Received: 15 May 2022 | Revised: 3 July 2022 | Accepted: 28 July 2022

IET Systems Biology

DOI: 10.1049/syb2.12049

The Institution of Engineering and Technology WILEY

ORIGINAL RESEARCH

Positive input observer-based controller design for blood glucose regulation for type 1 diabetic patients: A backstepping approach

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Abstract

In practice, there are many physical systems that can have only positive inputs, such as physiological systems. Most conventional control methods cannot ensure that the main system input is positive. A positive input observer-based controller is designed for an intravenous glucose tolerance test model of type 1 diabetes mellitus (T1DM). The backstepping (BS) approach is employed to design the feedback controller for artificial pancreas (AP) systems, based on the Extended Bergman's Minimal Model (EBMM). The EBMM represents the T1DM in terms of the blood glucose concentration (BGC), insulin concentration, and plasma level and the disturbance of insulin during medication due to either meal intake or burning sugar by doing some physical exercise. The insulin concentration and plasma level are estimated using observers, and these estimations are applied as feedback to the controller. The asymptotic stability of the observer-based controller is proved using the Lyapunov theorem. Moreover, it is proved that the system is bounded input-bounded output (BIBO) stable in the presence of uncertainties generated by uncertain parameters and external disturbance. For realistic situations, we consider only the BGC to be available for measurement and additionally inter-and intra-patient variability of system parameters is considered.

KEYWORDS

asymptotic stability, backstepping approach, blood glucose concentration, extended Bergman's minimal model, Lyapunov theorem, observer design, positive input, stability analysis

1 | INTRODUCTION

Positive input systems are a subset of dynamic systems whose input is limited to being positive or non-negative. It is very difficult to control these systems due to the fact that these systems are restricted to have a positive input. Most conventional control methods are designed in such a way that their input can have any signal, so they cannot take into account the restrictions imposed on the input. Most physiological systems are positive input, such as blood sugar control systems, tumour growth modelling systems [1]. One of the challenges of control science is controller design for these types of systems [2].

Diabetes is a chronic disease caused by insulin inadequacy to burn sugar or impaired insulin functioning due to numerous processes in the human body. Diabetes is categorised as type 1, noted as insulin-dependent diabetes, and type 2, noted as non-insulin-dependent diabetes.

The normal range of BGC is 70–130 mg/dl, which is called the euglycaemic range. The case in which the BGC rises above the normal level is called hyperglycaemia. On the other hand, hypoglycaemia is the case in which the BGC falls below the normal glucose level.

Diabetes type 1 affects 5%–10% of people and is caused due to the destruction of pancreas β-cells and results in hyperglycaemia. Type 2 diabetes is characterised as non-insulin-based diabetes, which affects 90%–95% of people and occurs due to defective insulin production.

Hyperglycaemia, if lasts for a long time, may cause macrovascular disorders and severely damage the kidneys, blood vessels, heart, and other body organs and reduce the expectancy of life. Diabetes is considered a life-threatening disease that burdens billions of dollars to the economy of societies. Accordingly, every 8 seconds, diabetes takes one person's life and every 30 seconds, causes a loss of limb. The World Health

Organization (WHO) announced that necessary action for diabetes treatment could decrease diabetes' negative effect on the economy.

To cure diabetes, the BGC should be monitored and controlled to its normal range. The traditional strategy for diabetes treatment requires the intermittent measurement of BGC and controlling the BGC by injecting the required insulin advised by the doctor [3]. Monitoring the BGC is incredibly difficult during the night.

The AP is a precise method used to control the BGC automatically. Research around the development of this treatment is still going on. Designing an AP controller is a challenging task due to variable meal intake, physical exercise, which is represented as a disturbance during medication, and also insulin sensitivity.

Artificial pancreas is a feedback controlled system involving three individual subsystems: continuous glucose measurement (CGM), feedback control unit, which determines the required quantity of insulin, and the insulin pump, which injects the required insulin via the intravenous or the subcutaneous route [4].

The schematic of the AP controlled system is shown in Figure 1.

A stabilising controller should be designed for regulating the BGC to the euglycaemic range. Designing a controller for AP systems requires the mathematical modelling of a T1DM patient. Bergman's minimal model is a simplistic but effective way for the mathematical modelling of T1DM.

The majority of controllers designed for AP systems require the measurement of all system states, which does not sound practical. Different linear and non-linear algorithms are presented in literature for the regulation of BGC to the normal level.

In Ref. [5], the linear quadratic Gaussian controller is proposed for the AP system to regulate the BGC to its normal level. The controller is designed based on the linear parameter-varying model. In Ref. [6], the linear quadratic algorithm is applied to control the BGC to its normal level.

The linear PID controller is employed in Ref. [7] to reduce the steady-state regulation error. In Ref. [8], the linear PD controller is designed to eliminate the oscillations in the PID controller regulating errors. In Ref. [9], the fuzzy approach is employed to improve the regulating performance of AP controlled systems. However, this method is computationally costly.

In the research studies mentioned above, linear control approaches are utilised for AP systems based on Bergman's minimal model (BMM). The BMM is intrinsically non-linear, and using the linear method for controlling non-linear systems may reduce the performance of the controller and cause the controller to ensure local stability only in a domain close to the operation point.

To ensure global stability, non-linear control approaches should be applied to control AP systems.

In Ref. [10], the non-linear control techniques are employed to stabilise AP systems; nevertheless, the internal dynamic's stability was not proved. In Ref. [11], the BS technique is employed to design the controller for AP systems. BS is the recursive non-linear control approach. However, BS controllers designed for AP systems provide bounded regulation errors.

In Ref. [12], a novel fully automated AP system based on the model predictive framework was proposed to treat subjects with T1DM. The controller requires the measurement of BGC and its time derivative. In Refs. [13–15], the sliding mode control (SMC) approach is used to design the controller for AP systems. However, the controller suffers from chattering, which may cause hypoglycaemia due to aggressive exogenous insulin infusions. In Refs. [16, 17], the H_∞ control technique is employed to design a robust controller for AP systems. Nevertheless, H_∞ controllers are of high order and fragile.

In Ref. [18], the BMM is linearised at specific points and the gain scheduling method is employed to design a controller, however, only local convergence is ensured. In Ref. [19], the controller is designed upon the state-dependent Riccati equation. Nevertheless, the controller ensures satisfactory control performance only in a region close to the equilibrium point, and in a realistic environment, the control performance is not acceptable.

In Ref. [20], the fuzzy approach is integrated with the SMC approach to design the AP controlled systems. However, these methods suffer from long settling time and chattering. In Ref. [21], the BS approach is employed to design an exponentially stable variable structure robust controller for T1DM.

All previously reviewed papers require the explicit measurements of the system states, including glucose concentration, remote insulin concentration, and plasma insulin concentration. The glucose concentration can be measured via glucose sensors, while the remote insulin concentration and the plasma insulin concentration are not measurable in practice. As mentioned in Refs. [22–24], the insulin measurement is costly and cumbersome due to reliability issues.

In Ref. [22], a linear Luenberger-like observer is designed to estimate the system states. In Ref. [25], linear quadratic (LQ) controllers and min–max controllers are designed using the estimation of states as feedback.

The blood glucose model is non-linear. In Refs. [25, 26], an observer is designed for the quasi-model of the non-linear blood glucose system. The quasi-model is the EBMM, which is linearised in the region close to the equilibrium point. In Ref. [27], the LMI approach is applied to design a robust observer-based controller for AP systems exposed to meal disturbance. The controller guarantees the boundedness of the BGC to the attractive ellipsoid.

In the aforementioned observer-based controllers designed for AP systems [22–27], controllers and observers are designed separately. In fact, in previous research studies, a stabilising observer is designed to estimate the system states, and a stabilising controller is designed considering that all the system states are available for measurement. These estimations are then used in place of actual states in the control law. In fact, in all the previous research studies, the stability of the controller and observer are analysed separately. As mentioned in Refs. [28, 29], studying the stability of the observer and controller

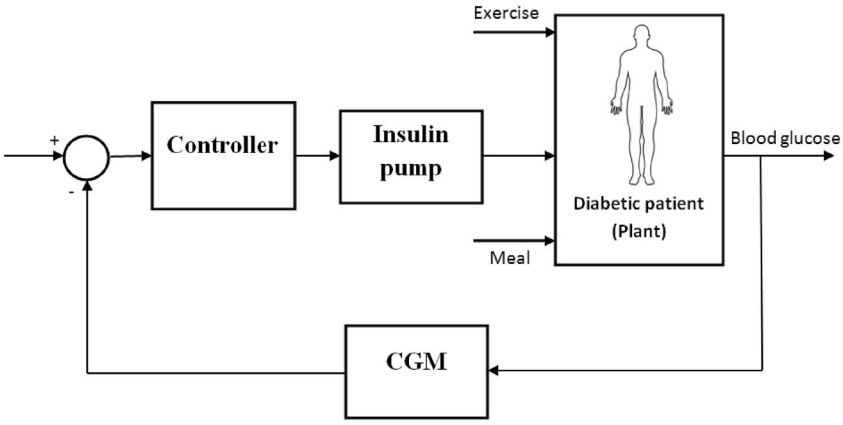


FIGURE 1 Closed-loop artificial pancreas (AP) controlled system

separately may destabilise the system for some initial conditions.

In this manuscript, the BS technique is employed to design an observer-based controller for AP systems. The stability of the observer and controller are analysed simultaneously using the Lyapunov theorem.

Recursive BS is an applicable control technique used for stabilising a special class of non-linear systems by combining the selection of the Lyapunov function with feedback system design. In BS methodology, due to its recursive structure, the full system is radiated out from a fundamental subsystem, which can be stabilised using other control techniques.

In Refs. [30, 31], a model predictive digital feedforward and feedback controller is designed with application to the type 1 diabetes control. In Ref. [32], feedforward controller is designed for a class of positive input linear systems. The controller is designed for the linearised model of the BGC. In Ref. [33], a feedforward controller is designed for a class of positive input non-linear systems. Because the BGC model is non-linear in nature, the system is modelled by linear and non-linear subsystems.

In this paper, two individual observers are designed to asymptotically estimate the insulin concentration and plasma concentration level. The controller guarantees the asymptotic stability of the system in the absence of measurements of remote insulin and plasma insulin concentrations. Finally, control variability grid analysis (CVGA) of 100 virtual T1DM patients using the proposed control law is introduced to evaluate the efficiency as well as confirm the reliability and robustness of the proposed control technique.

The principal novelties of the proposed control method are as follows:

1. Unlike most previous controllers designed to control BGC, the proposed controller ensures that the control input always remains positive.
2. Unlike Refs. [8–21], the controller just requires the measurement of the BGC, which can be easily measured by BGC sensors, and two individual observers are designed to estimate the insulin and plasma concentrations.
3. Unlike Refs. [4–9], the controller is designed using non-linear control methods, and the system's asymptotic stability is analysed using the Lyapunov theorem. The stability of the observer and observer-based controller are analysed simultaneously. Consequently, the controller ensures global asymptotic stability, and the performance of the system is improved compared with previous research studies.
4. The BS technique is employed to design the controller, and consequently, all the states concerning the EBMM are controlled. As a consequence, unlike Ref. [10], the instability of the internal dynamics does not occur using the proposed control method.
5. The controller is robust upon external disturbance and uncertainties in system parameters. It is proved mathematically and numerically that the system is BIBO stable in the presence of uncertainties.
6. Unlike Ref. [21], the control structure is not variable. Hence, the chattering phenomena is prevented.
7. Unlike Refs. [32, 33] in which feedforward controllers are designed, in this paper, a feedback approach is utilised to design the controller. The conclusion proposed in Refs. [32, 33] has to be understood with the caveat that the result assumes that the food pattern and the patient model are sufficiently well known so that the required feedforward bolus can be accurately computed. In practice, this assumption may not be valid. To address the caveat mentioned in Ref. [33], in this paper, we have designed a feedback controller using the BS approach. As a result, the proposed controller has the best advantages of feedback control compared to feedforward control.
8. In this paper, an analogue controller is designed while in Refs. [30, 31], a digital controller is presented. Also, digital control of a process over analogue control has the advantage that complex control calculations can be done easily; on the other hand, digital control has the disadvantages that sampling and quantisation processes lead to more errors that degrade system performance, and the design of digital controllers to compensate for such degradation is far more complex than the design of analogue controllers at an equivalent performance level [34].

The rest of the paper is arranged in the following manner: In Section 2, the system model is presented in terms of state

space, and the controller, the state observers and error dynamics are introduced in Section 3. The system stability is analysed using the Lyapunov theorem in Section 4. In Section 5, simulation results are presented, and in Section 6, some concluding remarks are presented.

2 | SYSTEM REPRESENTATION

In this section, initially, the system model is presented in state space, and afterwards, an appropriate transformation is given by which the system is transformed into the controllable canonical form.

2.1 | System modelling

Bergman modelled the T1DM using a three-state non-linear mathematical model as [17]

$$\dot{x}_1 = -p_1 x_1 - x_2(x_1 + G_b) + d, \tag{1a}$$

$$\dot{x}_2 = -p_2 x_2 + p_3 x'_3, \tag{1b}$$

$$\dot{x}'_3 = -n(x'_3 + I_b) + u(t), \tag{1c}$$

where x_1, x_2, x'_3 represent the glucose concentration, remote insulin concentration, and plasma insulin concentration, respectively, the control input u denotes the external insulin infusion rate and d denotes the meal disturbance. All the system parameters used in the simulation have been presented in Table 1. In the BMM, the meal disturbance effect is considered to be constant.

In Refs. [13, 16], the EBMM is suggested, which includes the meal disturbances as a time-varying dynamical state (here defined by x_4).

$$\dot{x}_1 = -p_1(x_1 - G_b) - x_1 x_2 + x_4, \tag{2a}$$

$$\dot{x}_2 = -p_2 x_2 + p_3(x'_3 - I_b), \tag{2b}$$

$$\dot{x}'_3 = -p_4(x'_3 - I_b) + u(t), \tag{2c}$$

TABLE 1 System parameters

Parameters	Values
Glucose effectiveness factor (p_1)	1×10^{-7} min^{-1}
Delay in insulin actions (p_2)	0.025 min^{-1}
Patient parameters (p_3)	0.000013 mU L^{-1} min^{-2}
Insulin degradation rate (p_4)	0.021 min^{-1}
Meal disturbance (p_5)	0.05 min^{-1}
Basal plasma insulin (I_b)	4.5 mU L^{-1}
Basal plasma glucose (G_b)	4.5 m Mol L^{-1}

$$\dot{x}_4 = -p_5\, x_4. \tag{2d}$$

The EBMM is more sensible compared with the BMM [16]. Let us define

$$x_3 = -x'_3,\ v = -u. \tag{3}$$

Considering Equation (3), Equations (2b) and (2c) can be rewritten as

$$\dot{x}_2 = -p_2 x_2 + p_3(-x_3 - I_b), \tag{4a}$$

$$\dot{x}_3 = -\dot{x}'_3 = p_4(x'_3 - I_b) - u(t) = -p_4(x_3 + I_b) + v(t) \tag{4b}$$

2.2 | Equivalence transformation

Let us define the auxiliary state X_1 as

$$X_1 = Ln\, x_1. \tag{5}$$

Similarly, the auxiliary reference state X_{1r} is defined as

$$X_{1r} = Ln\, x_{1r}, \tag{6}$$

where the constant x_{1r} defines the desired magnitude of state x_1.

Differentiating Equation (5) with respect to time and substituting Equation (2a) in the result, we have

$$\dot{X}_1 = \frac{\dot{x}_1}{x_1} = \frac{-p_1(x_1 - G_b) - x_1 x_2 + x_4}{x_1} = -p_1 + \frac{p_1 G_b}{x_1} - x_2 + \frac{x_4}{x_1}. \tag{7}$$

Consequently, we obtain

$$\dot{X}_1 = -p_1 + p_1\, G_b\, e^{-X_1} - x_2 + x_4\, e^{-X_1}. \tag{8}$$

Let us define the regulation error z_1 as

$$z_1 = X_1 - X_{1r}. \tag{9}$$

Differentiating Equation (9) with respect to time and considering that the reference magnitude x_{1r} is constant, we obtain

$$\dot{z}_1 = \dot{X}_1, \tag{10a}$$

$$\ddot{z}_1 = \ddot{X}_1. \tag{10b}$$

Differentiating Equation (8) with respect to time, we obtain

$$\ddot{X}_1 = -p_1\, G_b\, \dot{X}_1\, e^{-X_1} - \dot{x}_2 + \dot{x}_4\, e^{-X_1} - x_4\, \dot{X}_1\, e^{-X_1}. \quad (11)$$

Considering Equation (8), we have

$$x_2 = -\dot{X}_1 - p_1 + p_1\, G_b\, e^{-X_1} + x_4\, e^{-X_1}. \quad (12)$$

Substituting Equation (4a) with Equation (11) and considering Equation (12), we obtain

$$\begin{aligned}\ddot{X}_1 = \ddot{z}_1 = &-p_1 G_b \dot{X}_1 e^{-X_1} + p_2\left[-\dot{X}_1 - p_1\right. \\ &\left. + p_1 G_b\, e^{-X_1} + x_4 e^{-X_1}\right] + p_3(x_3 + I_b) \\ &- p_5 x_4 e^{-X_1} - x_4 \dot{X}_1 e^{-X_1}. \end{aligned} \quad (13)$$

Let us define

$$\begin{aligned}\overline{f}(X_1, \dot{X}_1) = &-p_1 G_b \dot{X}_1 e^{-X_1} + p_2\left[-\dot{X}_1 - p_1\right. \\ &\left. + p_1 G_b e^{-X_1}\right] + p_3 I_b, \\ Y(X_1, \dot{X}_1) = &\; p_2 e^{-X_1} - p_5 e^{-X_1} - \dot{X}_1 e^{-X_1}. \end{aligned} \quad (14)$$

Consequently, Equation (13) can be rewritten as

$$\ddot{z}_1 = \ddot{X}_1 = \overline{f}(X_1, \dot{X}_1) + Y(X_1, \dot{X}_1) x_4 + p_3 x_3. \quad (15)$$

2.3 | Canonical form

Let us define

$$z_1 = X_1 - X_{1r}, \quad (16a)$$

$$z_2 = \dot{X}_1 + \Lambda(X_1 - X_{1r}). \quad (16b)$$

where Λ is a positive constant. The state z_2 can be considered as z_1 which passes the filter with the transfer function of $G(s) = \frac{1}{s+\Lambda}$.

By simultaneously considering Equations (10a) and (16b), we obtain

$$\dot{z}_1 = z_2 - \Lambda\, z_1. \quad (17)$$

Differentiating Equation (16b), we have

$$\dot{z}_2 = \ddot{X}_1 + \Lambda\, \dot{z}_1. \quad (18)$$

Substituting Equation (15) in Equation (18), we obtain

$$\begin{aligned}\dot{z}_2 = &\overline{f}(X_1, \dot{X}_1) + Y(X_1, \dot{X}_1) x_4 + p_3 x_3 \\ &+ \Lambda(z_2 - \Lambda z_1). \end{aligned} \quad (19)$$

Let us define

$$f(\cdot) = \overline{f}(\cdot) + \Lambda\, z_2 - \Lambda^2\, z_1. \quad (20)$$

Considering definition Equation (20), Equation (19) can be rewritten as

$$\dot{z}_2 = f(X_1, \dot{X}_1) + Y(X_1, \dot{X}_1) x_4 + p_3 x_3. \quad (21)$$

In Appendix A, it is shown that Equation (21) can be rearranged as

$$\dot{z}_2 = F_1 z_1 + F_2 z_2 + f(X_{1r}, 0) + Y(X_{1r}, 0) x_4 + p_3 x_3. \quad (22)$$

In order for the actual input of the system (i.e. v) to always remain positive, the dummy input (i.e. u) is designed in such a way that the relationship between the actual and dummy input is calculated from the following equation

$$\dot{v} = -u\, v. \quad (23)$$

Considering Equation (23), it is clear that

$$\int_{v(0)}^{v(t)} \frac{dv}{v} = -\int_0^t u\, dt \;\Rightarrow\; v = v(0)\, e^{-\int_0^t u(\tau)\, d\tau}, \quad (24)$$

where $v(0)$ represents the initial magnitude of the dummy input variable $v(t)$. It is clear that if the initial value of the dummy input is selected as positive (i.e. $v(0) > 0$), the actual input of the system will always be positive.

3 | CONTROLLER DESIGN

In this section, initially, the procedure of designing the controller through the BS approach is introduced, and afterwards, the controller is given in theorem 1.

3.1 | Control procedure

In the following, two observers are designed to estimate the remote insulin and plasma concentrations. Initially, the state z_2 is estimated using an observer and afterwards, an observer is designed to estimate the state x_3. Let us define the estimation errors as

$$\tilde{z}_2 = z_2 - \hat{z}_2, \quad (25a)$$

$$e_1 = \frac{1}{\alpha}(x_3 - \hat{x}_3), \quad (25b)$$

where α is a positive constant, $\hat{z}_2$ represents an estimation of the state z_2 and $\hat{x}_3$ represents the estimation of the state x_3.

Considering the definition of Equation (25b), we can rewrite Equation (22) as

$$\dot{z}_2 = F_1 z_1 + F_2 z_2 + f(X_{1r}, 0) + Y(X_{1r}, 0)x_4 + p_3\ (\alpha e_1 + \widehat{x}_3). \tag{26}$$

Let us define

$$e_2 = \widehat{x}_3 - x_3^*, \tag{27}$$

where x_3^* represents the desired magnitude of $\widehat{x}_3$ and x_3^* calculated using Equation (28) is designed using the BS approach as

$$x_3^* = \frac{1}{p_3}[-f(X_{1r}, 0) - Y(X_{1r}, 0)x_4 - k_2\widehat{z}_2], \tag{28}$$

where k_2 is a positive constant. Considering the definition of Equation (27), Equation (26) can be rearranged as

$$\dot{z}_2 = F_1 z_1 + F_2 z_2 + f(X_{1r}, 0) + Y(X_{1r}, 0)x_4 + p_3(\alpha e_1 + e_2 + x_3^*). \tag{29}$$

Considering Equation (29), the desired variable x_3^* represents the governing variable designed for controlling the state z_2. Let us define

$$e_3 = v - v^*, \tag{30}$$

where v^* represents the desired magnitude of dummy control input v and is calculated using Equation (31), which is designed using the BS approach as

$$v^* = p_4(\widehat{x}_3 + I_b) + \left(p_3\alpha + \frac{1}{p_3}k_2k_1\right)\widehat{z}_2 + \frac{1}{p_3}Y(X_{1r}, 0) \times (p_5x_4) - \frac{1}{p_3}k_2k_1k_3e_2, \tag{31}$$

where the positive constant k_3 represents the control gain, $\widehat{x}_3$, $\widehat{z}_2$ represent the estimation of system states provided as an output of the observers proposed in Section 3.2, and e_2 represents the tracking error defined previously in Equation (27).

The control procedure using the BS approach is as follows:

1. Asymptotically stable observer is designed for the estimation of filtered state z_2, that is, $\widehat{z}_2$ tends to z_2 or $\tilde{z}_2$ tends to zero.
2. The desired variable x_3^* is appropriately designed such that z_2 tends to zero.
3. Asymptotically stable observer is designed to estimate state x_3, that is, the estimate state $\widehat{x}_3$ asymptotically converges to x_3 or $\tilde{x}_3$ tends to zero.
4. The desired variable v^* is designed properly such that the estimation error e_2 asymptotically converges to zero, that is, x_3^* tends to $\widehat{x}_3$.
5. The control law for dummy input (i.e. u) is designed properly such that the error e_3 asymptotically converges to zero, that is, v^* tends to v.

The schematic of the proposed observer-based control method is shown in Figure 2.

3.2 | Observer design

Let us design an observer for the estimation of state z_2 as

$$\widehat{z}_2 = k_1 z_1 + \eta, \tag{32}$$

where the positive constant k_1 is the observer gain and $\widehat{z}_2$ represents the estimation of state z_2 and η is the co-state calculated using the following differential equation

$$\dot{\eta} = \left(k_1\ \Lambda - {k_1}^2\right) z_1 - k_1\ \eta. \tag{33}$$

Moreover, let us design an observer to estimate the state x_3 as

$$\widehat{x}_3 = 2\alpha\ p_3\ z_1 + \sigma, \tag{34}$$

where $\widehat{x}_3$ represents the estimate of state x_3 and σ is the co-state calculated as

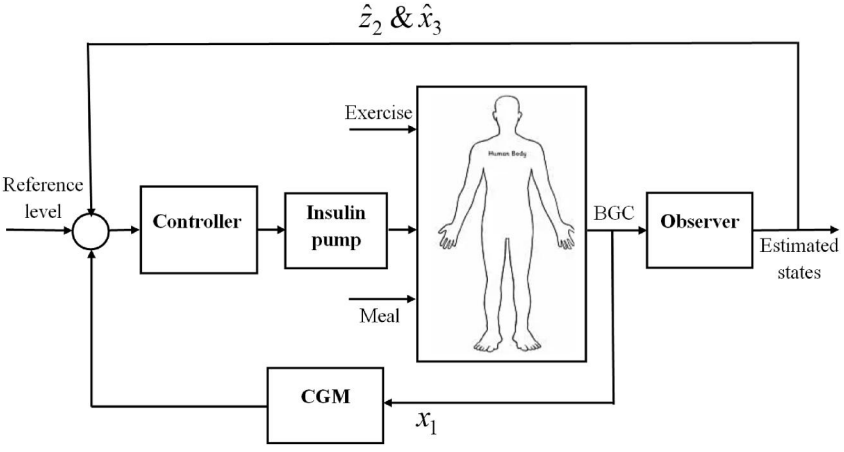
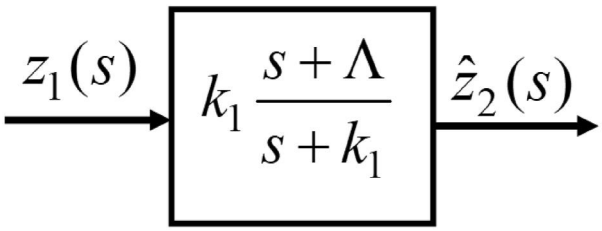


FIGURE 2 Observer-based AP controlled system



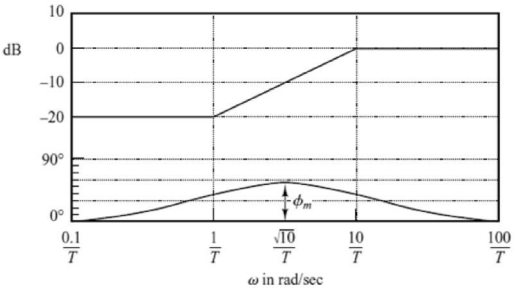


Figure 3a. Bode diagram of a lead compensator $k_1 \frac{s+\Lambda}{s+k_1}$ with $k_1 = 1, \Lambda = 0.1$.

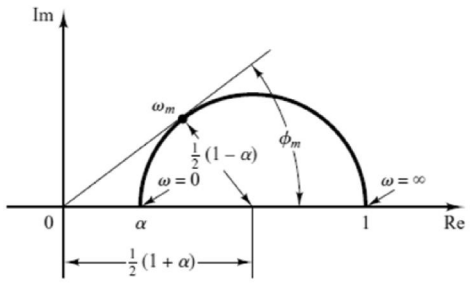


Figure 3b. Polar plot of a lead compensator $k_1 \frac{s+\Lambda}{s+k_1}$ with $\alpha = \frac{\Lambda}{k_1}$.

FIGURE 3 The schematic of block diagram and bode diagram of the filter

$$\dot{\sigma} = 2\alpha p_3 \Lambda z_1 - p_3 \alpha \, \hat{z}_2 - p_4(\hat{x}_3 + I_b) + v. \tag{35}$$

The schematic of block diagram and Bode diagram of the filter, calculated using Equarion (32), is shown in Figure 3.

Remark 1 Lead compensation essentially yields an appreciable improvement in transient response and a small change in steady-state accuracy. It will suppress the effects of high-frequency noise signals. As seen from Figure 3, the lead compensator is basically a high-pass filter (the high frequencies are passed, but low frequencies are attenuated). The primary function of the lead compensator is to reshape the frequency-response curve to provide a sufficient phase-lead angle to offset the excessive phase lag associated with the components of the fixed system. Lead compensation is commonly used for improving stability margins. Lead compensation achieves the desired result through the merits of its phase-lead contribution. Lead compensation yields a higher gain crossover frequency, which means a larger bandwidth. A large bandwidth means reduction in the settling time or fast response.

3.3 | BS controller design

In this subsection, the BS approach is employed to design the controller. The controller used the state x_1 as feedback. The states x_2 and x_3 are estimated using the observers proposed in Section 3.2. The controller is designed using the measurement of BGC (i.e. x_1) and $\hat{z}_2$, $\hat{x}_3$ (estimations of system states) as feedback.

Theorem 1 *The blood glucose control system is asymptotically stable ensuring that the actual system input (i.e. v)* always remains positive using the control input calculated as

$$u = -\frac{1}{v}\Big[p_4\big(2\alpha p_3(\hat{z}_2 - \Lambda z_1) + 2\alpha p_3 \Lambda z_1 - p_3 \alpha \hat{z}_2 - p_4(\hat{x}_3 + I_b) + v\big) - \frac{{p_5}^2}{p_3} Y(X_{1r}, 0) x_4 + k_4 e_3 - \frac{1}{p_3} k_1 k_2 k_3 \big(\alpha p_3 \hat{z}_2 - p_4(\hat{x}_3 + I_b) + v - \frac{p_5}{p_3} Y(X_{1r}, 0) x_4\big)\Big] \tag{36}$$

where the positive constant k_3 represents the control gain and $\widehat{x}_3$, $\widehat{z}_2$ represent the estimation of system states provided as an output of the observers proposed in Section 3.2, and e_2 represents the tracking error defined previously in Equation (27).

Remark 2 It is true that we designed the control law for the dummy input of the system, but in fact, we control the actual input of the system; in other words, the control law for the main input will be calculated then using Equation (24).

3.4 | Error dynamics

In Section 3.1, it was shown that the variable x_3^* could be considered as the governing variable to control the state z_2. Replacing x_3^* from Equation (28) in Equation (29), we have

$$\dot{z}_2 = F_1 z_1 + F_2 z_2 - k_2 \widehat{z}_2 + p_3(\alpha e_1 + e_2). \tag{37}$$

Considering the definition of Equation (25a), we can rearrange Equation (37) as

$$\dot{z}_2 = F_1 z_1 + F_2 z_2 - k_2(z_2 - \tilde{z}_2) + p_3 \alpha e_1 + p_3 e_2. \tag{38}$$

Moreover, in Appendix B, it is proved that the dynamic equation governing the estimation error $\tilde{z}_2$ is obtained as

$$\dot{\tilde{z}}_2 = F_1 z_1 + F_2 z_2 - k_2(z_2 - \tilde{z}_2) + p_3 \alpha e_1 + p_3 e_2 - k_1 \tilde{z}_2. \tag{39}$$

In Appendix C, the estimation error governing e_1 is obtained as

$$\dot{e}_1 = \frac{1}{\alpha}\left[-p_3 \alpha (z_2 + \tilde{z}_2) - p_4 \alpha e_1\right]. \tag{40}$$

As mentioned in Section 3.3, the control input v is considered as the guiding variable to control the state e_2. In Appendix D, it is proved that the dynamic governing the state e_2 can be considered as

$$\dot{e}_2 = 2\alpha\, p_3\, z_2 + \frac{1}{p_3} k_2\, k_1\, z_2 - \frac{1}{p_3} k_2\, k_1\, k_3\, e_2. \tag{41}$$

In Appendix E, it is proved that the error dynamics for e_3 is obtained as

$$\dot{e}_3 = \beta\, \tilde{z}_2 - k_4 e_3, \tag{42}$$

where

$$\beta = 2\alpha p_3 p_4 + p_3 \alpha k_1 - 2\alpha k_2 k_1 k_3 - \frac{1}{{p_3}^2}(k_2 k_1)^2 k_3 + p_3 \alpha k_1 + \frac{1}{p_3} k_2 {k_1}^2. \tag{43}$$

4 | STABILITY ANALYSIS

In this section, initially the stability of the origin is analysed. Afterwards, the BIBO (bounded input-bounded output) stability of the system is analysed in the existence of uncertainties in system parameters using the Lyapunov theorem.

4.1 | Stability of the equilibrium point

Consider the positive definite Lyapunov function

$$V = \frac{1}{2}\varepsilon\, {z_1}^2 + \frac{1}{2}{z_2}^2 + \frac{1}{2}{\tilde{z}_2}^2 + \frac{1}{2}\alpha\, {e_1}^2 + \frac{1}{2}\frac{p_3}{k_1 k_2}\, {e_2}^2 + \frac{1}{2}\gamma\, {e_3}^2, \tag{44}$$

where $\varepsilon, \alpha, \gamma$ are positive constants and k_1, k_2 are positive gains defined previously in Section 3.

In Appendix F, it is shown that the time derivative of the Lyapunov function can be upper-bounded as

$$\dot{V} \le -\lambda_1\, {z_1}^2 - \lambda_2\, {z_2}^2 - \lambda_3\, {\tilde{z}_2}^2 - \lambda_4\, {e_1}^2 - \lambda_5\, {e_2}^2 - \lambda_6\, {e_3}^2, \tag{45}$$

provided that control gains are selected as

$$\Lambda > \frac{1}{2} + \frac{f_1}{\varepsilon}, \tag{46a}$$

$$k_2 > \frac{\varepsilon}{2} + \frac{f_1}{2} + \frac{3}{2} f_2 + \frac{p_3}{2} + \frac{2\alpha {p_3}^2}{k_1 k_2} + \frac{1}{2}, \tag{46b}$$

$$k_1 > k_2 + \frac{f_1}{2} + \frac{f_2}{2} + \frac{1}{2} p_3 + \frac{1}{2}\gamma\, \beta, \tag{46c}$$

$$\alpha > 0, \tag{46d}$$

$$k_3 > p_3 + \frac{2\alpha {p_3}^2}{k_1 k_2} + \frac{1}{2}, \tag{46e}$$

$$k_4 > \frac{1}{2}\, \beta. \tag{46f}$$

Equation (45) implies that $\dot{V} \le 0$. Integrating both sides of Equation (45) with respect to time, we obtain

$$V(t) \le V(0) - \lambda_1 \int_0^t z_1^2(\tau) d\tau - \lambda_2 \int_0^t z_2^2(\tau) d\tau - \lambda_3 \int_0^t \tilde{z}_2^2(\tau) d\tau - \lambda_4 \int_0^t e_1^2(\tau) d\tau - \lambda_5 \int_0^t e_2^2(\tau) d\tau - \lambda_6 \int_0^t e_3^2(\tau) d\tau. \tag{47}$$

Since V is a positive definite function, from Equation (47), it can be deduced that

$$\lim_{t\to\infty} z_1 = 0,\ \lim_{t\to\infty} z_2 = 0,\ \lim_{t\to\infty} \tilde{z}_2 = 0,\ \lim_{t\to\infty} e_1 = 0,\ \lim_{t\to\infty} e_2 = 0,\ \lim_{t\to\infty} e_3 = 0. \tag{48}$$

Clearly, Equation (9) can be reconsidered as $z_1 = Ln\, x_1 - Ln\, x_{1r} = Ln\, \frac{x_1}{x_{1r}}$. Considering definitions of (5), (6), and (16a), the condition $\lim_{t\to\infty} z_1 = 0$ deduces

$$\lim_{t\to\infty} \left(Ln\, \frac{x_1}{x_{1r}}\right) = 0 \Rightarrow \lim_{t\to\infty} \left(\frac{x_1}{x_{1r}}\right) = e^0 = 1. \tag{49}$$

Consequently, we obtain

$$\lim_{t\to\infty} x_1(t) = x_{1r}. \tag{50}$$

4.2 | Robustness to parametric uncertainties

In this section, the robustness of the system is analysed in the existence of uncertainties in system parameters. In this paper, the nominal magnitude of system parameters are defined by the "¯" notation; for instance, $\bar{p}_1$ represents the nominal magnitude of parameter p_1.

Theorem 2 *For the system (2a)–(2d) in the presence of parametric uncertainties, the controller is calculated as*

$$u = \frac{1}{v}\Big[\bar{p}_4\left(2\alpha\bar{p}_3(\hat{z}_2 - \Lambda z_1) + 2\alpha\bar{p}_3\Lambda z_1 - \bar{p}_3\alpha\hat{z}_2 - \bar{p}_4(\hat{x}_3 + I_b) + v\right) - \frac{\bar{p}_5^{\,2}}{\bar{p}_3}Y(X_{1r},0)x_4 + k_4e_3 - \frac{1}{\bar{p}_3}k_1k_2k_3\left(\alpha\bar{p}_3\hat{z}_2 - \bar{p}_4(\hat{x}_3 + I_b) + v - \frac{\bar{p}_5}{\bar{p}_3}Y(X_{1r},0)x_4\right)\Big] \tag{51}$$

and ensures the boundedness of system errors, where $\hat{z}_2$ represents the estimation of system states provided as an output of the observer calculated using Equation (32). The variable $e_3 = v - v^*$ represents the deviation of the actual input from its desired magnitude v^* which is calculated using the nominal magnitude of system parameters as

$$v^* = \bar{p}_4\left(\hat{x}_3 + \bar{I}_b\right) + \left(\bar{p}_3\alpha + \frac{1}{\bar{p}_3}k_2k_1\right)\hat{z}_2 + \frac{1}{\bar{p}_3}Y(X_{1r},0)\left(\bar{p}_5x_4\right) - \frac{1}{\bar{p}_3}k_2k_1k_3e_2, \tag{52}$$

The variable $\hat{x}_3$ represents the estimation of state x_3 calculated as

$$\hat{x}_3 = 2\alpha\,\bar{p}_3\,z_1 + \sigma, \tag{53}$$

and σ is the co-state calculated as

$$\dot{\sigma} = 2\alpha\bar{p}_3\Lambda z_1 - \bar{p}_3\alpha\hat{z}_2 - \bar{p}_4\left(\hat{x}_3 + \bar{I}_b\right) + v. \tag{54}$$

Following the same procedure in Section 4.1, the error dynamics of the system in the presence of parametric uncertainties are calculated by

$$\dot{z}_2 = F_1z_1 + F_2z_2 - k_2(z_2 - \tilde{z}_2) + p_3\alpha e_1 + p_3e_2 + d_1, \tag{55a}$$

$$\dot{\tilde{z}}_2 = F_1z_1 + F_2z_2 - k_2(z_2 - \tilde{z}_2) + p_3\alpha e_1 + p_3e_2 - k_1\tilde{z}_2 + d_2, \tag{55b}$$

$$\dot{e}_1 = \frac{1}{\alpha}\left[-p_3\alpha(z_2 + \tilde{z}_2) - p_4\alpha e_1\right] + d_3, \tag{55c}$$

$$\dot{e}_2 = 2\alpha p_3z_2 + \frac{1}{p_3}k_2k_1z_2 - \frac{1}{p_3}k_2k_1k_3e_2 + d_4, \tag{55d}$$

$$\dot{e}_3 = \beta\tilde{z}_2 - k_4e_3 + d_5. \tag{55e}$$

where d_i $i = 1, \ldots, 5$ lumped the deviation of system parameters from their nominal magnitudes.

Proof Consider the Lyapunov function as

$$V = \frac{1}{2}\varepsilon\, {z_1}^2 + \frac{1}{2}{z_2}^2 + \frac{1}{2}{\tilde{z}_2}^2 + \frac{1}{2}\alpha\, {e_1}^2 + \frac{1}{2}\frac{p_3}{k_1k_2}\, {e_2}^2 + \frac{1}{2}\gamma\, {e_3}^2, \tag{56}$$

Consider the system errors in the presence of uncertainties calculated using Equations (55a–e) and take $r > 0$ and $r_d > 0$ such that $\|x\| \le r$ and $\|d\| \le r_d$. The Lyapunov function V satisfies

$$\frac{1}{2}c_1\|X\|^2 \le V \le \frac{1}{2}c_2\|X\|^2, \tag{57}$$

where $c_1 = \min\left\{\varepsilon, \alpha, \frac{p_3}{k_1k_2}, 1\right\}$ and $c_2 = \max\left\{\varepsilon, \alpha, \frac{p_3}{k_1k_2}, 1\right\}$.

The time derivative of the Lyapunov function can be calculated as

$$\dot{V} \le -c_3\,\|X(t)\|^2 + c_4\|X(t)\|\,\|d(t)\|, \tag{58}$$

where $X = [z_1, z_2, \tilde{z}_2, e_1, e_2, e_3]^T$, $d = [d_1, d_2, d_3, d_4, d_5]^T$.

Take $W = \sqrt{V(X)}$, when $V(X) \neq 0$, and use $\dot{W} = \dot{V}/2\sqrt{V}$ and Equation (58) to obtain

$$\dot{W} \le -\frac{1}{2}\left(\frac{c_3}{c_2}\right)W + \frac{c_4}{2\sqrt{c_1}}\|d(t)\|, \tag{59}$$

when $V(X) = 0$, it can be verified that

$$D^{+}W \leq \frac{c_4}{2\sqrt{c_1}}\|d(t)\|. \tag{60}$$

Hence,

$$D^{+}W \leq -\frac{1}{2}\left(\frac{c_3}{c_2}\right)W + \frac{c_4}{2\sqrt{c_1}}\|d(t)\|, \tag{61}$$

for all values of $V(x(t))$. By the comparison Lemma, $W(t)$ satisfies the inequality

$$W(t) \leq e^{-c_3/2c_2\,t}W(0) + \frac{c_4}{2\sqrt{c_1}}\int_0^t e^{-c_3/2c_2(t-\tau)}\|d(\tau)\|\,d\tau. \tag{62}$$

Using Equation (57), we obtain

$$\|X(t)\| \leq \sqrt{\frac{c_2}{c_1}}\|x(0)\|\,e^{-c_3/2c_2\,t} + \frac{c_4}{2c_1}\int_0^t e^{-c_3/2c_2(t-\tau)}\|d(\tau)\|\,d\tau. \tag{63}$$

It can be easily verified that

$$\|X(0)\| \leq r\sqrt{\frac{c_2}{c_1}},\quad \sup_{0\leq\sigma\leq t}\|d(\sigma)\| \leq \frac{c_1c_3r}{c_2c_4}, \tag{64}$$

ensure that $\|X(t)\| \leq r$; hence, $X(t)$ stays within the domain of validity of the assumptions.

5 | SIMULATION RESULTS

In this section, theoretical findings are evaluated by simulating the proposed method for glycaemic regulation in T1D patients in the presence of a high initial meal disturbance in MATLAB/Simulink software.

The proposed controller is simulated considering three scenarios: (i) the simulation results on the T1DM with exogenous meal disturbance and without uncertainties in system parameters, (ii) a 24 h (1440 min) multiple-meal scenario for random virtual T1DM patients to evaluate the robustness of the control method, considering uncertainties in system parameters and meal disturbance, and (iii) simulation for random initial conditions.

The control purpose is regulating the BGC to the reference range, assuring that (i) the control input always remains positive, (ii) only the BGC is accessible for feedback and the remote insulin and plasma concentration are not accessible for feedback, (iii) the BGC must not descend below the severe hypoglycaemic level (i.e. $x_1 > 50$ mg/dl), (iv) the BGC must not raise the postprandial hyperglycaemia level in the presence of external meal disturbance, (v) the magnitude of the control signal should be non-negative, and (vi) bringing the BGC below 180 mg/dl from the hyperglycaemic condition within a specified time of 120 min, which is a clinically recommended physiological necessity for T1DM.

5.1 | Scenario 1: Simulation with nominal magnitude of system parameters

In this scenario, the proposed control method and the BS and PID controller proposed in Ref. [11] and the variable structure controller proposed in Ref. [21] are simulated for the T1DM patients in the presence of meal disturbance modelled by Equations (2a)–(2d). In this scenario, the system parameters are considered to be certain and selected for all three controllers according to Table 1, and the control gains and initial conditions of plasma glucose–insulin are selected similar to Ref. [11] for a patient in the state of hyperglycaemia as $x_1(0) = 250$ mg/dl, $x_2(0) = 0.001$ min^{-1}, $x_3(0) = 7$ mU/L. As noted earlier, the level of BGC for a healthy person should be 70–180 mg/dl. The reference range of BGC for simulation is considered as $x_{1r} = 80$ mg/dl and the controller is designed to control the BGC to the reference level by the intravenous injection of insulin.

The system parameters and control gains used in the simulation are listed individually in Tables 1 and 2. Control gains are selected such that conditions (46a)-(46f) are satisfied. The PID and BS control gains are selected similar to Ref. [11]. For all three simulations, the same data set has been selected to make the results comparable with each other.

The time history of BGC is shown in Figure 4. The x-axis represents the time in seconds and the y-axis the BGC in mg/dl. In Figure 4, results of the proposed controller with and without observers are compared with the results of the PID and BS controller presented in Ref. [11] and the variable structure controller proposed in Ref. [21]. The comparisons confirm that the PID controller response has some steady-state error and has a very large settling time. The PID and BS controllers need the measurement of BGC, remote insulin, and plasma concentration. However, the proposed controller only requires the measurement of BGC, and the remote insulin and plasma concentrations are estimated by observers. It is worth mentioning that the proposed controller ensures asymptotic stability while the controllers proposed in Ref. [11] ensure bounded regulation error. As mentioned in Remark 1, the filter designed to estimate the system states represents as the lead compensator and the lead compensator improves the transient response and steady state accuracy of the system, which can be also verified from Figure 4.

Comparisons verify the improvement made by the proposed controller even in the presence of a lack of knowledge of remote insulin and plasma concentrations. Consequently, it can be observed that the performance of the PID controller is not satisfactory as compared with the proposed controller considering steady-state error and convergence time.

The time history of the required insulin that should be injected as the control input for the proposed controller, PID

and BS controllers and the variable structure controller are shown in Figure 5. The first control pulse of the proposed method in Figure 5 causes the BGC to fall from a higher to a lower level, and then other pulses are injected to regulate the BGC to the reference level. The insulin infusion rate is diminished as the BGC approaches the reference level of 80 mg/dl. Figure 5 verifies that the control input is always positive. As shown in Figure 5, the value of the controller presented in Ref. [21] for some time intervals is equal to zero. Since the controller produces negative values in these segments and the insulin injection can only be positive, the controller cannot control the system during these intervals. Hence, this may destabilise the system for some initial conditions. In this paper, the controller structure is designed to ensure that the control input is always positive.

The time history of estimation errors $\tilde{z}_2$, $\tilde{x}_3$ are shown in Figure 6. From Figure 6, it can be observed that the observers proposed in Section 3.2 can asymptotically estimate system states (z_2, x_3).

The time history of remote insulin concentration and plasma insulin concentration for the proposed control method is shown in Figures 7 and 8.

TABLE 2 Control and observer gains

Controller and observer gains	Values
Controller gain (k_2)	2
Controller gain (k_3)	1
Filter gain (Λ)	0.1
Observer gain (α)	1
Observer gain (k_1)	1

5.2 | Scenario 2: Simulation with random system parameters

In this section, the performance of the proposed controller is evaluated considering the intra-patient variability. The simulation is performed for 1 day (1440 min), considering three meal disturbances during the day.

The initial conditions of system states are considered as $x_1 = 80$ mg/dl, $x_2 = 0$ min^{-1}, $x_3 = 7$ mU/L and no initial meal disturbance is considered, that is, $x_4 = 0$ mg/dl/min. The subsequent aspects are considered in this outline for inter-patient variability: (i) 100 Monte-Carlo simulations are considered at the beginning of each new simulation. We simulate the controller with nominal magnitudes of system parameters. The model parameters are varied randomly from the range mentioned in Table 3. The value of the parameter p_1 is randomly selected between ±30% of its nominal value.

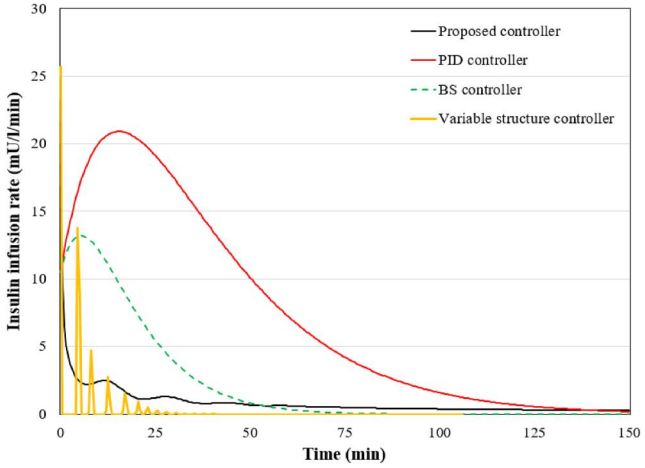


FIGURE 5 The time history of insulin infusion rate

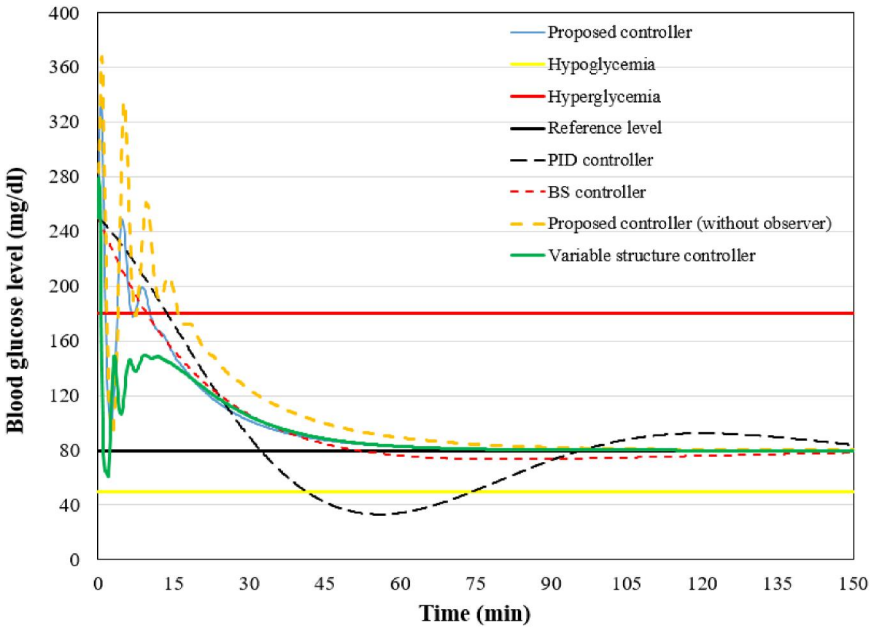


FIGURE 4 Time history of blood glucose concentration (BGC)

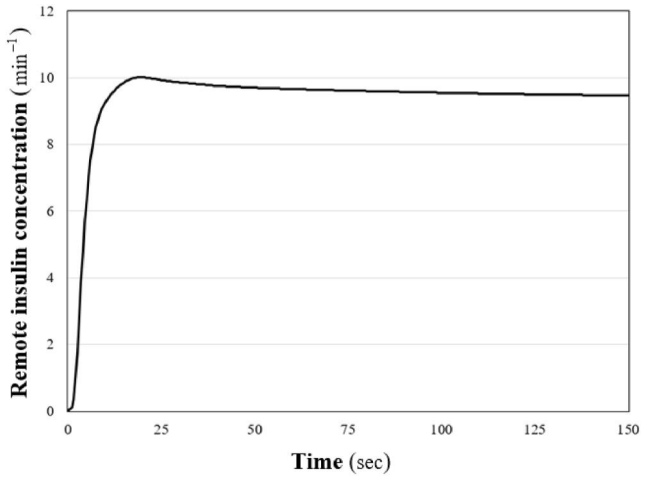


FIGURE 6 The time history of estimation errors

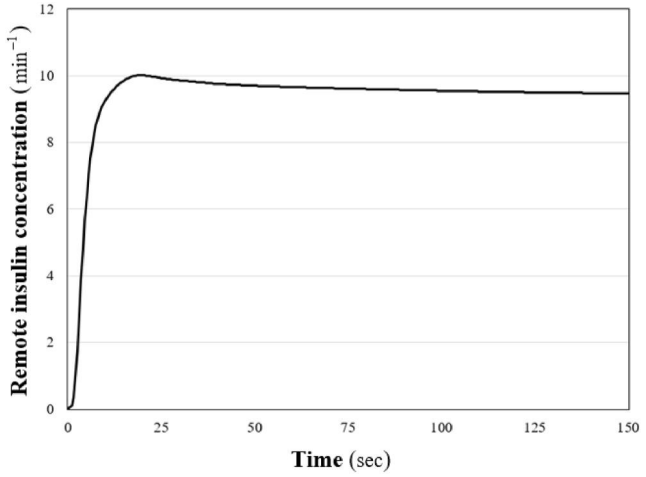


FIGURE 7 The time history of insulin concentration

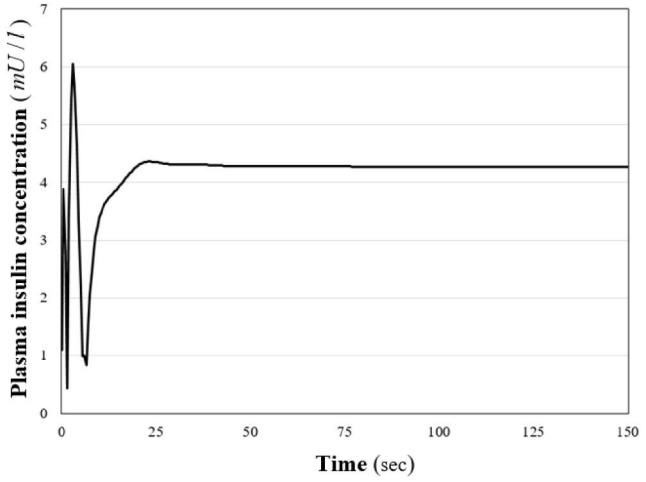


FIGURE 8 The time history of plasma concentration

(ii) To make the simulation more realistic, for the simulation purpose, the three meals with a high rate of glucose appearance in the blood, 5 mg/dl/min, 8 mg/dl/min, 5 mg/dl/min at 255, 575, and 750 min, accordingly. The control and observer gains for the simulation are considered similar to scenario 1.

To analyse the robustness of the controller against uncertainties in system parameters and external disturbance, the performance of the controller is analysed for 100 different random patients with different parameters, and the control grid variability analysis (CGVA) is shown in Figure 7. Inter- and intra-patient variability is performed considering the fact that the system parameters change randomly during the simulation, and the results are shown in Figure 8.

Figures 9 and 10 verify that 100% of the minimum BGC are greater than 70 mg/dl and 95% of the maximum BGC are less than 250 mg/dl.

TABLE 3 Uncertainty in system parameters

Parameters	Nominal value	Range
p_1	1×10^{-7}	$[0.7, 1.3] \times 10^{-7}$
p_2	0.015	[0.015, 0.055]
p_3	2×10^{-6}	$[1.4, 2.6] \times 10^{-6}$
p_4	0.2	[0.14, 0.26]
p_5	0.05	[0.04, 0.06]

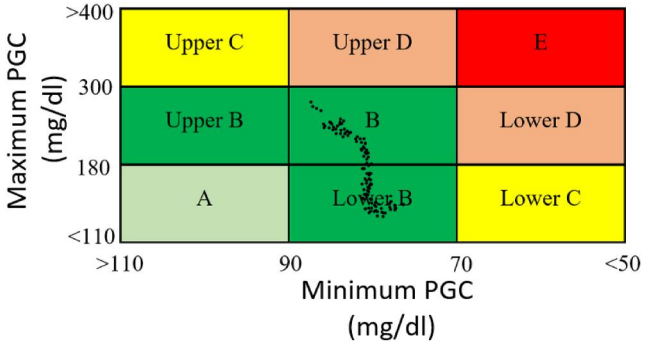


FIGURE 9 Control grid variability analysis (CVGA) plot of the type 1 diabetes mellitus (T1DM) subjects

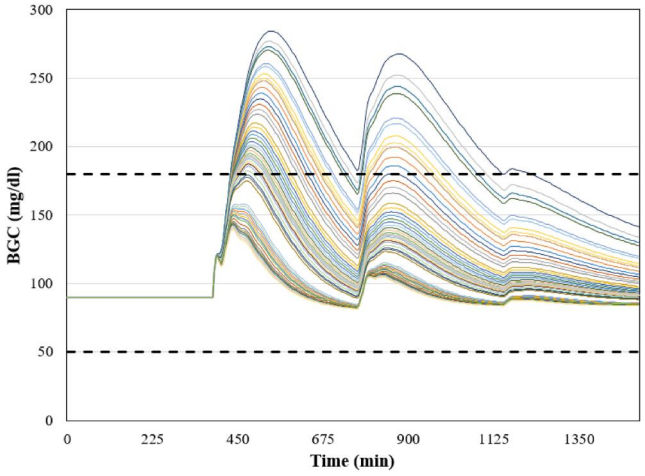


FIGURE 10 Blood glucose trajectories for virtual type 1 diabetes mellitus (T1DM) patients under parametric uncertainty

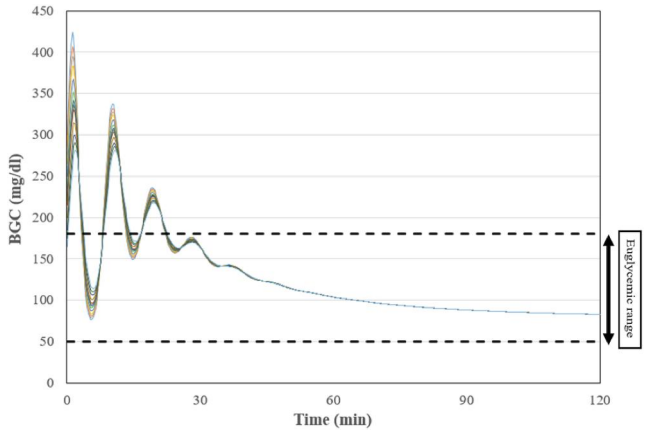


FIGURE 11 Blood glucose regulations for virtual type 1 diabetes mellitus (T1DM) patients for random initial conditions

5.3 | Scenario 3: Simulation with random initial conditions

The proposed observer-based controller is simulated in this section for different initial conditions selected within the range $x_1(0) \in [80, 350]$ mg/dl, $x_2(0) \in [0, 0.01]$ min^{-1}, $x_3(0) \in [0,20]$ mU/L. Figure 11 verifies that the proposed controller is asymptotically stable for different initial conditions, which are predictable, since the proposed controller ensures global asymptotic stability.

Remark 3 The simulation results in different scenarios verify that the proposed controller ensures asymptotic stability of the system without requiring the measurement of insulin and plasma concentrations. The controller also ensures that the system input always remains positive.

6 | CONCLUSION

This paper proposed a novel positive input observer-based blood glucose control method for EBMM using the BS approach. The asymptotic stability of the system was proved using the Lyapunov theorem. The proposed controller only requires the measurement of the BGC and ensures the asymptotic stability of the system. Simulation results verify the satisfactory performance of the proposed controller compared to previous related studies. Better regulation results were achieved without requiring the measurement of the remote insulin and plasma insulin concentration and without requiring a higher amount of insulin as the control input.

ACKNOWLEDGEMENT

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST

All authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: Homayounzade, M.: Positive input observer-based controller design for blood glucose regulation for type 1 diabetic patients: a backstepping approach. IET Syst. Biol. 16(5), 157–172 (2022). https://doi.org/10.1049/syb2.12049

APPENDIX A

Considering that the reference signal is constant, hence $\dot{X}_{1r} = 0$. Adding and subtracting $f(X_{1r}, \dot{X}_1)$ and $f(X_{1r},0)$ to the right side of Equation (21), we obtain

$$\begin{aligned}\dot{z}_2 = &\left(f(X_1,\dot{X}_1) - f(X_{1r},\dot{X}_1)\right) + \left(f(X_{1r},\dot{X}_1)\right.\\ &\left. - f(X_{1r},0)\right) + f(X_{1r},0) \quad + \left[\left(Y(X_1,\dot{X}_1)\right.\right.\\ &\left.\left. - Y(X_{1r},\dot{X}_1)\right) + \left(Y(X_{1r},\dot{X}_1) - Y(X_{1r},0)\right)\right.\\ &\left. + Y(X_{1r},0)\right] x_4 + p_3 x_3. \end{aligned} \tag{65}$$

Considering that

$$f(X_1,\dot{X}_1) - f(X_{1r},\dot{X}_1) = \overline{F}_1\,(X_1 - X_{1r}) = \overline{F}_1\, z_1, \tag{66a}$$

$$\begin{aligned} f(X_{1r},\dot{X}_1) - f(X_{1r},0) &= \overline{F}_2\,(\dot{X}_1 - 0)\\ &= \overline{F}_2\,(z_2 - \Lambda\, z_1), \end{aligned} \tag{66b}$$

$$\begin{aligned} Y(X_1,\dot{X}_1)x_4 - Y(X_{1r},\dot{X}_1)x_4 &= \overline{F}_3(X_1 - X_{1r})\\ &= \overline{F}_3\, z_1, \end{aligned} \tag{66c}$$

$$\begin{aligned} Y(X_{1r},\dot{X}_1)x_4 - Y(X_{1r},0)x_4 &= \overline{F}_4\,(\dot{X}_1 - 0)\\ &= \overline{F}_4\,(z_2 - \Lambda\, z_1), \end{aligned} \tag{66d}$$

we obtain

$$\dot{z}_2 = F_1\, z_1 + F_2\, z_2 + f(X_{1r},0) \; + Y(X_{1r},0)x_4 + p_3\, x_3, \tag{67}$$

where

$$\begin{aligned} F_1 &= \overline{F}_1 - \overline{F}_2\,\Lambda + \overline{F}_3 - \overline{F}_4\,\Lambda, \\ F_2 &= \overline{F}_2 + \overline{F}_4. \end{aligned} \tag{68}$$

APPENDIX B

Differentiating Equation (32) with respect to time, we obtain

$$\dot{\hat{z}}_2 = k_1\,\dot{z}_1 + \dot{\eta}. \tag{69}$$

Substituting $\dot{z}_1$ from Equation (17) and $\dot{\eta}$ from Equation (33), we obtain

$$\begin{aligned}\dot{\hat{z}}_2 = k_1(z_2 - \Lambda\, z_1) + \left(k_1\,\Lambda - k_1^{\,2}\right)z_1 - k_1\,\eta = k_1(z_2\\ - k_1\, z_1 - \eta) = k_1\,\tilde{z}_2. \end{aligned} \tag{70}$$

Differentiating the definition of Equation (25a) with respect to time and substituting for $\dot{z}_2$ from Equation (38) and $\dot{\hat{z}}_2$ from Equation (70), we obtain

$$\begin{aligned}\dot{\tilde{z}}_2 = \dot{z}_2 - \dot{\hat{z}}_2 = F_1\, z_1 + F_2\, z_2 - k_2(z_2 - \tilde{z}_2) + p_3\,\alpha\, e_1\\ + p_3\, e_2 - k_1\,\tilde{z}_2. \end{aligned} \tag{71}$$

APPENDIX C

Differentiating Equation (34) with respect to time, we obtain

$$\dot{\hat{x}}_3 = 2\alpha\, p_3\, \dot{z}_1 + \dot{\sigma}. \tag{72}$$

Substituting for $\dot{z}_1$ and $\dot{\sigma}$, respectively, from Equations (17) and (35), we obtain

$$\dot{\hat{x}}_3 = 2\alpha p_3(z_2 - \Lambda z_1) + 2\alpha p_3 \Lambda z_1 - p_3\alpha\hat{z}_2 - p_4(\hat{x}_3 + I_b) + v. \tag{73}$$

Differentiating Equation (25b) with respect to time, we obtain

$$\dot{e}_1 = \frac{1}{\alpha}\left(\dot{x}_3 - \dot{\hat{x}}_3\right). \tag{74}$$

Substituting $\dot{x}_3$ from Equation (4b) and $\dot{\hat{x}}_3$ from Equation (73) in Equation (74), we obtain

$$\alpha\dot{e}_1 = -p_4(x_3 + I_b) + v(t) - \left(2\alpha p_3(z_2 - \Lambda z_1) + 2\alpha p_3\Lambda z_1 - p_3\alpha\hat{z}_2 - p_4(\hat{x}_3 + I_b) + v\right). \tag{75}$$

Simplifying equal terms, we obtain

$$\alpha\dot{e}_1 = -p_3\alpha(z_2 + \tilde{z}_2) - p_4\alpha e_1. \tag{76}$$

APPENDIX D

Differentiating x_3^* from Equation (28) with respect to time to obtain

$$\dot{x}_3^* = \frac{1}{p_3}\left[-Y(X_{1r}, 0)\left(-p_5 x_4\right) - k_2 k_1 \tilde{z}_2\right]. \tag{77}$$

Differentiating the definition of e_2 from Equation (27), we obtain

$$\dot{e}_2 = \dot{\hat{x}}_3 - \dot{x}_3^*. \tag{78}$$

Substituting Equations (73) and (77), we obtain

$$\dot{e}_2 = 2\alpha p_3 z_2 - p_3\alpha\hat{z}_2 - p_4(\hat{x}_3 + I_b) + e_3 + v^* - \frac{1}{p_3}\left[-Y(X_{1r}, 0)\left(-p_5 x_4\right) - k_2 k_1 \tilde{z}_2\right]. \tag{79}$$

Substituting v^* from Equation (31) in the result, we obtain

$$\dot{e}_2 = 2\alpha\, p_3\, z_2 + \frac{1}{p_3} k_2\, k_1\, z_2 - \frac{1}{p_3} k_2\, k_1\, k_3\, e_2 + e_3. \tag{80}$$

APPENDIX E

Differentiating v^* from Equation (31) with respect to time to obtain

$$\dot{v}^* = p_4\dot{\hat{x}}_3 + p_3\alpha\dot{\hat{z}}_2 + \frac{1}{p_3} Y(X_{1r}, 0)\left(p_5\dot{x}_4\right) - \frac{1}{p_3} k_2 k_1 k_3 \dot{e}_2 + \frac{1}{p_3} k_2 k_1 \dot{\hat{z}}_2, \tag{81}$$

Substituting $\dot{\hat{x}}_3$ by Equation (73), $\dot{\hat{z}}_2$ by Equation (70), $\dot{x}_4$ by Equation (2d), and $\dot{e}_2$ by Equation (79) in Equation (81), we obtain

$$\begin{aligned}\dot{v}^* = {} & p_4\left(2\alpha p_3(z_2 - \Lambda z_1) + 2\alpha p_3\Lambda z_1 - p_3\alpha\hat{z}_2 - p_4(\hat{x}_3 + I_b) + v\right) + \left(p_3\alpha + \frac{1}{p_3} k_2 k_1\right)(k_1\tilde{z}_2) \\ & + \frac{p_5}{p_3} Y(X_{1r}, 0)\left(-p_5 x_4\right) \\ & - \frac{1}{p_3} k_2 k_1 k_3 \left(2\alpha p_3 z_2 - \alpha p_3\hat{z}_2 - p_4[\hat{x}_3 + I_b] + v \right. \\ & \left. - \frac{1}{p_3}\left(p_5 Y(X_{1r}, 0) x_4 - k_1 k_2 \tilde{z}_2\right)\right),\end{aligned} \tag{82}$$

Differentiating the definition of e_3 from Equation (30) and substituting Equation (23), we obtain

$$\begin{aligned}\dot{e}_3 &= \dot{v} - \dot{v}^*, \\ &= -uv - \dot{v}^*.\end{aligned} \tag{83}$$

Substituting u by Equation (36), $\dot{v}^*$ by Equation (82) and simplifying equal terms, we obtain

$$\dot{e}_3 = \left(2\alpha p_3 p_4 + p_3\alpha k_1 - 2\alpha k_2 k_1 k_3 - \frac{1}{{p_3}^2}(k_2 k_1)^2 k_3 + p_3\alpha k_1 + \frac{1}{p_3} k_2 {k_1}^2\right)\tilde{z}_2 - k_4 e_3 \tag{84}$$

APPENDIX F

Differentiating Equation (44) with respect to time to obtain

$$\dot{V} = \varepsilon\, z_1\, \dot{z}_1 + z_2\, \dot{z}_2 + \tilde{z}_2\, \dot{\tilde{z}}_2 + \alpha\, e_1\, \dot{e}_1 + \frac{p_3}{k_1 k_2} e_2\, \dot{e}_2 + \gamma\, e_3\, \dot{e}_3. \tag{85}$$

Substituting Equations (17), (38)–(42) in Equation (85) to obtain

$$\dot{V} = \varepsilon z_1[z_2 - \Lambda z_1] + z_2\left[F_1 z_1 + F_2 z_2 - k_2(z_2 - \tilde{z}_2) + p_3\alpha e_1 + p_3 e_2\right] + \tilde{z}_2\left[F_1 z_1 + F_2 z_2 - k_2(z_2 - \tilde{z}_2) + p_3\alpha e_1 + p_3 e_2 - k_1\tilde{z}_2\right] + e_1\left[-p_3\alpha(z_2 + \tilde{z}_2) - p_4\alpha e_1\right] + \frac{p_3}{k_1 k_2} e_2\left[2\alpha p_3 z_2 + \frac{1}{p_3}k_2 k_1 z_2 - \frac{1}{p_3}k_2 k_1 k_3 e_2\right] + \gamma e_3[\beta\tilde{z}_2 - k_4 e_3]. \quad (86)$$

Considering that for any arbitrary variables a and b we have $|a\,b| \le \frac{1}{2}\left(a^2 + b^2\right)$. Consequently, we obtain

$$\dot{V} \le \frac{\varepsilon}{2}\left({z_1}^2 + {z_2}^2\right) - \varepsilon\Lambda {z_1}^2 + \frac{1}{2}f_1\left({z_1}^2 + {z_2}^2\right) + f_2 {z_2}^2 + (z_2 + \tilde{z}_2)(-k_2(z_2 - \tilde{z}_2)) + \frac{1}{2}p_3\left({z_2}^2 + {e_2}^2\right) + \frac{1}{2}f_1\left({\tilde{z}_2}^2 + {z_1}^2\right) + \frac{1}{2}f_2\left({\tilde{z}_2}^2 + {z_2}^2\right) + \frac{1}{2}p_3\left({\tilde{z}_2}^2 + {e_2}^2\right) - k_1{\tilde{z}_2}^2 - p_4\alpha {e_1}^2 + \frac{2\alpha {p_3}^2}{k_1 k_2}\left({z_2}^2 + {e_2}^2\right) + \frac{1}{2}\left({e_2}^2 + {z_2}^2\right) - k_3 {e_2}^2 + \frac{1}{2}\gamma\beta\left({e_3}^2 + {\tilde{z}_2}^2\right) - \gamma k_4 {e_3}^2. \quad (87)$$

Consequently, we have

$$\dot{V} \le {z_1}^2\left[\frac{\varepsilon}{2} - \varepsilon\Lambda + \frac{1}{2}f_1 + \frac{1}{2}f_1\right] + {z_2}^2\left[\frac{\varepsilon}{2} + \frac{1}{2}f_1 + f_2 - k_2 + \frac{1}{2}p_3 + \frac{1}{2}f_2 + \frac{2\alpha {p_3}^2}{k_1 k_2} + \frac{1}{2}\right] + {\tilde{z}_2}^2\left[k_2 + \frac{1}{2}f_1 + \frac{1}{2}f_2 + \frac{1}{2}p_3 - k_1 + \frac{1}{2}\gamma\beta\right] + {e_1}^2\left[-p_4\alpha\right] + {e_2}^2\left[\frac{1}{2}p_3 + \frac{1}{2}p_3 + \frac{2\alpha {p_3}^2}{k_1 k_2} + \frac{1}{2} - k_3\right] + {e_3}^2\left[\frac{1}{2}\gamma\beta - \gamma k_4\right]. \quad (88)$$

Consequently, if the gains are selected such that Equations (46a)–(46f) are satisfied, we have

$$\dot{V} \le -\lambda_1 {z_1}^2 - \lambda_2 {z_2}^2 - \lambda_3 {\tilde{z}_2}^2 - \lambda_4 {e_1}^2 - \lambda_5 {e_2}^2 - \lambda_6 {e_3}^2. \quad (89)$$

where $\lambda_i\ i = 1:6$ are positive constants.