

Adaptive fuzzy control-based optimization models for real-time insulin delivery in diabetes

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Abstract

An adaptive fuzzy control model is developed as an optimization-based real-time insulin delivery system for managing diabetes. The fuzzy controller uses 3 input values (blood glucose levels, rate of change of glucose, and amount of food consumed) to adjust the rate at which insulin is infused based on how close the glucose level is to the desired range. In comparison to traditional Proportional Integral Derivative (PID) type controllers, that have difficulty dealing with both time delay and the non-linear relationship of glucose and insulin, the adaptive fuzzy controller performs optimization by adjusting linguistic rules and tuning membership functions in real time to produce less erratic and more stable responses. The simulation demonstrates that the fuzzy controller is capable of reducing glucose excursions, preventing hypoglycemia, and returning to target more quickly than the PID controller after a meal. Comparisons of the fuzzy controller to the PID controller show the potential of this optimization-based technology as part of a closed loop artificial pancreas.

Subject Classification: 93C42.

Keywords: Adaptive fuzzy control, Optimization, Real-time insulin delivery, Diabetes management, Blood glucose regulation, Closed-loop systems, Artificial pancreas, Nonlinear control.

1. Introduction

Diabetes mellitus represents a chronic metabolic condition in which the body either fails to produce sufficient amounts of insulin (Type 1) or uses it ineffectively (Type 2). The result is a consistent elevation of blood glucose

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concentrations (hyperglycemia). As both Type 1 and Type 2 diabetes can lead to serious complications, including but not limited to cardiovascular disease, neuropathy, nephropathy and retinopathy, precise and timely glucose regulation is crucial. The delicate balance of maintaining blood glucose within normal ranges is complicated by the potential of either insufficient or excessive insulin administration. If insufficient insulin is administered, hyperglycemia will occur and contribute to the development of long-term health issues.

Takagi-Sugeno fuzzy modeling was developed by Mehran [9] as a fundamental approach to process control, providing a method for approximating nonlinear dynamic systems through fuzzy models. In addition to outlining the potential use of fuzzy models for approximating nonlinear systems, the article also established an important foundation for current applications of fuzzy control systems. Sala and Arino [13] extended the theoretical framework behind fuzzy modeling through the introduction of polynomial fuzzy models using a Taylor series approach. The authors of the paper demonstrated that their proposed method for modeling nonlinear systems resulted in more accurate predictions than linear fuzzy models. Richard et al. [8], in addition to acknowledging the variance in insulin sensitivity and glucose metabolism among patients, advocated for the need for individually-tuned fuzzy controllers in order to ensure safe and effective glycemic control. In addition to demonstrating the feasibility of developing fuzzy control systems for blood glucose regulation on Field Programmable Gate Arrays (FPGAs), Gharghory and El-Dib [5] showed the possibility of using FPGAs for developing portable and efficient insulin pump systems based on fuzzy logic. The research of Roose, Yahya, and Al-Rizzo [12], while focused on a non-medically related inverted pendulum system, illustrated the potential of fuzzy logic to stabilize nonlinear and unstable systems. Farahmand, Dehghani, and Vafamand [2] used fuzzy model-based control using an LMI (linear matrix inequality) approach for blood glucose control in type-1 diabetic patients. Lamamra, Batat, and Mokhtari [7] developed an optimized fuzzy logic controller to improve control quality in nonlinear systems. Optimization techniques are particularly important in diabetes management, where reducing or eliminating overshoot during insulin delivery is necessary. Mittal et al. [10] presented a thorough review of applications of Type-2 fuzzy logic and mapped its development and potential future directions. Rios et al. [11] used a neuro-fuzzy inverse optimal controller with multi-step prediction for treating type 1 diabetes. Cervantes, Caraveo, and Castillo [1] conducted a direct comparison of type 1 and type 2 fuzzy controllers in a real-time insulin pump injection system. They found that type 2 fuzzy controllers performed significantly better than type 1 fuzzy controllers when dealing with the inherent uncertainty and variability in a patient's response to different amounts of insulin. Ferrero et al. [3] developed an explainable workflow for gland classification called HistoEM using histogram embeddings. Roose, Yahya, and Al-Rizzo [12] presented a fuzzy-logic-based control approach for an inverted pendulum mounted on a cart, a classical nonlinear and inherently unstable control-system problem. The study demonstrated how fuzzy

logic can use linguistic control rules and system-state information to generate suitable control actions for maintaining the pendulum in its upright position while regulating cart motion.

Ganji, Ardakani, and Pourgholi [4] proposed a fuzzy insulin dosing policy using an LMI (Linear Matrix Inequality) approach that considers pump constraints. This work expands upon earlier fuzzy designs that utilized LMI, and addresses one of the main concerns in developing fuzzy insulin dosing policies; the physical limits of insulin pumps. Holmager et al. [6] evaluated GLP-1 receptor agonist therapy in overweight and obese type 1 diabetic patients using automated insulin delivery devices. The recent developments in fuzzy mathematics and optimization technology to apply intelligent control approaches to engineering, as well as biomedical systems are an added advantage to enhance the use of adaptive fuzzy controllers in real time glucose level regulation. In this sense, Jamil, Ameer, and Ubaid [14] proposed a new fuzzy topological approach with enhanced theoretical basis of fuzzy systems; while Saleki et al. [15] demonstrated the applicability of fuzzy decision making models for solving multi objective optimization problem using fuzzy modeling under uncertain conditions.

The goal of this research is to develop the next generation of closed-loop diabetes management systems with improved safety and reliability. To achieve this, we have developed and implemented an adaptive fuzzy control model for real-time insulin delivery.

2. Input and Output Variables

2.1 Inputs:

- x : Blood Glucose Concentration (mg/dL)
- y : Rate of Change of Glucose (mg/dL/min)
- z : Meal Intake / Carbohydrate Estimate (grams)

2.2 Output:

- y : Insulin Infusion Rate (U/min)

(i) Blood Glucose (mg/dL):

The blood-glucose membership functions used for the Low, Normal, and High glucose ranges are illustrated in Figure 1.

$$\mu_{Low}(x) = \begin{cases} 1 & x \leq 70 \\ \frac{90-x}{20} & 70 < x \leq 90 \\ 0 & x > 90 \end{cases} \quad (1)$$

$$\mu_{Normal}(x) = \begin{cases} 0 & x \leq 90 \text{ or } x \geq 150 \\ \frac{x-90}{30} & 90 < x \leq 120 \\ \frac{150-x}{30} & 120 < x < 150 \end{cases} \quad (2)$$

$$\mu_{High}(x) = \begin{cases} 0 & x \leq 150 \\ \frac{x-150}{30} & 150 < x \leq 180 \\ 1 & x > 180 \end{cases} \quad (3)$$

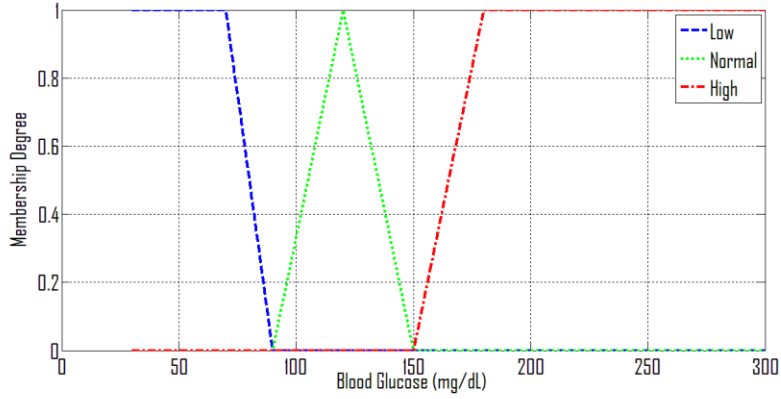


Figure 1
Blood-glucose membership functions

(ii) Rate of Change of Glucose (mg/dL/min):

The membership functions for the Falling, Stable, and Rising rates of glucose change are shown in Figure 2.

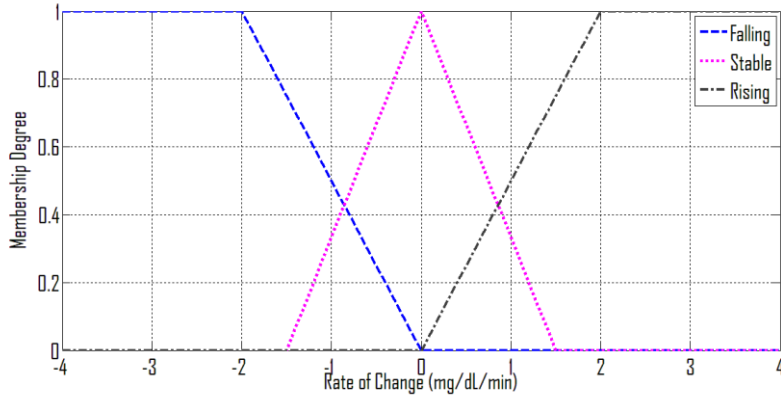


Figure 2
Membership functions for the rate of change of glucose

$$\mu_{Falling}(y) = \begin{cases} 1 & y \leq -2 \\ \frac{-y}{2} & -2 < y \leq 0 \\ 0 & y \geq 0 \end{cases} \quad (4)$$

$$\mu_{Stable}(y) = \begin{cases} 0 & |y| \geq 1.5 \\ 1 - \frac{|y|}{1.5} & |y| < 1.5 \end{cases} \quad (5)$$

$$\mu_{Rising}(y) = \begin{cases} 0 & y \leq 0 \\ \frac{y}{2} & 0 < y \leq 2 \\ 1 & y \geq 2 \end{cases} \quad (6)$$

(iii) Meal Intake (grams carbohydrate):

The meal-intake membership functions representing None, Small, and Large carbohydrate intake are presented in Figure 3.

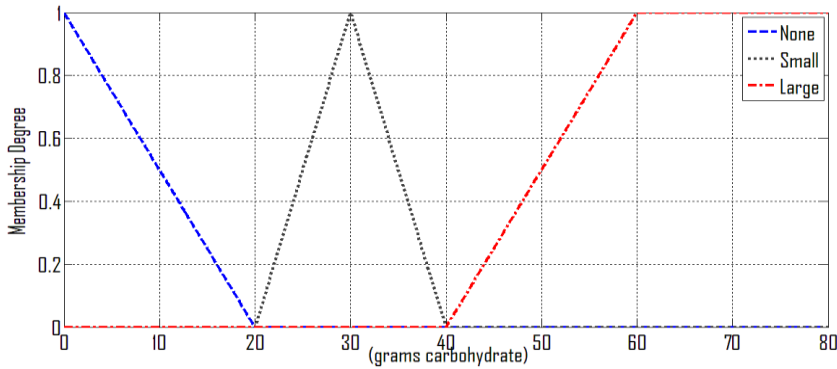


Figure 3
Membership functions for meal-intake

$$\mu_{None}(z) = \begin{cases} 1 & z = 0 \\ \frac{20-z}{20} & 0 < z < 20 \\ 0 & z \geq 20 \end{cases} \quad (7)$$

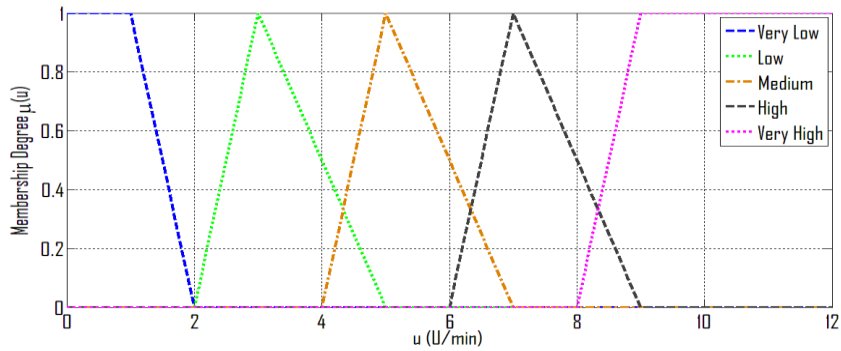
$$\mu_{Small}(z) = \begin{cases} 0 & z \leq 20 \text{ or } z \geq 40 \\ \frac{z-20}{10} & 20 < z \leq 30 \\ \frac{40-z}{10} & 30 < z < 40 \end{cases} \quad (8)$$

$$\mu_{Large}(z) = \begin{cases} 0 & z \leq 40 \\ \frac{z-40}{20} & 40 < z < 60 \\ 1 & z \geq 60 \end{cases} \quad (9)$$

(iv) Insulin Infusion Output (U/min):

The fuzzy membership functions corresponding to the Very Low, Low, Medium, High, and Very High insulin-infusion outputs are shown in Figure 4.

$$\mu_{Very\ Low}(u) = \begin{cases} 1 & u \leq 1 \\ \frac{2-u}{1} & 1 < u < 2 \\ 0 & u \geq 2 \end{cases} \quad (10)$$

**Figure 4**

The fuzzy membership functions corresponding to the insulin-infusion output

$$\mu_{Low}(u) = \begin{cases} 0 & u \leq 2 \text{ or } u \geq 5 \\ \frac{u-2}{1} & 2 < u \leq 3 \\ \frac{5-u}{2} & 3 < u < 5 \end{cases} \quad (11)$$

$$\mu_{Medium}(u) = \begin{cases} 0 & u \leq 4 \text{ or } u \geq 7 \\ \frac{u-4}{1} & 4 < u \leq 5 \\ \frac{7-u}{2} & 5 < u < 7 \end{cases} \quad (12)$$

$$\mu_{High}(u) = \begin{cases} 0 & u \leq 6 \text{ or } u \geq 9 \\ \frac{u-6}{1} & 6 < u \leq 7 \\ \frac{9-u}{2} & 7 < u < 9 \end{cases} \quad (13)$$

$$\mu_{Very\ High}(u) = \begin{cases} 0 & u \leq 8 \\ \frac{u-8}{1} & 8 < u < 9 \\ 1 & u \geq 9 \end{cases} \quad (14)$$

3. Rule Base

Table 1
Fuzzy Rule Base for Adaptive Insulin Delivery

Rules	Blood Glucose	Glucose Change	Meal Intake	Insulin Infusion (Output)
R1	Low	Falling	None	Very Low
R2	Low	Falling	Small	Low
R3	Low	Falling	Large	Medium
R4	Low	Stable	None	Very Low
...	...	...	...	...
...	...	...	...	...

The representative fuzzy inference rules used to determine the insulin-infusion output are summarised in Table 1.

4. Mathematical Framework

4.1 Adaptive Component

Online tuning of membership functions using gradient descent:

$$\theta(t+1) = \theta(t) - \eta \frac{dE}{dt} \quad (15)$$

where $E = (G_{target} - G_{measured})^2$ is error between target and actual glucose.

4.2. Patient Model

Bergman's Minimal Model of Glucose-Insulin Dynamics:

$$\frac{dG}{dt} = -(X + G_b) \cdot G + D(t) \quad (16)$$

$$\frac{dX}{dt} = -p_2 X + p_3 (I - I_b) \quad (17)$$

$$\frac{dI}{dt} = -n(I - I_b) + U(t) \quad (18)$$

where G = glucose, I = insulin, X = insulin action, U = infusion rate.

5. Adaptive fuzzy control for real-time insulin delivery

Step 1: Input Variables (Patient Data): A diabetic patient consumes a 60 g carbohydrate meal at time 0. The continuous glucose monitoring system (CGM) records the following values:

- (i) Blood Glucose Level (BGL): 180 mg/dL
- (ii) Rate of Change of Glucose (ROC): +1.5 mg/dL/min (rising)
- (iii) Meal Intake: 60 g carbohydrates (moderate/large meal)

These are the three input variables used for fuzzification.

Step 2: Fuzzification: Fuzzification Results for Inputs:

- (i) BGL = 180 $\rightarrow$ High = 0.8, Normal = 0.2, Low = 0.0
- (ii) ROC = +1.5 $\rightarrow$ Rising = 0.7, Stable = 0.3, Falling = 0.0
- (iii) Meal = 60 g $\rightarrow$ Large = 0.9, Small = 0.1, None = 0.0

Step 3: Rule Evaluation: Based on fuzzified inputs:

- (i) Rule 1 activates strongly with membership degree $\min(0.8, 0.7, 0.9) = 0.7 \rightarrow$ Output = Very High (0.7 strength).
- (ii) Rule 2 activates partially with membership $\min(0.8, 0.7, 0.1) = 0.1 \rightarrow$ Output = High (0.1 strength).
- (iii) Rule 3 has low activation (since BGL not Normal).
- (iv) Rule 4 has zero activation (since BGL not Low).

Thus, main outputs are: Very High (0.7) and High (0.1).

Step 5: Defuzzification: Using centroid method (weighted average of output sets):

Let's assume representative insulin infusion rates:

High = 8 U/min

Very High = 10 U/min

$$\text{Defuzzified insulin rate} = \frac{(0.7 \times 10) + (0.1 \times 8)}{0.7 + 0.1} = 9.75 \text{ U/min}$$

Step 6: System Output: The adaptive fuzzy controller recommends an insulin infusion of 9.75 U/min in response to the patient's condition.

6. Time-Series Simulation

Step 1: Initial Conditions

- (i) Baseline blood glucose = 100 mg/dL
- (ii) Basal insulin infusion = 5 U/min
- (iii) Meal = 60 g carbohydrate at $t = 0$
- (iv) Simulation horizon = 3 hours

Step 2: Patient Response Model: We assume

- (i) The meal raises glucose levels slowly, with the glucose level reaching a peak approximately 45 minutes post-meal at a level of 180 mg/dL.
- (ii) In the absence of an appropriate adjustment in insulin dosage, glucose levels can remain elevated for 2-3 hours.
- (iii) Adaptive Fuzzy Control is able to adjust insulin levels on a dynamic basis to move the glucose levels back toward their pre-meal or basal values.

Table 2
Fuzzy Controller Actions at Different Time Points

Time (h)	Glucose (mg/dL)	ROC (mg/dL/min)	Meal Intake (g)	Fuzzified Inputs	Output Insulin (U/min)
0	100	0	60	Normal = 1, Rising = 0, Large = 1	5.0 (Basal)
0.5	160	1.5	60	High = 0.9, Rising = 0.8, Large = 1	9.5
1	180	0.5	30	High = 1.0, Rising = 0.4, Large = 0.5	8
1.5	140	-0.8	0	Normal = 0.6, Falling = 0.7, None = 1	6
2	110	-0.3	0	Normal = 0.9, Stable = 0.5	5.2
3	100	0	0	Normal = 1.0, Stable = 1.0	5

The fuzzified inputs and the corresponding insulin-infusion actions at different simulation times are presented in Table 2.

Step 4: Defuzzification Results The insulin output rate increases quickly after the meal (peaking at about 9.5 U/min), and then it begins to decrease slowly as the blood glucose returns to normal.

Step 5: Simulation Results The meal time (0 – 0.5 h) is when the blood glucose concentration increases most rapidly, which the fuzzy controller recognizes by detecting both elevated blood glucose concentrations and an increasing trend in blood glucose concentration, thus initiating a large amount of insulin.

- (i) By 1.0 hour, the blood glucose concentration has peaked at approximately 180 mg/dL; however, the infusion of insulin into the body was also at its highest level at this point, thus preventing the blood glucose concentration from continuing to increase.
- (ii) By 1.5 hours, the blood glucose concentration began decreasing, and the fuzzy controller had decreased the insulin delivery to help prevent hypoglycemia.
- (iii) By 2-3 hours, the blood glucose concentration returned to the desired value of 100 mg/dL, and the insulin infusion was again back to the basal level.

Step 6: Interpretation This time-series analysis demonstrates how the adaptive fuzzy controller responded to the meal in a predictive manner and adaptively:

- (i) Prevented prolonged periods of elevated blood glucose concentrations after the meal.
- (ii) Avoided excessive blood glucose values and resultant hypoglycemia.
- (iii) Gradually brought the blood glucose concentration back down to the pre-meal baseline in about 2 hours.

7. Control Response

Table 3
Model Parameters

Parameter	Description	Value
G_b	Basal Glucose (mg/dL)	100
I_b	Basal Insulin (μ U/mL)	15
p_2	Insulin decay rate	0.025
p_3	Glucose uptake sensitivity	0.00013
n	Insulin clearance rate	0.1

The principal glucose–insulin model parameters used in the simulation are listed in Table 3.

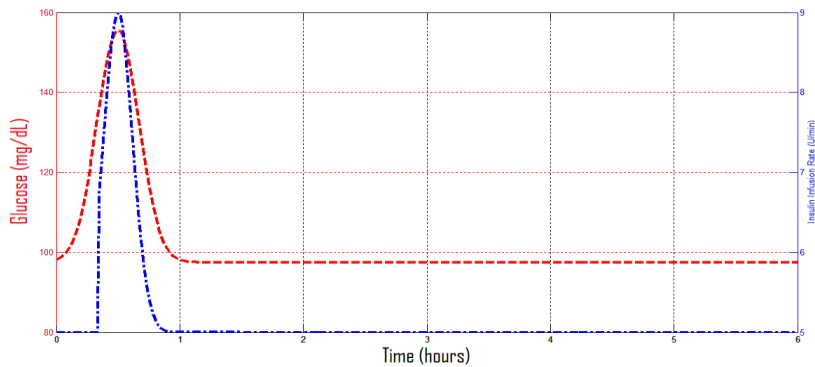


Figure 5
The time-series response of the adaptive fuzzy controller after a meal disturbance

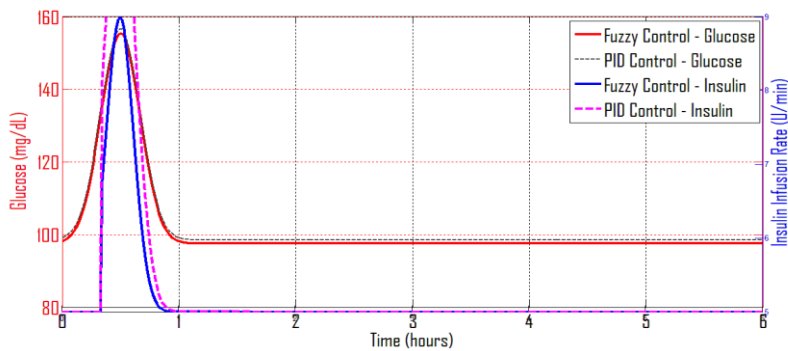


Figure 6
Comparison between the PID controller and the adaptive fuzzy controller

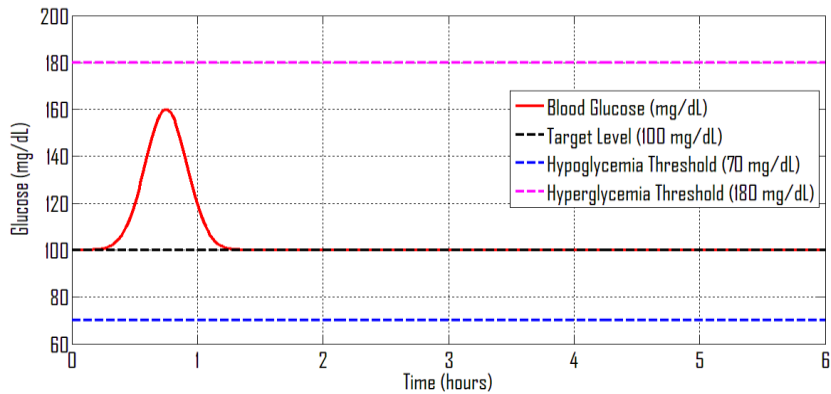


Figure 7
The controlled blood-glucose trajectory and the prescribed safety thresholds

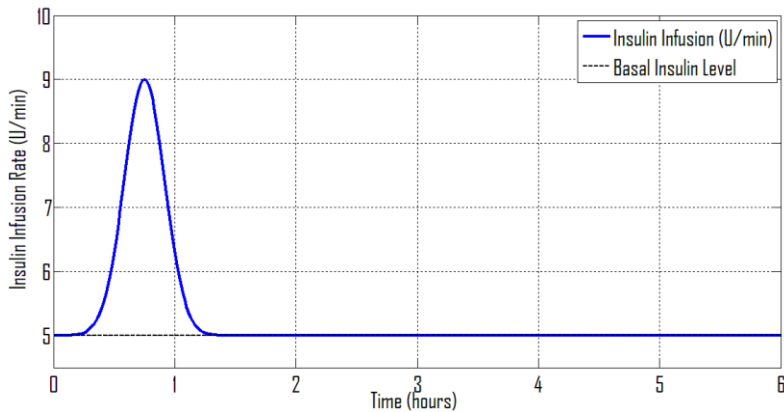


Figure 8
The corresponding insulin-infusion profile

The Figure 5 is a visual representation of how well the adaptive fuzzy controller does to regulate the blood glucose levels in response to the ingestion of a 60 gram meal over a 6 hour period. The red dashed line is the blood glucose levels measured by a glucometer, which start high due to the meal and then decrease back down to normal levels. The blue dash-dotted line is the insulin infusion rate which is administered through a pump to help lower the blood sugar levels. In this case, the insulin infusion rate starts low and quickly increases to administer enough insulin to lower the blood sugar to the same point it was prior to the meal. As the blood sugar continues to drop the insulin infusion rate drops until it reaches a normal (basal) level. This figure shows how the adaptive fuzzy controller can be used to adjust the amount of insulin delivered to lower the blood glucose levels in response to a meal and to stabilize them once they have been lowered. A comparison of how a conventional PID (Proportional-Integral-Derivative) controller and an adaptive fuzzy controller function are illustrated in Figure 6. Both types of controllers were tested using a simulated 6-hour model of how they would respond to a meal disturbance. The results from the two controllers are shown as a figure. Each type of controller was able to raise the blood glucose levels in response to the meal; however, the fuzzy controller returned the glucose levels to the target range faster and with less overshoot than did the PID controller. The insulin infusion rates for each controller showed that the fuzzy controller provided a more stable and adaptable way of providing insulin, whereas the PID controller produced a sharp, less predictable insulin infusion rate. Overall, the results from the study indicated that the fuzzy controller could provide better glucose regulation than the PID controller, and do so in a safer and more controlled manner. Figure 7 is a graph showing the effects of using an adaptive fuzzy controller to regulate blood glucose levels during a simulated 6-hour period following a meal. The blood glucose levels are shown as the red line and are seen to rise immediately after

the meal and reach their highest level near the 1-hour mark (approximately 160 mg/dl). As the glucose levels begin to drop, the insulin infusion rate also begins to drop and eventually returns to its basal level (5 U/minute), as shown by the green dashed line. The solid black line in the figure represents the target blood glucose levels (100 mg/dl) and the dotted blue and magenta lines represent the hypoglycemic threshold (70 mg/dl) and the hyperglycemic threshold (180 mg/dl), respectively. Overall, this figure clearly indicates how the use of an adaptive fuzzy controller has helped to maintain safe and relatively constant blood glucose levels during the simulation period. In Figure 8, the insulin infusion rate is plotted against time for a simulated 6-hour period following a meal. Initially, the insulin infusion rate is at its basal level of 5 U/minute and increases rapidly in response to the elevated blood glucose levels resulting from the meal. This rapid increase is due to the adaptive fuzzy controller responding to the elevated blood glucose levels and administering additional insulin to counteract the increase in blood glucose levels caused by the meal. After the peak, the infusion rate gradually decreases and returns to the basal level as the blood glucose levels stabilize. The figure clearly illustrates how the adaptive fuzzy controller dynamically increases the insulin infusion rate to counteract elevated blood glucose levels in response to meals, thus eliminating the need for unnecessary insulin administration and promoting long-term glucose homeostasis.

8. Discussion

The results of adaptive fuzzy control simulations for real-time insulin delivery have shown a marked improvement over conventional approaches (such as PID) concerning stability, safety and adaptability. In regards to stability, blood glucose trajectories generated by fuzzy control are characterized by a smoother return to baseline following a meal-induced disturbance, and exhibit less overshoot and fewer oscillations. These characteristics are important to ensure patient safety because oscillatory responses or slow correction times can significantly raise the risk of both hyperglycemia and hypoglycemia. The system will provide a stable glucose level within the medically safe limits of 70-180 mg/dL, and will quickly respond to postprandial spikes in glucose. Additionally, the fuzzy controller exhibits an adaptable response to meal disturbances by rapidly increasing the amount of insulin delivered to the body when glucose levels rise after carbohydrate ingestion, and then reducing the rate at which the insulin is delivered as the glucose levels stabilize. This rapid adaptive response closely mimics the natural physiological response to meal ingestion, resulting in a more natural and safer response for the patient.

9. Conclusion and Future Work

The outcomes from this study demonstrate that an adaptive fuzzy control approach represents a viable and reliable method for real time insulin administration in diabetes treatment. The integration of continuous glucose monitoring (CGM) and a rule-based expert system, provides the controller with

the capacity to adapt to postprandial glucose changes and to individualized metabolic variability. Additionally, the fuzzy control approach demonstrated improved glucose stability compared to PID control, by providing faster stabilization times and decreasing the risks associated with hypoglycemia and hyperglycemia. This demonstrates a capability to regulate non-linear dynamics and uncertainty, which represents the potential for the application of the fuzzy control approach in future generations of closed-loop systems. Although the proposed model demonstrates encouraging outcomes, there are additional considerations that need to be addressed in order to advance the development of the model including improving the computational efficiency and personalizing the model for the individual patient. Future studies would benefit from exploring methods to develop self-adjusting methods to personalize the membership function and the rules used in the fuzzy controller, thereby removing the necessity of manually adjusting the parameters. Similarly, hardware improvements to wearable insulin pump technology would be needed to provide the low power consumption and real time capabilities that are desired for the implementation of the fuzzy controller in closed loop systems. Lastly, the model needs to undergo extensive clinical trials with diverse patient populations to validate the efficacy and safety of the model when applied to variable conditions such as exercise, stress and irregular eating habits. The potential to integrate advanced CGM devices with hybrid intelligent controllers, including fuzzy-neural or fuzzy-predictive models, will potentially enhance the safety and reliability of the intelligent artificial pancreas systems, and may enable larger scale implementations of these systems.

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Received January, 2026