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Blood Glucose Regulation via Double Loop Higher Order Sliding Mode Control and Multiple Sampling Rate

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Abstract: Diabetes is a serious disease during which the body's production and use of insulin is impaired, causing glucose concentration level to increase in the bloodstream. The blood glucose dynamics is described using the Bergman minimal model. Higher order sliding mode control techniques, including the prescribed convergence law, the smooth second order, the quasi-continuous, and the super-twisting control algorithm, are studied for the double loop robust stabilization of the glucose concentration level of a diabetic patient in presence of the parameter variations and meal disturbance. In the inner loop super-twisting control stabilizes the glucose pump-actuator that yields a dynamical collapse of the loop. In the outer loop the higher order sliding mode controller generates a command to the pump-actuator in terms of insulin injection rate. The higher order sliding mode differentiator is employed to facilitate the controllers. The efficiency of the proposed controllers and observers/differentiators, i.e. robustness and high accuracy, in presence of physical disturbances like food intake and parametric uncertainties is confirmed via simulations. Two sampling rates are successfully employed in the simulations: a smaller one for the system and the controller and the larger one for the glucose sensor.

1. INTRODUCTION

The normal blood glucose concentration level in human is in the range of 70-110 mg/dl. This concentration is normally controlled within these limits by different factors in the body. The most important regulator of the glucose level is insulin.

Different factors including food intake, rate of digestion and exercise affect the glucose concentration. Failure in maintaining this value results in high blood sugar level, hyperglycemia, or low blood sugar level, hypoglycemia. Diabetes Mellitus is a disease in which blood glucose concentration is elevated because of deficient insulin secretion or abnormal insulin action due to autoimmune destruction of the insulin producing cells in pancreas. Patients diagnosed with this disease require lifetime exogenous insulin injections, which is the hormone necessary for absorption of glucose by the cells. The current treatments include three to four daily glucose measurements and an equivalent number of insulin injections (Jaremco and Rorstad, 1998).

An alternative approach is to close the broken insulin feedback loop outside the body and deliver it using an external device such as a pump (Jaremco and Rorstad, 1998; Chee et al, 2003). This pump that acts like an artificial pancreas would include a sensor and an insulin container. The sensor provides the measurements of the blood glucose concentration and passes the information to a feedback control system that would calculate the necessary insulin delivery rate using robust higher order sliding mode control algorithms (Levant, 2003, 2005, Shtessel et. al., 2003) to keep the patient under metabolic control. The pump injects insulin through a catheter placed under the patient's skin. Since the latest generation of the implantable pumps allows different infusion rates of insulin, the feedback control system mimics the normal function of a pancreas more closely.

In drug delivery to human body, certain requirements like robustness to uncertainties and external disturbances, should be satisfied. A small perturbation for a long period of time can cause in irreversible brain or heart damage. Also, it must be taken into consideration that a small change in some of the parameters can dramatically affect the patient and even result in the patient's death. Therefore, it is vital for the patients that controller used in designing the closed loop system be robust to any kind of perturbations and disturbances.

Several methods have been previously employed to design the feedback controller for insulin delivery, such as classical linear control (Chee et al, 2003; Hernjak and Doyle, 2005) and pole placement (Salzsieder et al., 1985), which require a linearized model for the design, as well as model predictive control (MPC) (Parker et. al., 1999). With this type of controller, hypoglycemia is the major concern. Insulin overdose can drop the glucose level below 50 mg/dl, which is even more dangerous than hyperglycemia and if left untreated can lead to loss of consciousness and eventually coma. Modeling the patients and the size and structure of the models, as well as nonlinear model versus linear models have been addressed in several works. Adaptation of the model is discussed as an improvement to the performance (Parker et. al., 2001) that can result in imposing some limitations on the model parameters. On the other hand, if linear models are employed for the patients, control algorithms like H_∞ can guarantee some levels of performance but full robustness cannot be achieved via this algorithm. However, as far as

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linear control algorithms are concerned, H_∞ control technique offers a promising result in maintaining blood glucose regulation in diabetic patients. Newer methods like run-to-run control are also employed in regulating the blood glucose level (Palerm, 2007).

In this work, sliding mode control (SMC) (Levant, 2003; Edwards, 1998) is used for designing the control algorithm for the glucose-insulin regulatory system. Insensitivity to internal and external disturbances, ultimate accuracy and robustness as well as finite time convergence that are main features of sliding mode control (Edwards, 1998) make it a suitable choice for the control algorithms related to human body, where extreme robustness is of great importance.

Traditional SMC has some intrinsic problems, such as discontinuous control that often yields chattering (Edwards, 1998). To cope with problem and achieve higher accuracy, higher order sliding mode (HOSM) is proposed (Levant, 2003, 2005, Shtessel et. al., 2003) in regulating the blood glucose concentration at the basal level. Obviously, $k-th$ order HOSM stabilizes the sliding variable at zero as well as its $k-1$ derivatives. On the other hand, since the high frequency switching can be hidden in the higher derivative of the sliding variable, the effect of chattering could be reduced dramatically. In other words, HOSM has two important features that make it a better choice in designing the controller.

Unlike in the paper (Kaveh and Shtessel, 2007) a double loop control structure is employed in this work. The outer loop controller generates an insulin rate control command that is followed by the actuator (an insulin pump). A double loop structure allows reducing relative degrees of the control systems designed in the outer and inner loops. Furthermore, using second order sliding mode control, for instance super-twisting control, allows achieving a dynamical collapse of the inner loop. It preserves a relative degree of the original input-output dynamics that allows avoiding (or significantly reducing) chattering.

Another new feature of the current work is in studying a multiple sampling rate performance of the designed glucose control system. The matter is that the HOSM control algorithms require a relatively high sampling rate, while a sensor of glucose in the blood performs at much lower rate. Figure 1 shows the block diagram of a closed loop control system of diabetic patients using insulin pumps.

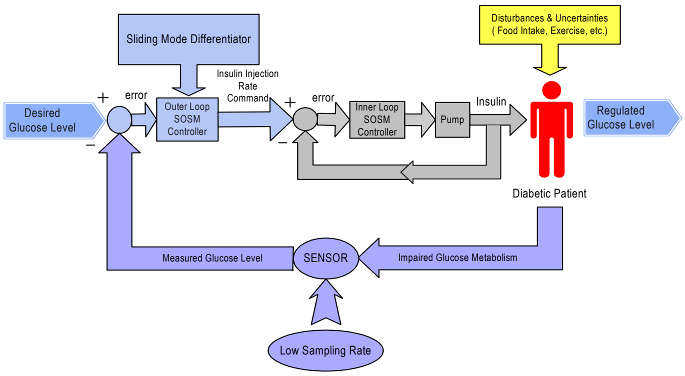

Fig. 1. The block diagram of a closed loop control system

2. INSULIN-GLUCOSE REGULATION DYNAMIC MODEL

To describe the insulin-glucose regulatory system dynamics in the human body, "Minimal Model", developed by Dr. Richard Bergman is used [16]

$$\begin{aligned} \dot{x}_1 &= -p_1[x_1 - G_b] - x_1 x_2 + D(t) \\ \dot{x}_2 &= -p_2 x_2 + p_3[x_3 - I_b] \\ \dot{x}_3 &= -n[x_3 - I_b] + \gamma[x_1 - h]^+ t \end{aligned} \qquad (1)$$

where *t=0* shows the time glucose enters blood, "+" sign shows the positive reflection to glucose intake and *G(t)* is the glucose concentration in the blood plasma (mg/dl); *X(t)* is the insulin's effect on the net glucose disappearance, the insulin concentration in the remote compartments (1/min); *I(t)* is the insulin concentration in plasma at time *t* (μ U/ml); G_b is the basal pre-injection level of glucose (mg/dl); I_b is the basal pre-injection level of insulin (μ U/ml); p_1 is the insulin-independent rate constant of glucose uptake in muscles and liver (1/min); p_2 is the rate for decrease in tissue glucose uptake ability (1/min), p_3 is the insulin-dependent increase in glucose uptake ability in tissue per unit of insulin concentration above the basal level [(μ U/ml) min^{-2}]; *n* is the first order decay rate for insulin in blood (1/min); *h* is the threshold value of glucose above which the pancreatic $\beta-$cells release insulin (mg/dl); γ is the rate of the pancreatic $\beta-$cells' release of insulin after the glucose injection with glucose concentration above the threshold [(μ U/ml min^{-2} (mg/dl)$^{-1}$].

The term, $\gamma[G(t)-h]^+$, in the third equation of the model acts as an internal regulatory function that formulates the insulin secretion in the body, which does not exist in diabetic patients. It has been also argued in (Fisher, 1991) that for diabetic subjects, the value of p_1 will be significantly reduced; therefore it can be approximated as zero. The parameters of the model and their values are introduced in (Fisher, 1991). It is worth noting that all the values are calculated for a person of average weight and these are not constant numbers and vary from patient to patient, which makes the design of the controller a more challenging task.

To show the complete dynamics of the glucose-insulin regulatory system, another term is considered in equation (1). *D(t)* shows the rate at which glucose is absorbed to the blood from the intestine, following food intake. Since in diabetic patients, the normal insulin regulatory system does not exist, this glucose absorption is considered as a disturbance for the system dynamics presented in (1). This is (Fisher, 1991)

$$D(t) = A\exp(-Bt), B > 0 \qquad (2)$$

where *t* is in (min) and *D(t)* is in (mg/dl/min).

The goal is to employ HOSM technique to design an appropriate control function to compensate the uncertainties and disturbances and to stabilize the blood plasma glucose concentration of a diabetic patient at the basal level. It should be mentioned that the dynamics of the pump is neglected in the model introduced in equation (1).

3. HOSM CONTROLLER DESIGN

The system (1) is rewritten in a state-space form as follows

$$\begin{aligned} \dot{x}_1 &= -p_1[x_1 - G_b] - x_1 x_2 + D(t) \\ \dot{x}_2 &= -p_2 x_2 + p_3[x_3 - I_b] \\ \dot{x}_3 &= -n[x_3 - I_b] + \gamma[x_1 - h]^+ t + u(t) \\ \dot{u}(t) &= \frac{1}{\tau}(-u(t) + w(t)) \end{aligned} \tag{3}$$

where x_1, x_2 and x_3 are blood plasma glucose concentration (mg/dl), the insulin's effect on the net glucose disappearance (1/min) and the insulin concentration in plasma (μ U/ml), respectively. $u(t)$ is the insulin injection rate at the output of the pump and $w(t)$ is the command to the insulin rate, the control function $u(t)$ defines the insulin injection rate and replaces the normal insulin regulatory system of the body, which does not exist in diabetic patients.

The double-loop control structure is proposed in order to reduce the input-output relative degree of the system (3). The outer loop SOSM controller is designed in terms of control $u(t)$. Next, inner loop SOSM controller is designed in terms of $w(t)$ in order to follow $u(t)$ treated as a command to the inner loop controller. Due to finite convergence time the inner loop (pump-actuator) dynamics will collapse preserving the overall relative degree of the system (3) that can be computed without taking into account the actuator dynamics.

3.1 Outer loop HOSM controller design

Stabilizing the glucose concentration in the diabetic patient's blood at the basal level G_b is an output-tracking problem thus; the tracking error is defined as the difference between the glucose concentration level and its basal value in the diabetic patient's blood as

$$e = G_b - G(t) = G_b - x_1 \tag{4}$$

Given the dynamical system introduced in equation (3) and disregarding the pump-actuator dynamics, the controller *u(t)* must be designed such that $e \to 0$ in presence of the uncertainties, parameter variations, and disturbances, oral food intake, *D(t)*.

First, the relative degree of the system must be defined. Using (3), the control function appears in the equations after the third differentiation of the output, i.e.

$$x_1^{(3)} = \phi(x,t) - p_3 x_1 u(t) \tag{5}$$

where

$$\begin{aligned} \phi(x,t) = {} & x_1[-p_1(p_1^2 + 3p_3 I_b) - p_3 I_b(p_2 + n) - p_3\gamma(x_1 - h)^+ t] \\ & + x_2[-p_1^2(1 + G_b) + p_1 p_2(2G_b - 1) + 2D(p_1 + p_2)] \\ & + x_3[-2p_3(p_1 + D)] + x_1 x_2[-(p_1 + p_2)^2 - 3p_3 I_b] \\ & + x_1 x_3[p_3(3p_1 + p_2 + n)] + x_1 x_2^2[-3(p_1 + p_2)] \\ & + x_2^2(p_1 G_b + D) + 3p_3 x_1 x_2 x_3 - x_1 x_2^3 + \ddot{D} \\ & + (p_1 G_b + D)(p_1^2 + 2p_3 I_b) \end{aligned} \tag{6}$$

Since $p_3 \neq 0, x_1 \neq 0$, and $p_3 x_1 \in [1.2\times10^{-4}, 3\times10^{-2}]$, the system (3) has a well-defined relative degree, $r = 3$. This allows us to design the controller for the system in equation (3) that satisfies $e \to 0$.

3.1.1 Prescribed Convergence (SOSM) Control Design

Designing the SOSM-based controller for glucose regulation is very important to select the desired smooth glucose regulation error dynamics with certain convergence rate that is recommended by medical procedures (De Fronzo, 2004). The settling time is supposed to be not lees than 2 hours, and undershoot should not exceed the hypoglycemia level. Therefore, the sliding variable is introduced in a form

$$\sigma = \ddot{e} + c_1\dot{e} + c_0 e \tag{7}$$

where c_1 and c_0 are real-valued constants chosen such that equation (7) has the desired behavior and the terms $\dot{e}, \ddot{e}$ can be obtained using the HOSM differentiator (Levant, 2003) which has the following generic form for *n*-differentiating a smooth function *f(t)*

$$\left.\begin{aligned} \dot{z}_0 &= v_0, \\ v_0 &= -\lambda_0 |z_0 - f(t)|^{(n/n+1)} sign(z_0 - f(t)) + z_1 \\ \dot{z}_1 &= v_1, \\ v_1 &= -\lambda_1 |z_1 - v_0|^{(n-1/n)} sign(z_1 - v_0) + z_2 \\ &. \\ \dot{z}_{n-1} &= v_{n-1}, \\ \dot{v}_{n-1} &= -\lambda_{n-1} |z_{n-1} - v_{n-2}|^{(1/2)} sign(z_{n-1} - v_{n-2}) + z_n \\ \dot{z}_n &= -\lambda_n sign(z_n - v_{n-1}) \end{aligned}\right\} \tag{8}$$

the sliding variable dynamics is derived using (7) as

$$\dot{\sigma} = \dddot{e} + c_1\ddot{e} + c_0\dot{e}, \quad \dot{u}(t) = v \tag{9}$$

where *v* is a virtual control. Then

$$\ddot{\sigma} = -\phi_1(x,t) + p_3 x_1 v \tag{10}$$

with

$$\begin{aligned} \phi_1(x,t) &= -\dot{\phi}(x,t) + p_3\dot{x}_1 u(t) + c_1\ddot{e} + c_0 \\ &= -\dot{\phi}(x,t) + p_3 u(t)[-p_1(x_1 - G_b) - x_1 x_2 + D(t)] + c_1\ddot{e} + c_0 \end{aligned} \tag{11}$$

It is assumed in the design procedure that (10) is bounded by some positive value, i.e. $|\phi_1| \leq L$.

HOSM (prescribed convergence law controller) that drives σ to zero in finite time is taken as

$$v = -\alpha\, sign(\dot{\sigma} + \beta|\sigma|^{1/2} sign(\sigma)), \quad \dot{u}(t) = v \tag{12}$$

It is obvious that introducing the virtual controller, adds one integration, which results in increasing the relative degree of the sliding variable dynamics i.e. *r=2*, instead of *1*. In order to compute $\sigma^{(k)}, k = 1$, the HOSM differentiator introduced in equation (8) is employed.

Remark 1: Increasing relative degree of the sliding variable dynamics from 1 to 2, yields high frequency switching in the virtual control, *v*, while the original control, *u*, is continuous since $u = \int v d\tau$. Also 2nd order quasi-continuous controller (Levant, 2005) can be used in (3) instead of the prescribed convergence law one given by equation (12). Chattering attenuation is expected to be better.

3.1.2 HOSM (Quasi-Continuous) Control Design

Following the work (Levant, 2005), quasi-continuous HOSM that drives the sliding variable (7) to zero in finite time, which dynamics are given by (9), is designed as follows:

$$\begin{aligned} v &= -\alpha(|\dot{\sigma}| + \beta_1 |\sigma|^{1/2})^{-1}(\dot{\sigma} + \beta_2 |\sigma|^{1/2}\, sign\sigma) \\ \dot{u}(t) &= v \end{aligned} \tag{13}$$

The introduced controller v in equation (13) is a continuous function everywhere except on the *2*-sliding mode, i.e., when $\sigma = \dot{\sigma} = 0$.

Remark 2: Although controller (13) is continuous everywhere except for $\sigma = \dot{\sigma} = 0$, its discontinuity and high frequency switching in the 2-sliding mode makes equation (12) preferable for controlling the system (3) providing continuity for the control function u .

3.1.3 SOSM (Super-Twist) Control Design

The super-twist control algorithm continuously controls the system with relative degree, *r=1*, in presence of bounded disturbances. In order to achieve relative degree 1, the sliding variable introduced in equation (7) will be employed.

To check the existence condition of the SMC, the dynamics of the sliding variable must be derived using (7) as

$$\dot{\sigma} = \dddot{e} + c_1\ddot{e} + c_0\dot{e} \tag{14}$$

Using (4) and (5), (14) can be written as

$$\begin{aligned} \dot{\sigma} &= \dddot{G}_b - \dddot{x}_1 + c_1\ddot{e} + c_0\dot{e} = -\dddot{x}_1 + c_1\ddot{e} + c_0\dot{e} \\ &= -\phi(x,t) + p_3 x_1 u(t) + c_1\ddot{e} + c_0 \end{aligned} \tag{15}$$

Combining and simplifying the terms in (15) will give

$$\dot{\sigma} = \psi(t) + p_3 x_1 u(t) \tag{16}$$

where

$$\psi(t) = -\phi(x,t) + c_1\ddot{e} + c_0\dot{e} \tag{17}$$

For the sliding mode to exist $\dot{\psi}(t)$ must be bounded by a positive real number [12], [17] i.e.

$$|\dot{\psi}(t)| \le N \tag{18}$$

From equations (3), (4) and (5) it is obvious that the above condition is met and therefore sliding mode exists and the controller can be designed for the system of (3).

Consider the following first order nonlinear differential equation

$$\dot{\sigma} + \alpha|\sigma|^{1/2} sign(\sigma) + \beta\int sign(\sigma)d\tau = f(t) \tag{19}$$

where $|\dot{f}(t)| \le L$. It has been proven [17] that the solution of this nonlinear differential equation and its first time-derivative will converge to zero in a finite time if $\alpha = 1.5\sqrt{L}$ and $\beta = 1.1L$, where L is a real positive constant. The super-twist control function can then be designed as

$$u = -\alpha_1 |\sigma|^{1/2} sign(\sigma) - \beta_1 \int sign(\sigma)d\tau \tag{20}$$

where $\alpha_1 = 1.25\times10^4\sqrt{N}$ and $\beta_1 = 0.92\times10^4 N$ for equation (20), taking into account $p_3 x_1 \in [1.2\times10^{-4}, 3\times10^{-2}]$.

By using this control law (20), the sliding variable σ of equation (7) will be stabilized at zero in finite time, assuming the meal disturbance *D(t)* in (2) is bounded by some real positive number like M , such that $|D(t)| \le M$.

Remark 3: It is worth noting that regardless of the *sign* function presented in the control introduced in equation (20), the control function is a continuous one.

Remark 4: The super-twist control algorithm (20) provides finite time convergence of the sliding variable (7) to zero but asymptotic convergence of the tracking error e due to the equation $\sigma = \ddot{e} + c_1\dot{e} + c_0 e = 0$, which parameters are selected in order to achieve a physiologically comfortable dynamics of the glucose level regulation.

3.2 Inner Loop Super-Twisting Controller Design

The pump-actuator dynamics is taken from equation (3)

$$\dot{u}(t) = \frac{1}{\tau}(-u(t) + w(t)) \tag{21}$$

The goal is to design super-twisting control $w(t)$ such that it provides finite time convergence for $u(t)$ of the commanded profile given by equation (20). This is equivalent to dynamic collapse of the pump-actuator compensated dynamics. The super-twisting control law is easily designed by the same analogy as equation (20)

$$w = -\bar{\alpha}_1 |\bar{\sigma}|^{1/2} sign(\bar{\sigma}) - \bar{\beta}_1 \int sign(\bar{\sigma})d\tau \tag{22}$$

where $\bar{\sigma} = u(t) - u_c(t)$ and $u_c(t)$ is given by equation (20).

4. GLUCOSE MONITORING SENSOR

A glucose sensor suitable for an insulin pump must be accurate, capable of frequent or continuous sampling, easy to calibrate and biocompatible. Glucose sensors are usually categorized in the two groups of minimal invasive and non-invasive (Koschinsky and Heinemann, 2001). Minimal invasive sensors measure the glucose concentration in the interstitial fluid of the skin instead of the blood. Most non-invasive methods are done using optical sensing.. The major problem with most of these kinds of the sensors is the precision of the measurement process. Implantable sensors that can be used in insulin pump, on the other hand, were introduced a few decades ago, but there is still no commercially available sensor that can work for a long time without the usual degradation. The ideal monitoring should be continuous, which is not achievable in real life. The main concern regarding this issue is to avoid hypoglycemia scenario. To avoid this, the sensor must be able to at least detect a decrease of 10 mg/dl in 5 minutes. Some of the newly developed continuous glucose monitoring sensors have achieved the sampling rate of every 5 minutes and other techniques are under study to reduce this rate significantly (Koschinsky and Heinemann, 2001). In this work, it is considered that the sensor is capable of updating the measurements every 0.6 seconds. The double loop controller introduced in the previous section of this paper is designed for the sensor sampled at the aforementioned time increments. Simulations are done for both of the cases and results are compared in the simulation section of this work.

5. SIMULATIONS

All three HOSM algorithms are studied for controlling the system (3) via simulations using MATLAB. The second order ($n = 2$) differentiator (8) is used to estimate $\dot{e}$ and $\ddot{e}$ while computing the sliding variable (7). Firstly, the simulation has been performed for the system of equation (3) assuming there is no controller, *u(t)*. Fig. 2 shows the glucose performances of the regulatory systems of a healthy person and a sick person. It is easy to see that the glucose value of the healthy person is finally stabilized at the basal level in the presence of the meal disturbance, but the sick person's glucose level stays out of range.

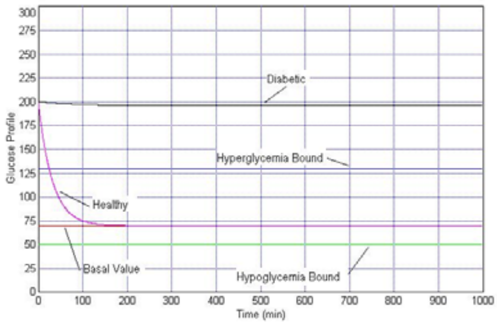

Fig.2 Performance of an open loop glucose regulatory system

Secondly, to validate the proposed algorithms introduced in equations (12), (13) and (20), the control function is applied to the system (3) and the response of a sick person in presence of the meal disturbance is examined. To compare the performances of the controllers, it is assumed the sensor is ideal. Figs. 3, 4 and 5 show the results obtained from the simulations for the above controllers, respectively.

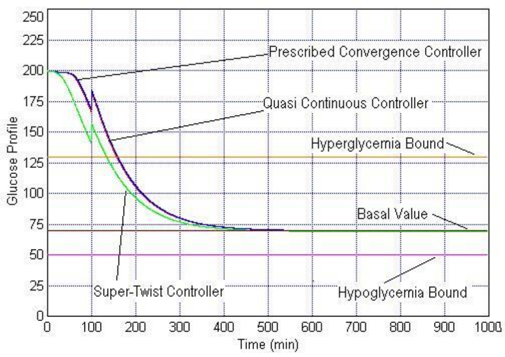

Fig. 3 Performance of close loop glucose regulatory systems with compensated pump dynamics and ideal sensor

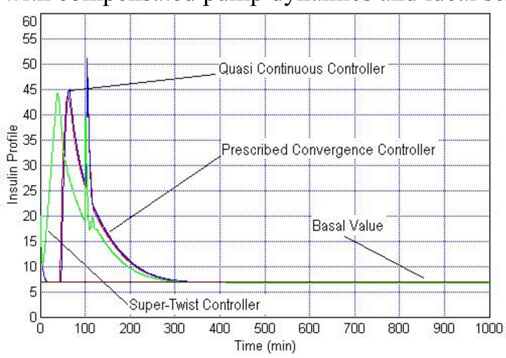

Fig. 4 Injected insulin profiles with compensated pump dynamics and an ideal sensor

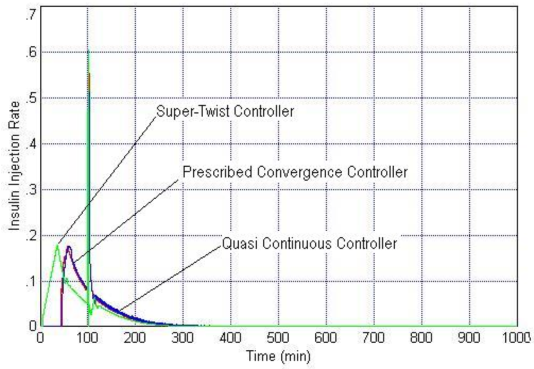

Fig. 5 Injected insulin rate profiles with compensated pump dynamics and an ideal sensor

It is obvious that in all the cases the glucose is completely stabilized at the basal level in a reasonable time interval. Finally, figs. 6, 7 and 8 show the glucose profile, insulin profile and the control function for system of equation (3) controlled by the algorithm proposed in equation (20), respectively using a realistic sensor.

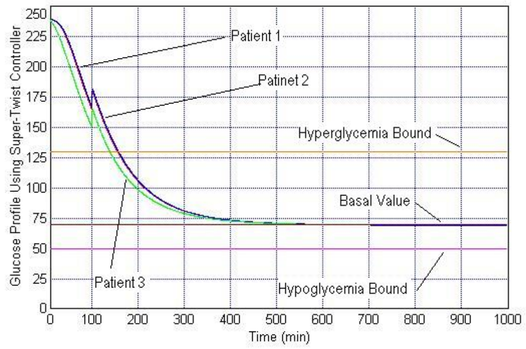

Fig. 6 Performance of close loop glucose regulatory system using super-twisting controller with compensated pump dynamics and a realistic sensor

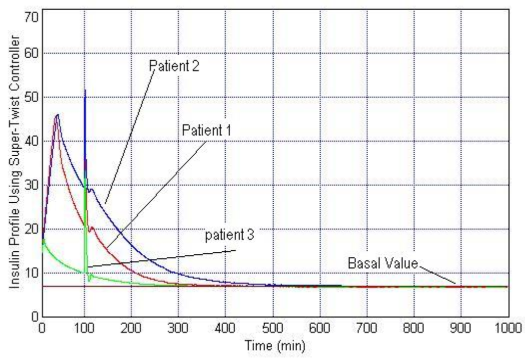

Fig. 7 Injected insulin profiles using super-twisting controller with compensated pump dynamics and a realistic sensor

The multiple sampling rate is used during the simulation study of the system controlled by the super-twisting controller: one sample data per 0.6 seconds for the glucose realistic sensor and 6×10^5 samples per second for the higher order sliding mode controllers, differentiators and the insulin - glucose dynamics. The values that have been used in implementing the model and its parameters are given in Table 1.

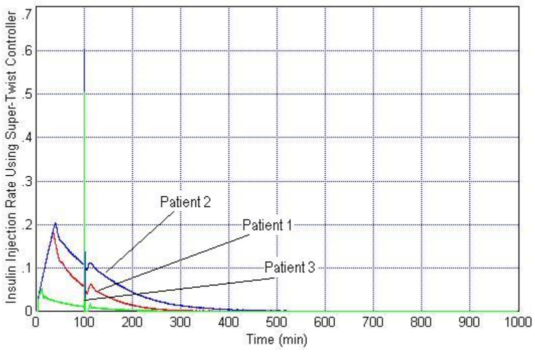

Fig. 8 Insulin rate profiles using super-twisting controller with compensated pump dynamics and an ideal sensor

Table (1): Parameter Values

	Normal	Patient
p_1	0.0317	0
p_2	0.0123	0.0123
p_3	8.2×10^{-8}	8.2×10^{-8}
γ	6.5×10^{-5}	0
n	0.2659	0.2659
h	79.0353	0
G_b	70	70
I_b	7	7
G_0	200	200
I_0	20	20

To represent the boundaries of hypo and hyperglycemia, a strip is added to all the glucose simulation profiles marking the range between 50 and 126 mg/dl. The sudden jumps in the corresponding profiles are due to its presence. It is obvious that all three controllers are able to deal with this sudden disturbance and maintain the profile.

Remark 5. In this work, a first order dynamics is considered for the actuator (insulin pump). Chattering analysis of the super-twisting control in equation (20) in presence of the higher order unmodeled dynamics of the actuator could be performed using the methods based on the describing function technique (Boiko, 2007, 2007).

5. CONCLUSIONS

The diabetes management as one of the challenging control problems in human regulatory systems has been studied. Three types of continuous HOSM algorithms in specific prescribed convergence law, quasi-continuous and super-twisting control algorithms are used for a feedback controller design that stabilizes the blood glucose concentration of a diabetic patient at the desired level. This stabilization has been done in presence of the external disturbances such as food intake and model parametric uncertainties. The robust high accuracy performance of the introduced controllers are checked and confirmed by computer simulations. The sliding mode differentiator has been used to facilitate the higher order sliding mode controllers. The double loop control strategy is employed for controlling the glucose level. This structure causes the dynamical collapse of the compensated actuator dynamics in the inner loop minimizing the actuator dynamics effect on the overall system performance. The discrete nature of the glucose sensors has been discussed and taken into account in the simulations. All three HOSM controllers/observers accurately and robustly handle the glucose regulation problem that was confirmed via the computer simulations.

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