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Generalized Super-Twisting Control for an Insulin Infusion System for Patients with Type 1 Diabetes

Control Super-Twisting Generalizado para un Sistema de Infusión de Insulina para Pacientes con Diabetes Tipo 1

GUERRERO, Jesús[1]†*, FRAUSTO-SAAVEDRA, Bryan[1], CHIMAL-CRUZ, Martín Alberto[2] and ORTIZ-SANTOS, Salvador[3]

[1]*Tecnológico Nacional de México/ ITS Abasolo, Departamento de Ingeniería Mecatrónica, México*
[2]*Universidad Politécnica de Guanajuato, Departamento de Ingeniería en Energía, México*
[3]*Universidad Autónoma de Querétaro, Facultad de Ingeniería, México*

ID 1er Autor: *Jesús, Guerrero* / **ORC ID**: 0000-0002-5873-8986, **CVU CONACYT ID**: 490978

ID 1er Coautor: *Bryan, Frausto-Saavedra* / **ORC ID**: 0000-0001-5290-8465

ID 2do Coautor: *Martin, Chimal-Cruz* / **ORC ID**: 0000-0002-1448-3221

ID 3er Coautor: *Salvador, Ortiz-Santos* / **ORC ID:** 0000-0001-9383-0705, **CVU CONACYT ID**: 491542

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Abstract

Type-1 diabetes is the number 1 disease in the world. When a person becomes ill, the patient's pancreas is no longer able to generate insulin to lower blood glucose levels when food is eaten. An alternative way to treat patients with diabetes is automatic insulin infusion systems. In this article, a control based on higher order sliding modes for the control of blood glucose is designed. The proposed controller is based on the Generalized Super-Twisting algorithm, which offers convergence in finite time, and is robust against external disturbances and parametric uncertainties. Also, the stability of the proposed controller is tested using Lyapunov arguments. Finally, the control performance is compared against other proposed methodologies. Those controllers were proven under several scenarios through computer simulations in MATLAB.

Diabetes, Sliding Mode Control, Stability, Robust

Resumen

La diabetes es la enfermedad número 1 en el mundo. Cuando una persona enferma, el páncreas del paciente ya no es capaz de generar insulina para reducir los niveles de glucosa en la sangre cuando un alimento es ingerido. Una alternativa para tratar a los pacientes con diabetes, son los sistemas de infusión de insulina automática. En este artículo se diseña un control basado en modos deslizantes de orden superior para el control de la glucosa en la sangre. El control diseñado se basa en el algoritmo Super-Twisting Generalizado, el cual ofrece convergencia en tiempo finito, es robusto ante perturbaciones externas e incertidumbres paramétricas. También, se prueba la estabilidad del controlador propuesto mediante argumentos de Lyapunov. Finalmente, se compara el desempeño del control contra otros propuestos en la literatura mediante simulaciones por computadora, bajo diversos escenarios.

Diabetes, Control por Modos Deslizantes, Estabilidad, Robusto

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* Correspondence to Author (email: jesus.gt@abasolo.tecnm.mx)
† Researcher contributing first author.

Introduction

Diabetes mellitus is a chronic metabolic disease characterized by elevated blood glucose levels. Diabetes is one of the leading causes of blindness, kidney failure, heart attacks, strokes, and lower-limb amputation. In 2021, according to the World Health Organization (WHO), an estimated 422 million people worldwide will have diabetes. However, its consequences can be avoided or delayed by adopting proper diets, physical activity, medication, and so on. The automatic glucose regulation system belongs to treatments based on medication. This system requires a robust control to regulate the glucose concentration to a basal state.

For this purpose, the minimum Bergman model is used, this represents the glucose dynamics and insulin kinematics [1], which is represented in three nonlinear differential equations [2]; this is also the most famous and widely used model in clinical assessments [3]. The first challenges to regulate blood glucose levels require precise measurements and specific assessment protocols that allow mitigate the adverse effects in treatments based on insulin application. In practice, measurement methods are used at the Point of Care (POC) with capillary or arterial blood. These analyzers can be based of gases, plasma, or serum of venous or arterial blood that are measured in the laboratory in an invasive way [4]. In the last years, there have been advances towards the development of nano biosensors or apt sensors [5] using various non-invasive nanomaterials for continuous glucose monitoring, especially optical biosensors [6], [7].

These tools have not been efficient by themselves. These devices require theoretical techniques to achieve accurate measurements in glucose prediction, such as Luenberger observer for state estimation [8], deep learning algorithms [9], incremental learning algorithms [10], machine learning [11], artificial neural networks [12], construction of prediction models [13], and so on. Classical or artificial intelligence predictors require models with Gaussian processes; however, this requirement cannot always be satisfied because unmeasurable disturbances and noise may not satisfy the mentioned distribution.

Consequently, a robust controller is proposed, the Generalized Super Twisting Algorithm (GSTA) [14], which is robust towards parameter uncertainties in the model and external disturbances. The GSTA is an extended version of the Super-Twisting Algorithm (STA) which has been applied successfully in several cases (see [15]-[19]).

For design purposes of the GSTA, this algorithm only requires knowledge of the external disturbance upper bound. This control method makes it possible to reduce blood glucose levels in the patients that are in situations of hyperglycemia. This process is made through an infusion pump that provides in real-time a variable insulin rate, and the controller can adjust the insulin concentration according to the readings of a continuous sensor.

The rest of the paper is organized as follows: The mathematical model that describes the glucose concentration dynamics in a human being is described in Section 2. In section 3, a glucose controller design based on a high order sliding modes control is shown. Additionally, the stability proof of the proposed controller is given. In Section 4, several computer simulations were carried out to test the proposed algorithm's robustness and effectiveness. Also, the behavior of the closed-loop control under different scenarios is analyzed. Finally, a concise conclusion about the article is offered in Section 5.

Mathematical Description

The mathematical model that describes the dynamic response of glucose concentration to an insulin injection of a patient with type 1 diabetes is known as the minimum Bergman model, which is described below:

$$\begin{aligned}\dot{x}_{b1}(t) &= -\left(p_1 + x_{b2}\,(t)\right)x_{b1}\,(t) + p_1\,G_{bl} + D(t)\\ \dot{x}_{b2}(t) &= -p_2 x_{b2}(t) + p_3(x_{b3}(t - I_{bl})\\ \dot{x}_{b3}(t) &= -n(x_{b3}(t) - I_{bl}) + u(t)\end{aligned} \tag{1}$$

Where $x_{b1}(t)$ is the concentration of glucose in the blood plasma [mg/dl], $x_{b2}(t)$ is the concentration of insulin in the remote compartment [1/min], $x_{b3}(t)$ represents the concentration of insulin in plasma at time t [μU/ml], G_{bl} is the basal glucose level [mg/dl], I_{bl} is the basal insulin level [μU/ml], p_1 is the insulin-independent rate constant of glucose uptake in muscles a liver [l/min]. The rate for decrease in tissue glucose uptake ability is defined by p_2 en [1/min]. p_3 represents the insulin-dependent increase in glucose uptake ability in tissue per unit of insulin concentration above the basal level [(μ/ml) $\min^{-2}$]. The parameter n is the first-order decay rate for insulin in blood [1/min].

From the study [20], it can be concluded that the value of p_1 is drastically reduced and approaches to zero for patients with diabetes. Note that the parameters shown in Table I have been calculated for an average person. However, it is necessary to mention that these parameters are not constant and vary from person to person, which makes the control design even more complex. Finally, from Eq. (2), the term $D(t)$ represents the rate at which glucose is absorbed into the blood by the intestine after food has been consumed. In patients with diabetes, glucose uptake is considered an external disturbance to the system's dynamics (2). This disturbance can be modeled as an exponential function as follows [20]:

$$D(t) = A_B e^{B_B t} \tag{2}$$

Where t is the time [min] and $A_B, B_B \in R^{+}$. The unit of D is in [mg/dl/min].

Finally, from model (1), the function *u(t)* represents the control signal, which is the function that will modify the system dynamics to regulate the glucose concentration in the diabetic patient's blood plasma.

Generalized Super-Twisting Control Design

The control objective is to regulate the blood's glucose concentration at the basal state value. Then, the error variable is defined as:

$$e(t) = x_{b1}(t) - G_{bl} \tag{3}$$

Where G_{bl} is the blood's glucose concentration in the basal state (desired value), and $x_{b1}(t)$ is the current patient blood's glucose concentration measured by the sensor. Moreover, the parameters shown in model (1) are not exactly known and vary from patient to patient. Also, the external disturbance is not completely known. For these reasons, the controller should be robust towards parameter uncertainties and external disturbances. At the same time, the controller requires fast convergence in finite time. Taking into consideration all the listed requirements, we will design a controller based on the high order sliding modes technique.

Considering the output $y = x_{b1}(t)$, we can observe that its relative degree is 3. Roughly speaking, the relative degree is the number of consecutive derivatives of the output until the signal control appears explicitly. In this particular case, the input signal comes out at the third derivative with respect the time of x_{b1}, this yields to:

$$\dddot{x}_{b1} = \varphi - p_3 x_{b1} u \tag{4}$$

Where φ is defined as:

$$\begin{aligned} \varphi = {} & [-p_1({p_1}^2 + 3p_3 I_{bl}) - p_3 I_{bl}(p_2 + n) - p_3\gamma[x_{b1} - h] + t]x_{b1} + [-{p_1}^2(1 + G_{bl}) + p_1 p_2(2G_{bl} - 1) + 2D(p_1 + p_2)]x_{b2} + [-2p_3(p_1 + D)]x_{b3} + [-(p_1 + p_2)^2 - 3p_3 I_{bl}]x_{1b}x_{b2} + [p_3(3p_1 + p_2 + n)]x_{b1}x_{b3} + [-3(p_1 + p_2)]x_{b1}{x_{b2}}^2 + (p_1 G_b + D){x_{b2}}^2 + 3p_3 x_{b1}x_{b2}x_{b3} - x_{b1}{x_{b2}}^3 + \ddot{D} + (p_1 G_{bl} + D)({p_1}^2 + 2p_3 I_{bl}) - p_3 x_{b1} u(t) \end{aligned} \tag{5}$$

The parameter φ will be relevant because, based on [21], it is part of the controller and is the term known as equivalent control. However, it is necessary to establish two critical implications: (1) φ depends on the dynamical model, which means that is crucial to know the exact value of the dynamical model's parameters, which is impossible to determine precisely in practice. (2) φ contains the disturbance D and its dynamics, which implies that is necessary to precisely known the disturbance D. In real terms, this is impossible. For these reasons, the parameter to determine φ, will be broken down into two terms, the nominal $\hat{\varphi}$, and the error term $\tilde{\varphi}$, as follows:

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$$\varphi = \hat{\varphi} + \tilde{\varphi} \qquad (6)$$

Where $\hat{\varphi}$ is the term that contains dynamical model nominal parameters and does not include the external disturbance. On the other hand, the term $\tilde{\varphi}$ encloses all the unknown terms and its dynamics. Substituting (6) in (4), yields to:

$$\dddot{x}_{b1} = \hat{\varphi} - p_3 x_{b1} u + \tilde{\varphi} \qquad (7)$$

Based on the relative degree of the output, we choose the sliding surface as in [21], which is defined as:

$$\sigma(e) = \ddot{e} + \alpha_2 \dot{e} + \alpha_1 e \qquad (8)$$

Where α_1 and α_2 are design positive constants.

Remark 1: The constants α_i are used to modify the convergence rate to the sliding surface.

Assumption 1: The external disturbance and its dynamics are considered bounded as follows:

$$\begin{aligned} \|D(t)\| &\leq \delta_1 \\ \|\dot{D}(t)\| &\leq \delta_2 \end{aligned} \qquad (9)$$

The main result of this manuscript is summarized in the following theorem.

Theorem 1. Consider the dynamical model of the blood's glucose concentration of the diabetes type 1 patient given by Eq. (1), assume that the external disturbance *D(t)* is bounded, and it satisfies the Assumption 1. Then, for every initial condition $\sigma(0)$, the sliding surface $\sigma = 0$ will be reached in finite time by the following Generalized Super-Twisting Controller:

$$u(t) = \frac{1}{p_3 x_{b1}} (\hat{\varphi} + \alpha_2 \ddot{e}_r + \alpha_1 \dot{e}_r - u_{ST}) \qquad (10)$$

Where the GSTA is represented by u_{ST}, and is defined as:

$$\begin{aligned} u_{ST} &= -k_1 \phi_1(\sigma) + \lambda \\ \dot{\lambda} &= -k_2 \phi_2(\sigma) \end{aligned} \qquad (11)$$

Where the functions $\phi_i(\sigma)$ have the following structure:

$$\begin{aligned} \phi_1(\sigma) &= |\sigma|^{\frac{1}{2}} sgn(\sigma) + \sigma \\ \phi_2(\sigma) &= \frac{1}{2} sgn(\sigma) + \frac{3}{2} |\sigma|^{\frac{1}{2}} sgn(\sigma) + \sigma \end{aligned} \qquad (12)$$

The feedback controller gains are k_1 and k_2.

Finally, when the sliding mode is reached ($\sigma = 0$), this means that the error converges to zero, and $x_{b1} \to G_b$ in finite time.

Proof: Consider the dynamic system (1) and the sliding surface (8). Computing the time derivative of σ, we have:

$$\dot{\sigma} = -k_1 \phi_1(\sigma) - k_2 \int_0^t \phi_2(\sigma) + d(t) \qquad (13)$$

Where *d(t)* encloses the system unknown dynamics and the external disturbances.
Let us define:

$$s_1 = \sigma$$

$$s_2 = -k_2 \int_0^t \phi_2(\sigma) + d(t) \qquad (14)$$

$$\dot{d}(t) = \beta(t)$$

Then, the sliding surface dynamics can be rewritten as:

$$\begin{aligned} \dot{s}_1 &= -k_1 \phi_1 + s_2 \\ \dot{s}_2 &= -k_2 \phi_2 + \rho(t) \end{aligned} \qquad (15)$$

Defining the vector $z = [\phi_1, s_2]^T$ and $\rho = \frac{\beta(t)}{\phi_1{}'}$. Next, the sliding Surface dynamics can be expressed as:

$$\dot{z} = \phi_1'(Az + B\rho) \qquad (16)$$

Where *A* and *B* are matrices defined as:

$$A = \begin{bmatrix} -k_1 & 0 \\ -k_2 & 0 \end{bmatrix} \text{ y } B = \begin{bmatrix} 0 \\ 1 \end{bmatrix} \qquad (17)$$

Considering the following Lyapunov function:

$$V = z^T P z \qquad (18)$$

Where P is a positive definite matrix which satisfies the Lyapunov's equation:

$$A^T P + PA = -Q \tag{19}$$

Where Q is a positive definite matrix. Based on results shown in [22], we assume that the disturbance satisfies the sector condition:

$$d = -\rho^2(\rho, z) + L^2 z^T C^T C z \geq 0 \tag{20}$$

Note that the upper and lower bounds of the sector are symmetric. Moreover, we choose $C = [1\ 0]$. For control design purpose, the matrix A can be rewritten as:

$$A = A_0 - K_0 C_0 \tag{21}$$

Where

$$A_0 = \begin{bmatrix} 0 & 1 \\ 0 & 0 \end{bmatrix}, K_0 = \begin{bmatrix} k_1 \\ k_2 \end{bmatrix}, C_0 = [1\ 0] \tag{22}$$

Computing the derivative of the Lyapunov function along the system trajectories, yields to:

$$\dot{V} = 2z^T P \dot{z}$$

$$\dot{V} = -\phi_1' \begin{bmatrix} z \\ \rho \end{bmatrix}^T \begin{bmatrix} A^T P + PA & PB \\ B^T P & 0 \end{bmatrix} \begin{bmatrix} z \\ \rho \end{bmatrix} \tag{23}$$

$$\leq -\phi_1' \left\{ \begin{bmatrix} z \\ \rho \end{bmatrix}^T \begin{bmatrix} A^T P + PA & PB \\ B^T P & 0 \end{bmatrix} \begin{bmatrix} z \\ \rho \end{bmatrix} + d \right\}$$

After some manipulations and considering the sector conditions, we obtain the following:

$$\dot{V} \leq -\phi_1' \left\{ \begin{bmatrix} z \\ \rho \end{bmatrix}^T W(K_0, P|\overline{\alpha}, L) \begin{bmatrix} z \\ \rho \end{bmatrix} - \overline{\alpha} z^T P z \right\} \tag{24}$$

Where

$$W(K_0, P|\overline{\alpha}, L) = \begin{bmatrix} W_{11} & W_{12} \\ W_{21} & W_{22} \end{bmatrix} \tag{25}$$

Each matrix element is described below:

$$W_{11} = A_0^T P + PA_0 + L^2 C^T C - C_0^T K_0^T P - PK_0 C_0 + \overline{\alpha} P$$

$$W_{12} = PB$$

$$W_{21} = B^T P$$

$$W_{22} = -1 \tag{26}$$

Choosing $K_0 > 0$ and the matrix $P > 0$,there exists a constant $\overline{\alpha} > 0$, such that $W(K_0, P|\overline{\alpha}, L)$ will be negative semidefinite. Therefore, the time derivative of V is expressed as:

$$\dot{V} \leq -\frac{\overline{\alpha}\, \lambda_{min}^{0.5}(P)}{2} V^{0.5} - \overline{\alpha} V \tag{27}$$

Therefore, it can be concluded that the time derivative of V will be negative definite if the gains k_1 and k_2 are selected large enough so that the matrix W will be negative semi-definite. If this condition is fulfilled, the states z will converge to zero, so the sliding surface will go to the origin, which implies that the errors tend to zero and, finally, the state x_{b1} will converge to the basal state in finite time.

Remark 2: In the proposed control law given by Eq. (10), the term that multiplies the control $\frac{1}{p_3 x_{b1}}$, depends on the state x_{b1}. However, this value is well defined and belongs to a neighborhood $p_3 x_{b1} \in [1.2 \times 10^{-4},\ 3 \times 10^{-2}]$.

Simulation Results

Several computer simulations were carried out to test the proposed controller effectiveness and robustness towards parametric uncertainties and external disturbances. The proposed controller was simulated with the MATLAB 2017a software, and the ODE45 solver with the variable step was used.

For the simulation, it is considered that the reference glucose level is $G_{bl} = 80$ [mg/dl]. The patient has hyperglycemia, so the initial condition was at 220 [mg/dl]. The control objective is that the sensor measurement tends to the baseline blood glucose state $G_{bl} = 80$ [mg/dl]. Three scenarios were tested to evaluate the performance of the control:

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1. **Nominal Scenario**: The patient is hyperglycemic; insulin is infused to reach a basal state. Disturbances are not considered in this case.
2. **Scenario with external disturbance**: It is simulated that the patient consumes food, affecting the system's dynamics. The disturbance acts at minute 600.
3. **Scenario with parametric uncertainty**: In this simulation, the controller is tested with a different patient, for which the system parameters change. The two previous cases are considered. That is, the nominal case and disturbances are tested. Table I shows the patient parameters used in the simulation.

1. Nominal Scenario

Figure 1 shows the controller performance under nominal conditions. In this case, the patient's glucose measurement is 220 mg/dl, and drops to the nominal reference level (dashed black line) of 80 mg/dl. A comparison of the proposed controller (green line) is made against the method proposed in [21] (pink line), and both controllers converge to the reference practically at the same time.

2. Robustness Towards External Disturbances Scenario

Figure 1 compares the proposed controller (red line) and Ahmad's (namely STA) method (blue line) [21]. In this scenario, the patient is hyperglycemia, and the controller acts by infusing insulin until the glucose is regulated in its basal state. Then, at minute 600, a food intake disturbance is introduced, and the patient's glucose goes lift again. The controller acts in regulation and causes the glucose to drop to the nominal value. From the graph, the disturbance affects the performance of the STA controller. In contrast, the GSTA controller converges to the nominal glucose value faster than the STA, demonstrating the effectiveness of the proposed methodology.

3. Robustness Towards Parametric Uncertainties Scenario

In this scenario, both controllers are simulated for a second patient. Therefore, the dynamical system parameters have changed. As seen in Figure 2, patient 2 starts with hyperglycemia with$x_{b1} = 220$ [mg/dl].

From the graph for a nominal scenario, both controllers converge to the reference practically simultaneously. For a second test, it is considered that the patient has eaten food and that this produces a disturbance of blood glucose, as observed at minute 600. After the disturbance, it is observed that the performance of the proposed controller in this item is higher than the nominal STA since it converges to the reference value in a shorter time. In contrast, the STA converges to a neighborhood of the nominal value.

Conclusions

In this article, a sliding mode controller based on the Generalized Super-Twisting Algorithm was designed for an insulin infusion system for patients with type 1 diabetes. The dynamic model of a patient with diabetes was shown. Afterward, a controller robust to external disturbances and parametric uncertainties based on sliding modes was designed. Using Lyapunov's theory, the stability of the developed control was demonstrated. Finally, its superior performance in rejecting disturbances was demonstrated through computer simulations compared to another similar methodology.

	Patient 1	Patient 2
p_2	0.02	0.0072
p_3	5.3×10^{-6}	2.15×10^{-6}
n	0.3	0.2465

Table 1 Parameters used in the simulation of the closed loop control

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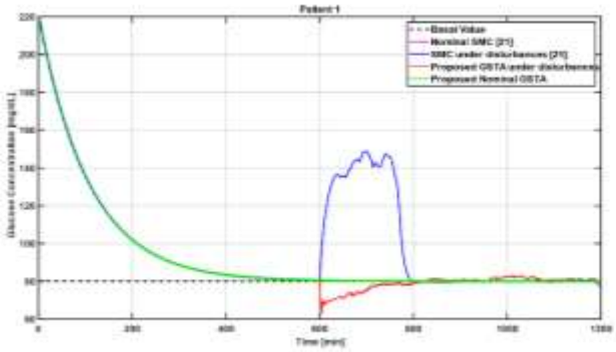

Figure 1. Performance of the proposed controller (GSTA) against the STA [21] for patient 1 for the nominal and disturbed case.

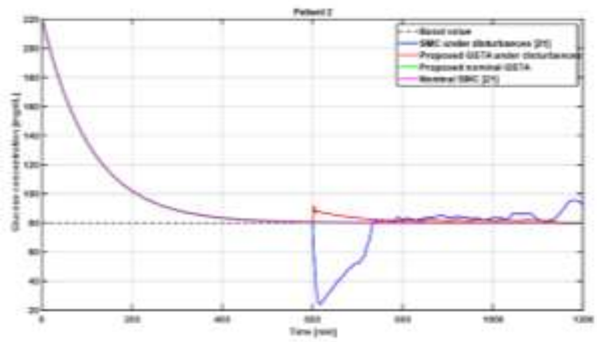

Figure 2 Performance of the proposed controller (GSTA) against the STA [21] for patient 2 for the nominal and disturbed case.