High-Order Sliding-Mode Control of Blood Glucose Concentration via Practical Relative Degree Identification

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Abstract— This research introduces a novel concept of practical relative degree and presents a numerical method of practical relative degree identification. The concept efficacy is demonstrated by computer simulation of a High-Order Sliding-Mode controller, effectively stabilizing the blood glucose concentration for two well known models with different relative degrees.

I. INTRODUCTION

Automatic insulin infusion for diabetic patients has been subject of an extensive research [1] [2] [3], but to date, all insulin pumps commercially available work with an open loop, except for a single model that has a hypoglycemia detection to avoid insulin overshot. The glucose-insulin regulation system is non linear and time variable. The identification of the patient's parameters is expensive, and invasive and uncertainties are always present due to the most important parameters, such as insulin resistance, can be temporarily or permanently changed depending on the personal habits. The operation range is wide, in a diabetic patient, blood glucose can vary from 40 to $500mg/dl$ [4]. These characteristics make difficult to use a linear control.

High Order Sliding Mode Control (HOSMC) [5] [6] [7] [8] [9] is a *black-box* oriented control i.e. it only needs knowledge of the relative degree of the system and reasonable bounds for few expressions. Thus HOSMC presents an attractive alternate approach to blood glucose control. Due to its nonlinearity, it can work in the whole operating range of the system. Its design does not depend on parametric or system model uncertainties, which guarantees the required robustness.

There are several known mathematical models describing the glucose insulin regulatory system. Improved models

involve additional dynamics, which significantly increase the model order.

The Bergman Minimal Model (BeM) has relative degree 3, and it contains the fewest number of parameters that describe the glucose-insulin regulatory system with sufficient accuracy. There are some other models, such as the Candas and Radziuk Model [10], and the Cobelli Model [11], which concur with BeM and also have relative degree 3. More detailed models are the Hovorka Model [12] and the Dalla Model [13], having relative degree 5. One of the most complete models is the Sorensen Model (SoM). It describes the action of each group of organs, having some influence on glucose regulation. SoM has relative degree 5.

The same patient can be physiology described by all the mentioned models, while the output and the input of the system, the glucose concentration and the insulin infusion, remain the same. It is assumed in this research that all models share the same *practical relative degree* featuring the actual process. The idea is that all models might be considered as general small perturbations of some unknown simple model. The perturbations can include small disturbances, as well as singular perturbations. Both types of perturbations can change the relative degree [14]. The relative degree of this unknown simplest model is functionally called the practical relative degree. This *practical relative degree* is to be identified and used in order to construct a HOSMC to be effective for all models. The resulting HOSMC reveals robustness with respect to the corresponding relative-degree fluctuations [14].

In this work a black-box HOSMC of third order is designed for the two most accepted models, BeM and SoM, using the novel concept of practical relative degree. The practical relative degree of the glucose insulin regulatory system is identified by a numerical method, while SoM is assumed to be a singular perturbed representation of BeM. The same HOSMC blood glucose concentration controller has been tested via simulation for both models, BeM and SoM, and has demonstrated very good performance.

II. MODELS

A. Bergman Model

Following is the Bergman Model (BeM):

$$\begin{aligned}
\dot{B}_1 &= -p_1[B_1 - G_b] - B_1 B_2, \\
\dot{B}_2 &= -p_2 B_2 + p_3[B_3 - I_b], \\
\dot{B}_3 &= -n[B_3 - I_b] + \gamma[B_1 - h]t + u(t).
\end{aligned} \tag{1}$$

Here B_1, B_2 and B_3 are plasma glucose concentration, the insulin influence on glucose concentration reduction, and insulin concentration in plasma respectively. The control input $u(t)$ represents the insulin infusion rate, p_1 is the insulin-independent glucose-utilization rate, p_2 is the rate of decrease of the tissue glucose uptake ability, p_3 is the insulin-dependent increase of the glucose uptake ability. The term $\gamma[B_1 - h]t$ represents the pancreatic insulin secretion after a meal intake at $t = 0$. As this work is focused on insulin therapy which is usually administrated to type-1 diabetes mellitus patients, the parameters p_1 and γ are assumed to be zero in order to represent the dynamic of this disease [15]. The parameter n is the first order decay rate for insulin in blood. The parameters to simulate the BeM *in silico* patients where obtain from [16].

The relative degree r is defined as the order of the total time derivative of σ where the input variable u explicitly appears for the first time [17]. Thus, calculating

$$B_1^{(3)} = \phi_B(B, t) - p_3 B_1 u(t) \tag{2}$$

where

$$
\begin{aligned}
\phi_B(B&,t) = \\
B_1&[-p_1(p_1^2 + 3p_3 I_b) - p_3 I_b(p_2 + n) - p_3\gamma[(B_1 - h)^+ t]] \\
+B_2&[-p_1^2(1 + G_b) + p_1 p_2(2G_b - 1) + 2D(p_1 + p_2)] \\
+B_3&[-2p_3(p_1 + D)] + B_1 B_2[-(p_1 + p_2)^2 - 3p_3 I_b] \\
+B_1&B_3[p_3(3p_1 + p_2 + n)] + B_1 B_2^2[-3(p_1 + p_2)] \\
+B_2^2&(p_1 G_b + D) + 3p_3 B_1 B_2 B_3 - B_1 B_2^3 \\
+\ddot{D}& + (p_1 G_b + D)(p_1^2 + 2p_3 I_b)
\end{aligned}
\tag{3}
$$

shows that the relative degree BeM is 3.

B. Sorensen Model

SoM is a physiological model with tissue and organs compartments, 8 for glucose and 7 for insulin. It was developed writing the mass balance equation account for blood flow, the exchange between the compartments and metabolic processes causing addition or removal of glucose, insulin and glucagon [18]. SoM is a non-linear model of relative degree five. The original model and the detailed explanation of parameters can be found in [18]. In order to get a form comparable with BeM, SoM could be rewritten as

$$\dot{S}_1 = \frac{1}{V_H^G}(-Q_H^G S_1 + Q_L^G S_2 + S_7 - F_{RBGU})$$

$$\dot{S}_2 = \frac{1}{V_L^G}(Q_A^G S_1 + Q_G^G S_6 - Q_L^G S_2 + f_{HGP} S_8 - f_{HGU} S_3)$$

$$\dot{S}_3 = \frac{1}{\tau_1}(2\tanh(0.55 S_4^N) - S_3)$$

$$\dot{S}_4 = \frac{1}{V_L^I}(Q_A^I S_5 + Q_G^I S_{10} - Q_L^I S_4 - F_{LIC})$$

$$\dot{S}_5 = \frac{1}{V_H^I}(Q_L^I S_4 - Q_H^I S_5 + S_9 + u(t))$$

$$\dot{S}_6 = \frac{Q_G^G}{V_G^G}(S_1 - S_6) + \frac{1}{V_G^G}(F_{MEAL} - R_{GGU})$$

$$\dot{S}_7 = Q_K^G \dot{G}_K + G_P^G \dot{G}_{PV} + Q_B^G \dot{G}_{BV}$$

$$\dot{S}_8 = \frac{1}{\tau_1}(1.21 - 1.14\tanh[1.66(S_4^N - 0.89)] - S_8)$$

$$\dot{S}_9 = Q_B^I \dot{I}_B + Q_K^I \dot{I}_K + Q_P^I \dot{I}_{PV}$$

$$\dot{S}_{10} = \frac{Q_G^I}{V_G^I}(S_5 - S_{10})$$

$$\dot{S}_{11} = \frac{1}{V_C}(F_{PCR} - F_{MCC} S_{11}^N)$$

where

$$
\begin{aligned}
f_{HGP} &= F_{HGP}^B 2.7 tanh(0.39 S_{11}^N) - f_2 \\
&\quad [1.42 - 1.41 tanh(0.62(S_2^N - 0.497))] \\
f_{HGU} &= F_{HGU}^B 5.66 + 5.66 tanh(2.44(S_2^N - 1.48))
\end{aligned}
\tag{4}
$$

TABLE I

SORENSEN MODEL STATE SPACE VARIABLES

Variable	Description	Units
S_1	Glucose in blood	mg/dl
S_2	Glucose in liver circulation	mg/dl
S_3	Hepatic glucose uptake	mg/dl
S_4	Insulin in liver circulation	mg/dl
S_5	Insulin in blood	mg/dl
S_6	Glucose in gut circulation	mg/dl
S_7	Glucose in kidney, periphery and brain circulation	mg/dl
S_8	Hepatic glucose production	mg/dl
S_9	Insulin in kidney, brain an periphery circulation	mU/l
S_{10}	Insulin in gut circulation	mU/l
S_{11}	Glucagon secretion	pg/ml

The upper index N means the normal value of the corresponding variable.

To simulate the SoM *in silico* patients the parameters where obtained from [18], but the parameters that describe patient metabolic portrait where significantly changed in order to have patients with the same complexion, but different disease characteristics (Table II).

TABLE II
SoM *in silico* PATIENTS METABOLIC PORTRAIT

Variable	Patient 5	Patient 4	Patient 6	Units
F_{BGU}	70	70	70	mg/min
F_{RBGU}	10	5	15	mg/min
R_{GGU}	20	10	11	mg/min
F_{PGU}^{B}	35	20.5	11	mg/min
F_{HGP}^{B}	155	123.5	200	mg/min
F_{HGU}^{B}	20	10	10	mg/min
F_{PIC}	0	0	0	

Calculate the SoM relative degree. Differentiating S_1 obtain that for the first time the control appears in its fifth derivative. Indeed,

$$S_1(t)^{(5)} = \phi_S(S,t) + S_{id}u(t) \tag{5}$$

$$S_{id} = (-2f_{HGU}0.55Q_A^I)(V_G^H \tau_1 V_L^I V_H^I I_L^B)^{-1} \tag{6}$$

$$\phi_S(S,t) = \frac{1}{V_G^H}(Q_H^G S_1^{(4)} + \frac{Q_L^G}{V_L^G}Q_A^G S_1^{(3)} \tag{7}$$

$$+ S_7^{(4)} + \frac{Q_L^G}{V_L^G}(S_6^{(3)} - S_2^{(3)}) + f_{HGP}S_8^{(3)}$$

$$- \frac{f_{HGU}}{\tau_1}(-S_3^{(2)} - 1.1S_4^N S_4^{(2)}tanh(0.55S_4^N S_4)^2$$

$$- 1.1S_4^N S_4^{(1)}(2tanh(0.55S_4^N S_4))$$

$$(1 - tanh(0.55S_4^N S_4)^2 0.55S_4^N S_4))$$

Thus, the SoM relative degree equals 5.

III. HOSMC ROBUSTNESS WITH RESPECT TO RELATIVE DEGREE FLUCTUATIONS

It is well known that any small general perturbation or model inaccuracy can lead to a decrease of the model relative degree, or even to its disappearance. On the other hand unaccounted-for fast dynamics of the system can increase the system's relative degree. It was recently proved that homogeneous HOSMC with a HOSM differentiator inside feature ultimate robustness with respect to all such perturbations [14]. In particular, singular perturbations often appear at the inputs and outputs of systems [19], [20]. For simplicity the following consideration is restricted to singular perturbations at the system input. Consider the system

$$\dot{x} = a(t,x) + b(t,x)v, \quad \sigma = \sigma(t,x) \tag{8}$$

where $x \in \mathbf{R}^n$, $v \in \mathbf{R}$ is the input, a, b and $\sigma : \mathbf{R}^{n+1} \to \mathbf{R}$ are unknown smooth functions, n can be also uncertain. The output σ is measured in real time.

Assumption 1. Smooth uncertain functions a, b and σ are defined in some open region $\Omega \subset \mathbf{R}^{n+1}$. It is supposed that provided the input v is a Lebesgue-measurable function of time, $|V| \leq v_M$, all solutions starting from an open region $\Omega_x \subset \mathbf{R}^n$ at $t \in t_a$ can be extended in time up to $t = t_b > t_a$ without leaving the region Ω. The constant $v_M > 0$ is introduced in Assumption 4.

Assumption 2. The relative degree r_p of the system is assumed to be constant and known. It means that for the first time the input variable v appears explicitly in the r_pth total time derivative of σ [21]. It can be checked that

$$\sigma^{(r_p)} = h(t,x) + g(t,x)v \tag{9}$$

where $h(t,x) = \sigma^{(r_p)}|_{v=0}, g(t,x) = \frac{\partial}{\partial v}\sigma^{(r_p)}$ are some unknown smooth functions, which can be expressed in the terms of Lie derivatives. The set Ω_x is supposed to contain r_p-sliding points at the time $t = t_a$.

Assumption 3. It is supposed that

$$0 < K_m \leq \frac{\partial}{\partial v}\sigma^{(r_p)} \leq K_M, |\sigma^{(r_p)}|_{v=0}| \leq C \tag{10}$$

hold in Ω for some K_m, K_M, $C > 0$. Conditions (10) are formulated in terms of input-output relations.

Let the unaccounted-for dynamics is described by the equations

$$\mu\dot{z} = f(z,u), v = v(z) \tag{11}$$

where $z \in \mathbf{R}^m$, $u \in \mathbf{R}$ is the control and the input of the unaccounted-for dynamics, output $v(z)$ is continuous and $f(z,u)$ is a locally bounded Borel-measurable function, the time constant $\mu > 0$ is a small parameter. All differential equations are understood in the Filippov sense [22].

The control u is determined by a feedback

$$u = U(\sigma, \dot{\sigma}, \ldots, \sigma^{(r-1)}) \tag{12}$$

where U is a function continuous almost everywhere, and bounded by some constant u_M, $u_M > 0$, in its absolute value. Being applied directly to (8), i.e. with

$$v = u, \tag{13}$$

it is supposed to locally establish the r_p-sliding mode $\sigma \equiv 0$.

Assumption 4. Initial values of z belong to some compact region Ω_{z0}. The unaccounted-for dynamics is assumed to be

Bounded-Input-Bounded-State (BIBS), with $\mu = 1$. Since $|u| \leq u_M$, this provides for the infinite extension in time of any solution of (12) and for z belonging to another compact region Ω_z independent of μ. Indeed, μ can be excluded by the time transformation $\tau = t/\mu$. This assumption causes also the "internal" output v to be bounded in its absolute value by some constant $v_M > u_M > 0$.

Assumption 5. The dynamic output feedback (12) is supposed to be r_p-sliding homogeneous [21], which means that the identity

$$U(\sigma, \dot{\sigma}, \ldots, \sigma^{(r_p-1)}) \equiv U(\kappa^{r_p}\sigma, \kappa^{(r_p-1)}\dot{\sigma}, \ldots, \kappa\sigma^{(r_p-1)}) \tag{14}$$

is kept for any $\kappa > 0$. It is also assumed that the control function U is locally Lipschitz everywhere except a finite number of smooth manifolds comprising a closed set Γ in the space with coordinates $\Sigma = (\sigma, \dot{\sigma}, \ldots, \sigma^{(r_p-1)})$. Note that, due to the homogeneity property (14), the set Γ contains the origin $\Sigma = 0$, where the function U is inevitably discontinuous [21].

Quasi Continuous HOSMC [23] satisfies Assumption 5. As follows from (9) and (10),

$$\sigma^{(r_p)} \in [-C, C] + [K_m, K_M]v. \tag{15}$$

Assumption 6. It is assumed that with control (12) applied directly to inclusion (15), a finite-time stable inclusion, (12), (13), (15) is created. Note that the right-hand sides of the differential inclusions are enlarged at the points of the control discontinuity according to the Filippov procedure [21].

Assumption 7. The unaccounted-for dynamics are assumed exact in the following sense. With $\mu = 1$ and any constant value of u the output v uniformly tends to u. That means that for any $\delta > 0$ there exists $T > 0$ such that with any u, $u = const$, $|u| \leq u_M$, $z(0) \in \Omega_z$, the inequality $|v - u| \leq \delta$ is kept after the transient time T. It is required also that the function $f(z, u)$ in (11) be uniformly continuous in u, which means that $||f(z, u) - f(z, u + \triangle u)||$ tends to 0 with $\triangle u \rightarrow 0$ uniformly in $z \in \Omega_z$, $|u| \leq u_M$.

Assumption 8. It is supposed that the change of (12), (13) at the set Γ to

$$v \in \begin{cases} U(\Sigma), & \Sigma \notin \Gamma \\ [-V_M, V_M], & \Sigma \in \Gamma \end{cases} \tag{16}$$

does not destroy the finite-time convergence, i.e. (15), (16) is also finite-time stable.

Theorem 1: [19] Let assumptions 1-8 hold. Then there exist a vicinity Q of the r_p-sliding set in Ω_x at $t = t_a$, a time moment $t_1 \in (t_a, t_b)$, and $a_0, a_1, \ldots, a_{r-1} > 0$, such that with sufficiently small $\mu > 0$ for any trajectory of (8), (11), (12) starting within Q at $t = t_a$ the inequalities

$|\sigma| < a_0\mu_p^r, |\dot{\sigma}| < a_1\mu^{r_p-1}, \ldots, |\sigma^{(r_p-1)}| < a_{r_p-1}\mu$ are kept within $t \geq t_1$.

Usually different system variables feature different rates, some of them are faster than the others and do not affect the controllable outputs [24]. Unfortunately, it is very difficult to check the assumptions of theorem 1 in practice. For example, in our case BeM and SoM have the same output and input, but dimensions of the models are different, and, moreover, the physical meaning of variables is also different. This means that it is also difficult to rewrite SoM in the form (8), (11), as a singularly perturbed reduced system, while the reduced system is close to BeM.

IV. PRACTICAL RELATIVE DEGREE

According to theorem 1, HOSMC are robust with respect to relative degree fluctuations due to singular perturbations, that are always present in practice. In fact they are robust also with respect to much more general perturbations [20], [14]. Therefore, it is important to identify a reasonable value of the relative degree, in order to use HOSMC as a black box control for a real process.

HOSMC robustness with respect to relative degree fluctuations allows the use of a controller of order r_p for system (8), neglecting the increment of the relative degree due to (11). However, it is not easy to present the original mathematical model of blood glucose dynamics given by eqs. (4) in the singular perturbation form (8), (11). It makes difficult to construct a robust HOSMC controller that can stabilize the blood glucose concentration using a variety of mathematical models of glucose dynamics with different relative degrees.

A. Practical relative degree identification method

It is supposed that practical relative degree (r_p) of system (8) exists, but it is unknown. In order to identify practical relative degree, a Heaviside step function $u = H(x - t_H)$ is applied to equation (9):

$$\sigma^{(r_p)} = h(t, x) + g(t, x)H(x - t_H) \tag{17}$$

If a discontinuity is observed in $\sigma^{(r_p)}$ at $t = t_H$, and consequently a slope change appears in $\sigma^{(r_p-1)}$, with the increment of $\sigma^{(r_p)}$ always having the same sign, then the *practical relative degree* of the system is identified as r_p.

V. IDENTIFICATION OF THE PRACTICAL RELATIVE DEGREE OF THE GLUCOSE-INSULIN REGULATORY SYSTEM

A Heaviside step function, $u = H(x - 15)$ was applied. The third derivative was analyzed to find the discontinuity at $t = 15min$ and the second derivative was analyzed to find the slope change which takes place at the same time. The robust third-order differentiator [25] was used for this sake.

It is clear from Fig. 1 that the relative degree of BeM is three, which concurs with the theoretical relative degree. One can see from Fig. 2 that for SoM the discontinuity appears
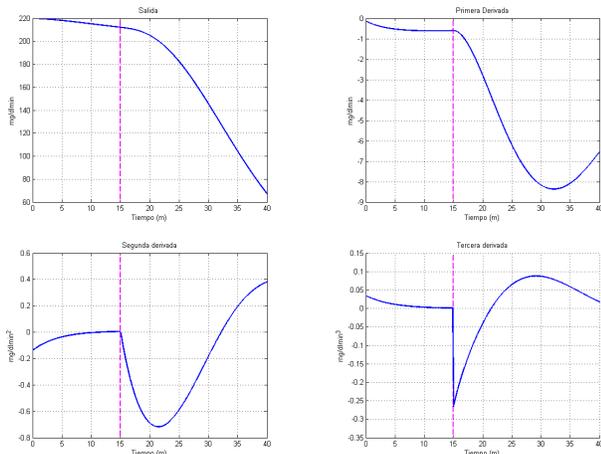
Fig. 1. BeM output and its derivatives, response to an step function $u = H(x-15)$. A discontinuity appears in the third derivative, a sudden change of slope is seen in the second derivative, then the model's practical relative degree is clearly 3.
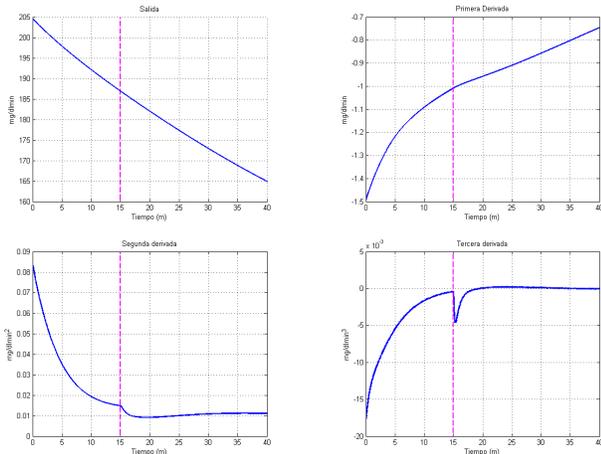
Fig. 2. SoM output and its derivatives, response to an step function $u = H(x-15)$. A discontinuity is first seen in the third derivative, and a sudden change of slope in the second then it is possible to control this system with a third order controller, due to its *practical relative degree* is 3.

at $t = 15m$, in the third derivative and the second derivative has a inflection change. Thus, both models have the same practical relative degree $r_p = 3$, and the same controller can be applied to both models.

VI. CONTROLLER

Quasi Continuous Control (QC-HOSMC) [23] was chosen in this work, for it produces less chattering than the Nested Control. QC-HOSMC u, is chosen according to the system relative degree 3, since it has been shown that BeM and SoM have the same practical relative degree $r_p = 3$.

$$
\begin{aligned}
u &= -\alpha[\ddot{\sigma} + \beta_2(|\dot{\sigma}| + \beta_1|\sigma|^{2/3})^{1/2}(\dot{\sigma} + \\
&\quad \beta_1|\sigma|^{2/3}sign\sigma)]/[|\ddot{\sigma}| + \beta_2(|\dot{\sigma}| + \beta_1|\sigma|^{2/3})^{1/2}]
\end{aligned} \tag{18}
$$

where $\beta_1 = 0.2$, $\beta_2 = 0.4$, $\alpha = 30$. The first and second

derivatives of σ are calculated using finite differences [26], with a sample step $\delta = 0.1m$, according to an amperometric glucose sensor sample time [27].

According to the glycemic recommendations for non-pregnant adults with diabetes of the American Diabetes Association (ADA), 1-2 hours after a meal ingestion blood glucose concentration (G) should be $G < 180mg/dl$. ADA considers hypoglycemia for $G \leq 70mg/dl$.

The control aim is to lower the blood glucose concentration in a smooth way to avoid a hypoglycemia episode. Therefore reference is created as a dynamical profile based on BeM and the parameters tuned in order to satisfy ADA recommendations ($p_1 = 0.022$, $p_2 = 0.0123$, $p_3 = 6.92e-6$, $\gamma = 0.0039$, $n = 0.2659$, $h = 79.0353$, $G_b = 90$, $I_b = 7$).

Simulations represent a postprandial event of a poorly controlled diabetic patient starting in 350mg/dl. The controller was tested with SoM and BeM, with no special retuning. For each model three different *in silico* patients.
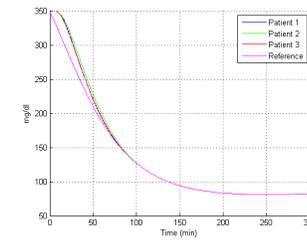
Fig. 3. Glucose concentration for BeM, representing a postprandial event, controlled by a third order QC-HOSMC. There is no hypoglycemic overshot, and normoglycemia is achieved in acceptable time (100 min). Controller gains are the same for the three patients.
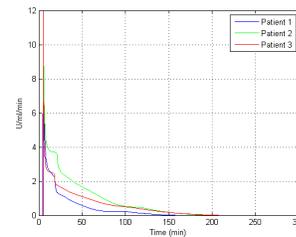
Fig. 4. Insulin dose prescribed by the controller to achieve normoglycemia. Notice the different dose for each patient.

It is seen from Figs. 3 and 5 that for BeM and SoM the final target is achieved. It means controller can be designed according to the *practical relative degree* identified for SoM.

The insulin infusion remains constant in Fig. 6 after the basal level is achieved, since SoM describes the insulin effect not only on glucose extraction, but also on hepatic glucose production. Therefore a small infusion is needed to maintain a balance in glucose concentration. In BeM this effect is not taken into account, hence the insulin infusion is zero, as soon as the equilibrium point is achieved (see Fig. 4).

VII. CONCLUSIONS

High-order sliding-mode controllers for blood glucose regulation can designed based on the relative degree approach.
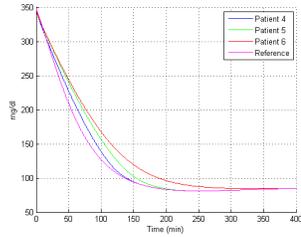
Fig. 5. Glucose concentration for SoM, representing a postprandial event, controlled by the same third order QC-HOSMC, as BeM. SoM relative degree is 5, but its practical relative degree is 3. There is no hypoglycemia overshot.
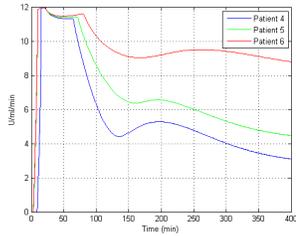
Fig. 6. Insulin dose prescribed by the controller to achieve normoglycemia. Notice the different dose for each patient.

Two different well-known mathematical models, Bergman Minimal Model (BeM) and Sorensen Model (SoM), are used. Obviously, the complete model of any biological system never exists. This means that the true relative degrees and orders of biological models are unknown, since they vary from model to model. Therefore, it is difficult to analytically determine a system's relative degree. Experimental identification of the practical relative degree is proposed for these kind of systems. In this work the practical relative degree of the glucose-insulin regulatory system is determined, based on BeM and SoM. The practical relative degree of the both models is found to be $r_p = 3$. And, therefore, the same HOSM controller is applied. The controller has been tested via simulation for 6 *in silico* patients, and the results demonstrate the accurate robust regulation of blood glucose concentration for both mathematical models of glucose dynamics.

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