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Rapid insulin stabilization via sliding modes control for T1DM therapy

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***Abstract*— Blood glucose control through exogenous insulin infusion is the main paradigm on Type 1 Diabetes Mellitus Therapy. The artificial pancreas is a technological approach that seeks an automatic insulin infusion by means of continuous subcutaneous insulin infusion systems, continuous glucose monitoring systems and a control algorithm that compute the required insulin that must be infused. In this sense, most of the blood glucose control schemes seeks blood glucose control without taking care of the dynamic of infused insulin (not the transient neither the stable state). In this contribution a novel method for rapid stabilization of positive and compartmental linear systems is presented. We proposed a stabilization approach using a sliding mode control. Such methodology is used to stabilizing the linear insulin system of a well known glucose-insulin dynamical model.**

Keywords: Sliding modes, positive systems, Type 1 Diabetes Mellitus.

I. Introduction

Automatic insulin infusion is the main paradigm for blood glucose control in Type 1 diabetes Mellitus (T1DM) via the called artificial pancreas, a technological approach to glycemic management in insulin-depend diabetic patients (Cobelli, 2011). The automation of insulin delivering has given rise to the understanding of glycemic management as a control problem, and the main goal around is to compute a time-varying insulin delivery profile able to reach the glycemic control target. Many blood glucose control algorithms have been developed since then, but the effectiveness of all of them depends on the glucose control via the insulin infusion; nevertheless, the dynamics of delivered insulin is not considered as a relevant parameter as the glucose concentration usually is. In this contribution, the stabilization of delivered insulin is considered as a control problem, inherent to the glucose one. In the glucose metabolism of a healthy subject, the pancreatic insulin release is perturbed by the glucose imbalance, but after the perturbation, the insulin release goes to the homeostatic equilibrium, or the so called, basal insulin release. This fact, is a starting point towards the study of the glucose control from a integrative point of view, where we must take care of insulin control as well as the traditional glucose one.

The stabilizing of insulin dynamics is carried out by a sliding mode control. Some contributions of sliding modes control theory have been presented in applications of artificial pancreas (Kaveh, 2008)-(Abu, 2010); nevertheless such contributions are devoted to the typical control problem, that is the glucose control and stabilizing without taking care of the insulin dynamics.

II. A class of positive systems

Novel solutions on stabilizing positive linear system via positive control can be obtained from the Frobenius-Perron Theorem for Metzler matrices and known results of sliding modes theory, particularly the sliding dynamic on hyperplanes $Lx - k = 0$ of $(n-1)$-dimension. Firstly, we will discussed a preliminary issues.

Let $\sigma(A)$ be the set of eigenvalues of A. $\mathbb{C}^+ = \{z \in \mathbb{C} \mid \text{Re}(z) > 0\}$ and $\mathbb{C}^- = \{z \in \mathbb{C} \mid \text{Re}(z) < 0\}$. A matrix $A = [a_{ij}] \in \mathbb{R}^{n\times n}$ is *Metzler* if $a_{ij} \geq 0$, for $i \neq j$. Also, matrix $A = [a_{ij}] \in \mathbb{R}^{n\times n}$ is *Hurwitz* if $\sigma(A) \subset \mathbb{C}^-$.

Theorem 1: Frobenius-Perron for Metzler matrices
Let $A \in \mathbb{R}^{n\times n}$ be a Metzler matrix. Then, there exists a real number μ_0 and a vector $x_0 \geq 0$, such that the follow holds:

a) μ_0 is an eigenvalue of A and x_0 is its respective eigenvector, i.e. $Ax_0 = \mu_0 x_0$;
b) If $\mu \neq \mu_0$ is any other eigenvalue of A, then $\text{Re}(\mu) < \mu_0$.

Remark 1: Inverse property of Metzler matrices.
Let $A \in \mathbb{R}^{n\times n}$ be a Metzler matrix. There exist a matrix $-A^{-1}$ if and only if A is Hurwitz (i.e. $\mu_0 < 0$).

Corollary 1: Let $A \in \mathbb{R}^{n\times n}$ be an irreducible Metzler matrix. Then, there exist a strictly positive matrix $-A^{-1}$ if and only if A is Hurwitz.

Consider the next homogeneous linear system in continuous-time:

$$\dot{x} = Ax \tag{1}$$

where $x \in \mathbb{R}^n$ and $A = [a_{ij}] \in \mathbb{R}^{n\times n}$. If $x(t_0) = x_0 \in \mathbb{R}^n$, $t \geq 0$, then the solution $x(t, t_0, x_0) \in \mathbb{R}^n$, for all $t \geq 0$, if and only if matrix A is Metzler.

Theorem 2: Let us consider the positive linear system:

$$\dot{x} = Ax + c \tag{2}$$

where $x \in \mathbb{R}^n$, A is a Metzler matrix and $c \in \mathbb{R}^n$ is a positive vector. Then, the non-trivial equilibrium state $\overline{x} = -A^{-1}c$ is asymptotically stable (i.e. A is Hurwitz) if and only if there exists such equilibrium state and it is positive.

Definition 1: A matrix $A = [a_{ij}]$ is compartmental if the follow two conditions hold:

1. A is a Metzler matrix.
2. $\sum_i a_{ij} \leq 0$ for each $i, j = 1, \ldots, n$.

The second condition is the called *diagonal dominance* (by columns). From Gerschgorin Theorem (see (Leenheer and Aeyels, 2001) and (Bellman, 1970)), if A is compartmental, then $\sigma(A) \cap \mathbb{C}^+ = \emptyset$.

III. Stabilization of positive-systems/positive-control via sliding mode

Let us consider the positive linear control system:

$$\dot{x} = Ax + bu \tag{3}$$

of which state is $x \in \mathbb{R}^n_+$, matrix A is Metzler and Hurwitz, $b \in \mathbb{R}^n_+$ and control parameter $u \geq 0$; the system can be restricted to an interval: $u \in [r_1, r_2]$, with $r_2 > r_1 \geq 0$.

If A in system (3) is Meztler and Hurwitz, the unique positive equilibrium point $\overline{x} = -A^{-1}b\bar{u}$ (with constant $\overline{u} > 0$) is globally asymptotically stable. Then the follow question rises: *Is it possible to obtain a rapid stabilization on $\overline{x}$ if we consider $u \in [r_1, r_2]$ instead of $u = \overline{u}$?*. To answer the last question we most consider that the system (3) is not-controllable; according to Brammer's controllability Theorem. Due to A is a Meztler matrix, it has at least a real eigenvalue, then the system is not fully controllable via positive control. Now, a sliding method to solve the rapid stabilization in positive linear systems via positive control is presented.

Let us consider system (3) with $a_{ij} \geq 0$ for $i \neq j$. In state space, the positive equilibrium points are:

$$\overline{x}_1 = -A^{-1}br_1 \quad \text{and} \quad \overline{x}_2 = -A^{-1}br_2$$

such that $\|\overline{x}_1\| < \|\overline{x}_2\|$, due to $\|\overline{x}_1\| = \left\|-A^{-1}br_1\right\| = \left\|-A^{-1}b\right\| r_1 < \left\|-A^{-1}b\right\| r_2 = \left\|-A^{-1}br_2\right\| = \|\overline{x}_2\|$.

The hypothesis of A Hurwitz implies that each equilibrium point $\overline{x}_i$ is global attractor for solution of the feedback system $\dot{x} = Ax + br_i$, $i = 1, 2$. For sliding purposes, let us consider a constant vector $L \in \mathbb{R}^n_+$ and a constant scalar $k > 0$, in such a manner that the embedded hyperplane in $\mathbb{R}^n_+$ given by:

$$Lx = k \tag{4}$$

with numerical values L and k arbitrarily chosen such that the sliding condition, given by the next inequalities, is satisfied:

$$\begin{array}{l} L(Ax + br_1) < 0 \quad \text{for} \quad x \in \mathbb{R}^n_+ \text{ such that } Lx > 0 \\ L(Ax + br_2) > 0 \quad \text{for} \quad x \in \mathbb{R}^n_+ \text{ such that } Lx < 0 \end{array} \tag{5}$$

Determining magnitude k involves the straight line segment joining the equilibrium points

$$x = \lambda\overline{x}_1 + (1 - \lambda)\,\overline{x}_2, \text{ for } \lambda \in (0, 1)$$

We can chose k in such a manner that hyperplane given by $Lx - k = 0$ reaches a predetermined equilibrium point $\overline{x}$ obtained with $\lambda = \frac{1}{2}$;

$$\overline{x} = \frac{1}{2}\overline{x}_1 + \frac{1}{2}\overline{x}_2$$

Then,

$$k = L\overline{x} \tag{6}$$

Considering inequalities (5) and parameters r_1, r_2, $\overline{x}$, k and L, it is known that applying the no-continuous control

$$u = \begin{cases} r_1 & \text{if} \quad Lx - k > 0 \\ r_2 & \text{if} \quad Lx - k < 0 \end{cases}, \tag{7}$$

any solution $x(t)$ with initial condition out of hyperplane $Lx = k$ reaches it in a finite time. It also known that no-continuous control (7), evolving in the extremes of restriction interval $[r_1, r_2]$, minimizes the time to reach hyperplane $Lx = k$, see (Leyva and Solis-Daun, 2009), due to considering the Lyapunov function $V = \frac{1}{2}(Lx - k)^2$, control (7) is the solution of the follow optimization problem:

$$\min_{u \in [r_1, r_2]} \frac{dV}{dt} = \min_{u \in [r_1, r_2]} \{(Lx - k)\, L\,(Ax + bu)\}.$$

Once inequalities (5) are satisfied an invariant dynamic over hyperplane $Lx = k$ rises, and this dynamics corresponds to the application of the so called equivalent control, given by u_{eq} and defined for x such that $Lx = k$, and computed from $L\dot{x} = 0$. That is,

$$L(Ax + bu_{eq}) = 0,$$

Consequently;

$$u_{eq} = -\frac{LAx}{Lb}.$$

This results defines a globally stabilizing control:

$$u = \begin{cases} r_1 & \text{if} \quad L(x - \overline{x}) > 0 \\ -\frac{LAx}{Lb} & \text{if} \quad L(x - \overline{x}) = 0 \\ r_2 & \text{if} \quad L(x - \overline{x}) < 0 \end{cases} \tag{8}$$

for all $x \in \mathbb{R}^n_+$ in the feedback system (3)–(8).

Now, we must proceed to select the hyperplane $Lx = k$. Let us consider the Metzler matrix A given in (3) with inputs $a_{ij} \geq 0$ for $i \neq j$. Such that term LAx is:

$$\begin{array}{rcl} LAx & = & -x_1p_1 - x_2p_2 - x_3p_3 \cdots - x_np_n \\ & = & -\langle p, x\rangle < 0 \quad \text{for } p \in int\mathbb{R}^n_+ \end{array}$$

that means, $p = \begin{pmatrix} p_1 & p_2 & p_3 & \cdots & p_n \end{pmatrix}^T \in \mathbb{R}^n_+$ gives that equality:

$$\begin{aligned} l_1a_{11} + l_2a_{21} + l_3a_{31} + l_4a_{41} + \cdots + l_na_{n1} &= -p_1 \\ l_1a_{12} + l_2a_{22} + l_3a_{32} + l_4a_{42} + \cdots + l_na_{n2} &= -p_2 \\ l_1a_{13} + l_2a_{23} + l_3a_{33} + l_4a_{43} + \cdots + l_na_{n3} &= -p_3 \\ &\vdots \\ l_1a_{1n} + l_2a_{2n} + l_3a_{3n} + l_4a_{4n} + \cdots + l_na_{nn} &= -p_n \end{aligned}$$

written in a matricial form:

$$A^T L^T = -p$$

consequently, $L^T = (-A^{-1})^T p \in \mathbb{R}^n_+$; due to A is Metzler and Hurwitz. That is, for each $p \in \mathbb{R}^n_+$ we have a vector $L = -p^T A^{-1} \in \mathbb{R}^n_+$ such that $u_{eq} = -\frac{LAx}{Lb} > 0$. Then

$$\begin{aligned} u_{eq} &= -\frac{LAx}{Lb} \\ &= \frac{p^T x}{p^T(-A^{-1})\, b} > 0 \text{ for } x \in \mathbb{R}^n_+. \end{aligned}$$

Matrix $A_{eq} = A + b\left(\frac{p^T}{p^T(-A^{-1})b}\right)$ is Metzler because it is the sum of a Metzler matric and a matrix with non-negativa inputs. Let us consider the positive control system and the plane $S = \left\{x \in \mathbb{R}^n_+ \; L(x - \overline{x}) = 0\right\}$.

Proposition 1: If $p \in int\mathbb{R}^n_+$ (that is: $p_i > 0$ for $i = 1, ..., n$), if there exists a slide over S.

Proof: The condition $p \in int\mathbb{R}^n_+$ implies that $u_{eq}(x) > 0$ for $x \in \mathbb{R}^n_+$. According to Theorem 1 in (Sira, 1988), if the control bounds r_1 and r_2 are selected such that $r_1 < u_{eq} < r_2$ remains, then the affine closed-loop system has a sliding mode. In this manner, considering $r_2 > 0$ large enough ($\|\overline{x}\| < \|\overline{x}_2\|$) there exist a slide over hyperplane S.

Lema 1: $\det A_{eq} = 0$.

Proof: It is enough to prove that $b \in \ker\left(I - b\frac{L}{Lb}\right)$, due to

$$\left(I - b\frac{L}{Lb}\right) b = b - b\frac{L}{Lb}b = 0,$$

We can conclude that $\det A_{eq} = 0$. □

The last Lemma can be interpreted as follows: the $n-$dimensional dynamics of $\dot{x} = Ax$ is restricted to the $(n-1)$-dimensional dynamics, by means of the equivalent control u_{eq}, defined at the hyperplane S and represented by $\dot{x} = A_{eq}x$.

We have proved that $\lambda = 0$ is the eigenvalue of matrix $A_{eq} = A + b\left(\frac{p^T}{p^T(-A^{-1})b}\right)$; moreover such matrix is Metzler because it is defined as the sum of a Metzler matrix an a matrix with no-negative inputs.

In the other hand, if $x^* \in \text{Ker}\left(I - b\frac{L}{Lb}\right)$, then $x^* = \frac{1}{Lb}bLx^*$. Thus, $x^* \in \text{Im}(b)$, implying that $\lambda = 0$ is a simple eigenvalue with the corresponding eigenvector x^*. In the application exposed in the follow, we show that $\lambda = 0$ is a dominant eigenvalue of A_{eq} (according yo to the Frobenius-Perron Theorem for Metzler matrices); this implies that the dynamics of system $\dot{x} = A_{eq}x$ has a state $\overline{x} = -A^{-1}b\bar{u}$ as an unique equilibrium point .

Furthermore, from inequalities (5) it is easy to see that, for x such that $s(x) = 0$ the follow is satisfied:

$$L(Ax + br_1) < 0 < L(Ax + br_2)$$

As $Lb > 0$, we have

$$Lbr_1 < -LAx < Lbr_2 \quad \Leftrightarrow \quad r_1 < \frac{-LAx}{Lb} < r_2$$

we can conclude that $u_{eq} \in [r_1, r_2]$. In particular, the next is also satisfied:

$$u_{eq}(\overline{x}) = -\frac{1}{Lb}LA\overline{x} = -\frac{1}{Lb}LA\left(-A^{-1}b\overline{u}\right) = \overline{u}.$$

IV. Stabilization of insulin implies glucose stabilization

IV-A. Model of insulin dynamics

Many mathematical models about glucose-insulin dynamics in T1DM have been proposed; nevertheless the Sorensen's model is one of the most accepted because its completeness in representing glucose metabolism in a compartmental approach (Sorensen, 1985). The use of Sorensen's model for control purposes has been discussed in (Quiroz, 2007); there, a brief discussion about the main structure of the model is presented. The model is divided in three subsystems: glucose, insulin and glucagon-metabolic rates. Glucose subsystem is a 8-dimensional nonlinear of ordinary differential equations, meanwhile insulin subsystem is a 7-dimensional linear one. Both systems are coupled by the nonlinear glucagon-metabolic rates subsystem. It is important to remark that the Sorensen's model has been validated and the involved parameters are known.

A typical approach of glucose control on T1DM consists on design a function $u(t)$ to control the measured output signal, that is the glucose concentration of the peripheral vascular tissue. The control objective on glucose concentration is reached by the exogenous supply of insulin in the subcutaneous route (control signal) defined by designed $u(t)$. In this contribution, a stabilization of the insulin subsystem is proposed. This intent obeys to the necessary control of insulin infusion; that is, it isn't sufficient to get glucose concentration on physiologic ranges, but of infused insulin must be controlled in order to reduce excess of infused doses to prevent hyperinsulinemia and diabetic coma.

Here, we propose an algorithm for insulin control based in rapid stabilization of a linear control system by means of a sliding modes theory for positive systems. The controlled

system is the insulin subsystem of the Sorensen's model, which is rewritten here and considering nominal parameters:

$$\begin{aligned}
\dot{x}_1 &= 1{,}73x_2 - 1{,}73x_1 \\
\dot{x}_2 &= 0{,}454x_1 + 0{,}909x_4 + 0{,}727x_5 + 1{,}06x_6 - \\
&\quad 3{,}151x_2 \\
\dot{x}_3 &= 0{,}765x_2 - 0{,}765x_3 \\
\dot{x}_4 &= 0{,}094x_2 + 0{,}378x_3 - 0{,}789x_4 \\
\dot{x}_5 &= 1{,}411x_2 - 1{,}835x_5 \\
\dot{x}_6 &= 1{,}418x_2 - 1{,}874x_6 + 0{,}455x_7 \\
\dot{x}_7 &= 0{,}05x_6 - 0{,}111x_7
\end{aligned}$$

where, x_i, for $i \in 1, ..., 7$ is the insulin concentration in brain, arterial, gut, liver, kidney, periphery vascular, periphery interstitial compartments, respectively. This submodel is use to design a stabilizing controller according to the methodology given in the previous section. Next, the parameters of the no-continuos control u for rapid insulin stabilization is computed.

IV-B. Rapid stabilization analysis

Let us consider the state space representation of the insulin linear subsystem described before:

$$\begin{aligned}
\dot{x} &= Ax + bu \\
\dot{y} &= g(x, y)
\end{aligned} \tag{9}$$

with $x = (x_1, ..., x_7)^T \in \mathbb{R}^7_+$ representing insulin levels. The parameter of positive control u represents insulin infusion, that is, a bounded parameter $u \in [r_1, r_2]$, with $r_2 > r_1 \geq 0$. We can see that the matrix A of this model is Metzler and Hurwitz, in such a manner that the positiveness and sliding condition on Equation (5) hold.

The stabilization problem assumes exogenous insulin infusion on the subcutaneous tissue, that is, the mass balance equation of insulin concentration on the peripheral vascular compartment $\dot{x}_6$ is modified by the addition of the input u:

$$\dot{x}_6 = 1{,}418x_2 - 1{,}874x_6 + 0{,}455x_7 + 1{,}418u$$

The multiplicative term 1.418 preserves the mass balance on equation, using nominal values of caudal and volumen parameters on the peripheral vascular compartment ($\frac{Q_P^I}{V_{PV}^I} = 1{,}418$) (Sorensen, 1985).

In this manner, $b = [0 \quad 0 \quad 0 \quad 0 \quad 0 \quad 1{,}418 \quad 0]^T$ and the parameters of hyperplane $Lx - k = 0$ are $L = [a_1 \quad a_2 \quad a_3 \quad a_4 \quad a_5 \quad a_6 \quad a_7]$. Once inequalities (5) hold, we can define a sliding control u_{eq} in the segment of hyperplane $Lx = k$. From $L\dot{x} = 0$

$$u_{eq} = -\frac{LAx}{Lb} \in [r_1, r_2].$$

According to (6), we have: $k = (r_1 + r_2)(0{,}45781a_1 + 0{,}45781a_2 + 0{,}45781a_3 + 0{,}27387a_4 + 0{,}35202a_5 + 0{,}6885a_6 + 0{,}31014a_7)$. We can prove that there exists L such that a stable sliding rises over hyperplane $H = \{x \in \mathbb{R}^7_+ / Lx = k\}$. Values $a_i > 0$ for $i = 1, 2, ..., 7$ and $k > 0$ must be fixed such that the inequalities (5) hold. In this manner:

$$\begin{aligned}
LAx &= x_6(1{,}06a_2 - 1{,}874a_6 + 0{,}05a_7) - x_3(0{,}765\,a_3 \\
&\quad -0{,}378a_4) + x_2(1{,}73a_1 - 3{,}151a_2 + 0{,}765\,a_3 + \\
&\quad 0{,}094\,a_4 + 1{,}411a_5 + 1{,}418a_6) - x_5(1{,}835a_5 - \\
&\quad 0{,}727\,a_2) - x_4(0{,}789a_4 - 0{,}909a_2) - x_1(1{,}73a_1 \\
&\quad -0{,}454a_2) - x_7(0{,}111a_7 - 0{,}455a_6)
\end{aligned}$$

For simplicity in the last expression numerical values are assigned to some a_i, in particular to eliminate x_1, x_3, x_4, x_5 and x_7 having the next linear system

$$\begin{bmatrix} 1{,}73 & -0{,}454 & 0 & 0 & 0 \\ 0 & 0 & 0{,}765 & -0{,}378 & 0 \\ 0 & -0{,}909 & 0 & 0{,}789 & 0 \\ 0 & -0{,}727 & 0 & 0 & 1{,}835 \end{bmatrix} \begin{bmatrix} a_1 \\ a_2 \\ a_3 \\ a_4 \\ a_5 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

with the following non-trivial solution: $[a_1 \quad a_2 \quad a_3 \quad a_4 \quad a_5]^T = [0{,}66239 \quad 2{,}5241 \quad 1{,}4369 \quad 2{,}9080 \quad 1{,}0]^T$. Furthermore, we consider that $0{,}111\,a_7 - 0{,}455\,a_6 = 0$ and $a_6 = 0{,}243\,96a_7$, and we have:

$$L = \begin{bmatrix} 0{,}662 & 2{,}524 & 1{,}436 & 2{,}908 & 1 & 0{,}243a_7 & a_7 \end{bmatrix}$$

such that:

$$LAx = [0{,}345a_7 - 4{,}023]x_2 + [2{,}675 - 0{,}407a_7]x_6$$

Due to $b^T u = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 1{,}418u & 0 \end{bmatrix}^T$ we have $Lbr_1 = a_6 r_1 = 0{,}243a_7 r_1$. To determine the values of positive parameter such that inequalities (5) hold, the following operations must be considered:

$$\begin{aligned}
L\dot{x} &= (Ax + bu) \\
&= (0{,}345a_7 - 4{,}023)x_2 + (2{,}675 - 0{,}407a_7)x_6 + \\
&\quad 0{,}243a_7 u
\end{aligned}$$

We most also consider: $Lx - k = 0{,}662x_1 + 2{,}524x_2 + 1{,}436x_3 + 2{,}908x_4 + x_5 + 0{,}243a_7x_6 + a_7x_7 - k = 0$. That is;

$$\begin{aligned}
x_2 &= \frac{1}{2{,}524}k - \frac{1}{2{,}524}(0{,}662x_1 + 1{,}436x_3 + 2{,}908x_4 + \\
&\quad x_5 + 0{,}243a_7x_6 + a_7x_7) \\
&= \frac{1}{2{,}524\,1}k - (0{,}262x_9 + 0{,}569x_3 + 1{,}152x_4 \\
&\quad +0{,}396x_5 + 9{,}665 \times 10^{-2}a_7x_6 \\
&\quad 0{,}396a_7x_7) \\
&= \frac{1}{2{,}524}k - L_m x_m
\end{aligned}$$

In such a manner that:

$$\begin{aligned} Lx-k &> 0 \quad \Leftrightarrow \quad x_2 > \frac{1}{2{,}524\,1}k - L_m x_m \\ &\Leftrightarrow \quad u = r_1 \\ Lx-k &< 0 \quad \Leftrightarrow \quad x_2 < \frac{1}{2{,}524\,1}k - L_m x_m \\ &\Leftrightarrow \quad u = r_2 \end{aligned}$$

If we assume that $0{,}345a_7 - 4{,}023 = 0$, then $a_7 = 11{,}632$; such that:

$$L = [0{,}662 \quad 2{,}524 \quad 1{,}436 \quad 2{,}908 \quad 1 \quad 2{,}837 \quad 11{,}63] \quad (10)$$

and $L\dot{x} = 2{,}837u - 2{,}060x_6$, the inequalities (5) result:

$$\begin{aligned} \lim_{s\to 0^+} L\dot{x} &= \lim_{s\to 0^+} L\left(Ax + br_1\right) = 2{,}837r_1 - 2{,}060x_6 < 0 \\ &\Leftrightarrow \; x_6 > \frac{2{,}837r_1}{2{,}060} = 1{,}377r_1 \\ \lim_{s\to 0^-} L\dot{x} &= \lim_{s\to 0^-} L\left(Ax + br_2\right) = 2{,}837r_2 - 2{,}060x_6 > 0 \\ &\Leftrightarrow \; x_6 < \frac{2{,}837r_2}{2{,}060} = 1{,}377r_2 \end{aligned}$$

which can be summarized in conditions for r_1 and r_2:

$$r_1 < 0{,}726x_6 < r_2$$

if we agree with $13{,}770 = \min\{x_6\} \leq x_6 \leq \max\{x_6\} = 34.425$, then we can chose $r_1 > 10$ and $r_2 < 50$. We can also consider $k = 552{,}75$. The equivalent control results in $u_{eq} = -\frac{LAx}{Lb} = 0{,}726\,22x_6$, due to $L\dot{x} = 0$ implies that $u_{eq} = 0{,}726\,22x_6$. Then, control can be redefined:

$$u = \begin{cases} r_1 & \text{if} \quad Lx - 552{,}75 > 0 \\ 0{,}726\,22x_{14} & \text{if} \quad Lx - 552{,}75 = 0 \\ r_2 & \text{if} \quad Lx - 552{,}75 < 0 \end{cases}$$

with $0 < r_1 < \min\{0{,}726x_6\} \leq 0{,}726x_6 \leq \max\{0{,}726x_6\} < r_2$, where we chose $k = 552{,}75$. Now, we compute the equilibrium point $\overline{x}$ the sliding system: $\dot{x} = Ax + bu_{eq}(x)$; that is:

$$A\bar{x} + bu_{eq}(\overline{x}) = 0$$

Due to $\overline{x}$ must be on the hyperplane, then $L\overline{x} = k$ must hold. From Equation (10) and selected $k = 552{,}75$, then $\overline{x} = [28{,}672 \quad 28{,}672 \quad 28{,}672 \quad 17{,}153 \quad 22{,}059 \quad 43{,}114 \quad 19{,}421]^T$.

IV-C. Simulations

The no-continuous controller u proposed in the last section seeks to stabilize the insulin subsystem of Sorensen's model in a desirable equilibrium point with physiological meaning such that it can be able to regulate the glucose subsystem through the coupling equations of the Sorensen's model (Quiroz, 2007). The numerical simulations of this process were carried out using ®MatLab-Simulink, considering L given in (10) and $k = 552{,}75$. First, the dynamic evolution of glucose subsystem is observed just considering a constant value $u = 22$ mUI emulating a basal subcutaneous insulin infusion, as it is shown in circle-marked line of Figure 1. Figure 2 shows the temporal evolution of peripheral vascular glucose concentration (G_{pv}) of Sorensen's model, here we can see the effect of the constant basal infusion on G_{pv} (circle-marked line). In the same manner, the temporal evolution of peripheral vascular insulin concentration is shown in circle-marked line of Figure 3. This open-loop experiment is for realizing that without parametric uncertainties nor external perturbations, a continuous insulin infusion is enough to regulate a T1DM patient on the physiological glucose range (70-120 mg/dl).

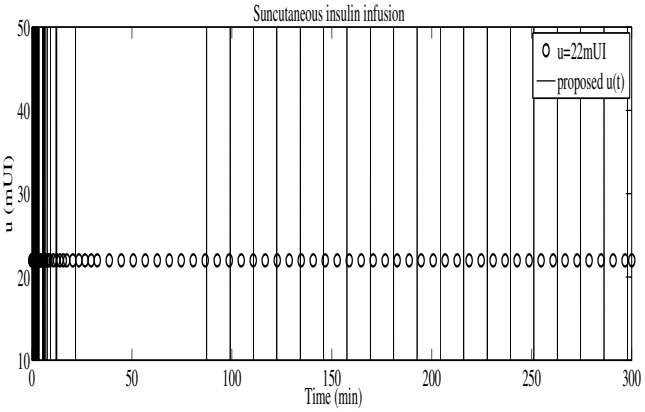

Figura 1. Control signal corresponding to the subcutaneous insulin.

After that, the stabilizing controller u is proved for different initial conditions. First the proposed u was proved with initial conditions $x_0 = [22 \quad 22 \quad 22 \quad 22 \quad 22 \quad 22 \quad 22]^T$, which is the initial condition closer to hyperplane $Lx - k = 0$, the corresponding control signal of the no-continuous u is shown in solid line in Figure 1, and the insulin stabilization insulin subsystem is depicted by the trajectory of state x_6 (I_{pv}) in solid line of Figure 3. The computed control signal reaches insulin stabilization and it is able to hold G_{pv} in the physiological range (see solid line in Figure 2).

Finally, a set con initial conditions x_0 of the insulin subsystem were selected in order observe the stabilizing property of the insulin subsystem and the regulation of the glucose subsystem. Figure 3 shows the time evolution and stabilization of x_6 considering ten different initial conditions: five above the hyperplane (dash lines) and five down (dotted lines). The corresponding glucose regulation for each insulin profile with different initial condition are shown in Figure 2, where dash lines correspond to initial conditions above hyperplane and the dotted lines for the initial conditions down hyperplane.

V. Conclusions

This contribution has the main intention to pointed out the importance of insulin stabilization in the general problem of automatic insulin infusion required in the paradigm of artificial pancreas, the technological approach to improve

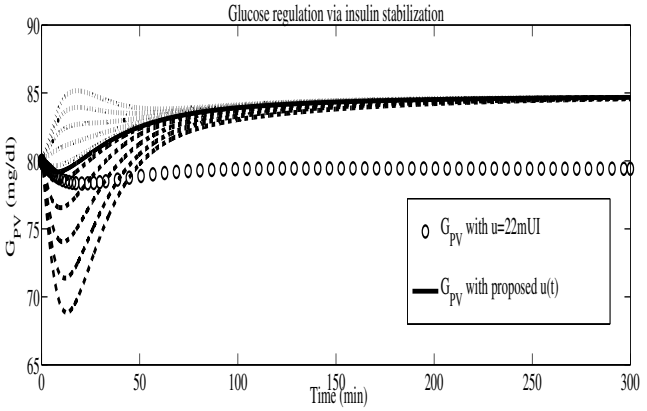

Figura 2. Regulated peripheral vascular glucose concentration.

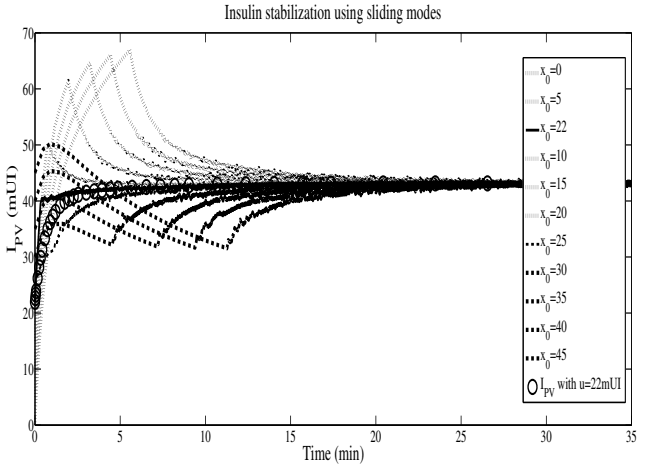

Figura 3. Stabilization of insulin subsystem with different x_0.

conventional T1DM therapy. The stabilization of the insulin concentration in human body has relevant medical advantages due to excess or deficiency of insulin in target tissues has negative effects over their correct function and in general it affects the complete glucose metabolism.

The proposed control scheme based in sliding modes control theory allows that a positive compartmental linear system, such as the insulin subsystem of Sorensen's model, can be stabilized on a desired equilibrium point, able to regulate the blood glucose concentration on peripheral tissue of a T1DM patient. Simulations results shows that the stabilization is preserved for different initial conditions of insulin state. This results shows that the sliding control theory is an exploitable tool for this class of biomedical systems.

VI. Acknowledges

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