IEEE Control Systems Letters paper presented at
2023 62nd IEEE Conference on Decision and Control (CDC)
December 13-15, 2023. Marina Bay Sands, Singapore

Computing control invariant sets for waiting-time switched systems: a study case of glucose regulation

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***Abstract*— Waiting-time constraints, bounding the minimum and maximum time of permanence in a given mode of a switched system, can be included in optimization-based control formulations by means of hard constraints. However, basic concepts such as equilibrium and invariance sets are modified by these constraints, affecting the formal stability analysis. This paper explores general regions of the state space wherein switched system trajectories under waiting-time constraints can feasibly (and indefinitely) remain inside, replacing the concept of invariance with those of permanence. Explicit algorithms to compute these regions inside an (out of the origin) target window are provided, while the glucose regulation problem for Type 1 Diabetes Mellitus (T1DM) patients is considered as an example to highlight its main properties.**

I. INTRODUCTION

The problem of keeping the states of a dynamical system inside a region over time by control laws has been studied since the seminal work of [1]; this region is referred as *Control Invariant Set* (CIS) in the control-theory literature. A CIS plays a fundamental role on the stabilization of control dynamical systems by generalizing the concept of control equilibrium states (i.e., a fixed point of the control system $x^+ = f(x, u)$) and therefore the control-target sets can be formally analyzed using the Lyapunov Theory [2]. Also, a CIS offers a framework to properly handle uncertain systems with bounded disturbances [3].

Although the set invariance characterization is widely addressed for linear systems, it is not completely understood in non-linear systems such as hybrid systems (which is a usual framework for biomedical problems). The particular type called switched system - defined by a set of discrete modes that selects the continuous dynamic that governs the states and a rule to manage the switches among the modes [4], [5] - presents a complex dynamical structure that complicates the proper characterization of regions such as the CIS. The problem was studied for the case of control linear switched systems on [6], and for an autonomous non-linear switched system on [7]. Also, on [8] and [9] it was approached for an autonomous linear switched system with and without dwell-time restriction respectively (the dwell-time constraint imposes a minimum-time of permanence on a mode as a stability condition [10], [11]).

As stated earlier, a switched system can serve as a framework for biomedical problems where the treatment (or drug administration) is represented by a mode and the schedule of treatments is associated with an optimal control problem [12]. Frequently, each treatment may be subject to waiting-time constraints (WTCs), which impose (i) a minimum time of administration for effectiveness and (ii) a maximum time of administration to avoid the onset of resistance (or to reduce toxicity effects). Moreover, for Type 1 Diabetes Mellitus (T1DM) treatment, switched systems can be employed for modeling patients' intraday variability [13], [14]. Under this scheme, each mode represents a particular set of parameters (i.e. insulin sensitivity) while the waiting-time constraint (minimum and maximum admissible time in each one) can be related to the physiological time variability, that is, embedding the time-variability of parameters as a constraint instead of a precomputed switching path.

From a dynamical point of view, WTCs drastically modify the control invariant regions of a switched system, since they prevent remaining too much or too little time in a given mode. Indeed, the literature lacks results on this subject except for the preliminary outputs presented in [15] and [16], where a conservative approximation of the structure of invariance regions with an application on control of ecological systems was studied.

This paper explores the Set-Invariance Theory for Switched Systems subject to WTCs. The discussion is focused on general regions of the state space - denoted as Permanence Regions (PR) - where the system can feasibly remain indefinitely without breaking the WTCs. Simulations illustrate the algorithms performance and the potential benefits for Glycemia regulation on patients with T1DM when the model is affected by variations of insulin sensitivity.

II. SWITCHED SYSTEMS

Switched systems dynamics can be described by the following equation [17]:

$$x(k+1) = A_{\sigma(k)}x(k) + B_{\sigma(k)}u(k), \tag{1}$$

with $x(k) \in \mathbb{X} \subset \mathbb{R}^n$ is the state of the system, $u(k) \in \mathbb{U} \subset \mathbb{R}^m$ is the control input and $\sigma(k) \in \Sigma := \{1, 2, \ldots, q\}$ is the switching signal that selects the mode $\sigma(k)$, at time $k \in \mathbb{N}$, among $q > 1$ possible values. The *switching path* $\boldsymbol{\sigma} := \{\sigma(k)\}_{k=0}^{\infty}$ is a sequence that indicates, through its elements, the selected subsystem that governs the dynamics of Eq. (1).

*This work was not supported by any organization

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Remark 1: The switching signal σ could be (i) externally manipulated (chronic infections and cancer application [12]) or (ii) time-dependent signal (diabetes application [18]).

A. Waiting-time constraints

Let $\boldsymbol{\sigma}$ be a switching path and $\kappa_{\boldsymbol{\sigma}} = \{k_j\}$ the sequence of *jump time instants* k_j, given recursively by $k_j = \min\{k \in \mathbb{N} : k > k_{j-1} \text{ and } \sigma(k) \neq \sigma(k+1)\}$, for $j \in \mathbb{N}$, with $k_0 = 0$.

A switching path $\boldsymbol{\sigma}$ restricted to a maximal and a minimal time of permanence for any selected mode is said to be restricted by the *Waiting-Time Constraints* or simply Waiting-Time (WTCs). It can be formalized as follows.

Definition 1 (Waiting Time Constraints, WTCs): Consider two values $L_\sigma \in \mathbb{N}$ and $U_\sigma \in \mathbb{N}$, for each $\sigma \in \Sigma$, denoted as *minimal and maximal waiting times* for σ, respectively, with $L_\sigma \leq U_\sigma$. We say that a switching path $\boldsymbol{\sigma}$ fulfills the *waiting time constrains* if its sequence of jump time instants $\kappa_{\boldsymbol{\sigma}}$ satisfies that $L_{\sigma(k_j)} \leq |k_j - k_{j-1}| \leq U_{\sigma(k_j)}$.

III. SET INVARIANCE FOR SWITCHED SYSTEMS

Let us review first the scenario without waiting times.

A. Set Analysis (Without Waiting-Time)

Let us recall that a control equilibrium for a linear control system is given by all states x_s for which there is a feasible input u_s such that $x_s = Ax_s + Bu_s$ [2]. Now, let us generalize this concept for switched systems.

Definition 2 (Control equilibrium set, CES): Consider the switched system (1). Its control equilibrium set, $\mathbb{X}_s \subset \mathbb{X}$, is given by all admissible states $x_s \in \mathbb{X}$ such that there is a pair $(\sigma_s, u_s) \in \Sigma \times \mathbb{U}$ that fulfills $x_s = A_{\sigma_s} x_s + B_{\sigma_s} u_s$. The generalization of equilibria is the concept of invariance presented next.

Definition 3 (Control Invariant Set, CIS): A nonempty set $\Omega \subset \mathbb{X}$ is said to be a *control invariant set* for switched system (1) if for every initial state $x(0) \in \Omega$ there is a control sequence $\boldsymbol{\sigma} \times \boldsymbol{u} = \{(\sigma(k), u(k)\}_{k=0}^{\infty}$ such that $x(k) \in \Omega$ for all $k \geq 0$.

A trivial (but Non-Maximal) CIS for the switched system without WTCs is given by an invariant set of any particular mode or the union of CIS of different modes. In order to characterize the Maximal CIS of the system, the following concept of controllable sets can be used.

Definition 4 (Controllable set of mode σ): Consider a nonempty set $\Omega \subset \mathbb{X}$. The one step controllable set to Ω for mode σ is given by

$$\mathcal{S}(\sigma, \Omega) = \{x \in \mathbb{X} : \exists\ u \in \mathbb{U} \text{ s.t. } A_\sigma x + B_\sigma u \in \Omega\}.$$

The k-step controllable set to Ω for mode σ can be defined iteratively by $\mathcal{S}^k(\sigma, \Omega) := \mathcal{S}(\sigma, \mathcal{S}^{k-1}(\sigma, \Omega))$ for $k \geq 1$, with $\mathcal{S}^0(\sigma, \Omega) := \Omega$.

The following is a known result on set-invariance of switched systems, which proof can be found at [16].

Proposition 1: A nonempty set $\Omega \subset \mathbb{X}$ is a control invariant set for the switched system (1) if and only if $\Omega \subset \bigcup_{\sigma \in \Sigma} \mathcal{S}(\sigma, \Omega)$.

The above proposition provides a criterion to determine if a region is (or not) a CIS for the switched system and a hint to obtain invariant regions within an arbitrary set $\mathbb{T} \subseteq \mathbb{X}$ by the following reasoning (i) compute $S(\sigma, \mathbb{T})$ (ii) test if $\mathbb{T} \subset \bigcup_{\sigma \in \Sigma} \mathcal{S}(\sigma, \mathbb{T})$ and (iii) if $\mathbb{T} \subset \bigcup_{\sigma \in \Sigma} \mathcal{S}(\sigma, \mathbb{T})$ is true then $\mathbb{T}$ is a CIS and the algorithm stops, if not replaced $\mathbb{T}$ by a *'appropriate set'* contained on $\mathbb{T} \cap \mathcal{S}(\sigma, \mathbb{T})$ for all modes σ, and repeat the procedure. This criteria (if it converges) provides the Maximal CIS within $\mathbb{T}$. From a practical perspective, the crucial part is that the union of the controllable sets could be nonconvex. Then, computing this 'appropriate set' (such as the maximum convex set inside the union) is not an easy task. Even when this starting point looks promising and the problem itself is interesting and challenging, we leave the discussion for future works.

B. Set Analysis (Including Waiting-Time)

A natural way of maintaining the states on-time between certain critical values (usually related to a healthy states in biomedical systems) is by the steady-states concept. Unfortunately, the intersection of the steady-states of every mode may not lie inside a desire region (see Fig. 3 for the T1DM case). Hence, it is necessary to generalize the invariance concept. A particular case of CIS that covers all switching signal natures (all cases mentioned on Remark 1) is the Full Control Invariant Set defined below.

Definition 5 (Full Control Invariant Set, FCIS ([16])): A set $\Omega \subset \mathbb{X}$ is said to be a *full control invariant set* for the switched system (1) under WTCs if for all $x \in \Omega$ and every $\sigma \in \Sigma$ there exists a control input $u \in \mathbb{U}$ such that $A_\sigma x + B_\sigma u \in \Omega$.

The concept of FCIS will be tested on the application example in Section IV. Next, we relax the conditions of permanence in a set by the concept of permanence set, which covers more general regions that can be stabilized by the switched system (1).

Definition 6 (Permanence Set, PS): Given the set $\mathbb{T} \subset \mathbb{X}$, the set $\Omega \subseteq \mathbb{T}$ is said to be a *permanence set* of $\mathbb{T}$ for system (1) under WTCs if for every $x(0) \in \Omega$ there exists a control sequence $\boldsymbol{\sigma} \times \mathbf{u} := \{(\sigma(k), u(k))\}_{k=0}^{\infty}$ such that $x(k) \in \mathbb{T}$ for every $k \geq 0$.

Consider a given target window $\mathbb{T} \subset \mathbb{X}$ (target of control). The next Algorithm 1 finds a PS inside $\mathbb{T}$.

The equilibrium set of the switched system, $\mathbb{X}_s$, is given by $\mathbb{X}_s = \mathbb{X}_s^1 \cup \mathbb{X}_s^2$. Algorithm 1 finds $\mathcal{Y}_s^1 \subset \mathbb{T}$ which is a subset of $\mathbb{X}_s^1$, and $\mathcal{Y}_s^2 \subset \mathbb{T}$ which is a subset of $\mathbb{X}_s^2$, such that $\mathcal{Y}_s^1 \subset \mathcal{S}^{k_1}(\sigma_1, \mathcal{Y}_s^2)$ and $\mathcal{Y}_s^2 \subset \mathcal{S}^{k_2}(\sigma_2, \mathcal{Y}_s^1)$. Then, every steady-sate on $\mathcal{Y}_s^1$ can be reached from $\mathcal{Y}_s^2$ in k_2 steps with mode σ_2, and every steady-sate on $\mathcal{Y}_s^2$ can be reached from $\mathcal{Y}_s^1$ in k_1 steps with mode σ_1. This ensures that the system can be in mode σ_1 the time it requires to fulfill the minimal WT by remaining at any steady-state of $\mathcal{Y}_s^1$ and switch to mode σ_2 by reaching first any steady-state on $\mathcal{Y}_s^2$, which can be done in less than U_1 steps; so the maximal WT for mode σ_1 can be fulfilled as well. The reasoning can be applied for mode σ_2 also and applied indefinitely, which implies that

Algorithm 1: Compute a PS of $\mathbb{T}$ given by equilibrium subsets of each mode

Data: Matrix A_i, B_i, sets $\mathbb{T}, \mathbb{U}$ and scalar U_i ; $\triangleright\ i = 1, 2$
Require: $k_i \leq U_i$; $\triangleright\ i = 1, 2$
Result: $\mathcal{Y}_s^1 \cup \mathcal{Y}_s^2$
1: $\mathcal{Y}_s^i =$ Compute the maximal control equilibrium set inside $\mathbb{T}$ of mode i; $\triangleright\ i = 1, 2$
2: $k_i =$ Choose any number less than U_i; $\triangleright\ i = 1, 2$
3: **while** *true* **do**
4: $\quad S_1 = \mathcal{S}^{k_1}(\sigma_1, \mathcal{Y}_s^2)$; $\triangleright$ in every of the k_1 steps $\cap\mathbb{T}$
5: $\quad S_2 = \mathcal{S}^{k_2}(\sigma_2, \mathcal{Y}_s^1)$; $\triangleright$ in every of the k_2 steps $\cap\mathbb{T}$
6: $\quad$ **if** $(\mathcal{Y}_s^1 \subset S_1)$ **and** $(\mathcal{Y}_s^2 \subset S_2)$ **then**
7: $\quad\quad$ **return** $\mathcal{Y}_s^1 \cup \mathcal{Y}_s^2$
8: $\quad$ **end**
9: $\quad \mathcal{Y}_s^1 = \mathcal{Y}_s^1 \cap S_1$;
10: $\quad \mathcal{Y}_s^2 = \mathcal{Y}_s^2 \cap S_2$;
11: **end**

Algorithm 2: Compute a PS of $\mathbb{T}$ given by CIS of each mode

Data: Matrix A_i, B_i, sets $\mathbb{U}, \mathbb{T}$ and scalar U_i ; $\triangleright\ i = 1, 2$
Require: $k_i \leq U_i$; $\triangleright\ i = 1, 2$
Result: $\Omega := \Omega^1 \cup \Omega^2$
1: $\Omega^i =$ Compute the maximal control invariant set inside $\mathbb{T}$ of mode i; $\triangleright\ i = 1, 2$
2: $k_i =$ Choose any number less than U_i; $\triangleright\ i = 1, 2$
3: **while** *true* **do**
4: $\quad S_1 = \mathcal{S}^{k_1}(\sigma_1, \Omega^2)$; $\triangleright$ in every of the k_1 steps $\cap\mathbb{T}$
5: $\quad S_2 = \mathcal{S}^{k_2}(\sigma_2, \Omega^1)$; $\triangleright$ in every of the k_2 steps $\cap\mathbb{T}$
6: $\quad$ **if** $(\Omega^1 \subset S_1)$ **and** $(\Omega^2 \subset S_2)$ **then**
7: $\quad\quad$ **return** $\Omega^1 \cup \Omega^2$
8: $\quad$ **end**
9: $\quad \Omega^1 =$ Compute the maximum control invariant set inside $\Omega^1 \cap S_1$ of system 1;
10: $\quad \Omega^2 =$ Compute the maximum control invariant set inside $\Omega^2 \cap S_2$ of system 2;
11: **end**

the set $\mathcal{Y}_s^1 \cup \mathcal{Y}_s^2$ is a PS of $\mathbb{T}$, as shown in the following proposition.

Proposition 2: If Algorithm 1 converges to a set $\Omega = \mathcal{Y}_s^1 \cup \mathcal{Y}_s^2$ then Ω is a permanence set of $\mathbb{T}$ for system (1) under WTCs.

Proof: Let us consider $x(0) \in \Omega = \mathcal{Y}_s^2 \cup \mathcal{Y}_s^2$. Then $x(0) \in \mathcal{Y}_s^1$ or $x(0) \in \mathcal{Y}_s^2$, without loss of generality consider that $x(0) \in \mathcal{Y}_s^1$ (the other case is analogous). Since $\mathcal{Y}_s^1 \subset S_1 = \mathcal{S}^{k_1}(\sigma_1, \mathcal{Y}_s^2)$ the system can be feasible driven to $\mathcal{Y}_s^2$ in k_1 steps (without leaving $\mathbb{T}$, since the computation of $\mathcal{S}_i$ is intersect with $\mathbb{T}$ in every step). Therefore, the maximal waiting time U_1 is fulfilled because $k_1 \leq U_1$. In the case that $k_1 < L_1$, apply $L_1 - k_1$ times the input that keeps the subsystem (mode 1) on the equilibrium point $x(0)$, in order to fulfill the minimal waiting time L_1. After that, switch to mode 2 and keep the system on $\mathcal{Y}_s^2 \subset S_2 = \mathcal{S}^{k_2}(\sigma_2, \mathcal{Y}_s^1)$ and repeat the argument indefinitely. Then the system can remain on Ω fulfilling the WTCs and its permanence on set $\mathbb{T}$. ■

Algorithm 2 follows the same idea as Algorithm 1 to construct another PS but replace equilibrium sets with invariant sets.

The algorithms were formulated for two modes for simplicity but these can be applied for q modes when the switching signal is externally manipulated. It is sufficient to find two of the q modes for which the algorithms converge (since it is not mandatory to use all the q modes). For the case of a time-dependent switching signal, where the q modes must be used, the algorithms can be formally generalized by forming a q-cycle (instead of the 2-cycle of lines 4 and 5) in which we construct the k-step controllable sets from one CIS to other.

Proposition 3: If Algorithm 2 converges to a set $\Omega = \Omega^1 \cup \Omega^2$ then Ω is a permanence set of $\mathbb{T}$ for system (1) under WTCs.

Proof: It follows by the same steps of Proposition 2 proof with the difference that in this case, it used invariance properties to fulfill the minimal waiting time, instead equilibrium ones. ■

Parameters k_1 and k_2 from Algorithm 1 (and Algorithm 2) are free parameters only restricted to $k_1 \leq U_1$ and $k_2 \leq U_2$. The increase in these parameters corresponds to a greater computational cost. However, it corresponds with more probability of convergence as well, as the following property indicates.

Property 4: Consider a target window $\mathbb{T}$ and the switched system (1) under WTCs. If Algorithm 1 (and Algorithm 2) converges for a given choice of $k_1 > 0$ and $k_2 > 0$, then it also converges for any other choice $\hat{k}_1$ and $\hat{k}_2$ greater that k_1 and k_2, respectively.

Proof: Immediate from the general fact that controllable sets satisfy $\mathcal{S}^{j+1}(\sigma, \Omega) \subset \mathcal{S}^{j}(\sigma, \Omega)$ when Ω is a CIS. ■

Remark 2: Property 4 shows that a larger value of k_i implies a better chance of convergence for Algorithm 1 and 2. Naturally, the convergence depends on the preexistence of such PS as those searched by Algorithm 1 and 2. However, there is no a priori characterization (up to our knowledge) to guarantee such existence. In any case, if they exist then the algorithms can recover them. As might be expected, in practical application we will start our search with low values of k_i (since the bigger they are the bigger the computational cost) and we will increase them as long the algorithm does not converge. If at some point both k_1 and k_2 reach the upper bounds U_1 and U_2, respectively, and even then the algorithms do not converge, thus we can assure the nonexistence of PS of that kind.

C. Simulation example

Consider the switched system (1) given by modes

$$A_1 = \begin{bmatrix} 1.5 & 0 \\ 0 & -0.8 \end{bmatrix}, \quad A_2 = \begin{bmatrix} 0.34 & -1.05 \\ 1.05 & 0.34 \end{bmatrix},$$

$$A_3 = \begin{bmatrix} 1.02 & -0.27 \\ 0.27 & 1.02 \end{bmatrix}, \quad A_4 = \begin{bmatrix} 1.4 & 0.3 \\ 1 & -2.7 \end{bmatrix},$$

with $B_\sigma = [1,1]^T$ for $\sigma = 1,2,3$ and $B_4 = [1,-1]^T$, where $x \in \mathbb{R}^2$ and $u \in \mathbb{R}$. The waiting-time constraints are assumed to be the same for each mode σ, and are given by $L_\sigma = 2$ and $U_\sigma = 5$ for all $\sigma \in \Sigma$, and the target window given by $\mathbb{T} = \{(x_1, x_2) : 0.1 \leq x_1 \leq 1, -0.5 \leq x_2 \leq 0.5\}$.

For different results on convergence, a simple option is to test different target windows. Table I shows the results of convergence for all Algorithms with a tolerance of convergence given by $\varepsilon = 10^{-5}$ and $k_1 = k_2 = 5$ (which are the maximum values for the convergence, see Property 4).

MODES	FCIS [16]	ALGORITHM 1	ALGORITHM 2
1 & 2	✓	✗	✓
1 & 3	✗	✓	✓
1 & 4	✗	✓	✓
2 & 3	✗	✗	✓
2 & 4	✗	✓	✓
3 & 4	✓	✓	✓

TABLE I: Symbol ✓ means the Algorithm for the two pairs of modes converges to a nonempty set and ✗ it does not. The FCIS corresponds to Algorithm 1 presented on [16], and it shows convergence only in two cases. As expected, Algorithm 2 shows the best performance in all scenarios.

IV. APPLICATION TO TYPE 1 DIABETES MELLITUS (T1DM)

Insulin-on-board (IOB) estimation is used in modern insulin therapy with subcutaneous insulin infusion to prevent insulin stacking that may lead to hypoglycemia. IOB calculations that take into account variations of insulin sensitivity appear to promote effective and safe insulin therapy on multiple-meal scenarios [18]. Insulin sensitivity (S_I) variations affecting the excursion of blood glucose on T1DM can be modeled by a switched system. The following equations - based on a linearization of an oral minimal model (insulin action on glucose consumption independent on glycemia level) [19] and under a quasi-steady-state assumption (remote insulin at the equilibria with plasmatic insulin) - represent a model for T1DM without carbohydrate intakes[1].

$$\begin{bmatrix} \dot{x}_1(t) \\ \dot{x}_2(t) \\ \dot{x}_3(t) \end{bmatrix} = \begin{bmatrix} -\theta^1 & -\theta^2_{\sigma(t)} & 0 \\ 0 & -\frac{1}{\theta^3} & \frac{1}{\theta^3} \\ 0 & 0 & -\frac{1}{\theta^3} \end{bmatrix} \begin{bmatrix} x_1(t) \\ x_2(t) \\ x_3(t) \end{bmatrix} + \begin{bmatrix} 0 \\ 0 \\ \frac{1}{\theta^3} \end{bmatrix} u(t) + \begin{bmatrix} \theta^0_{\sigma(t)} \\ 0 \\ 0 \end{bmatrix}, \tag{2}$$

where $x_1(t)$ is the blood glucose concentration (i.e., the glycemia to be controlled) [mg/dL], $x_2(t)$ the insulin delivery rate in plasma [U/min], $x_3(t)$ the insulin delivery rate in the subcutaneous compartment [U/min], and $u(t)$ the continuous subcutaneous insulin rate [U/min].

The time-varying insulin sensitivity is given by $\theta^2_{\sigma(t)}$ [mg/(dL·U)] while the endogenous glucose production at basal levels is given by $\theta^0_{\sigma(t)}$. From [20] it can be shown that glucose production at basal level depends on the insulin sensitivity by $\theta^0_{\sigma(t)} = \theta_1 G_b + \theta^2_{\sigma(t)} u_b(t)$ [mg/(dL·min)], where $u_b(t)$ corresponds to a basal infusion which maintains glycemia at a constant level, G_b (i.e., diurnal profiles of $u_b(t)$ [21]). Moreover, θ^1 is the glucose effectiveness (or glucose self-regulation effect to promote its own metabolism independent of insulin levels) [1/min] and θ^3 is the insulin absorption time constant (time-to-maximum effective insulin concentration) [min].

To account for physical limitations and safety operation, the system (2) is constrained in both, state and inputs, hereby $u \in \mathbb{U} = \{u \in \mathbb{R}_{\geq 0} : u \leq U_{\max}\}$ with $U_{\max} \approx 0.25$ [U/min] (maximal basal rate of insulin pump) and $x \in \mathbb{X}$ with:

$$\mathbb{X} = \left\{x \in \mathbb{R}^3_{\geq 0} : G_{\text{hypo}} \leq x_1 \leq G_{\text{hyper}}, x_2 + x_3 \leq \tfrac{\text{IOB}}{\theta^3}\right\},$$

where $G_{\text{hypo}} = 60$ and $G_{\text{hyper}} = 300$ [mg/dL] (physiological limits for x_1). In addition, IOB (maximal admissible IOB) is assumed to be a stationary level given by IOB$= 2\theta^3 U_{b,\max}$, where $U_{b,\max} := (\theta^0 - \theta^1 G_{b,\min})/\theta^2$, $\theta^2 = \min_{t^* \in [0,\infty)} \theta^2_{\sigma(t)}$ and $\theta^0 = \theta^0_{\sigma(t^*)}$ ($G_{b,\min} = 60$ [mg/dL]).

Remark 3 (Insulin sensitivity, S_I): S_I is a fundamental parameter that measures the ability of insulin to enhance the disappearance of glucose by inhibiting endogenous glucose production (liver) and by stimulating glucose utilization in insulin-dependent tissues. It can be estimated at steady-state as well as dynamics conditions [22]. As it was reported in [14], for most T1DM patients it is significantly lower at breakfast than at lunch and dinner.

Within this framework, the therapeutic objective is to maintain glycemic levels within the near-normal target range - called normoglycaemia ($\geq$ 70 [mg/dL] and $\leq$ 140 [mg/dL]). Accordingly, our goal is to characterize a permanence set for model (2) inside the normoglycaemia ranges (target set $\mathbb{T}$), which provides a stabilizable control target to design control strategies to feasibly maintain normal glycemic levels over time.

A. Simulation Results

Results are based on the model identified in [23] where two modes were considered, $\sigma \in \Sigma = \{\sigma_1, \sigma_2\}$. The signal σ_1 represents higher insulin sensitivity from 6hs to 22hs and signal σ_2 represents a lower insulin sensitivity from 22hs to 6hs, so WTCs[2] for σ_1 are $L_{\sigma_1} = U_{\sigma_1} = 16T$ and for σ_2 are $L_{\sigma_2} = U_{\sigma_2} = 8T$, where T is the discrete-sampling time.

The target window $\mathbb{T}$ is defined by the normoglycaemia values, i.e., we are interested in maintaining the system inside $\mathbb{T} = \{x \in \mathbb{X}\colon 70 \leq x_1 \leq 140\}$. Considering a tolerance given by ε equal to 10^{-2}, 10^{-4} and 10^{-4} for each state respectively, the FCIS algorithm that we proposed on

[1]The main results (Algorithm 1 and 2) can be easily extended to the affine system 2 by considering the computation of the involved sets on the Algorithms for the affine system instead of the linear case.

[2]Note that in this case, the switched system is time-switched depending (see Remark 1).

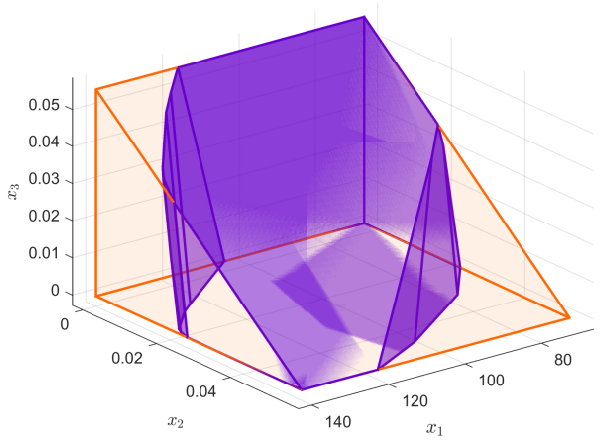

Fig. 1: Maximal FCIS (purple) within the target set $\mathbb{T}$ (orange) given by Algorithm proposed on [16]. This FCIS represents a CIS for higher and lower insulin sensitivities subsystems simultaneously.

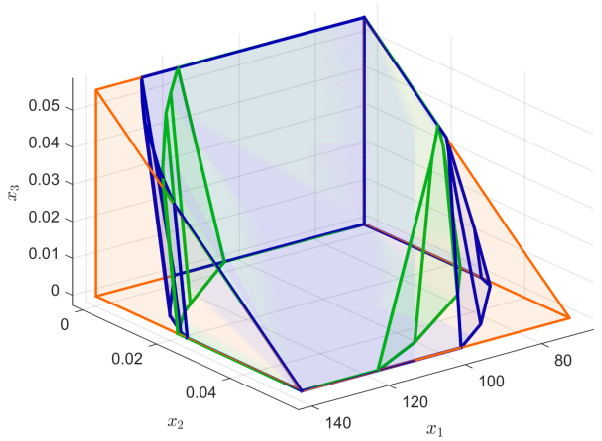

Fig. 2: A PS within $\mathbb{T}$ (orange) given by Algorithm 2. The PS is given by the union of two invariant sets; a control invariant set of mode σ_1 (blue) and a control invariant set of mode σ_2 (green), such that the system can be feasibly driven from one invariant set to the other without leave the target set $\mathbb{T}$.

[16] converges to a nonempty FCIS within $\mathbb{T}$. We show in Figure 1 the FCIS (in purple) inside the target window $\mathbb{T}$ (in orange). Because of the system limitations (for both modes), a large region of $\mathbb{T}$ does not belong to the FCIS; for instance, the value inside $\mathbb{T}$ with minimum glucose concentration and maximum insulin in plasma does not belong to the FCIS. This is so because large values of x_2 increase the value of IOB, which in turn decreases the values of glucose x_1 and this value is already at its minimum value inside $\mathbb{T}$, (which means the system will escape $\mathbb{T}$).

On the other hand Algorithm 1 provides a nonempty PS of $\mathbb{T}$ for system (2) (see Figure 3), which is computed using $k_1 = 5$ and $k_2 = 4$, the minimum values such that Algorithm 1 converges (see Remark 2). The PS, $\mathcal{Y}_1 \cup \mathcal{Y}_2$, in Figure 3 is projected on the dimension of glucose concentration (x_1) and IOB (which depends on x_2 and x_3) to improve interpretation. Figure 3 also shows that the only common equilibrium for the two modes (intersection of equilibrium sets) does not belong to the target window $\mathbb{T}$, therefore it is useless as a control target.

Finally, as we can see in Figure 2, Algorithm 2 also converges to a nonempty PS for system (2) for $k_1 = k_2 = 2$, given by the union of an invariant set of mode σ_1 (blue) with an invariant set of mode σ_2 (green). As expected, this Algorithm gives the larger target set inside $\mathbb{T}$ (larger than the FCIS or the PS given by Algorithm 1) that can be stabilized by the switched system (2).

To conclude, Figure 4 shows two feasible glucose excursions inside the FCIS (blue) and the PS (pale blue), respectively, and their respective input sequence for several days. The initial state is given by an extreme point of $\mathbb{T}$ $(116, 0.09, 0.001)$. The feasible trajectories inside the FCIS and PS are obtained by minimizing the insulin input from the initial condition and with a hard restriction of not leaving the target set $\mathbb{T}$.

V. CONCLUSIONS

The characterization and computation of Permanence Regions in the state space that can be feasibly stabilized by a Waiting-Time Constrained Switched System were addressed in this work. The proposed algorithms applied to the problem of Glycemia regulation in patients with Type 1 Diabetes Mellitus yielded several interesting findings. Future work includes the analysis of Permanence Sets within target regions without equilibrium points and the application of the results to the multidrug resistance problem.

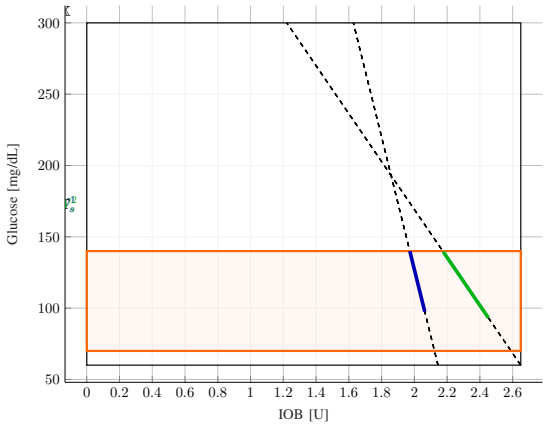

Fig. 3: A PS within $\mathbb{T}$ given by Algorithm 1. The PS is given by the union of two equilibrium sets; a control equilibrium set of mode σ_1, $\mathcal{Y}_1$ (blue), and a control equilibrium set of mode σ_2, $\mathcal{Y}_1$ (green), such that the system can be feasibly driven from one equilibrium set to the other without leave the target set $\mathbb{T}$.

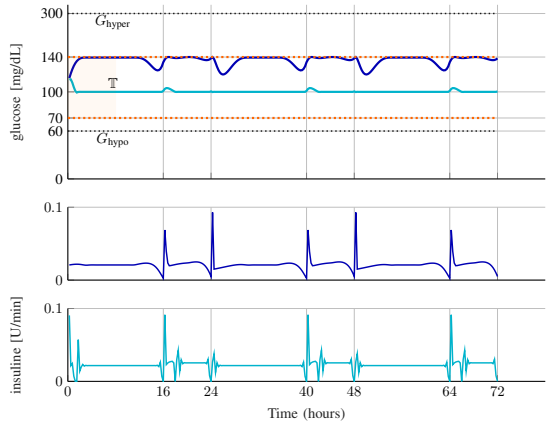

Fig. 4: Two feasible glucose excursions inside the FCIS (blue) of and the PS given by equilibrium sets (pale blue), and the corresponding input sequence for every trajectory. The initial time $k = 0$ represents the day hour 6 am with the initial signal $\sigma(0) = \sigma_1$ accounting for higher S_I. Vertical lines represent the time there is a switch of model. Higher S_I from 6hs to 22hs and lower S_I from 22hs to 6hs.

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