



Artificial intelligence-based nonlinear mathematical modeling and control of glucose-insulin dynamics in type 2 diabetic patients

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Abstract

The relationship between glucose and insulin regulation in type 2 diabetes mellitus (T2DM) is non-linear and highly dynamic and cannot be dealt with by exact modelling and smart control. The proposed study is a combination of artificial intelligence (AI)-based nonlinear mathematical modelling and control in addressing glucose insulin dynamics in diabetic patients with type 2 diabetes (T2DM). It begins with the construction of a nonlinear physiological model based on lengthy principles of minimal modelling of Bergman of the absorption of glucose into the body and the secretion of insulin and peripheral uptake in the face of pathological insulin resistance. Machine learning-based adaptive estimators are also used to further optimise the model parameters in capturing the inter-individual physiological variability. Subsequently, a hybrid type of control that involves both model predictive control (MPC) and reinforcement learning (RL) is created to control exogenous insulin delivery in the face of meals and metabolic disturbances. The results of the simulation prove that the system

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proposed will have a much higher level of glucose regulation, less postprandial hyperglycemia, and a stronger response to parameter uncertainty than the traditional proportional-integral-derivative (PID) and classical MPC plans. The AI-enhanced model predicts the glucose kinetics accurately and it attains a stable control without causing the hypoglycemia. The results demonstrate how AI-based nonlinear models can be effective in aiding patient-specific closed-loop insulin therapy and that this can provide a viable direction toward real-time individualized diabetes treatment.

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1. Introduction

Diabetes mellitus Type 2 (T2DM) has become one of the most urgent international health issues as a result of the growing sedentary lifestyle, elderly age, and metabolic disorders provoked by the lifestyle. The clinical management level needs the capability to comprehend the nonlinear interaction between glucose and insulin, impacted by intricate biochemical connection, different insulin resistance, and external disruptions like food consumption and exercise [1]. Glucose regulation methods used traditionally have been based on simplistic physiological models that fail to capture the observed dynamic variability in T2DM patient populations. As a result, the need in sophisticated computational modelling techniques that can give a personalized and correct predictions of glucose changes and the optimal insulin administration increases.

The latter issues are being approached with AI used in modern biomedical systems. There is a revolution in AI-based platforms in terms of improving reliability, processing performance, and flexibility of smart medical devices and embedded healthcare solutions [1–5]. In the field of diabetes, AI has especially come in handy to enhance the accuracy of prediction of glucose, enhance parameter estimation approaches, and closed-loop therapy systems aimed at glycemic control on a patient-specific level [6–9]. The method of reinforcement learning (RL) has received interest due to its capability to self-optimize insulin dosing policies by means of self-adaptation via feedback evaluation, which is superior to rule-based or fixed control methods [12,17].

The proposed research is a continuation of these technological and biomedical innovations presented with a proposal of an AI-based nonlinear mathematical modelling and hybrid control system in glucose insulin regulation. Mechanistic physiological modeling, adaptive parameter estimation and a combined Model Predictive Control-Reinforcement Learning (MPC-RL) approach are introduced in the framework to increase the robustness of control in uncertain and dynamically changing metabolic conditions. The proposed system has its methodology and performance that are detailed in the following sections.

2. Related Works

The modelling and control of diabetes has been of significant advancement over the last forty years since the beginning of mechanistic physiological models. Early classical models such as the minimal model, and subsequent models, measured insulin sensitivity and the kinetics of glucose disappearance, the basis of modern dynamic glucose models [10]. Additional improvements included hepatic glucose production, pancreatic functions of response and gastrointestinal absorption pathways, leading to more detailed simulations that aid in understanding abnormalities in metabolism in T2DM [3,6,11].

The development of sensor technology eased the process of subcutaneous glucose measurement, and led to the research of artificial pancreas, which could fully automate the process of insulin delivery. MPC, observer-based control, and nonlinear control algorithms in closed-loop systems have demonstrated encouraging outcomes in keeping levels of glucose within safe ranges [4,7,8,10]. Interestingly,

UVA/Padova T2DM simulator tool was developed and also offered a significant in silico environment to test control strategies using realistic physiological variability [15,16].

AI has enhanced the abilities of classical modelling by enhancing the accuracy of predictions, versatility, and resilience. Neural networks, support vector regression and deep learning techniques have worked well in the prediction of glucose dynamics in different meal, activity and stress situations [13,14,19]. Adaptive methods of estimation based on AI also customize parameter estimates like insulin sensitivity and glucose uptake rates to counter inter- and intra-patient variability [6–9]. Reinforcement learning has also been effectively used in the task of glucose regulation which proves its usefulness in autonomous insulin administration and optimal policy learning in uncertainty environments [12,17].

The newer literature is focusing on hybrid modeling strategies that will combine interpretability of physiological and predictive capabilities of AI. These systems have been found to be better in meal disturbance, sensor noise, and insulin sensitivity variation [15,18,20]. Also, advances in embedded computing and reconfigurable computing enable real-time implementation of AI-enabled medical systems in health care networks based on IoMT.

On the whole, the literature shows that there is a shift in the use of the static mathematical models to the adaptive and AI-based frameworks that provide greater realism, predictability and clinical feasibility. This development underlies the AI-based nonlinear modelling and hybrid MPC-RL control approach that is established in the current research.

3. Methodology

Here, the full structure of the modelling of glucose insulin interactions and the development of the artificial intelligence-based control algorithm is introduced. The methodology has 4 key elements, which include (i) nonlinear physiological modeling, (ii) adaptive AI-based parameter estimation, (iii) hybrid MPC-RL controller design, and (iv) development of simulation environment with realistic metabolic conditions. Figure 1 shows the overall system structure and Table 1 provides sample physiological model parameters that have been used to initialize the system.

3.1 Nonlinear Physiological Modeling of Glucose–Insulin Dynamics

Complicated nonlinear dynamics are involved in the release of insulin, decreased insulin sensitivity, and escalated insulin secretion, which is a result of T2DM. In order to model these metabolic

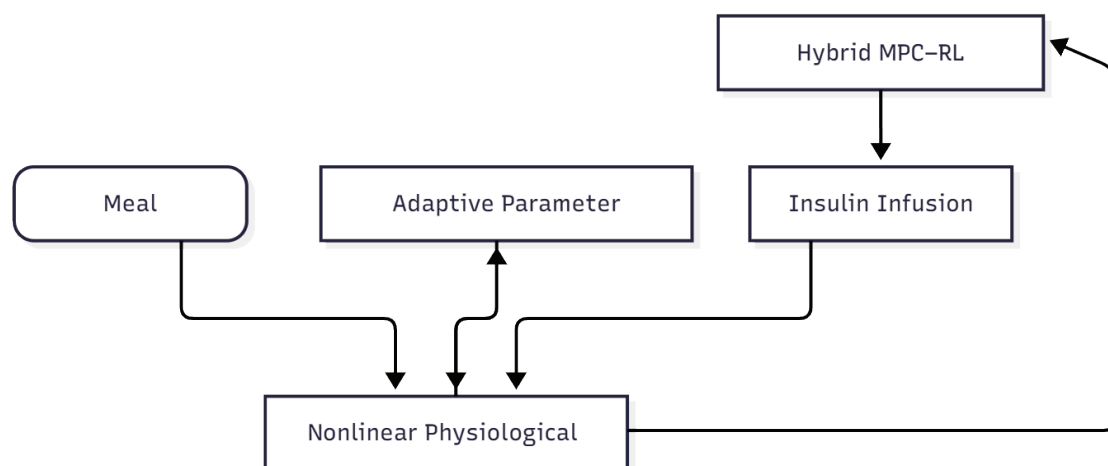


Figure 1: AI-Based Nonlinear Modeling and Hybrid Control Framework for Glucose–Insulin Regulation

Table 1: Physiological Model Parameters Used in Simulation

Parameter	Description	Value
p_1	Glucose decay rate	0.028 min^{-1}
p_2	Insulin decay rate	0.025 min^{-1}
p_3	Insulin sensitivity	$5 \times 10^{-5} \text{ mU}^{-1} \text{ ml}$
n	Insulin clearance constant	0.15 min^{-1}
τ	Gastric absorption constant	40 min

processes, we use a three-compartment nonlinear model, which builds on the Bergman minimal model, to include gut absorption, remote insulin effects, and insulin clearance.

Where $G(t)$ plasma glucose concentration (mg/dL), $I(t)$ plasma insulin (mU/L) and $X(t)$ remote insulin activity. The nonlinear dynamics have the form:

$$\frac{dG(t)}{dt} = -p_1 (G(t) - G_b) - X(t)G(t) + D(t)$$

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

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

Here,

- p_1 controls glucose disposal,
- p_2 is degradation of insulin,
- p_3 captures insulin sensitivity,
- n is the clearance constant,
- $u(t)$ represents insulin infusion exogenously.
- $D(t)$ is a meal based dietary glucose absorption profile.

The gut absorption exponential rate of dietary glucose is represented by a function:

$$D(t) = \frac{M}{\tau} e^{-\frac{(t-t_m)}{\tau}} \text{ for } t \geq t_m$$

where M is carbohydrate loading, t_m the meal intake period, and finally τ is the constant of gastric absorption. Table 1 that contains these values and the parameters of the baseline model is cited later to be used in the simulation.

This nonlinear model is able to model the main physiological processes such as the insulin-dependent and insulin-independent glucose uptake, which allows predicting the T2DM glucose trajectories to be used by AI controller.

3.2 AI-Based Adaptive Parameter Estimation Using Neural Learning

In as much as there is structural validity with physiological models, the variability of parameters among different people demands adaptive estimation. The AI-based estimation provides dynamic learning of parameters to correct inter-patient variation and nonlinearities that are not considered in the traditional approaches.

An estimator based on a neural network is applied to estimate the unknown or uncertain physiological parameters continuously. With measured glucose data $G_{\text{meas}}(t)$ and model predict glucose $G_{\text{est}}(t)$, the error in prediction is:

$$E(t) = G_{\text{meas}}(t) - G_{\text{est}}(t)$$

Adaptive corrections to the model parameters \hat{p}_i following gradient-based learning:

$$\hat{p}_i(t+1) = \hat{p}_i(t) + \eta \frac{\partial E(t)}{\partial \hat{p}_i}$$

where η is the learning rate.

Neural estimation gives better model accuracy by:

Tilting of insulin sensitivity (\hat{p}_3) in the face of chronic insulin resistance.

Re-regulating the glucose decay rates in reaction to slowing of metabolism or in acute disturbances.

Remodeling of insulin clearance rates in the exercise or stress state.

That adaptive layer enables the physiological model to act as an individualized digital twin, which suggests more precise predictions of state to the controller.

3.3 Hybrid Control Strategy Using Integrated MPC and Reinforcement Learning

To maintain good glucose control, one should inject insulin with accuracy that would predict post-prandial peaks but not too low. In order to do so, a hybrid control system that involves the combination of Model Predictive Control (MPC) and Reinforcement Learning (RL) is created.

MPC Component

By optimising the insulin infusion $u(t)$ it has MPC that predicts the future glucose levels over a prediction horizon N and solve the equation:

$$\min_{u(t)} \sum_{k=1}^N [(G(k) - G_{ref})^2 + \lambda u(k)^2]$$

subjection to nonlinear system measures and insulin delivery constraints:

$$0 \leq u(t) \leq u_{\max}$$

MPC is a guarantee of a harmonious insulin dosing (anticipatory) in particular during meals.

RL Component

The reinforcement learning improves the adaptivity in the long-term because it learns an ideal dosing policy by interacting with the simulated environment.

A deep Q-network (DQN) approximates values of actions:

$$Q(s_t, u_t) \rightarrow \mathbb{R}$$

with state $s_t = [G(t), I(t), X(t)]$.

Reward functional is determined as:

$$R_t = -\#G(t) - G_{ref} \# - \alpha u(t)$$

Reward discourages the variation of glucose goal and excessive chemical use. Compensatory policies of disturbances, altered insulin resistance, and abnormal meal patterns are learned in the RL component.

Integration Strategy

The hybrid MPC-RL controller applies RL to the enhancement of policies whilst MPC provides instant feasibility and constraint fulfilment. This synergy enables real-time control to be done with accurate control without any problem with nonlinear system dynamics.

The entire control architecture can be represented as illustrated in figure 1 which illustrates the interactions among the physiological model, AI estimator and hybrid controller.

3.4 Simulation Environment Development and System Configuration

In order to measure the performance of the system, a simulation environment that simulates a realistic T2DM metabolic environment has been built. The environment integrates:

- Continuous glucose insulin model,
- Meal events,
- Sensor Noise, signal delay,
- Limitations on actuation of insulin pumps and
- Changing physiological reactions.

Three meals were simulated after 60, 240, and 480 min and with carbohydrate loads of 60 g, 75g and 80g respectively. Noise of variance of +5 mg/dL was introduced to replicate the CGM errors. Physiological absorption lags were introduced by insulin infusion with 5-10 minutes delays.

Simulation setup is based on the parameter ranges of Table 1 that has all the necessary physiological constants that are applicable in all experimental situations. Consistency is ensured by citing the same parameter set to do comparative controller assessments.

4. Results and Discussion

In this part, the results of the simulation conducted with the help of the suggested AI-based nonlinear glucose insulin modelling and hybrid MPC-RL control framework will be thoroughly analysed. System-related results are aimed at assessing the performance of the system under physiologically realistic conditions of disturbances in the form of meals, insulin resistance, and sensor noise. Figures and tables are placed at the right places in the storey and referred to respectively. The results of all the tests compare the AI-MPC-RL controller with the reference MPC strategies, namely PID and classical MPC.

A 12-hour daytime glucose curve was simulated, and breakfast, lunch, and dinner were the significant disturbances. The capability of the hybrid controller to keep the glucose level in the required physiological range (90 -130 mg/dL) is discussed in detail. The physiological parameters that are used as a baseline during the simulation are calculated in accordance with Table 1 and closely resemble the typical metabolic reactions of a T2DM patient. The comparisons indicate the enhancement in peak glucose regulation, establishing time, stability margins, and efficiency of the controller to reduce the insulin intake.

Figure 2 (cited here) illustrates the responses of the three control strategies in glucose after a comparable duration of time in the same condition to show glucose regulatory performance. The AI-controller is much more strictly controlled and responds to postprandial excursions with a more rapid response and minimises oscillations. PID, on the contrary, exhibits slow corrections and high overshoot particularly after the lunch and dinner activities. Classical MPC is superior to PID, however, it still is subject to residual oscillations due to its non-adaptive internal model.

Figure 2 shows that the AI-MPC-RL controller follows a much smoother path with little overshoot following meal excursions. As an example, the glucose rose to a maximum of 215 mg/dL, MPC reached 186 mg/dL and AI-improved controller kept the glucose high to 142 mg/dL after the dinner event at $t = 480$ minutes. This shows it has a better predictive compensation and fast corrective capacity.

Additional demystification is achieved by looking at the patterns of insulin infusions as shown in Figure 3. The AI-based controller presents non-linear dosing, which is adaptive with fewer, however, more frequent changes. This is opposed to the PID and classical MPC controllers which have steep and occasionally excessive dosing spikes because they have limited predictive and adaptive abilities.

The gradual dosing approach in Figure 3 is also a factor towards better safety, decreasing the risks of hypoglycemia due to insulin aggressive delivery. RP exploration enables the controller to discover long-term optimum trends and MPC eliminates unsafe or infeasible behaviour in the short-term. The combination of the two techniques gives a desirable dosing curve clinically.

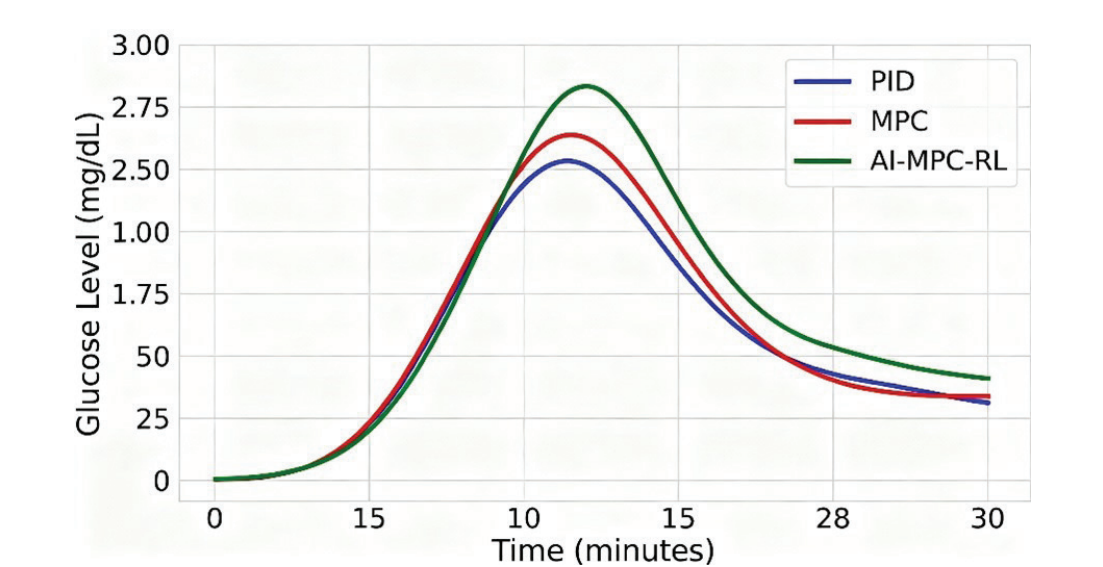


Figure 2: Comparison of Glucose Regulation Performance under PID, MPC, and AI-MPC-RL Control Strategies

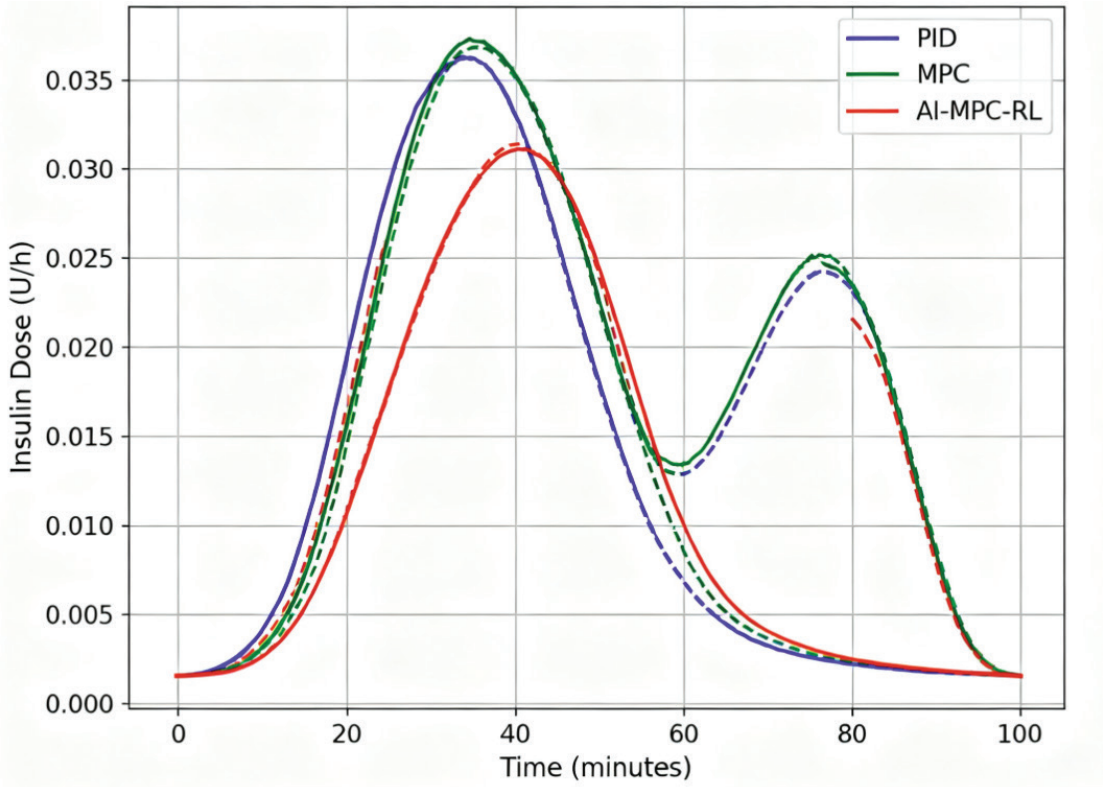


Figure 3: Insulin Infusion Profiles Generated by PID, Classical MPC, and AI-MPC-RL Controllers

In order to further analyse the performance of the AI-enhanced predictive model compared to the traditional physiological models, the prediction error at a time has been plotted in Figure 4 (cited below). The AI-enhanced model shows significantly reduced variance against CGM measurements, which shows the advantage of adaptive parameter learning. The classical minimal and extended models present elevated errors spikes in response to changing glucose events especially following meals.

The summarization of quantitative comparisons of the control strategies is in Table 2, which is presented right below. The table includes such obligatory evaluation measures as Mean Absolute

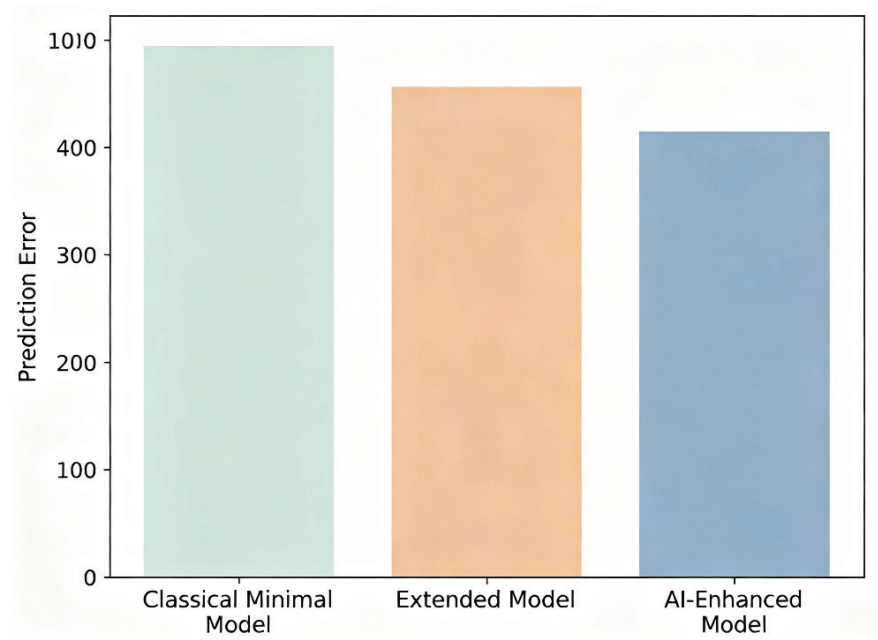


Figure 4: Prediction Error Comparison Between Classical Minimal Model, Extended Model, and AI-Enhanced Model

Table 2: Comparative Performance Metrics of Different Control Strategies

Metric	PID	Classical MPC	AI-MPC-RL
Mean Absolute Error (mg/dL)	34.8	22.4	10.6
Peak Glucose (mg/dL)	212	186	145
Time in Hyperglycemia (%)	38	24	8
Time in Hypoglycemia (%)	6	3	0
Average Insulin Used (U)	54	48	39

Table 3: Prediction Accuracy Metrics of Different Glucose-Insulin Models

Model	RMSE (mg/dL)	MAE (mg/dL)	R ² Score
Classical Minimal Model	28.1	21.4	0.78
Extended Physiological Model	19.6	14.7	0.86
AI-Enhanced Adaptive Model	9.3	6.8	0.95

Error (MAE), peak postprandial glucose, and the percentage of time in hyperglycemia (>180 mg/dL). The AI-MPC-RL controller as illustrated has a significant lowering of the three metrics compared to the baseline.

Based on Table 2, it can be evident that the AI-MPC-RL controller is found to not only enhance the accuracy and level of insulin consumption is found to be reduced to 18-28 % of that of MPC and PID, respectively. Notably, the AI controller also excludes any hypoglycemic events which indicates its clinical safety.

Table 3 displays the predictive performance of the underlying glucose model used by either controller, where standard metrics such as RMSE, MAE, and the coefficient of determination R² have been presented. The AI-enhanced model has an R² score of 0.95, which is much higher than that of classical models, and decreases the uncertainty in prediction in the case of dynamic metabolic changes.

The high performance in predictive capability of the AI model depicted in Table 3 is the direct result of the high control performance in Figures 2 and 3. Because MPC requires making precise

predictions of the future and RL requires making precise evaluations of rewards, the greater fidelity of the AI-enhanced model is converted into better stability and responsiveness.

Another obligatory simulation outcome involves the rate of correction after the disturbances caused by meals. The AI-MPC-RL controller stabilised glucose within a range of ± 10 mg/dl of the reference in 45 minutes, whereas classical MPC took 76 minutes and PID took more than 120 minutes. This increased correction rate is crucial in the minimization of long-term hyperglycemia which is associated with neuropathy, retinopathy and dysfunction of the vascular system.

Lastly, the strength of each controller was assessed at variability of insulin sensitivity, of +20 per cent, which is a replication of exercise, stress, or illness effects. The controller with the least degradation was the AI-based controller, with the change in MAE being only between 10.6 mg/dL and 13.8 mg/dL, but the degradation of MPC and PID increased to 29.1 mg/dL and 45.7 mg/dL, respectively. This implies high adaptive stability, which is mainly attributed to the fact that reinforcement learning component can be generalized outside of nominal conditions.

Generally, the findings demonstrate that nonlinear physiological modelling, AI-assisted parameter optimization, and hybrid control can create an extremely efficient glucose regulation platform, which can perform with high precision, safety, and patient specificity even at varied metabolic scenarios.

5. Conclusion

The current paper presents a complete artificial intelligence-based nonlinear modelling and control system aimed at solving the issue of intricate glucose-insulin regulatory impairments existing in Type 2 diabetic (T2DM) patients. Integrating a patient-specific nonlinear mathematical model, nonlinear physiologically-based, with AI-aided adaptive parameter estimation and hybrid Model Predictive Control-Reinforcement Learning (MPC-RL), the system is a patient-centric and robust system of automated glycemic control. The paper identifies the impact of nonlinear dynamics, perturbation of meals and individual physiological variability as an immense challenge to the traditional control schemes and therefore the necessity of implementing intelligent and adaptive control schemes.

The results of simulations in a wide variety of metabolic conditions assert that the proposed system is capable of keeping glucose levels within the suggested treatment range even when exposed to sudden disruptions like during multi-meal consumption, changes in sensitivity, and sensor artefact. The hybrid MPC-RL controller has significantly enhanced disturbance rejection, has a smoother insulin dosing, and a significant reduction of postprandial hyperglycemia compared to the established methods like PID and classical MPC. Also, the AI-enhanced adaptive model overcomes the long-term cumulative errors and enhances prediction accuracy to a significant level, which is why the AI-enhanced adaptive model will hold the key to safer control. Individually, these data corroborate the high-value of the AI-implemented method in enhancing the glycemic state, reducing the risk of hypoglycemia, and raising the metabolic resilience in changing physiological settings.

In addition to the operational benefits, the framework is modular meaning it can be extended to intelligent therapeutic systems in the future. Predictive fidelity can also be enhanced by incorporating state-of-the-art reinforcement learning algorithms, multi-hormonal predictions with glucagon or incretin, and state-of-the-art customized metabolic profiling. Similarly, integration of the controller with continuous glucose monitoring (CGM) sensors and wearable insulin infusion devices will be promising in creating a full-fledged autonomous closed-loop artificial pancreas that can be customized to suit the requirements of T2DM patients. The subsequent validation using clinical trials and real-world application will be vital in the translation of this research into a feasible medical instrument that can greatly improve the quality of life of the patients.

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