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Model free sliding mode controller for blood glucose control: Towards artificial pancreas without need to mathematical model of the system

Nahid Ebrahimi, Sadjaad Ozgoli*, Amin Ramezani

Systems, Life Sciences and Control Engineering (SyLiCon) LAB, Department of Electrical and Computer Engineering, Tarbiat Modares University, Tehran, Iran

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ABSTRACT

Background: The mechanism of glucose regulation in human blood is a nonlinear complicated biological system with uncertain parameters and external disturbances which cannot be imitated accurately by a simple mathematical model. So to achieve an artificial pancreas, a method that does not need a model is necessary.

Methods: In this paper, a model free third order terminal sliding mode controller is developed and applied to blood glucose regulation system. So in this paper, a data driven control method is proposed which doesn't need a pre specified mathematical model of the system. The proposed method uses a third order terminal sliding mode controller to overcome the problem in finite time without chattering. It also uses a disturbance estimation technique to reject external disturbances. The sliding mode algorithm is equipped with a regression algorithm to release its need to model of the system. It is proved theoretically that the method is stable and the error converges to zero. In order to determine the parameters needed in this method, an algorithm is provided.

Results: Simulation studies are carried out with different scenarios and compared with Model Free Adaptive Control method. At the first scenario, the proposed method is applied to a virtual type- 1 diabetic patient without considering of external disturbances. The blood glucose level of 110 mg/dl is considered as the goal and it is illustrated that the desired glucose concentration is obtained. It is illustrated that the proposed method shows better performance against Model Free Adaptive Controller. Then in the next scenario, blood glucose of the patient is controlled in presence of three meal times during a day with different values of carbohydrate. The maximum of the blood glucose in this scenario is obtained as 168.5 mg/dl and the minimum of it stays on 85.5 Mg/dl. So the patient blood glucose level is almost within acceptable range (70–180 mg/dl) unlike the Model Free Adaptive Controller. In the last scenario, 22 tests are done for different patients (by randomly varying simulator parameters in $\pm$ 40% range) and the control performance is evaluated by the well-known Control Variability Grid Analysis CVGA. For all of them, the blood glucose remains in the green zone (safe region) of the CVGA .

Conclusion: Simulation results show that the proposed method acts robustly and can overcome uncertainties and external disturbances. The blood glucose level remains in safe region in all case. So the proposed method can be used in an artificial pancreas.

1. Introduction

Diabetes mellitus is a metabolic disease characterized by inadequate production of insulin or deficient sensitivity to insulin. Diabetes is classified into: "type1 diabetes" and "type 2 diabetes". In type 1 diabetes (T1D), the immune system attacks the b-cells in pancreas which produce insulin. Therefore the blood glucose concentration cannot be regulated by pancreas and maintains high level that may lead to some complications such as neural damages, blindness and chronic renal malfunction [1,2]. To survive, T1D patients must treat with multiple daily exogenous insulin injections.

In recent decades, researchers and engineers are going to automate the insulin management procedure in order to make artificial pancreas. These device consists of a glucose concentration sensor, a control algorithm and an infusion insulin pump [3]. Until now several control algorithms have been proposed for blood glucose regulation such as PID control [4,5], model predictive control [6–9], adaptive control [10,11], robust control [12–14] and sliding mode

* Corresponding author.
E-mail addresses: n.ebrahimimeymand@modares.ac.ir (N. Ebrahimi), ozgoli@modares.ac.ir (S. Ozgoli), ramezani@modares.ac.ir (A. Ramezani).

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control [15–17]. For example A new feedforward–feedback blood glucose controller is designed for type 1 diabetes patients in [18]. The proposed strategy in this paper is based on a ratio controller in which the insulin to CHO ratio is regulated based on the estimation of CHO meal. In [19], an adaptive controller is designed in order to keep blood glucose in normal range. A model-based strategy is used to obtain the insulin infusion rate, while the model parameters are tuned recursively. In [20] Internal Model Control (IMC) and enhanced IMC is presented for a diabetic patient. The first order plus time delay (FOPTD) model is used in order to approximate the first principles physiological model which is then used for developing the IMC and EIMC

Among these controllers, Sliding Mode Control has received a lot of attention in biomedical studies due to its unique features such as strong robustness, fast convergence rate, and simplicity [21,22]. In [23] a model free Nonsingular Fast Terminal Sliding Mode (NFTSM) Control is proposed in order to control the blood glucose concentration. The control algorithm in this paper is designed by adding a NFTSM component to the Nonlinear Integral Backstepping based Model Free (NIB-MFC) Control in order to compensate the estimation error of the time delay estimation module of NIB-MFC.

In spite of good features, the traditional SMC suffers from high-frequency oscillations called chattering phenomena and infinite convergence time. To solve the first issue many solutions has been proposed up to now. Among these methods, implementation of a high order SMC is of significant importance [24]. The main idea of high order sliding mode control is to drive the sliding variable and its derivatives to zero [25,26].

The second issue of traditional SMC is that the convergence time to the equilibrium point may not be finite. To solve this problem, the Terminal Sliding Mode Control (TSMC) method has been presented [27], where a nonlinear sliding surface is considered instead of a linear one. The chosen surface behaves as an attractor for the state trajectories [28].

In addition, the SMC method has the third and yet not solved problem: It is model based, i.e., a mathematical model of Glucose-insulin dynamics is required in order to design controller. On the other hand, glucose-insulin dynamics in the human body is complicated and includes nonlinearities and a large number of model parameters must be found. It has large variations from patient to patient and day-to-day for the same patient. Therefore an accurate model is unavailable or the computation cost of an accurate and reliable model is high. To overcome these problems, In many studies, Model free controllers, which utilize merely input and output data in their design procedures, have been considered [29–31].

Among the Data Driven Control (DDC) methods, Model Free Adaptive Control (MFAC) has obtained intensive attention due to its unique properties: First, MFAC uses only I/O data of the control systems; second, the MFAC method does not need any external “test and train” process and third, its scheme is simple and can easily be implemented [32].

MFAC is established on a new concept called pseudo-partial derivative (PPD), which is estimated only by using the I/O data of the controlled plant. Based on this concept, instead of identifying a global nonlinear model, an equivalent dynamical linearization data model is built along the dynamic operation points of the plant under control.

In this paper, in order to regulate blood glucose level, a model-free third order terminal sliding mode controller based on MFAC has been proposed and compared with Model Free Adaptive Control method. The model of the glucose-insulin system is not required in the proposed method. However, in order to test the effectiveness and performance of the method, a virtual diabetic patient is needed, For this, Dalla Man model [1,33] is used in this paper. In compare to most of in silico models, Dalla Man model is validated on more subjects and is more accurate [1].

The model-free terminal SMC has been basically provided by the authors in [34]. There, it is proved theoretically that the system trajectories are pushed into a bounded domain in the vicinity of the sliding surface and remains in it forever [34]. In addition, it is proved that the tracking error is bounded [34]. Here in this paper, the method is modified to be used for control of glucose level in blood. Practical limits are considered and a new parameter estimation algorithm is provided. In order to evaluate the proposed method, three different scenarios are assumed for simulation study: In the first scenario, it is considered that the external disturbances do not exist. In the second study, three meal ingestions are considered in simulations (as disturbance) and the blood glucose is controlled in presence of disturbances; and in the last scenario, the blood glucose control of different patients is considered and the Control Variability Grid Analysis (CVGA) is done.

In summary the contribution of this study is that a new approach is proposed in order to blood glucose control of type 1 diabetes. Since the glucose- insulin system is a complex nonlinear one that its model parameters are varying from one patient to patient and is continuously in presence of disturbances and uncertainties. The proposed method in this paper is only based on input and output data, therefore an accurate mathematical model is not needed and the proposed controller can adapt with different scenarios unlike the model based controllers.

On the other hand, the proposed method uses a new third order terminal sliding mode controller in order to decrease chattering phenomena and to obtain faster convergence rate in comparison to previous applied traditional sliding mode controllers.

One of the major problems for blood glucose controllers is to deal with many disturbances such as taking meals, exercises, stress and so on. In order to cope with this problem, we employ a disturbance estimation technique and show that the proposed controller can reject the external disturbances perfectly.

Another contribution of this paper is that a novel Parameter Tuning Algorithm is proposed in order to select design parameters properly which is an important issue in every controller design procedure. The results of the proposed controller are compared by Model Free Adaptive Controller and the superiority of the proposed method is shown in different scenarios.

This paper is organized as follows: The Proposed method is presented in Section 2. Simulation results are provided in Section 3. Discussion is made in Section 4. Glucose insulin model is presented in Appendix 1. Finally, Control Variability Grid Analysis is described in Appendix 2.

2. Methods

2.1. Problem formulation

It is considered that the relationship between plasma glucose concentration G and the injected insulin u(k) can be described as:

$$G(k+1) = f(G(k), \ldots, G(k-n_y), u(k), \ldots, u(k-n_u)) \quad (1)$$

where n_u and n_y are unknown orders of input, $u(k)$ and output, $G(k)$ respectively. $f(k)$ represents an unknown nonlinear function.

In order to apply the proposed method, the Glucose-insulin system described by (1) should meet following assumptions.

Assumption 1. Partial derivatives of $f(.)$ are continuous with respect to all variables, namely $u(k)$, ..., $u(k - L + 1)$, where $L > 1$ is the linearization length of the input.

Assumption 2. The system is generalized Lipschitz, which means

$$|G(k_1 + 1) - G(k_2 + 1)| \leq g_L \|U_L(k_1) - U_L(k_2)\| \quad (2)$$

for $U_L(k_1) \neq U_L(k_2)$ and any $k_1 \neq k_2, k_1, k_2 \geq 0$, where

$U_L(k) = [u(k), \ldots, u(k-L+1)]$

And g_L is the Lipschitz constant which is a positive constant.

Remark 1. According to Eqs. (A1) and (A23), it can be concluded that the partial derivatives are continuous, i.e. the glucose insulin system satisfies Assumption 1.

Remark 2. According to the proposed method in [35], the Lipschitz constant is calculated numerically for the glucose-insulin system by different tests. For this, the input signal is considered to be a random numeric sequence and k_1 and k_2 in (2) are changed randomly in each test. The test has been repeated 10,000 times and in all test runs the system satisfies the Lipschitz condition. The obtained results also show that the Lipschitz constant (computed as the maximum of all constants obtained in each test) is about $g_L = 304$.

Lemma 1. *(See [32]) For the discrete nonlinear system in (1) which satisfies Assumption 1 and Assumption 2 for any $L > 1$ if $\|\Delta U_L(k)\| \neq 0$, there exists a time-varying vector $\Phi_L \in R^L$ called the pseudo gradient vector such that the system can be described as the following Partial Form Dynamic Linearization (PFDL), i.e.*

$$\Delta G(k+1) = G(k+1) - G(k) = \Phi_L^T(k)\Delta U_L(k) \tag{3}$$

where

$$\Phi_L(k) = [\emptyset_1(k), \emptyset_2(k), \ldots, \emptyset_L(k)]^T$$

and

$$\Delta U_L(k) = U_L(k) - U_L(k-1)$$

□

The pseudo gradient, $\Phi_L(k)$, vector can be estimated by a minimization problem on the following criterion function:

$$J(\Phi_L(k)) = \left|G(k) - G(k-1) - \Phi^T{}_L(k)\Delta U_L(k-1)\right|^2 + \mu\|\Phi_L(k) - \hat{\Phi}_L(k)\|^2 \tag{4}$$

where $\mu > 0$ is a weighting factor and $\hat{\Phi}_L(k)$ is the estimation of the pseudo gradient vector. The estimation algorithm is obtained by minimizing the cost function (4) with respect to $\Phi_L(k)$, which yields

$$\hat{\Phi}_L(k) = \begin{cases} \hat{\Phi}_L(1) & \text{if} \begin{cases} \|\hat{\Phi}_L(k)\| \leq e \text{ or} \\ \|\Delta U_L(k-1)\| \leq e \text{ or} \\ sign(\hat{\emptyset}_1(k)) \neq sign(\hat{\emptyset}_1(1)) \end{cases} \\ \hat{\Phi}_L(k-1) + a & else \end{cases} \tag{5}$$

where

$$a = \frac{\eta\Delta U_L(k-1)\left(G(k) - G(k-1) - \hat{\Phi}_L(k-1)\Delta U_L(k-1)\right)}{\mu + \|\Delta U_L(k-1)\|^2}$$

In order to consider the effect of estimation error and external disturbances, a term modelling this effect, $D(k)$ is augmented as

$$G(k+1) = G(k) + \emptyset_1(k)u(k) + F(k) + D(k) \tag{6}$$

where

$$F(k) = \sum_{i=2}^{L} \emptyset_i(k)\Delta u(k-i+1) - \emptyset_1(k)u(k-1)$$

Based on disturbance estimation technique [36], external disturbance can be estimated as

$$\hat{D}(k) = D(k-1) = G(k) - G(k-1) - \emptyset_1(k-1)u(k-1) - F(k-1) \tag{7}$$

so, Eq. (6) can be rewritten as:

$$G(k+1) = G(k) + \emptyset_1(k)u(k) + F(k) + D(k-1) \tag{8}$$

In order to facilitate theoretical analysis, the following property should be considered for external disturbances:

Propery 1. There is a constant, $\Delta > 0$, such that:

$$|(D(k) - 2D(k-1) + D(k-2))| < \frac{\Delta}{\alpha_1} < \lambda_s \tag{9}$$

Where α_1 and λ_s are design parameters that will be introduced later.

Note that the amount of food which is taken by the patient in every meal time is bounded, so this property is satisfied by glucose-insulin system.

2.2. Proposed controller

In this section, in order to develop a robust controller against uncertainties, a third order model free discrete time sliding mode controller is designed based on the following switching function:

$$S_{i+1}(k) = S_i(k) + \beta_i S_i(k-1) \quad i = 1, 2 \tag{10}$$

Where β_1 and β_2 are design parameters and $S_1(k)$ is a terminal sliding function as

$$S_1(k) = \alpha_1 e(k) - \alpha_2 e(k-1) + \alpha_3 e(k-1)^{\alpha} \tag{11}$$

where $0 < \alpha_2 < \alpha_1$ and $\alpha_3 > 0$ are positive design parameters, $\alpha = \frac{p}{q}$, where p and q are two odd numbers such that $0 < p < q$. In addition $e(k)$ shows the tracking error $e(k) = G(k) - r(k)$ where $r(k)$ is the desired output.

In the next section, the model-free third order discrete TSMC is designed based on two theorems of [34]. In the first theorem, the convergence of $\sigma(k)$ into a quasi-sliding domain is mentioned. In the second theorem, the ultimately boundedness of the tracking error is guaranteed.

Theorem 1. *For the glucose-insulin system, described in Appendix 1, the control law (12) causes the $S_3(k)$ to converge into a quasi-sliding band with a band width of $|S_3(k)| < \alpha_1\lambda_s + \Delta$ in finite time and causes it to remain in this domain forever.*

$$u(k) = u_{eq}(k) + u_s(k) \tag{12}$$

Where $u_{eq}(k)$ is designed to be

$$u_{eq}(k) = (\alpha_1\emptyset_1(k))^{-1}\begin{pmatrix} \alpha_1 r(k+1) + \alpha_2 e(k) - \alpha_3 e(k)^{\alpha} - \alpha_1 G(k) \\ -\alpha_1 F(k) - \alpha_1 D(k-1) - \sum_{i=1}^{n-1} \beta_i S_i(k) \end{pmatrix} \tag{13}$$

And $u_s(k)$ is defined as

$$u_s(k) = (\emptyset_1(k))^{-1}\left(\emptyset_1(k-1)u_s(k-1) - \lambda_s sign(\sigma(k))\right) \tag{14}$$

where λ_s is a positive design parameter as mentioned in (9) and $sign(.)$ is the signum function.

Proof. As said in the previous section, the system satisfies Assumptions 1 and 2. In addition the disturbance satisfies property 1. So refer to details that can be found in [34], the proof completes.

2.2.1. Error dynamics analysis

Theorem 2. *For the system described by (1), if the nonlinear sliding function is chosen as (10) and the sliding control law is considered as (12), then the tracking error is ultimately bounded, which means that there is a number $K^* > 0$ such that*

$$|e(k)| \leq \psi(\alpha).max\left\{\left(\frac{\varepsilon}{\alpha_3}\right)^{\frac{1}{\alpha}}, \left(\frac{\alpha_3}{\alpha_2}\right)^{\frac{1}{1-\alpha}}\right\} \quad \forall k > K^* \tag{15}$$

where ε is a small positive number and $\psi(\alpha)$ is

$$\psi(\alpha) = 1 + \alpha^{\frac{\alpha}{1-\alpha}} - \alpha^{\frac{1}{1-\alpha}} \tag{16}$$

Proof. Considering $V(k) = |S_3(k)|$ as a Lyapunov function candidate, it can be proved that $S_1(k)$ and $S_2(k)$ tends to zero as k converges to infinity and consequently it is proved that the tracking error is ultimately bounded. More details can be found in [34].

Until now, a robust model free sliding mode controller is designed and analysed in order to regulate the blood glucose concentration. One of the main issues in the controller design procedure is to choose proper controller parameters. For a unique controller structure, different controller parameters may cause different control performances. Therefore, a parameter tuning approach is proposed to improve the controller performance in the next section.

2.3. Parameter tuning algorithm

An important problem in every controller design procedure is to select design parameters properly. In this case (blood glucose regulation), a new approach is proposed to tune deign parameters. This approach can also be used for other cases. The main idea of this method is based on making an analogy to a PID controller and use of PID design knowledge as a starting point. For this purpose, we consider some simple assumptions which convert structure of the proposed controller to PID format. It should be emphasized that these assumptions are just considered for construction of a parameter designing algorithm and this issue does not apply any limitation on the controller and its properties.

2.3.2. The algorithm

The following algorithm can converge to a set of proper parameters for the control law (12).

1- Design and tune a simple discrete time PID controller for system (1) as follows.

$$u(k) = u(k-1) + ae(k) + be(k-1) + ce(k-2) \tag{17}$$

2- Knowing a, b, c, solve the following nonlinear equations, (18) to (20), for α_is, β_is and $\emptyset_1(0)$

$$a = \frac{\alpha_2 - \alpha_1 - \alpha_3 - \alpha_1(\beta_1 + \beta_2)}{\alpha_1 \emptyset_1(0)} \tag{18}$$

$$b = \frac{(\beta_1 + \beta_2)(\alpha_2 - \alpha_3) - \alpha_1\beta_1\beta_2}{\alpha_1 \emptyset_1(0)} \tag{19}$$

$$c = \frac{\beta_1\beta_2(\alpha_2 - \alpha_3)}{\alpha_1 \emptyset_1(0)} \tag{20}$$

subject to the following constraints by a numerical method such as Genetic Algorithm (GA).

$0 < \alpha_2 < \alpha_1$

$\alpha_3 > 0$

$0 \le |\beta_1| < 1$

$0 \le |\beta_2| < 1$

3- Apply the proposed controller with the obtained parameters.

4- Evaluate the performance of the proposed controller. If the desired performance has not obtained, return to step 1 in order to tune the parameters. □

proof of convergence: First the control law, (12), is changed to PID format. For this, assume the following simplifying assumptions are met.

$$u_s(k) = 0 \tag{21}$$

$$G(k) - r(k+1) = e(k) \tag{22}$$

$$\alpha \approx 1 \tag{23}$$

$$D(k-1) = 0 \tag{24}$$

$$F(k) = -\emptyset_1(k)u(k-1) \tag{25}$$

According to Eqs. (13), (10) and (11) and by considering the above assumptions, the control law (12) can be rewritten as

$$\begin{aligned}(\alpha_1\emptyset_1(k))u(k) = {} & \alpha_1\emptyset_1(k)u(k-1) \\ & + \big(\alpha_2 - \alpha_1 - \alpha_3 - \alpha_1(\beta_1 + \beta_2)\big)e(k) \\ & + \big((\beta_1 + \beta_2)(\alpha_2 - \alpha_3) - \alpha_1\beta_1\beta_2\big)e(k-1) \\ & + \big(\beta_1\beta_2(\alpha_2 - \alpha_3)\big)e(k-2)\end{aligned} \tag{26}$$

Since in the first step we have $\emptyset_1(k) = \emptyset_1(0)$, the above equation changes to

$$u(k) = u(k-1) + ae(k) + be(k-1) + ce(k-2) \tag{27}$$

where a, b and c are as defined in (18) to (20). This has a discrete time PID format.

So if the controller parameters are founded via this algorithm, we expect it to have such a performance as the PID controller (27) may have. The performance may be degraded due to simplifying assumptions, but the PID tuning procedure works well and it is well known that a PID controller can be tuned up to reaching acceptable performance.

It should be noted that this analogy to the PID structure is just used for tuning the design parameters. We should not forget that the structure of the proposed controller is a sliding mode controller and it works well, as proved theoretically.

3. Results

In order to apply the proposed method in real word, the blood glucose control diagram shown in Fig. 1 should be implemented. The plasma glucose concentration is the measurement used to implement the control algorithm.

The model for the insulin pump is supposed to be 1 (i.e. no gain and no any delay is considered). For the model of patient, one of the most complete models from literature is considered which is introduced in Appendix 1. Nominal parameters of the model are given in Table 1. It should be noted that the model is not used in the insulin calculation method. It is just to simulate the patient and lies outside of the artificial pancreas. Performance of the proposed controller is investigated for virtual type-1 diabetic patients during a day.

Three different simulation scenarios are assumed. In the first scenario, the blood glucose level of 110**mg/dl** is considered as the goal and it is considered that any disturbance does not effect on the system. The Nominal parameters given in Table 1 are used for simulator in this scenario. The controller parameters are obtained according to mentioned tuning algorithm. The obtained parameters are set to be $\alpha_1 = 0.9964$, $\alpha_2 = 0.99$, $\alpha_3 = 0.0029$, $\beta_1 = -0.7707$, $\beta_2 = -0.0879$, $\mu = 0.9$, $\eta = 0.001$.

In order to show the effectiveness of the method, the proposed controller and Model Free Adaptive Control (MFAC) are

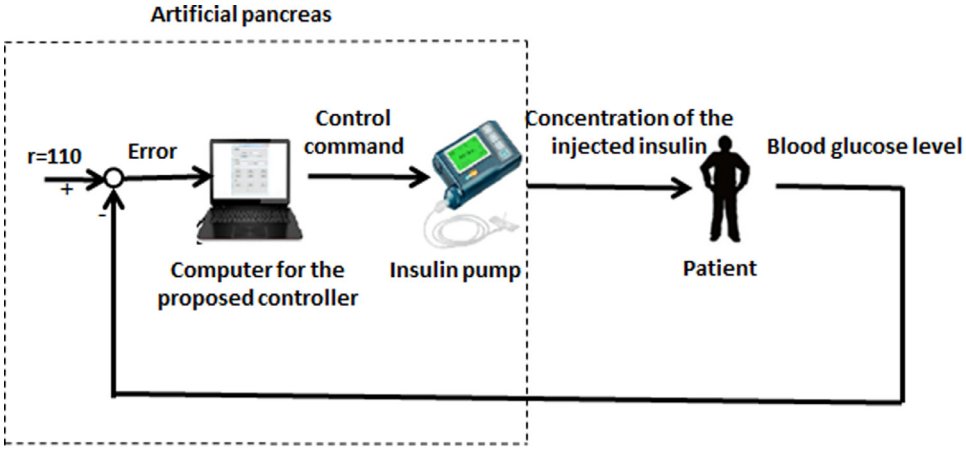

Fig. 1. Artificial pancreas in control loop.

Table 1
Model Parameters for diabetic patient.

Parameter	Value	Parameter	Value
Vg	1.88	k_{p1}	3.1106
k_2	0.079	k_{p2}	0.0021
k_1	0.065	k_{p3}	0.009
k_i	2.6114	p_{2u}	0.0331
V_{mx}	0.047	k_{max}	0.0558
k_{m0}	225	k_{min}	0.008
F_{snc}	1	k_{abs}	0.0568
b	0.82	m_3	0.285
d	0.01	m_4	0.1936
f_1	0.9	k_{e1}	0.005
m_1	0.19	k_{e2}	339
m_2	0.4840	BW	78

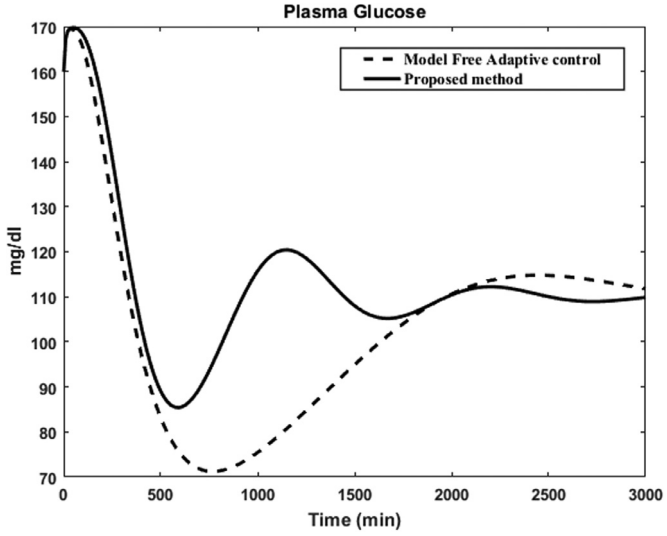

Fig. 2. Plasma glucose of a type 1 diabetic patient with the proposed method and MFAC without meal disturbances.

implemented for a virtual type-1 diabetic patient. The tracking performance of both methods is illustrated in Figs. 2 and 3. As seen, the controller performance of the proposed method is satisfactory and the proposed method follows the desired blood glucose level better than MFAC.

In the second scenario, three meal disturbances are set in the daily program of the patient. At 7 AM, the patient has breakfast containing 35**gr** of carbohydrates. At 13 PM, the patient takes a meal containing 50**gr** of carbohydrates. At 19 PM, the patients has

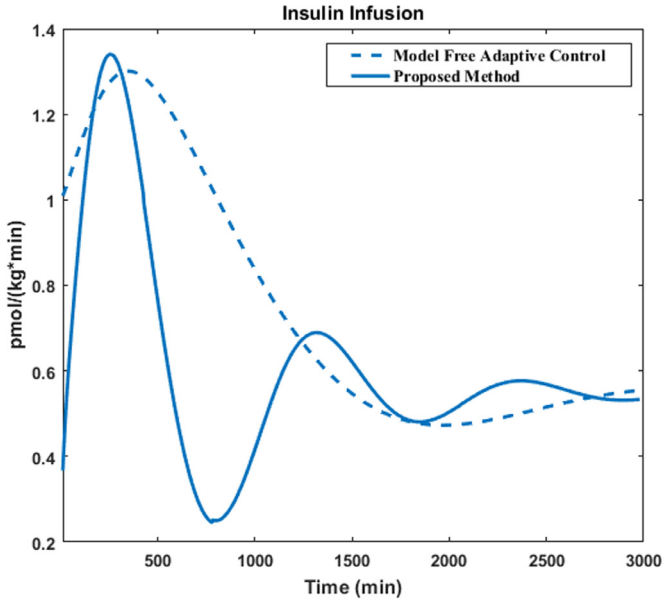

Fig. 3. Infusion insulin of the proposed method and MFAC without meal disturbances.

dinner which contains 70 ***gr*** of carbohydrates. In this scenario, the nominal model parameters given in Table 1 are used also.

The simulation results of the both approaches are shown in Figs. 4 and 5. As seen, the patient blood glucose level is almost within acceptable range of $70-180\,^{\mathbf{mg}}/_{\mathbf{dl}}$. By applying the proposed method no hyperglycaemic phenomenon is occurred and the minimum values of blood glucose are also regulated very well but the simulation result of the MFAC is unacceptable and hyperglycaemic phenomenon is occurred.

In the third scenario, in order to test the performance and robustness of the proposed method, the control variability grid analysis (CVGA) is used (see Appendix 2). For this, all parameters of the model are varied randomly within ± 40% range. The control performance obtained in this scenario is illustrated in CVGA plane for 22 tests depicted at Fig. 6.

As seen, almost all of the test results lay in the green zone, which is the safe region.

In order to evaluate the performance of the proposed method in presence of the measurement noise, we perform two other simulations. At the first simulation, we consider that we have no meal disturbances and the measured blood glucose effected by a random

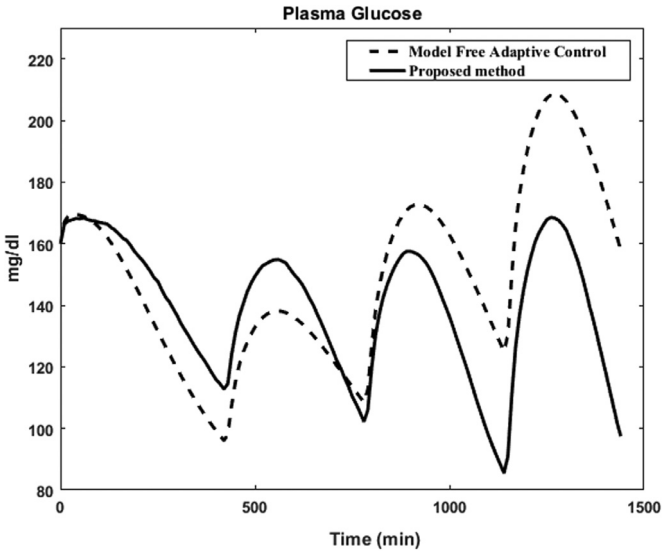

Fig. 4. Plasma glucose results of a type 1 diabetic patient with the proposed method compared to MFAC in presence of three meal disturbances.

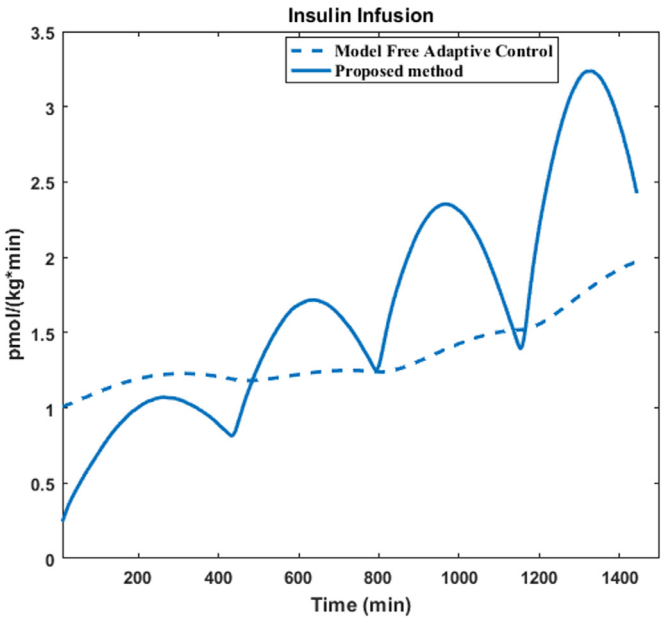

Fig. 5. Infusion insulin of the proposed method and MFAC in presence of three meal disturbances.

noise as follows:

$$\boldsymbol{G_n(k) = G(k) + n(k)} \tag{28}$$

where $\boldsymbol{n(k)} = 2^*(\boldsymbol{rand}(1) - 0.5)$.

In this condition, the blood glucose level and insulin infusion are demonstrated in Figs. 7 and 8.

Simulation results show that the proposed method is able to regulate the blood glucose under the influence of measurement noise.

In the next simulation, we consider that the daily program of the patient includes three meal disturbances and glucose sensor include measurement noise same as (28).

The simulation results are shown in Figs. 9 and 10. As it can be seen, the blood glucose level maintains in the safe region and the proposed method has acceptable response.

3.1. Implementation notes for artificial pancreas

The glucose- insulin system is a nonlinear complex system which is related to other biological system of the patient. On the other hand the model parameters vary from patient to patient, so the designed control algorithm should be robust and adaptive.

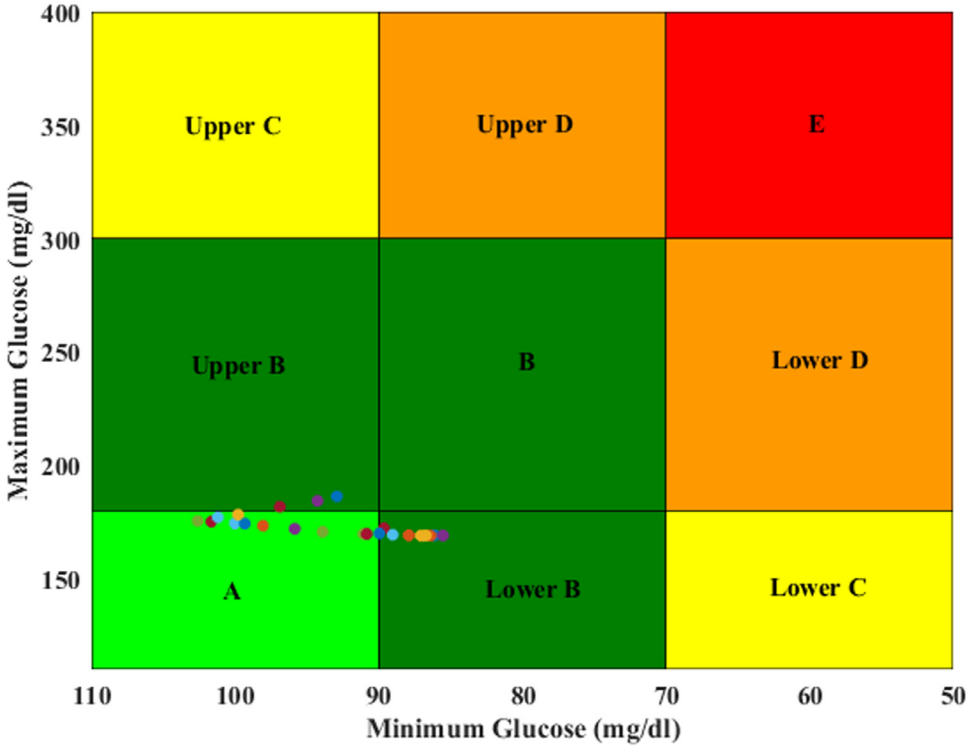

Fig. 6. Control Variability Grid Analysis with ± 40% change in parameters for different patients.

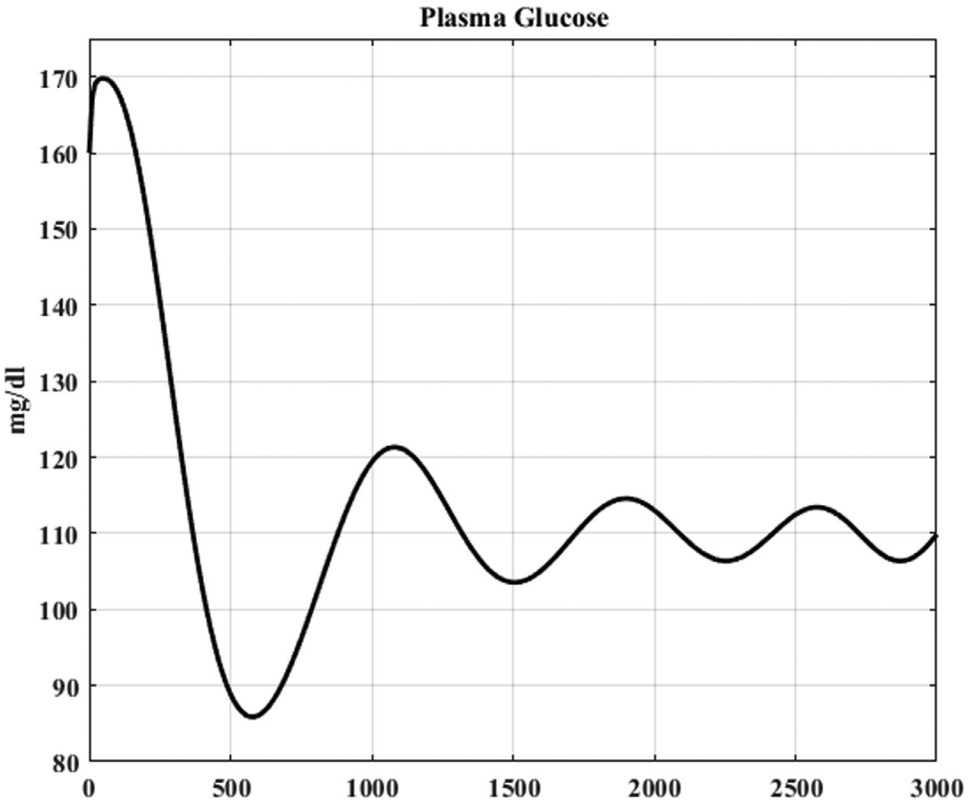

Fig. 7. Plasma glucose of a type 1 diabetic patient with the proposed method in presence of measurement noise regardless of the meal disturbances.

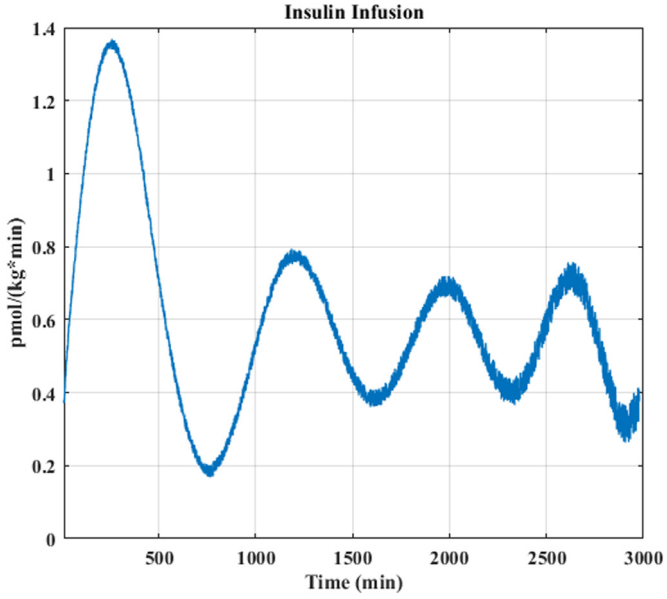

Fig. 8. Insulin infusion of a type 1 diabetic patient with the proposed method in presence of measurement noise regardless of the meal disturbances.

The proposed method in this paper satisfies this issue but there are more notes that should be considered to implement an algorithm as a real safe artificial pancreas. Selecting an accurate sensor with small delay is one of them. In order to guarantee the safety of the system, multiple sensors can be used. The delayed action of the insulin pump is other point for glucose control algorithms. This would be considered for future studies. The time interval at which the control algorithms determine the output should be on the proper order. In order to deal with the risk of hypoglycemia for automated system, the use of glucagon can be a safety measure; also necessary alarms should be given to the patient to take carbohydrates in this case. It should be possible for the control algorithms to stop for a few minutes for maintenance operations such as sensor replacement. Another aspect that has to be considered for practicality of the control algorithms is handling data dropout. This case can be a future work in order to develop the proposed algorithm. Proper selecting of the desired signal has also great importance. Maximum and minimum of the infusion insulin, Reasonable changes in blood glucose are some of the main constraints that must be applied to control algorithms in order to practical implementing.

4. Discussion

In this paper, a new data driven controller has been proposed to regulate blood glucose level. The controller uses third-order discrete time terminal sliding mode method. The proposed method utilizes merely input and output data of glucose-insulin system. Since control design procedure does not need a mathematical model of the glucose-insulin system, it is very suitable to be applied in practice. The controller parameters are tuned by a novel algorithm which uses analogy to a PID controller. This enables the designer to make benefits of his/her skills of PID controller design.

In addition in the proposed method, external disturbances have been handled by using a disturbance estimation method. Hence, it has robust performance in presence of external disturbances such as meal disturbances.

In order to evaluate the effectiveness of the proposed method, three scenarios are investigated via simulations and the results compared with Model Free Adaptive Controller. At first, blood glucose control is considered for a virtual type- 1 diabetic patient regardless of external disturbances and it is shown that the desired

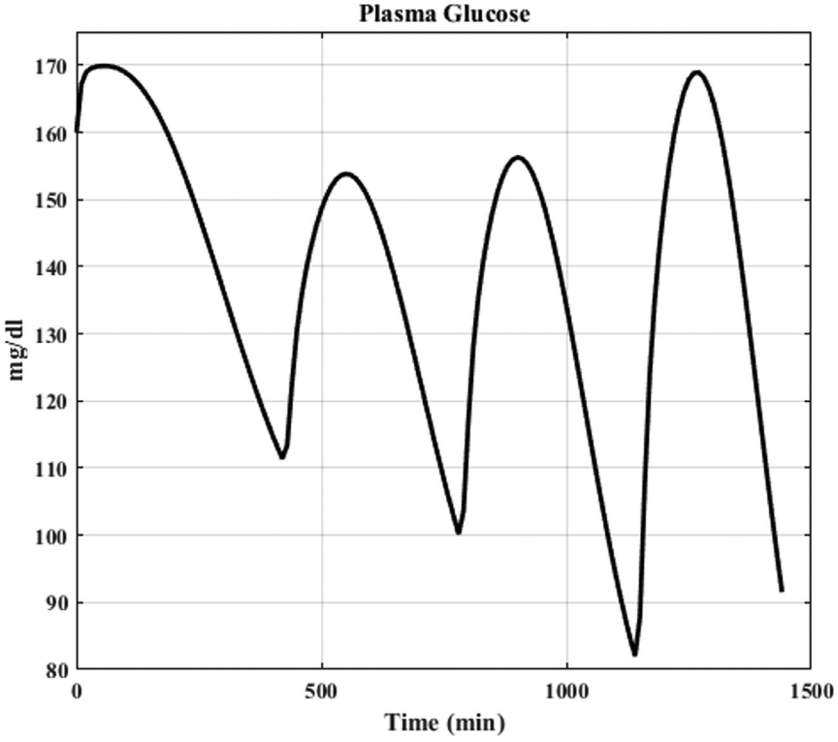

Fig. 9. Plasma glucose of a type 1 diabetic patient with the proposed method in presence of measurement noise and meal disturbances.

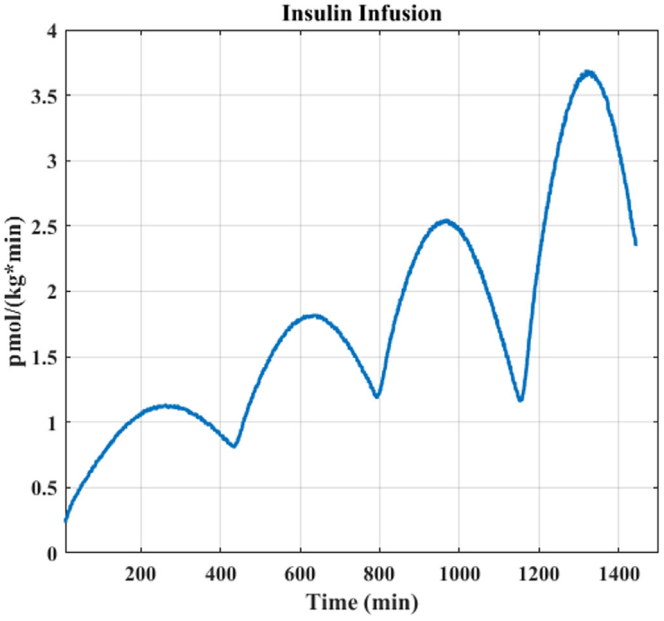

Fig. 10. Insulin infusion of a type 1 diabetic patient with the proposed method in presence of measurement noise and meal disturbances.

glucose level is achieved. The superiority of the proposed method against MFAC is illustrated. Then in the second scenario, blood glucose control of the patient is performed in presence of three meal takings and it is shown that the proposed method is robust against external disturbances and the blood glucose level remains in the acceptable range unlike the MFAC method. In the last scenario, different patients are considered and the control performance is evaluated by CVGA by 40% change in parameters. The blood glucose level, remains in the safe region in this case too.

It should be noted that the glucose insulin system is a complex nonlinear system which is subjected to different disturbances such as food intake, emotional stress, exercise, hormonal changes and so on. In this paper we take account the effect of food intake. More studies on the impact of other disturbances and their interactions would be considered as future works.

Declaration of Competing Interest

The authors have no conflict of interest.

Appendix 1. Glucose insulin model for people with T1D

In [1,33] a state space ODE model has been introduced by Dalla Man et.al. for the variations of blood glucose level in a human. The model is presented in [1,33] in 7 subsystems. Here we just provide the model equations without description of parameters. The reader is referred to [1,33] for details. The model is republished here, just to make familiarization with its structure and properties (Assumption 1 and 2). The equations are as follows:

$$\dot{\mathbf{Q}}_{\mathbf{sto1}}(\mathbf{t}) = -\mathbf{k}_{\mathbf{gri}}\mathbf{Q}_{\mathbf{sto1}}(\mathbf{t}) \tag{A1}$$

$$\dot{\boldsymbol{Q}}_{\boldsymbol{sto2}}(\boldsymbol{t}) = -\boldsymbol{k}_{\boldsymbol{empt}}\boldsymbol{Q}_{\boldsymbol{sto2}}(\boldsymbol{t}) + \boldsymbol{k}_{\boldsymbol{gri}}\boldsymbol{Q}_{\boldsymbol{sto1}}(\boldsymbol{t}) \tag{A2}$$

$$\dot{\boldsymbol{Q}}_{\boldsymbol{gut}}(\boldsymbol{t}) = -\boldsymbol{k}_{\boldsymbol{abs}}\boldsymbol{Q}_{\boldsymbol{gut}}(\boldsymbol{t}) + \boldsymbol{k}_{\boldsymbol{empt}}(\boldsymbol{t}, \boldsymbol{Q}_{\boldsymbol{sto}}(\boldsymbol{t}))\boldsymbol{Q}_{\boldsymbol{sto2}}(\boldsymbol{t}) \tag{A3}$$

$$\boldsymbol{Q}_{\boldsymbol{sto}}(\boldsymbol{t}) = \boldsymbol{Q}_{\boldsymbol{sto1}}(\boldsymbol{t}) + \boldsymbol{Q}_{\boldsymbol{sto2}}(\boldsymbol{t}) \tag{A4}$$

$$\boldsymbol{R}_{\boldsymbol{a}}(\boldsymbol{t}) = \frac{\boldsymbol{f}\boldsymbol{k}_{\boldsymbol{abs}}\boldsymbol{Q}_{\boldsymbol{gut}}(\boldsymbol{t})}{\boldsymbol{BW}} \tag{A5}$$

$$\boldsymbol{k}_{\boldsymbol{empt}}(\boldsymbol{t}, \boldsymbol{Q}_{\boldsymbol{sto}}(\boldsymbol{t})) = \boldsymbol{k}_{\boldsymbol{max}} + \frac{\boldsymbol{k}_{\boldsymbol{max}} - \boldsymbol{k}_{\boldsymbol{min}}}{2}[\boldsymbol{A}(\boldsymbol{t})] \tag{A6}$$

$$\boldsymbol{A}(\boldsymbol{t}) = \tanh\left[\boldsymbol{\alpha}(\boldsymbol{Q}_{\boldsymbol{sto}}(\boldsymbol{t}) - \boldsymbol{bD}(\boldsymbol{t})\right] - \tanh\left[\boldsymbol{\beta}(\boldsymbol{Q}_{\boldsymbol{sto}}(\boldsymbol{t}) - \boldsymbol{dD}(\boldsymbol{t}))\right]$$

$$\alpha = \frac{5}{2D(t)(1-b)}$$

$$\beta = \frac{5}{2D(t)d}$$

$$D(t) = \int_{t_i}^{t_f} d(t)dt$$

$$\dot{G}_p(t) = -k_1 G_p(t) + k_2 G_t(t) + EGP(t) + R_a(t) - U_{ii} - E(t) \quad \text{(A7)}$$

$$\dot{G}_t(t) = k_1 G_p(t) - k_2 G_t(t) - U_{id}(t) \quad \text{(A8)}$$

$$G(t) = \frac{G_p(t)}{V_G} \quad \text{(A9)}$$

$$E(t) = max\{0, k_{e1}(G_p(t) - k_{e2})\} \quad \text{(A10)}$$

$$EGP(t) = max\left\{0,\ EGP_b - k_{p2}\left(G_p(t) - G_{pb}\right) - k_{p3}\left(I_d(t) - I_b\right)\right\} \quad \text{(A11)}$$

$$\dot{I}_1(t) = k_i I(t) - k_i I_1(t) \quad \text{(A12)}$$

$$\dot{I}_d(t) = k_i I_1(t) - k_i I_d(t) \quad \text{(A13)}$$

$$U_{id}(t) = V_m(X(t)) \frac{G_t(t)}{k_m + G_t(t)} \quad \text{(A14)}$$

$$V_m(X(t)) = V_{m0} + V_{mx} X(t) \quad \text{(A15)}$$

$$\dot{X}(t) = p_{2u}(I(t) - I_b) - p_{2u} X(t) \quad \text{(A16)}$$

$$\dot{I}_p = m_1 I_l(t) - (m_2 + m_4) I_p(t) + s(t) \quad \text{(A17)}$$

$$\dot{I}_l = m_2 I_p(t) - (m_1 + m_3) I_l(t) \quad \text{(A18)}$$

$$I(t) = I_p(t)/V_I \quad \text{(A19)}$$

$$\dot{S}_1 = -(k_{a1} + k_d) S_1(t) + u(t) \quad \text{(A20)}$$

$$\dot{S}_2 = k_d S_1(t) - k_{a2} S_2(t) \quad \text{(A21)}$$

$$s(t) = k_{a1} S_1(t) + k_{a2} S_2(t) \quad \text{(A20)}$$

$$\dot{G}_M = k_{sc} G(t) - k_{sc} G_M(t) \quad \text{(A23)}$$

Appendix 2. Control variability grid analysis

The Control Variability Grid Analysis (CVGA) is a known graphical tool to evaluate the quality of the closed loop glucose control [1]. It represents the min/max values of blood glucose in a group of subjects. In this method, each patient presented by a single data point over a specified time period.

Various regions on the CVGA plane are associated with different qualities of blood glucose regulation. In order to categorize patients, nine square zones are considered as follows [1]:

Zone A ($G_{max}\langle 180, G_{min}\rangle 90$): Accurate control.
Zone Upper B ($180 < G_{max}\langle 300, G_{min}\rangle 90$): Benign trends towards hyperglycemia.
Zone Lower B ($G_{max} < 180,\ 70 < G_{min} < 90$): Benign trends towards hypoglycaemia.
Zone B ($180 < G_{max} < 300,\ 70 < G_{min} < 90$): Benign control.
Zone Upper C ($G_{max} > 300,\ G_{min} > 90$): Overcorrection of hypoglycaemia
Zone Lower C ($G_{max} < 180,\ G_{min} < 70$): Overcorrection of hyperglycaemia
Zone Upper D ($G_{max} > 300,\ 70 < G_{min} < 90$): Failure to deal with hyperglycaemia.
Zone Lower D ($180 < G_{max} < 300,\ G_{min} < 70$): Failure to deal with hypoglycaemia.
Zone E $G_{max} > 300,\ G_{min} < 70$): Erroneus control.

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