International Journal on Advanced Science Engineering Information Technology

Vol.12 (2022) No. 1
ISSN: 2088-5334

Artificial Pancreas: Avoiding Hyperglycemia and Hypoglycemia for Type One Diabetes

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***Abstract*— The objective of this work is to automatically regulate glycemia of Type 1 Diabetes Mellitus (T1DM) avoiding both hyperglycemia and hypoglycemia risks. A positive state feedback controller was designed previously to regulate Blood Glucose Concentration (BGC) in the fasting phase maintaining the system in the positively invariant set (PIS). The drawback of this positive controller is that when tested in the postprandial phase it couldn't avoid hyperglycemia. Therefore, in this work, the positive state feedback controller was developed to avoid both hypoglycemia and hyperglycemia maintaining the system inside the PIS. Meal disturbance is estimated by a sliding mode perturbation observer to be included in the control law. Such that meal effect is canceled early enough preventing glycemia from raising to hyperglycemia, but the positivity of the new controller isn't guaranteed. Therefore, a hybrid controller is designed to switch to the previous positive controller whenever the new controller has a negative action. A positive control is essential in this problem since the control input (insulin) can only be infused and it cannot be taken back from the bloodstream in case of any overdoses. The hybrid positive controller is tested *in silico* on five virtual T1DM patients. The results shown that the average percentage of time for glycemia over 180mg/dl (3.6%), normal range (80-120mg/dl) (78.2%), and below (80mg/dl) (0%) from overall simulation time. In conclusion, the hybrid positive control law succeeded to maintain the system inside the PIS avoiding hypoglycemia and preventing hyperglycemia keeping BGC in normal range rejecting meal disturbance.**

***Keywords*— Type 1 diabetes mellitus (T1DM); positively invariant set; sliding mode perturbation observer; hybrid control.**

Manuscript received 2 May 2021; revised 31 Jul. 2021; accepted 12 Aug. 2021. Date of publication 28 Feb. 2022.

I. INTRODUCTION

Before the discovery of insulin in 1921, T1DM was a deadly illness. The current treatment consists of a series of regular insulin injections based on glycemia and carbohydrate (CHO) intake measurements or continuous subcutaneous insulin infusion (CSII) through a pump [1], [2]. The aim is to keep Blood Glucose Concentration (BGC) in a healthy range (80 mg/dl to 140 mg/dl) [3]. Hyperglycemia (BGC > 180 mg/dl) must be prevented because cerebral stroke, cardiac arrest, renal failure, and vision loss become more likely when BGC levels exceed 180 mg/dl [4]. Exogenous insulin may be injected/infused to get glucose levels back to normal. Since insulin can only be injected, the controller must only have one direction of operation [5]. Any insulin overdose will result in hypoglycemia. Hypoglycemia has a faster onset and can quickly escalate to life-threatening levels, increasing the risk of diabetic coma [4].

Model Predictive Control (MPC) has gotten much attention in the last decade as an advanced control technique that can be used in an AP device [6], [7]. For people with (T1DM), zone model predictive control has proved to be an efficient closed-loop method of blood glucose regulation [8]. AP, in diabetes, refers to a closed-loop control to automate BGC regulation [9], [10]. The patient avoids manual insulin injections throughout the day [11]. MPC was chosen because of its demonstrated ability to estimate the best control action and deal with feedback, state constraints, and disturbances [12], [13]. These formulations, in general, use discrete-time control behavior and are based on the Bergman T1DM patient model and its linearization [14]. The disadvantage of these models, as shown by the Magdelaine *et al.* [2] model, is that this apparent model equilibrium in fasting periods so that a different insulin infusion rate is needed for each value of (BGC) in order to maintain a constant BGC level. Magdelaine *et al*. [2] demonstrated that this is not true in practice, with patients displaying only one single insulin infusion rate, known as the basal rate, independent of glycemia and capable

of maintaining equilibrium for any glycemia value during fasting periods.

Since insulin can only be injected, the positive-control design was presented in Nath *et al.* [4]. Furthermore, since glucose and insulin are both positive factors, the positive area for the device model must be measured to ensure that these variables remain positive. The positive invariant set for the glucose-insulin dynamic was calculated in Mohammad Ridha *et al.* [15] for the Magdelaine dynamic.

In addition, for glycemic regulation in the fasting phase, a positive Sliding Mode Control (SMC) was built in Nath *et al.* [4]. Just two states were used to measure the PIS (plasma insulin and subcutaneous insulin). The tradeoff was relatively hard between maintaining positive i/p – o/p bounds and regulation speed. A positive state feedback control was then devised [16]. Hypoglycemia was avoided during the fasting phase, and the controller kept the system inside PIS. After meal intake, glycemia is raised because meal intake is a positive factor. Thus the positive properties for the system and control action will not change.

Hyperglycemia under positive control in (Mohammad Ridha *et al.* [16] was not completely treated after meal intake. As a result, this is the primary issue discussed in this research. This depends on the controller's development in Mohammad Ridha *et al.* [16], by putting the estimated meal with a controller in the same channel. The meal intake is estimated via SMPO; it is a robust observer that is used to estimate the bounded disturbances. In other words, the development controller calculates the insulin amount required to minimize the expected meal's impact on BGC. In comparison, keeping the positivity constrained and also preventing hypoglycemia events. This paper is arranged as follows: in Section II, A. some useful preliminaries are presented, in B. the T1DM, in C. positive control problem, D&E. SMPO F. the control design and G. switching operation. Section III shows the results of simulation and discussion, and Section IV ends with a conclusion and future work.

II. Materials and Method

A. Preliminaries

If the state variables remain nonnegative for all nonnegative inputs and initial conditions, the system is said to be positive. Therefore consider the autonomous linear system;

$$\dot{x}(t) = Ax(t) + Bu(t),\ x(0) = x_0$$
$$y(t) = Cx(t) \tag{1}$$

where $x \in \mathbb{R}^n, y \in \mathbb{R}^p, u \in \mathbb{R}^m, A \in \mathbb{R}^{n\times n}, B \in \mathbb{R}^{n\times m}$ $C \in \mathbb{R}^{p\times n}$

Definition 1: "[17] If for every $x_0 \in \mathbb{R}_+^n, u \in \mathbb{R}_+^m$, the state $x(t) \in \mathbb{R}_+^n$ and output trajectories $y(t) \in \mathbb{R}_+^p$ for any $t \geq 0$, system (1), is named internally positive".

Definition 2:[17] "If $x_0 \in M$ implies $x(t, x_0) \in M$ for any $t \geq 0$, the nonempty set $M \subseteq \mathbb{R}^n$ is a positively invariant set (PIS), for system (1)".

Corollary 1: "[17] System (1) is internally positive if and only if, A is Metzler and $B \geq 0, C \geq 0$ (i.e. $b_{ij}, c_{ij} \geq 0\ \forall(i,j)\big)$".

B. Glucose – Insulin Mathematical Model

The glucose-insulin dynamics were modeled by the Magdelaine model, which was used in the *in-silico* research. Clinical data from diabetic patients with T1DM are used to build this simulator [2]. After adjusting variables to give them a more physiological sense, the following model represents the glucose-insulin dynamics [18].

$$\begin{pmatrix}\dot{x_1}\\ \dot{x_2}\\ \dot{x_3}\end{pmatrix} = \begin{pmatrix}0 & -\theta_2 & 0\\ 0 & -\frac{1}{\theta_3} & \frac{1}{\theta_3}\\ 0 & 0 & -\frac{1}{\theta_3}\end{pmatrix}\begin{pmatrix}G\\ x_{n_1}\\ x_{n_2}\end{pmatrix} + \begin{pmatrix}0\\ 0\\ \frac{1}{\theta_3}\end{pmatrix}u + \begin{pmatrix}\theta_1\\ 0\\ 0\end{pmatrix} + \begin{pmatrix}1\\ 0\\ 0\end{pmatrix}D(t) \tag{2}$$

Where, $x_1(t)\left[\frac{\text{mg}}{\text{dL}}\right]$ is glycemia , $\text{x}_2[U.min^{-1}]$ is plasma insulin rate, $\text{x}_3[U.min^{-1}]$ is the subcutaneous insulin rate. $\Theta_1\ \left[\frac{mg}{dl.min^{-1}}\right]$ the deference between liver production of glucose and its consumption by the brain. $\Theta_2\ \left[\frac{mg}{dl.U^{-1}}\right]$, the insulin sensitivity factor, $\theta_3\ [min^{-1}]$, the transfer time of insulin [19].

The model was re-represented in [18], after some change of variable so that basal insulin $(u_b = \frac{\theta_1}{\theta_2})\ [U.min^{-1}]$ that keeps BGC level constant was lumped in the controller, plasma insulin and subcutaneous insulin [18]. In other words, that the basal insulin is continuously injected.

$$\begin{cases}\begin{pmatrix}\dot{\tilde{x}}_1\\ \dot{\tilde{x}}_2\\ \dot{\tilde{x}}_3\end{pmatrix} = \begin{pmatrix}0 & -\theta_2 & 0\\ 0 & -\frac{1}{\theta_3} & \frac{1}{\theta_3}\\ 0 & 0 & -\frac{1}{\theta_3}\end{pmatrix}\begin{pmatrix}\tilde{x}_1\\ \tilde{x}_2\\ \tilde{x}_3\end{pmatrix} + \begin{pmatrix}0\\ 0\\ \frac{1}{\theta_3}\end{pmatrix}\tilde{u} + \begin{pmatrix}1\\ 0\\ 0\end{pmatrix}D(t)\\ \tilde{y} = C\tilde{x}, \tilde{x}_o \triangleq \tilde{x}(0)\end{cases} \tag{3}$$

Via the following change of variables:

$$\begin{aligned}\tilde{x}_1 &= x_1 - G_r\\ \tilde{x}_2 &= x_2 - u_b,\\ \tilde{x}_3 &= x_3 - u_b,\\ \tilde{u} &= u - u_b\end{aligned} \tag{4}$$

where $C = (1\quad 0\quad 0), G_r\ \left[\frac{mg}{dl}\right]$ is the glucose reference level (i.e. $\frac{110\text{mg}}{\text{dL}}\big), u_b\ \left[\frac{\text{U}}{\text{min}}\right]$.

C. Positive control and problem formulation

The main problem of this model is that it is not a positive realization according to definition (1) and corollary (1) [15]. So, this leads to finding the positive invariant set (PIS) for this system where insulin and glucose remain positive. In Mohammad Ridha *et al.* [15], the authors found the PIS in an open loop. Then in Mohammad Ridha *et al.* [16], the authors found the PIS under a positive state feedback control. This controller showed a good performance in the fasting phase. Hypoglycemia is totally prevented, and the control action remained positive for all time because of the system inside the PIS. The state feedback control was obtained as in Mohammad Ridha *et al.* [16]:

$$\tilde{u}(x) = F.x(t) \tag{5}$$

Where

$$F = k\left(\frac{1}{\theta_2}\quad -\theta_3\quad -\theta_3\right), k > 0 \tag{6}$$

The output of the positive controller is evaluated on the nominal system during the fasting phase and then under meal

perturbations, as described in Mohammad Ridha *et al.* [16]. The controller was active in preventing hypoglycemia in the fasting and postprandial phases, but it was unsuccessful in preventing hyperglycemia after meal intake. As known, meal intake is a positive disturbance. This results in glycemia remaining in the PIS, and the control action stays positive. Thus, the previous properties (in the fasting phase) are still true in a scenario that includes a disturbance meal [1].

In this work, the controller in (5) is developed with the same positivity properties to include hyperglycemia avoidance. This is accomplished by enabling the meal effect in the controller after estimating it as shown in the flowchart below:

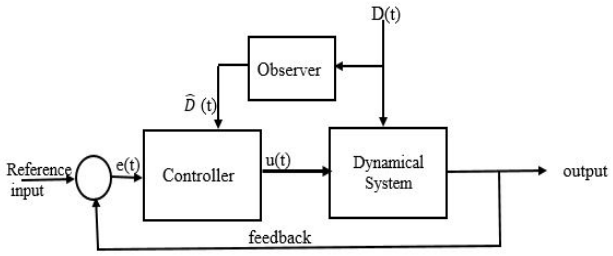

Fig. 1 Flowchart of the proposed controller

Therefore, the controller detects the amount and timing of the meal intake in this situation. The next section explains the meal estimation.

D. Sliding Mode Observer (SMO)

The Sliding Mode Perturbation Observer (SMPO) in this study will be used to estimate the disturbance meal D(t) based on equivalent control methodology. The control law will use this approximation after estimating D(t) to reduce its effect, shown later. To reconstruct the unknown input (the meal) for the (3), the following procedure uses the SMPO [20].

In the first step, with certain parameters let the observer dynamic be given by:

$$\dot{\tilde{x}}_1(t) = -\theta_2\, x_2(t) + k * sgn\left(\tilde{x}_1(t) - \hat{\tilde{x}}_1(t)\right)$$

$$\hat{\tilde{x}}_1(t_0) = \tilde{x}_1(t_0) \tag{7}$$

Where it is supposed that the only unknown element is the unpredictable meal. Then, the sliding variable s can be described as:

$$s(t) = \tilde{x}_1(t) - \hat{\tilde{x}}_1(t) \tag{8}$$

And its time derivative as:

$$\dot{s}(t) = \dot{\tilde{x}}_1(t) - \dot{\hat{\tilde{x}}}_1(t) \tag{9}$$

This leads to;

$$\dot{s}(t) = D(t) - k * sgn(\, s(t) \tag{10}$$

Thus, during sliding mode $\dot{s}(t) = s(t) = 0; \forall\, t \geq t_0$ [21],

$$D(t) = [k * sgn(\, s(t)]_{eq} \tag{11}$$

Where $[k * sgn(\, s(t)]_{eq}$ is the equivalent operator of the discontinue term.

The meal D(t) estimate is obtained according to the equivalent control principle [21]. The following Low Pass Filter (LPF) mathematically approximates meal from (12):

$$\dot{v}(t) = \frac{1}{\tau 1}\Big(-v(t) + k * sgn\big(s(t)\big)\Big) \tag{12}$$

And according to Utkin *et al.* [21]

$$v(t) \approx D(t) \tag{13}$$

The value of k is selected such that Falah *et al.* [22] $k > \max_t |D|$

$$\text{or; } k = k_0 + \max_t |D(t)|\,, k_0 > 0 \tag{14}$$

Assuming that the meal disturbance is constrained by a positive real number, such as M ($\max_t |D(t)| \leq M$) hence we have;

$$k = k_0 + M \tag{15}$$

Only the perturbation is estimated using this form of SMPO. In addition, when deriving a controller for BGC, the first and second derivatives for the estimated perturbation $\big(\mathrm{v}(t)\big)$are required, as shown in section F.

E. SMO with Approximate Signum Function (ASMO)

The chattering behavior is inherent in the sliding mode controller and observer. Hence the chattering will exist in observing the meal when it is estimated according to the above design. The sign function is replaced by an approximation signum function as follows in Falah *et al.* [22] and Al-samarraie [23], to remove the chattering that occurs in SMO.

$$sgn(s) \approx \frac{2}{\pi}\, tan^{-1}(\gamma s) \tag{16}$$

Where $\gamma \geq 1$ is a design parameter for the observer. By selecting the observer parameters k and γ (see Appendix A), the error in estimating the meal δ is given by [22].

$$|v(t) - \delta| \leq \frac{2}{\tau 1 \gamma} \tan\frac{\pi}{2k}\, M \tag{17}$$

Where $M = \sup_t D(t)$.

In addition, the time derivative for the estimated perturbation ($\dot{v}(t)$) is required when deriving a robust controller for BGC in the next section. This can be obtained from LPF in (12).

F. Control Design

In the construction of a realistic control problem, there will always be a discrepancy between the real model and the mathematical model used for the control strategy. These variations (or discrepancies) are caused by unknown input changes, model parameter variability, and unmolded dynamics.

Designing a control law that provides the desired output to the closed-loop system in the event of disturbance (input disturbances/parameter uncertainty) is a critical task for a control engineer. One design principle for this situation is to cancel the perturbation term after estimating it.

The Mohammad Ridha et al. [16] controller is used in this study to avoid hypoglycemia and hyperglycemia after meals. The system in equation (3) gets a new variable change. This is to add the meal with the controller designed in Mohammad Ridha *et al.* [16], with the same channel. The new control design will reduce the meal's action on the BGC. The variable

change begins with the assumption that:

$$z_1(t) = x_1(t) \tag{18}$$

and

$$\dot{z_1}(t) = -\theta 2\, z_2(t) \tag{19}$$

from equation (19) $\dot{z}_1(t) = \dot{x}_1(t)$, and from equation(3)

$$\dot{z_1}(t) = -\theta_2\, x_2(t) + \mathrm{D(t)} \tag{20}$$

Equating equation (20) with equation (3), leads to:

$$z_2(t) = x_2(t) - \frac{D(t)}{\theta 2} \tag{21}$$

Assume that $z_2(t)$ dynamic as follows;

$$\dot{z_2}(t) = -\frac{z_2(t)}{\theta 3} + \frac{z_3(t)}{\theta 3} \tag{22}$$

From equation (3);

$$\dot{x_2}(t) = -\frac{x_2(t)}{\theta 3} + \frac{x_3(t)}{\theta 3} \tag{23}$$

Differentiating equation (21), and equating with equation (22), and from equation (23), get:

$$z_3(t) = x_3(t) - \frac{D(t)}{\theta 2} - \dot{D}(t)\frac{\theta 3}{\theta 2} \tag{24}$$

Differentiating equation (24):

$$\dot{z_3}(t) = -\frac{z_3(t)}{\theta 3} + \frac{\tilde{u}(t)}{\theta 3} - \frac{D(t)}{\theta 2 * \theta 3} - \frac{\dot{D}(t)}{\theta 2} - \ddot{D}(t)\frac{\theta 3}{\theta 2} \tag{25}$$

Design $\tilde{u}(t)$ such that the dynamics of z_3 is similar to the dynamics of x_3 in fasting phase as follows:

$$\dot{z_3}(t) = -\frac{z_3(t)}{\theta 3} + \frac{\vartheta(t)}{\theta 3} \tag{26}$$

Where $u_z(t)$ is the new controller,

$$u_z(t) = \vartheta(z) + \theta 3 * \delta\left(D, \dot{D}, \ddot{D}\right) \tag{27}$$

Note that $\tilde{u}_z(t) = \tilde{u}(t)$ in (5), when D(t)=0.

Equation (27), express the new controller including the meal input and its derivative with the $\vartheta(z)$ is the same controller in the fasting phase but with a new state variable, where;

$$\vartheta(z) = F.z(t) \tag{28}$$

$$F = k\left(\frac{1}{\theta_2} \quad -\theta_3 \quad -\theta_3\right), k > 0$$

$$\delta\left(D, \dot{D}, \ddot{D}\right) = \frac{D(t)}{\theta 2 * \theta 3} + \frac{\dot{D}(t)}{\theta 2} + \ddot{D}(t)\frac{\theta 3}{\theta 2} \tag{29}$$

Equation (29) represents the amount of meal disturbance to be estimated. The new system after the change of variables become:

$$\begin{aligned} \dot{z}_1 &= -\theta_2 z_2 \\ \dot{z}_2 &= -\frac{1}{\theta_3} z_2 + \frac{1}{\theta_3} z_3 \\ \dot{z}_3 &= -\frac{1}{\theta_3} z_3 + \frac{1}{\theta_3} u + \delta\left(D, \dot{D}, \ddot{D}\right) \end{aligned} \tag{30}$$

The system then becomes similar to the system in equation (3) in the fasting phase after applying the new controller in equation (27). The new controller in (27) containing the positive controller in (28) and the estimated meal to cancel the effect of the meal intake. As a result, the new controller reduces the effect of the meal intake on the system in equation (6). While preserving the good propriety of the fasting controller [16].

The controller in equation (26) is composed of $\vartheta(z) \geq 0$ and $\delta\left(D, \dot{D}, \ddot{D}\right)$, is prevented both hypoglycemia and hyperglycemia completely. The derivative of meal intake isn't always positive. As a result, the control action cannot be guaranteed to remain positive for all times. Therefore, the next section will demonstrate a switching operation that results in a hybrid positive controller. The second derivative of meal intake is calculated numerically by *Matlab Simulink* in this study.

G. Switching Operation

Switching control is a term used to describe time-dependent optimal control problems with a vector-valued control system in which only one variable should be active at any given time [24]. Switching control theory is used in multi-objective control systems to solve regulation and safety control problems; figure (2) illustrates the architecture of a multi-controller [25].

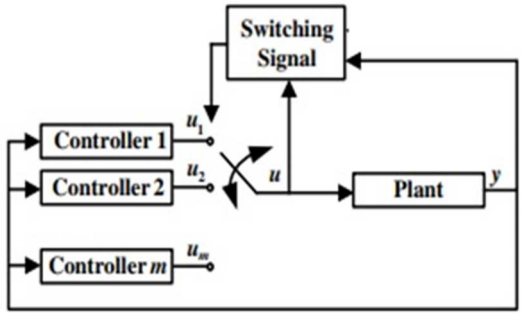

Fig. 2 Architecture of multi-controller

The main goal of this activity is to keep the system trajectory within the PIS. As discussed in the previous section, there are no guarantees that the controller $u_z(t)$ in (27) will remain positive at all times. As a result, there's a chance that the system trajectory will leave the PIS. As a result, switching operations must be performed between the new controller $u_z(t)$ in equation (27) and the original controller $\tilde{u}(t) = \mathrm{F.x(t)}$, which is positive, in equation (7). This ensures that the state trajectory stays inside the PIS. The switching operation is based on the condition that before the new controller's value drops below zero (negative control), the control is automatically switched to the controller in the previous position in (7).

$$u_s(t) = \begin{cases} u_z(t) & ; if\ u_z(t) \geq 0 \\ \tilde{u}(t) & ; if\ u_z(t) < 0 \end{cases} \tag{31}$$

Where, $u_s(t)$ the switching control or the hybrid control.

Appendix A

Appropriate selection of γ and k are obtained according to Eq. (15) and inequality (17). The SMO gain k is set equal to (Eq. (17))),[the max bound on the disturbance meal as $\max|D| \leq 2$];

$$\left.\begin{aligned} k &= k_o + \sup_t D(t) \\ &= 0.2 + 1.1372 \\ &= 1.3372 \end{aligned}\right\} \quad (32)$$

Now set the maximum estimation error to 0.1 in inequality (17) yield;

$$\left.\begin{aligned} |v(t) - \delta| &\le \frac{2}{\tau\gamma}\tan\frac{\pi}{2k}\sup_t D(t) \\ 0.1 &= \frac{2}{\tau_1 * \gamma}\tan\frac{\pi}{2k}\sup_t D(t) \\ \Rightarrow \gamma &= \frac{20}{0.08}\tan\frac{\pi}{2*1.3372} * 1.1372 \\ \gamma &= 5.8298 \end{aligned}\right\} \quad (33)$$

Appendix B

For the new hybrid controller, a Luenberger observer is used to estimate the insulin states x_2, x_3:

$$\dot{\hat{x}} = A\hat{x} + B\tilde{u}(t) + LC\left(\tilde{x} - \hat{\tilde{x}}\right) \quad (34)$$

The observer gain matrix L was generated using the pole placement method with the following poles:

$\lambda_L = -\left(10K \ \frac{1}{\theta_3} \ \frac{1}{\theta_3}\right)$, that resulted in relatively fast convergence.

III. Results and Discussion

This section compares the performance of the control strategies, taking into account the rejection of unannounced meal disturbances, the percentage of time spent within and outside the normoglycemia region, hypo and hyperglycemic incidents, and so on.

Lehmann and Deutsch [26] presented the function as a disturbance meal as in Fadhel and Raafat [27]. It gives a Gaussian shape meal operation, as shown in figure (3)

$$D(t) = \left(\frac{mt}{b^2}\right) e^{\left(\frac{-t^2}{2b^2}\right)} \quad (35)$$

Where $time\ t$ is in (min) and $D(t)$ is in $(mg/dl.min^{-1})$, m denoted the quantity of the carbohydrate in the meal $\left(\frac{mg}{dl}\right)$, and $(b = 80)$ is the constant value taken from Lehmann and Deutsch [26]. The ASMPO parameters are listed in table (1), [see appendix A].

TABLE I
ASMPO PARAMETERS

Parameter	Value	Unite
K	1.3372	-------
τ_1	0.08	min

Figure (3) displays the chatter elimination result using the Approximated Sliding Mode Observer ASMO.

Note that BGC1 means, blood glucose concentration under fasting phase positive state feedback controller. BGC2 means the blood glucose under a postprandial positive hybrid controller. $u_s(t)$ means the positive hybrid controller, switched controller means a positive controller that the new postprandial controller switched to it when it has a negative action, and $\tilde{u}(t)$is the fasting phase positive state feedback controller.

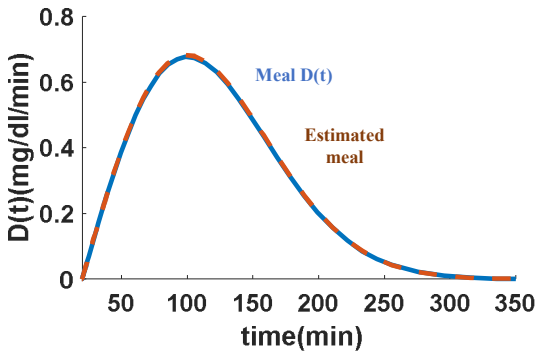

Fig. 3 Meal estimated using ACSMO

For the fasting phase equation (5), with $D(t) = 0$. The conventional positive state feedback controller steering glucose concentration (G= $\tilde{x}_1 + G_r$) to normal zone as fast as possible as shown in figure (4). While preventing hypoglycemia occurrence. This is true for patient 1. The virtual patient parameters are given in [18], where $\theta_2 = 10.78, \theta_3 = 122$ min , with initial glucose concentration $\left(G(0) = 140\frac{\text{mg}}{\text{dl}}\right)$.

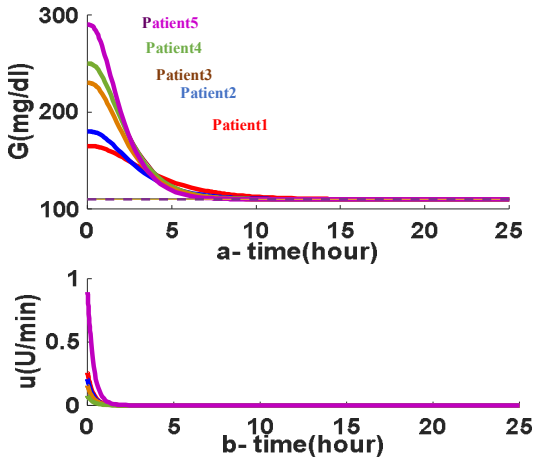

Fig. 4 Closed-loop response for all patients in the fasting phase

A 1-day virtual protocol taken from Sereno *et al.* [19] is used to evaluate the control strategies' effectiveness. Assume that the patients are given a different starting level of BGC at 00 hours and that the control loop is then closed. The patient took a breakfast (40g) of glucose at 7:00h, lunch (50g) at 13:00h, and dinner (70g) at 21:00h. After 24 hours, the virtual scenario ends. This scenario is shown simultaneously in figure (5-a) after meal estimation, under the new and conventional controller, and the control action for this process is also shown in figure (5-b). The hybrid controller $u_s(t)$ gives an adequate action (depending on the ASMPO accuracy estimation) that reduces the effect of the meal and keeps BGC in the normal zone. In contrast to the conventional positive state feedback controller $\tilde{u}(x)$. The state feedback gain is designed as; K = 0.05 [18]. The $u_z(t)$ remain positive for this scenario. Thus, the switching operation is not activated.

Figure (6) shows the Luenberger observer result for the insulin subsystem x_2, x_3. See that the initial starting point for the original state and estimated state are different. This is due

to the fact that the original state is unknown. Therefore, the starting point is chosen arbitrarily. [see Appendix B].

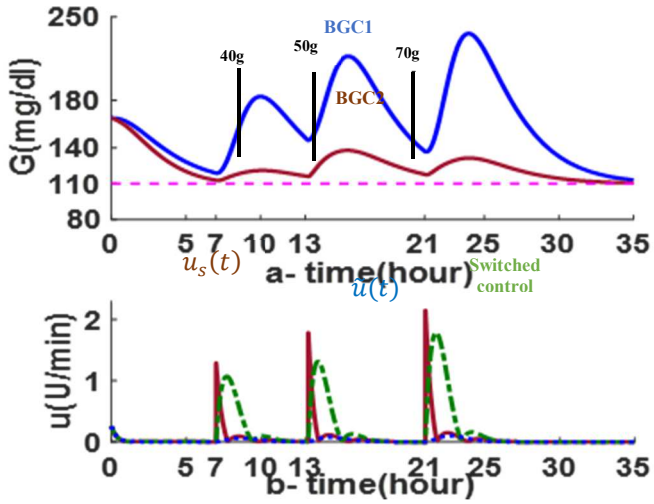

Fig. 5 Virtual protocol response for patient 1 a-BGC and b-control action

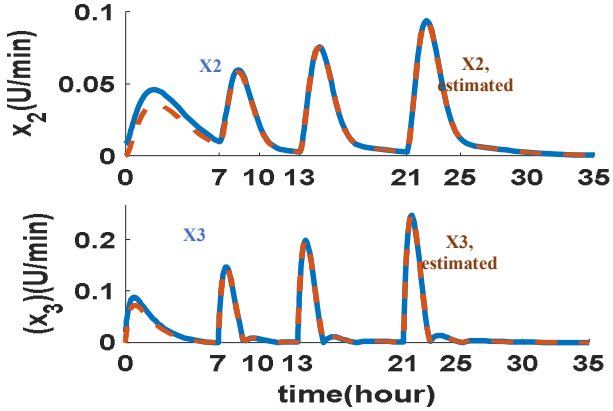

Fig. 6 Luenberger Observer behavior: insulin states and their estimation in closed-loop

The same scenario is repeated to patient 2 with initial glucose concentration $\left(G(0) = 70\frac{\text{mg}}{\text{dl}}\right)$ and $\theta_2 = 10.0634, \theta_3 = 58.5\ min$. Figure (7-a), shows the glucose concentration behavior, and figure (7-b), shows the control action behavior.

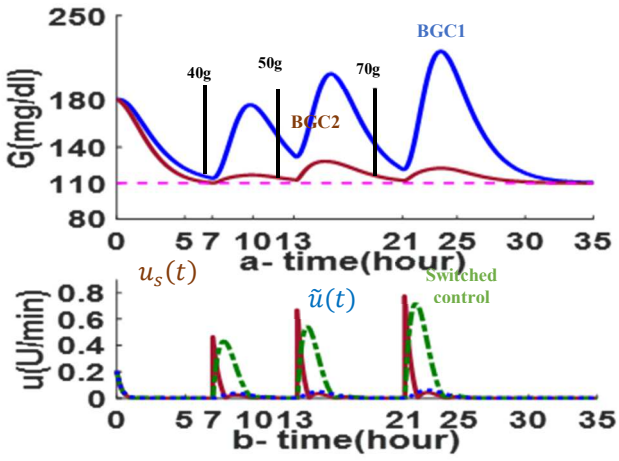

Fig. 7 Virtual protocol response for patient 2 a-BGC and b-control action

The figures below show the response behavior for the other three patients with the same protocol scenario. the information for each patient is listed in the caption of the figure.

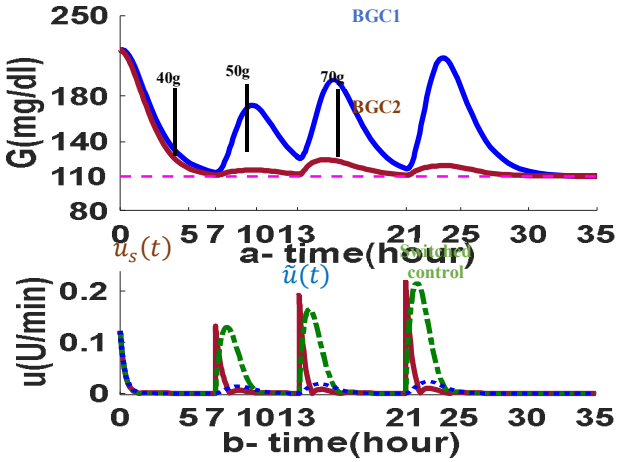

Fig.8 Virtual protocol response for patient 3 with $\left(G(0) = 100\frac{\text{mg}}{\text{dl}}\right), \theta_2 = 17.0154, \theta_3 = 88\ min$

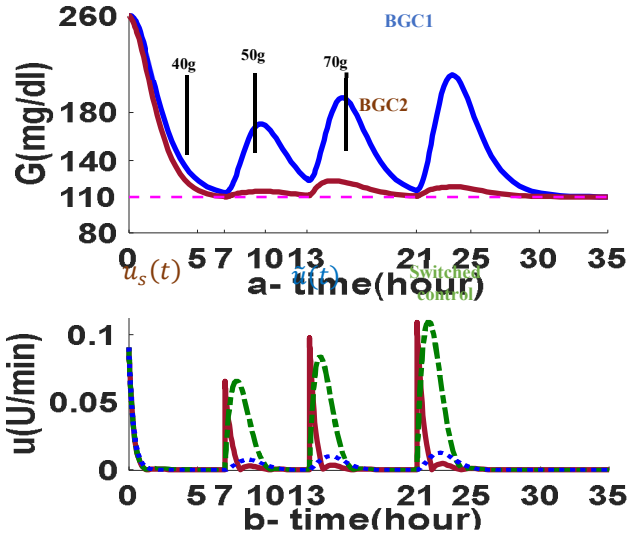

Fig. 9 Virtual protocol response for patient 4 with $\left(G(0) = 150\frac{\text{mg}}{\text{dl}}\right), \theta_2 = 45.22, \theta_3 = 74\ min$

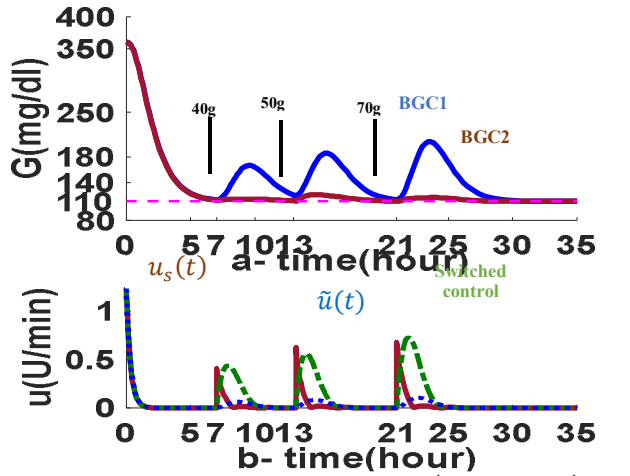

Fig. 10 Virtual protocol response for patient 5 with $\left(G(0) = 240\frac{\text{mg}}{\text{dl}}\right), \theta_2 = 83.079, \theta_3 = 70\ min$

The results for the five T1DM patients show that the hybrid controller reduced the effect of disturbance meal at any time. It is preventing both hypos and hyperglycemia episodes. Moreover, it is keeping the system inside the PIS with positive action. The -tables below illustrate the statistical results for all patients with the two controllers.

TABLE II
STATISTICAL RESULTS WITH $\tilde{u}(x)$

BGC mg/dl	Pat.1	Pat.2	Pat.3	Pat.4	Pat.5	Avg.
<80	0%	0%	0%	0%	0%	0%
80-120	10%	16%	17%	19%	14%	15.2%
120-140	23%	30%	22%	20%	24%	23.8%
140-180	36%	30%	33%	28%	32%	31.8%
>180	31%	24%	28%	33%	30%	29.2%

TABLE III
STATISTICAL RESULTS WITH $u_s(t)$

BGC mg/dl	Pat.1	Pat.2	Pat.3	Pat.4	Pat.5	Avg.
<80	0%	0%	0%	0%	0%	0%
80-120	69%	79%	76%	82%	85%	78.2%
120-140	26%	11%	14%	10%	10%	14.2%
140-180	3%	4%	5%	6%	2%	4%
>180	2%	6%	5%	2%	3%	3.6%

In table (II & III) the initial point was taken into account. The conventional positive state feedback controller success in preventing hypoglycemia events only. It is failed in preventing the risk of hyperglycemia. The percentage of glucose concentration in the range (80-120 g/dl) overall patients (15 % of simulation time), while in the range over 180 mg/dl (30% of simulation time).

The hybrid positive controller success in preventing both hypoglycemia and hyperglycemia. The overall percentage of glucose concentration in the safe zone (80-120 mg/dl) for all patients (75 % from the simulation time), and (16% of the time) in the range (120-140 mg/dl). Also, it is good to note that the percentage of glucose concentration below 80 mg/ dl is (0%). For all patient responses, the control action (insulin injection) remains positive for all times. This is due to the technique of the hybrid controller.

IV. CONCLUSION

A previous design positive state feedback controller is developed in this work to include meal effect estimation. The postprandial controller reduces the meal effect to prevent hyperglycemia, which was the main drawback of the previous positive controller. This development depends on meal disturbance estimated using SMPO and included in the control law (controller and disturbance in the same channel) such that the meal effect is canceled and hyperglycemia is prevented. Also, a Luenberger observer is used to estimate unmeasured system states that need in the feedback control.

This postprandial control law does not guarantee positivity; thus, a hybrid controller is designed. Therefore, whenever the new postprandial controller has a negative action, the hybrid controller switches to the original fasting phase positive state feedback controller. The overall hybrid controller is positive, and the system remains inside PIS. From the simulation results, the new hybrid positive controller has the advantages of the previous design, avoiding hypoglycemia (average percentage of glycemia below 80mg/dl is 0%), and the new achievement prevents hyperglycemia (average percentage glycemia over 180mg/dl is 3.6%). In the end, to complete the design. It would be appropriate to test controller robustness against parameter change.

REFERENCES

[1] N. Magdelaine *et al.*, "Hypoglycaemia-free artificial pancreas project," *IET Syst. Biol.*, vol. 14, no. 1, pp. 16–23, 2020, doi: 10.1049/iet-syb.2018.5069.

[2] N. Magdelaine *et al.*, "A long-term model of the glucose-insulin dynamics of type 1 diabetes," *IEEE Trans. Biomed. Eng.*, vol. 62, no. 6, pp. 1546–1552, 2015, doi: 10.1109/TBME.2015.2394239.

[3] M. J. Schoelwer *et al.*, "Predictors of Time-in-Range (70–180 mg/dL) Achieved Using a Closed-Loop Control System," *Diabetes Technol. Ther.*, vol. 23, no. 7, pp. 1–7, 2021, doi: 10.1089/dia.2020.0646.

[4] A. Nath, R. Dey, and C. Aguilar-Avelar, "Observer based nonlinear control design for glucose regulation in type 1 diabetic patients: An LMI approach," *Biomed. Signal Process. Control*, vol. 47, pp. 7–15, 2019, doi: 10.1016/j.bspc.2018.07.020.

[5] K. Menani, T. Mohammadridha, N. Magdelaine, M. Abdelaziz, and C. H. Moog, "Positive sliding mode control for blood glucose regulation," *Int. J. Syst. Sci.*, vol. 48, no. 15, pp. 3267–3278, 2017, doi: 10.1080/00207721.2017.1381893.

[6] A. Nath and R. Dey, "Robust observer-based control for plasma glucose regulation in type 1 diabetes patient using attractive ellipsoid method," *IET Syst. Biol.*, vol. 13, no. 2, pp. 84–91, 2019.

[7] P. Abuin, P. S. Rivadeneira, A. Ferramosca, and A. H. González, "Artificial pancreas under stable pulsatile MPC: Improving the closed-loop performance," *J. Process Control*, vol. 92, pp. 246–260, 2020, doi: 10.1016/j.jprocont.2020.06.009.

[8] Z. Cao, R. Gondhalekar, E. Dassau, and F. J. D. Iii, "Extremum Seeking Control for Personalized Zone Adaptation in Model Predictive Control for Type 1 Diabetes," vol. 9294, no. c, pp. 1–12, 2017, doi: 10.1109/TBME.2017.2783238.

[9] B. K. Abd-Al Amear, S. M. Raafat, and A. Al-Khazraji, "Glucose controller for artificial pancreas," *2019 Int. Conf. Innov. Intell. Informatics, Comput. Technol. 3ICT 2019*, pp. 1–6, 2019, doi: 10.1109/3ICT.2019.8910295.

[10] A. El Fathi, V. Gingras, and B. Boulet, "The artificial pancreas and meal control: an overview of postprandial glucose regulation in type 1 diabetes," *IEEE Control Syst. Mag.*, vol. 38, no. February, pp. 67–85, 2018.

[11] B. Moreano and J. Pumisacho, "Comparison between PID-Fuzzy and Numerical Methods based on linear Algebra controllers for Glucose control in Type 1 Diabetes treatment.," *2019 Int. Conf. Inf. Syst. Comput. Sci.*, pp. 156–162, 2019, doi: 10.1109/INCISCOS49368.2019.00033.

[12] A. K. Patra, A. K. Mishra, and P. K. Rout, "Backstepping Model Predictive Controller for Blood Glucose Regulation in Type-I Diabetes Patient," *IETE J. Res.*, vol. 66, no. 3, pp. 326–340, 2020, doi: 10.1080/03772063.2018.1493404.

[13] A. H. González, P. S. Rivadeneira, A. Ferramosca, N. Magdelaine, and C. H. Moog, "Stable impulsive zone model predictive control for type 1 diabetic patients based on a long-term model," *Optim. Control Appl. Methods*, vol. 41, no. 6, pp. 2115–2136, 2020, doi: 10.1002/oca.2647.

[14] C. Cobelli *et al.*, "Advancing Our Understanding of the Glucose System via Modeling: A Perspective," *IEEE Trans. Biomed. Eng.*, vol. 61, no. 5, pp. 1577–1592, 2014.

[15] T. Mohammadridha, P. S. Rivadeneira, J. E. Sereno, M. Cardelli, and C. H. Moog, "Description of the Positively Invariant Sets of a Type 1 Diabetic Patient Model," *17th CLCA Lat. Am. Conf. Autom. Control.*, 2016.

[16] T. MohammadRidha, P. S. Rivadeneira, N. Magdelaine, M. Cardelli, and C. H. Moog, "Positively invariant sets of a T1DM model: Hypoglycemia prediction and avoidance," *J. Franklin Inst.*, vol. 356, no. 11, pp. 5652–5674, 2019, doi: 10.1016/j.jfranklin.2019.03.022.

[17] L. F. S. Rinaldi, *Positive linear systems Theory and Application*, vol. 50. 2011.

[18] T. Mohammadridha, P. S. Rivadeneira, M. Cardelli, N. Magdelaine, and C. H. Moog, "Towards hypoglycemia prediction and avoidance for Type 1 Diabetic patients," *2017 IEEE 56th Annu. Conf. Decis. Control. CDC 2017*, doi: 10.1109/CDC.2017.8264264.

[19] J. E. Sereno, M. A. Caicedo, and P. S. Rivadeneira, "Artificial pancreas: Glycemic control strategies for avoiding hypoglycemia," *DYNA*, vol. 85, no. 207, pp. 198–207, 2018, doi:

10.15446/dyna.v85n207.71535.
[20] S. Ahmed, Y. K. Al-nadawi, M. H. Mshari, and M. M. Salih, "Electronic Throttle Valve Control Design Based on Sliding Mode Perturbation Estimator †," *IJCCCE*, vol. 15, no. 2, pp. 65–74, 2015.
[21] J. S. V. I. Utkin, J. Guldner, *Sliding Mode Control in Electro-Mechanical Systems. London, Taylor & Francis Group*. 2009.
[22] A. Falah, A. J. Humaidi, A. Al-dujaili, and I. K. Ibraheem, "Robust Super-Twisting Sliding Control of PAM- actuated Manipulator Based on Perturbation Observer Robust Super-Twisting Sliding Control of PAM- actuated Manipulator Based on Perturbation Observer," *Cogent Eng.*, vol. 7, no. 1, pp. 1–30, 2021, doi: 10.1080/23311916.2020.1858393.
[23] S. A. Al-samarraie, "A Chattering Free Sliding Mode Observer with Application to DC Motor Speed Control," *2018 Third Sci. Conf. Electr. Eng.*, pp. 259–264, 2018.
[24] C. Clason, A. Rund, and K. Kunisch, "Systems & Control Letters Nonconvex penalization of switching control of partial differential equations," *Syst. Control Lett.*, vol. 106, pp. 1–8, 2017, doi: 10.1016/j.sysconle.2017.05.006.
[25] M. I. Tomera, "Hybrid Switching Controller Design for the Maneuvering and Transit of a Training Ship," *Int. J. Appl. Math. Comput. Sci.*, vol. 27, no. 1, pp. 63–77, 2017, doi: 10.1515/amcs-2017-0005.
[26] E. D. Lehmann and T. Deutsch, "A physiological model of glucose-insulin interaction in type 1 diabetes mellitus," *J. Biomed. Eng.*, vol. 14, no. 3, pp. 235–242, 1992, doi: 10.1016/0141-5425(92)90058-S.
[27] S. F. Fadhel and S. M. Raafat, "H ∞ loop Shaping Robust Postprandial Glucose Control for Type 1 Diabetes," *Eng. Technol. J.*, vol. 39, no. 02, pp. 268–279, 2021.