model, assumptions and simplifications made, and unanticipated real-world non-linearities create uncertainty in the feasibility of the approach. The proposed controller design provides a strong theoretical building block for future insulin pump control systems, however, actuator capabilities and investigation on fitness of the model is required to ensure safety of a real-world patient.

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