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Impulsive Zone Model Predictive Control with Application to Type I Diabetic Patients

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***Abstract*—In this work the problem of regulating glycemia in type I diabetic patients is studied by means of a novel impulsive zone model predictive control. According to the control objective of steering the system to an arbitrary desired target set, weak stability is demonstrated based on a novel dynamic characterization of two underlying discrete-time subsystems of the original impulsive system. To evaluate the proposed strategy, a new patient model is used. A long-term scenario - including meals - is simulated, and the results appear to be satisfactory as long as every hyperglycemia and hypoglycemia episodes are suitably controlled/minimized.**

***Keywords*—Impulsive Systems, non-zero regulation, model predictive control, stability, type I diabetes.**

I. Introduction

Recently, a version of model predictive control (MPC) for ICS has been developed in [1]. The MPC strategy proposed there also covers the problem to steer a linear ICS (LICS) to a zone defined by a 'therapeutic window', which does not contains the origin in its interior, and accounts for feasibility not only at the impulsive time, but also in continuous time. The formulation is based on appropriated invariant sets for ICS [2]. However, the calculation of the invariant sets is not a trivial task and it could be difficult in many applications. Besides, the computational effort appears to be high as the prediction horizon is quite large to account for a given (moderate) domain of attraction.

A zone control MPC ([3], [4], [5]) is an MPC formulation that is less general than the one having invariants sets as target sets ([1], [6]), but more general than the typical one having equilibrium points as set-points [7]. In this framework, the system state is steered to an equilibrium set - instead to an equilibrium point - making no differences between points inside the set. Furthermore, this control strategy is formulated in a tracking scenario where the equilibrium set can be far from the origin. By means of the use of artificial/intermediary variables that are forced to lie in the equilibrium space, this kind of controllers ensure feasibility for any change of the target set, and they provides an enlarged domain of attraction, given by the controllable set to the entire equilibrium subspace, instead of the controllable set to a given point or invariant terminal set (as described, for instance, in [7]). In [5] the basis of an impulsive zone-MPC (iZMPC) was given, but no stability analysis was shown theoretically.

In this paper, an interesting case-study is analyzed: the type 1 diabetes mellitus (T1DM) patient dynamic. Type 1 diabetes is a chronic autoimmune disease affecting approximately 25 million individuals in the world. Current treatment requires either multiple daily insulin injections or continuous subcutaneous (SC) insulin infusion (CSII) delivered *via* a pump. More than 30 years ago, the idea of an artificial endocrine pancreas for patients with type 1 diabetes mellitus (T1DM) was envisioned [8]. In recent years, MPC has received increasing attention as a promising algorithm for an artificial pancreas [9], [10], [11]. These approaches use discrete-time control actions, as a natural form of control design. However, the novel approach of iZMPC seems to be a suitable alternative, since the injection of insulin can be seen as an impulsive input. Another important point regarding the T1DM control problem is the model used to describe the patient behavior (independently of the control strategy). In this regards, a new interesting linear model for T1DM patients was recently presented in [12]. This model reveals some wrong dynamic functioning of the simulator of UVA/Padova (the simulator used in the cited works), and represents more accurately the behaviors of Type I diabetic patients for a long-term scenario.

The contributions of this paper are in two-folds: first, based on a novel dynamic description of a linear impulsive control system (LICS), an efficient iZMPC is developed where weak stability and weak attractivity to the state window target are demonstrated. Second, the performance of the strategy is illustrated by using the new model for T1DM patients presented in [12]. Good performances are achieved in long-term intervals including meals, avoiding hyperglycemia and hypoglycemia episodes.

II. Preliminaries

The class of dynamic systems of interest in this paper consists in a set of linear impulsive first-order differential equations of the form

$$\left\{ \begin{array}{rcl} \dot{x}(t) & = & A_c x(t), \quad x(0) = x_0, \quad t \neq \tau_k, \\ x(\tau_k^+) & = & A_d x(\tau_k) + B u(\tau_k), \quad k \in \mathbb{N}. \end{array} \right. \tag{1}$$

The variable $t \in \mathbb{R}$ denotes time, τ_k, $k \in \mathbb{N}$, denotes the impulse time instants, τ_k^+ denotes the time instant after τ_k, $x \in \mathcal{X} \subseteq \mathbb{R}^n$ denotes the (constrained) state vector and $u \in \mathcal{U} \subseteq \mathbb{R}^m$ denotes the (constrained) impulsive control inputs. Both constraint sets, $\mathcal{X}$ and $\mathcal{U}$, are compact sets and contain the origin in their interior. Matrix $A_c \in \mathbb{R}^{n\times n}$ and $A_d \in \mathbb{R}^{n\times n}$ are the continuous and discrete transition matrices, while $B \in \mathbb{R}^{n\times m}$ is the impulsive input matrix. Furthermore, as part of the system description, a target state set $\mathcal{X}^{Tar} \subset \mathcal{X}$ is defined, where the system is desired to be steered and kept.

Let $\kappa(\cdot)$ be a control law, in such a way that $u(\tau_k) = \kappa(x(\tau_k))$, for $k \in \mathbb{N}$. Then, the closed-loop impulsive system is described by:

$$\left\{ \begin{array}{rcll} \dot{x}(t) & = & A_c x(t), \quad x(0) = x_0, & t \neq \tau_k, \\ x(\tau_k^+) & = & A_d x(\tau_k) + B\kappa(x(\tau_k)), & k \in \mathbb{N}, \end{array} \right. \tag{2}$$

This way, the closed-loop trajectory is denoted by $x(t) = \phi_{cl}(t; x_0, \kappa(\cdot))$, for $t \geq 0$, with $\phi_{cl}(0; x_0, \kappa(\cdot)) = x_0$, and clearly, the jump depends now only on the state.

III. Underlying discrete time systems

The discrete sequence of impulsive system is represented by the 'algebraic equation' in (1), and relates the state at time τ_k^+ with the state and the impulsive input at times τ_k. However, it is possible to expand this characterization adding two discrete time systems, which can be obtained by sampling the state at τ_k and τ_k^+, for $k \in \mathbb{N}$, respectively. This way the first discrete system results

$$x(\tau_k) = M_{k-1}^* x(\tau_{k-1}) + e^{A_c\delta_{k-1}} B u(\tau_{k-1}). \tag{3}$$

while the second one is given by

$$x(\tau_k^+) = M_{k-1} x(\tau_{k-1}^+) + Bu(\tau_k), \tag{4}$$

where $\delta_i \triangleq \tau_i - \tau_{i-1}$, $M_i^* \triangleq e^{A_c\delta_i} A_d$, $M_i \triangleq A_d e^{A_c\delta_i}$, $i = 0, 1, \cdots$. Notice that the inputs $u(\tau_k)$ are already known at time instants τ_k^+. Here, it is assumed that $\delta_i = T$ (period), for $i = 0, 1, \cdots$, and so $M_i = M$, $M_i^* = M^*$ are constant maps. Then, the discrete systems become

$$x^\bullet(j+1) = A^\bullet x^\bullet(j) + B^\bullet u^\bullet(j), \quad x^\bullet(0) = x_0, \tag{5}$$

$$x^\circ(j+1) = A^\circ x^\circ(j) + B^\circ u^\circ(j), \quad x^\circ(0) = x_0, \tag{6}$$

where $A^\circ = M = A_d e^{A_cT}$, $A^\bullet = M^* = e^{A_cT}A_d$, $B^\circ = B$, $B^\bullet = e^{A_cT}B$, and $u^\circ(j+1) = u^\bullet(j)$, for $j \geq 0$. Notice that there is only one input u (shifted one time instant) for both discrete time systems.

A. Impulsive System Equilibrium Set Characterization

The only formal **equilibrium point of the ICS** (1) is given by $(u_s, x_s) = (0, 0)$, which is the only pair verifying $\dot{x} = 0$ and $x(\tau_k^+) = x(\tau_k)$. However, by abstracting the general concept of equilibrium and taking into account the ICS only at times τ_k and τ_k^+, it is possible to find some generalization that accounts for equilibrium entities out of the origin. In what follows assume that $A_d = I$.

Definition 1: **(Generalized control equilibrium of ICS)** Consider a ICS (1), a period T and a non-empty convex set Ω. A state $x_s^\bullet \in \mathcal{X}$ is a **generalized control equilibrium point with respect to** Ω if there exists an input $u_s \in \mathcal{U}$ such that

$$\begin{array}{rcl} \phi(T; x_s^\bullet, u_s) & = & x_s^\bullet \qquad (7) \\ o_s(x_s^\bullet, u_s) & \in & \Omega, \qquad (8) \end{array}$$

where $o_s(x_s^\bullet, u_s) \triangleq \{\phi(t; x_s^\bullet, u_s), \quad t \in [0, T]\}$.

Given that, by definition, $\phi(0; x_s^\bullet, u_s) = x_s^\bullet$, the state trajectory in a period T, $\phi(t; x_s^\bullet, u_s)$, for $t \in [0, T]$, uniquely define an orbit (closed trajectory), o_s. More precisely, the orbit is given by two trajectories, one going from $x_s^\bullet$ to x_s° in a time instant (jump):

$$\phi(0^+; x_s^\bullet, u_s) = x_s^\bullet + Bu_s \triangleq x_s^\circ, \tag{9}$$

and the other going back from x_s° to $x_s^\bullet$, for $0 < t \leq T$ (free response):

$$\phi(t, x_s^\bullet, u_s) = e^{A_ct} \underbrace{\phi(0^+; x_s^\bullet, u_s)}_{x_s^\circ}, \quad \text{for} \quad t \in (0, T]. \tag{10}$$

For the closed-loop ICS (2), the following definition arises:

Definition 2: **(Generalized equilibrium point of ICS)** Consider the closed-loop system (2). A generalized control equilibrium point with respect to Ω, for $u = \kappa(x)$, is a **generalized equilibrium point with respect to** Ω.

Next an algebraic characterization of the Feasible Generalized Control Equilibrium of ICS, based on the UDS, is presented.

Property 1: Define first the set of feasible pairs, $z \triangleq (u, x^\bullet) \in \mathbb{R}^{m+n}$, as $\mathcal{Z} \triangleq \mathcal{U} \times \mathcal{X}$. A **Feasible Generalized Control Equilibrium**, $x_s^\bullet$, is uniquely characterized by the pairs $z_s \triangleq (u_s, x_s^\bullet) \in \mathcal{Z} \subseteq \mathbb{R}^{m+n}$ that fulfill the (simultaneous) equilibrium condition

$$\left[\begin{array}{cc} B^\bullet & (A^\bullet - I_n) \\ A^\circ B^\circ & (A^\circ - I_n)A_d \end{array} \right] \left[\begin{array}{c} u_s \\ x_s^\bullet \end{array} \right] = 0, \tag{11}$$

The first condition in (11) clearly represents an equilibrium condition for the UDS (5). The second one, given that $x_s^\circ = x_s^\bullet + Bu_s$, represents an equilibrium condition for the UDS (6), and it is equivalent to $B^\circ u_s + (A^\circ - I_n)x_s^\circ = 0$.

The generalized equilibrium defined before plays the role of the equilibrium point in a discrete time system. Now, the next step is to describe the analogue to the equilibrium set (a set or aggregation of equilibrium point), which will be useful for control proposes.

Definition 3: **The generalized equilibrium set of an ICS**, $\mathcal{X}_s^\bullet$, is simply defined by all the feasible generalized equilibrium points $x_s^\bullet$.

This latter set implicitly defines the equilibrium input set, $\mathcal{U}_s$, given by all the input associated to $\mathcal{X}_s^\bullet$[1]. Also, directly related to $\mathcal{X}_s^\bullet$ is $\mathcal{X}_s^\circ$, which is given by $\mathcal{X}_s^\circ \triangleq \{\mathcal{X}_s^\bullet + Bu_s, \quad \text{for all} \quad u_s \in \mathcal{U}_s\}$.

[1]If the set $\mathcal{Z}_s$ is defined as all pairs $(u_s, x_s^\bullet)$ that fulfill condition (11); then $\mathcal{X}_s^\bullet = \text{proj}_{x^\bullet}(\mathcal{Z}_s)$ and $\mathcal{U}_s \triangleq \text{proj}_u(\mathcal{Z}_s)$, where $\text{proj}_{x^\bullet}(\mathcal{Z}_s)$ and $\text{proj}_u(\mathcal{Z}_s)$ denote the projection of the set $\mathcal{Z}_s$ on the state space of subsystem (5), and on the the input space, respectively.

B. Target equilibrium sets for control purposes

The goal of the control of the ICS (1) is to steer it to an arbitrary target set $\mathcal{X}^{Tar} \subseteq \mathcal{X}$, and once the system reaches this set, to keep it there indefinitely. To accomplish this objective, it is necessary to define the so called target counterpart of the equilibrium sets of subsection III-A. This way, the sets $\mathcal{X}_s^{\bullet Tar}$, $\mathcal{X}_s^{\circ Tar}$, $\mathcal{U}_s^{Tar}$ and $\mathcal{Z}_s^{Tar}$ are well defined as the counterpart of $\mathcal{X}_s^{\bullet}$, $\mathcal{X}_s^{\circ}$, $\mathcal{U}_s$ and $\mathcal{Z}_s$, respectively, by replacing $\mathcal{X}$ by $\mathcal{X}^{Tar} \subseteq \mathcal{X}$ in the corresponding definitions.

Remark 1: Note that the parameter that decides if there exist two sets $\mathcal{X}_s^{\circ Tar}$ and $\mathcal{X}_s^{\bullet Tar}$ inside a given target set $\mathcal{X}^{Tar}$ is the period T. Given a non-empty set $\mathcal{X}^{Tar}$, there exists a maximal T such that the these conditions hold. According to this requirement, the maximum value of T, T_{max}, allowed by the problem is well defined. On the other hand, the minimum value, T_{min}, is assumed to be given by practical restrictions (since maximal frequency of impulses is always determined by the control problem itself), and also it is assumed that for this T_{min}, sets $\mathcal{X}_s^{\circ Tar}$ and $\mathcal{X}_s^{\bullet Tar}$ are nonempty.

C. Weak Atractivity and Weak Stability

Once the equilibrium sets are characterized, the next step is to establish some stability definitions. In this paper, only the stability at time instants τ_k will be considered, which is defined as weak stability in [1]. First, weak attractivity is defined considering the general case of possible non null equilibrium

Definition 4: **(Weakly attractive sets, [1])** A nonempty convex target set $\mathcal{Y} \subseteq \mathcal{X}$ is **weakly attractive** for the closed-loop system (2), if there exists a ϵ_0 such that $\lim_{k\to\infty} \mathrm{dist}_{\mathcal{Y}}(\phi(\tau_k; x_0, \kappa(\cdot))) = 0$, for all x_0 such that $\mathrm{dist}_{\mathcal{Y}}(x_0) < \epsilon_0$.

In the latter definition, $\mathrm{dist}_{\mathcal{Y}}(x)$ represent the distance from x to set $\mathcal{Y}$, and it is defined as $\mathrm{dist}_{\mathcal{Y}}(x) = \min_{y\in\mathcal{Y}} \|x - y\|$.

Theorem 1: The set $\mathcal{X}_s^{\bullet Tar}$ is **weakly attractive** for the closed-loop system (2) if and only if it is **attractive** - in the sense of attractivity of discrete-time systems - for the discrete-time closed-loop system: $x^\bullet(k+1) = A^\bullet x^\bullet(k) + B^\bullet \kappa(x^\bullet(k))$.

Proof: The proof follows directly from the fact that $x^\bullet(k) \triangleq \phi(\tau_k; x_0, \kappa(\cdot))$, provided that $x^\bullet(0) = \phi(0; x_0, \kappa(\cdot)) = x_0$. ■

An **asymptotic stability** definition is also presented in [1]. Roughly speaking, a nonempty convex target set $\mathcal{Y} \subseteq \mathcal{X}$ is **weakly asymptotically stable**, if it is **weakly stable** and **weakly attractive**. Weak stability refers to the so called ϵ-δ stability [7]. In this work, however, only the attractivity of the proposed control strategy will be considered for simplicity, given that an extension to weak asymptotic stability can be obtained by finding Lyapunov-type functions in MPC [7].

IV. MODEL PREDICTIVE CONTROL STRATEGY

In this section a MPC formulation is stated to steer the system from a given initial state x_0 to an equilibrium objective set defined by $\mathcal{X}_s^{\bullet Tar} \subset \mathcal{X}^{Tar}$. The cost of the optimization problem that MPC solves on-line is

$$V_N(x, \mathcal{X}_s^{\bullet Tar}, \mathcal{U}_s^{Tar}; \mathbf{u}, u_a, x_a) \tag{12}$$
$$= V_{dyn}(x; \mathbf{u}, u_a, x_a) + V_f(\mathcal{X}_s^{\bullet Tar}, \mathcal{U}_s^{Tar}; u_a, x_a), \tag{13}$$

where

$$\begin{aligned} V_{dyn}(x; \mathbf{u}, u_a, x_a) &= \sum_{j=0}^{N-1} (x(j) - x_a)^T Q\, (x(j) - x_a) \\ &+ (u(j) - u_a)^T R\, (u(j) - u_a), \end{aligned}$$

with $Q > 0$ and $R > 0$, is a term devoted to steer the system to a certain **artificial open-loop equilibrium variable** given by $(u_a, x_a) \in \mathcal{U}_s \times \mathcal{X}_s^{\bullet}$, and

$$V_f(\mathcal{X}_s^{\bullet Tar}, \mathcal{U}_s^{Tar}; u_a, x_a) = p\left(\mathrm{dist}_{\mathcal{X}_s^{\bullet Tar}}(x_a) + \mathrm{dist}_{\mathcal{U}_s^{Tar}}(u_a)\right)$$

with $p > 0$, is a terminal cost devoted to steer x_a to the whole sets $\mathcal{X}_s^{\bullet Tar}$ and u_a to $\mathcal{U}_s^{Tar}$, respectively. Notice that in the latter cost, the current state x, $\mathcal{X}_s^{\bullet Tar}$, and $\mathcal{U}_s^{Tar}$ are parameters, while $\mathbf{u} = \{u(0), u(1), \cdots, u(N-1)\}$, u_a and x_a are the optimization variables (being N the control horizon).

The optimization problem to be solved at time k by the MPC is given by

$P_{MPC}(x, \mathcal{X}_s^{\bullet Tar}, \mathcal{U}_s^{Tar})$:

$$\begin{aligned} \min_{\mathbf{u}, u_a, x_a} \quad & V_N(x, \mathcal{X}_s^{\bullet Tar}, \mathcal{U}_s^{Tar}; \mathbf{u}, u_a, x_a) \\ s.t. \quad & \\ & x(0) = x, \\ & x(j+1) = A^\bullet x(j) + B^\bullet u(j), \qquad j \in \mathbb{I}_{0:N-1} \\ & x(j) \in \mathcal{X},\ u(j) \in \mathcal{U}, \qquad j \in \mathbb{I}_{0:N-1} \\ & A^\bullet(t)x(j) + B^\bullet(t)u(j) \in \mathcal{X},\ t \in (0, T],\ j \in \mathbb{I}_{0:N-1} \\ & x(N) = x_a, \\ & x_a \in \mathcal{X}_s^{\bullet}, \quad u_a \in \mathcal{U}_s. \end{aligned}$$

where $A^\bullet(t) \triangleq e^{A_c t} A_d$ and $B^\bullet(t) \triangleq e^{A_c t} B$. The constraint $x(N) = x_a$ is the terminal constraint that forces the terminal state - at the end of control horizon N - to reach the artificial equilibrium state x_a. Furthermore, the last constraint forces the artificial variable pair (u_a, x_a) to be in $\mathcal{X}_s^{\bullet} \times \mathcal{U}_s$, and it is equivalent to force the pair (u_a, x_a) to fulfill the equilibrium condition $x_a = A^\bullet x_a + B^\bullet u_a$.

Remark 2: The continuous constraint that forces the entire state trajectories to stay in $\mathcal{X}$ is necessary to ensure the state trajectory feasibility not only at the impulsive time steps, but at each time instant.

The control law, derived from the application of a **receding horizon control** policy (RHC), is given by $\kappa_{MPC}(x, \mathcal{X}_s^{\bullet Tar}, \mathcal{U}_s^{Tar}) = u^0(0; x)$, where $u^0(0; x)$ is the first element of the solution sequence $\mathbf{u}^0(x)$. The domain of attraction of the closed loop is given by the N steps controllable set to the **entire equilibrium set** $\mathcal{X}_s^{\bullet}$, $\mathcal{X}_N^{\bullet}$.

A. Weak Attractivity of $\mathcal{X}_s^{\bullet Tar}$ under the MPC controller

In this section, the attractivity of the set $\mathcal{X}_s^{\bullet Tar}$ under the control law derived from the proposed MPC formulation is established. First, to ensure that the continuous feasibility constraint will be satisfied, the following assumption is made.

Assumption 1: For each $x \in \mathcal{X}_N^\bullet$ there exists an input $u \in \mathcal{U}$ such that

$$\begin{aligned} A^\bullet x + B^\bullet u &\in \mathcal{X}_N^\bullet, \quad (14) \\ A^\bullet(t)x + B^\bullet(t)u &\in \mathcal{X}, \quad t \in (0,T]. \quad (15) \end{aligned}$$

By definition of the controllable set $\mathcal{X}_N^\bullet$, condition (14) is always fulfilled. If condition (15) is not fulfilled, $\mathcal{X}_N^\bullet$ should be reduced, maintaining its invariant condition for system (6).

A stronger condition that ensures condition (15) (but not necessary for condition (15) to be satisfied) is as follows:

$$ch\{A^\bullet(t)\mathcal{X}_N^\bullet, \quad t \in (0,T]\} \subseteq \mathcal{X}. \quad (16)$$

This condition implies that $u = 0$ will produce always a feasible continuous response. To practically check if this condition is fulfilled, the convex hull can be computed on a discrete family of mappings, for a number M of time instants $t(i) \in (0,T]$, with $i \in \mathbb{N}_{0:M}$. If the condition is not fulfilled, then the controllable set $\mathcal{X}_N^\bullet$ must be recompute according to a scaled (reduced) constraint state set, $\gamma\mathcal{X}$, with $0 < \gamma < 1$.

Theorem 2: Suppose that Assumption 1 holds, and that $\mathcal{X}_s^{\bullet Tar}$, is a generalized equilibrium set with respect to $\mathcal{X}^{Tar}$:

1) the MPC controller is recursively feasible.
2) $\mathcal{X}_s^{\bullet Tar}$ is an **equilibrium sets for the UDS (5) controlled by the MPC**: $x^\bullet(j+1) = A^\bullet x^\bullet(j) + B^\bullet \kappa_{MPC}(x^\bullet(j))$.
3) $\mathcal{X}_s^{\bullet Tar}$ is a **generalized equilibrium set for system (1) controlled by the MPC**, with respect to $\mathcal{X}^{Tar}$.
4) $\mathcal{X}_s^{\bullet Tar}$ is **weakly attractive for system (1), controlled by the MPC**, for all $x_0 \in \mathcal{X}_N^\bullet$.

Proof: See the Appendix. ■

This way, following a different procedure than the one used [3], [4], it can be shown that this MPC formulation ensures the weak attractivity of the objective set $\mathcal{X}_s^{\bullet Tar}$, and furthermore, because of the use of the artificial variables (u_a, x_a), the domain of attraction is given by the N-step controllable set to the equilibrium set $\mathcal{X}_s^\bullet$.

Remark 3: Weak asymptotic stability can also be established by finding a Lyapunov function, following similar steps as the one shown in the stability proofs in [3].

V. CASE-STUDY: TYPE 1 DIABETIC PATIENTS

The glucose dynamics x_1 (mg/dl) consists in a single equation, where $\dot{x}_1$ represents the production of glucose minus the consumption of glucose. The increase of glucose includes the liver endogenous glucose production (EGP) and the digestion of carbohydrate food intake (CHO). The EGP k_1 is assumed to be constant for simplicity, but a more accurate model may be derived. The glucose absorption rate includes the consumption by the brain k_b without need of insulin, the storage by the liver and the consumption by the muscles under the action of insulin [12]. The parameters k_1 and k_b are compacted in $\theta_1 = k_1 - k_b$.

The relationship between the insulin infusion rate, u (U), and the insulinemia, x_2 (U/l), is derived from the pharmacokinetic characteristics of insulin. As it is described in [12], the insulin dynamic is given by a second-order model with a single time constant T_u. A similar second-order system is used to model the relationship between amount of carbohydrates CHO in meals and x_4 (g/l), where T_r is the time constant. r is the ingestion of CHO in each meal of the patient. A state-space representation of the model is as follows:

$$\begin{aligned} \dot{x}(t) &= \begin{pmatrix} 0 & -k_{si} & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & -\frac{1}{T_u^2} & -\frac{2}{T_u} & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & -\frac{1}{T_r^2} & -\frac{2}{T_r} \end{pmatrix} x(t) \quad (17) \\ &+ \begin{pmatrix} 0 & 0 \\ 0 & 0 \\ \frac{k_u}{V_i T_u^2} & 0 \\ 0 & 0 \\ 0 & \frac{k_r}{V_B T_r^2} \end{pmatrix} \begin{pmatrix} u(t) \\ r(t) \end{pmatrix} + \begin{pmatrix} \theta_1 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}. \end{aligned}$$

The state and input constraints are given by $\mathcal{X} = \{x : [0\ 0\ -0.1\ 0\ -0.1]^T \preceq x \preceq [300\ .5\ 0.1\ 1\ 0.1]^T\}$ and $\mathcal{U} = \{u : 0 \leq u \leq 30\}$, respectively. The state target window should be decided by the treating physician, and in this simulated scenario will be defined by $\mathcal{X}^T = \{x : [70\ 0\ -0.1\ 0\ -0.1]^T \preceq x \preceq [140\ 0.2\ 0.05\ 0.5\ 0.05]^T\}$.

The simulated scenario is based on an hospitalized patient tagged as IF2 and extracted from [12]. The model parameters are given by: $\theta_1 = 0.1385\ mg/dl/min$, $k_{si} = 197\ mg/U/min$, $T_u = 122\ min$, $T_r = 183\ min$, $k_u = 10.62\ min$, $V_i = 180\ dl$, $k_r = 0.11232$, and $V_B = 46.8\ dl$.

The initial condition for x_1 is set up inside the hyperglycemia zone ($x_1 > 140$), *i.e* $x_1(0) = 250$. The first goal is to steer the system from this condition to the normoglycemia zone ($70 < x_1 < 140$). Once the system is in this zone, the second objective is to maintain the system inside these limits even when strong 'perturbations' (as food intake) enter to the system. Since the patient is hospitalized, regular meals are considered: the breakfast at 8 a.m, the launch at 1 p.m. and the dinner at 8 p.m. Furthermore, it is assumed that the counting of CHO in the meals is accurate and known.

A. *iZMPC for T1DM patients*

In this subsection, the iZMPC controller is tested to regulate glycemia using the T1DM patient model described above, together with the constraints and the target window. The optimization horizon is settled in 80 h. This horizon is larger than the one used in other works [10], [9], [8], since the used linear model is able to reproduce accurately the behaviors for long-time intervals. In spite of the simplicity of the model, this is an advantage when control strategies are designed.

The iZMPC controller is tuned as: $N = 40$, and $R = 1$ are fixed, and Q and p are variant (see Figs. 1-2). Notice that the control horizon was chosen very small (≈ 3.4 h) in contrast to the optimization horizon (80 h), due to the enlarged domain of attraction generated by the artificial variables (x_a, u_a). In the other MPC strategies (see [1]) N needs to be much larger than 40 to obtain the same domain of attraction.

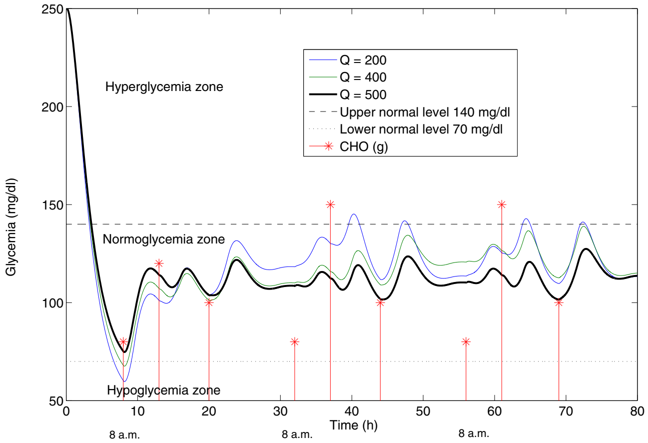

Fig. 1. Glycemia evolution including 3 meals by day, and $p = 50000$.

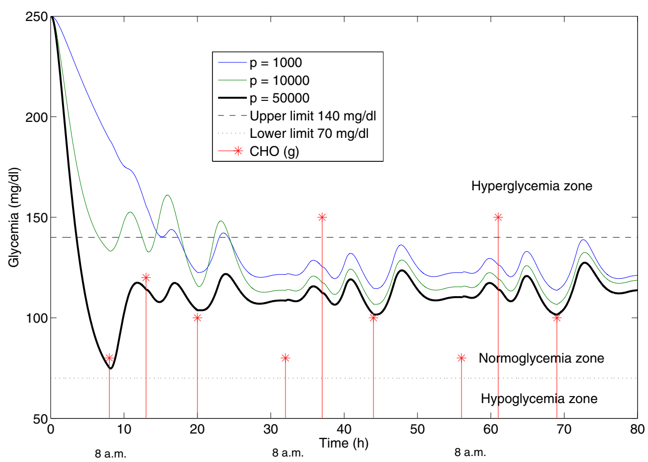

Fig. 2. Glycemia evolution including 3 meals, and $Q = 500$.

Fig. 1 shows the glycemia behavior. It initiates in a hyperglycemia condition but it is effectively driven to the normozone in only 3.5 h in all cases, as it is recommended by physicians. After that, the glycemia is maintained in this zone even after meals (represented by the starts $*$ in Fig. 1).

For $Q = 200$ there are some episodes of high and low glycemia. So, this value must be taken as a lower bound in the setup of the iZMPC. For $Q = 400$, and $Q = 500$, the correct amount of insulin was injected when necessary. As a consequence, hyperglycemia and hypoglycemia episodes were avoided. This is a very important result, accounted for the predictive nature of the controller, which not only predict the patient behavior but also the eventual limit saturation for the variables (in this case, it anticipates $u(.)$ cannot be negative).

In Fig. 2, the parameter p took 3 different values: 1000, 10000 and 50000. The effect of this parameter was to accelerate the regulation at the beginning of the optimization

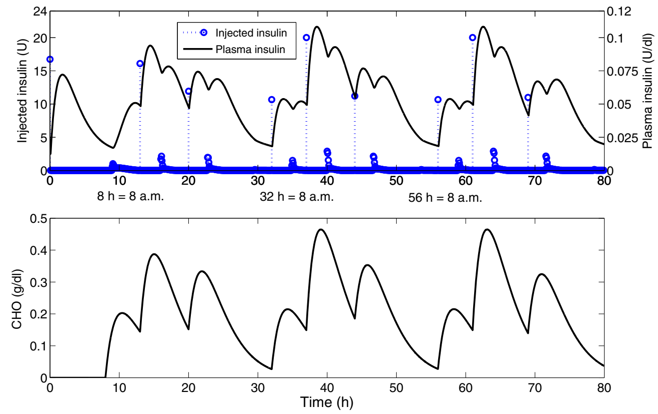

Fig. 3. Upper figure: $u(\tau_k)$, and plasma insulin x_2 evolution. Lower figure: CHO x_4 evolution. In both subfigures, $Q = 500$, and $p = 50000$.

horizon. Note that for $p = 1000$ the system takes too much time to enter to the normozone ($\approx$ 14 h). For $p = 10000$, this time was reduced to 8 h, and for the last value, to 3.5 h. In Fig. 3 the input, x_2, and x_4 time evolutions are depicted for $Q = 500$, and $p = 50000$. As it is desired, each state is steered to its corresponding therapeutic window relatively fast. Besides, the input makes the main effort first, and after its settling time, it reacts only at the meal intake times.

All these results show that the tuning procedure - which is a matter of future study - is a crucial point. Furthermore, these are only preliminary (good) results, and they should be validated with a larger cohort of patients.

VI. Conclusions

The problem of regulating glycemia in type I diabetic patients has been tackled in this paper. Based on linear impulsive systems, and by means of a proper subsystems characterization, a suitable impulsive Zone MPC (iZMPC) strategy was developed.

The main benefits of the this controller are: (i) It can steer the system to any feasible state window target, including those which does not contain the origin in its interior, (ii) it does not need to compute invariant sets as a target set, and (iii) it has an enlarged domain of attraction (for a given control horizon), because of the use of artificial intermediary variables.

By simulating a hospitalized patient scenario, satisfactory performances were achieved. It is shown that the iZMPC maintains the glycemia in a normal range of $70 \sim 140\ mg/dl$, injecting appropriated insulin bolus when necessary, which means that hyperglycemia and hypoglycemia episodes were successfully avoided. The obtained results encourage to continue with this case-study, where there are still many open problems to solve in order to get an artificial pancreas.

VII. Appendix

Proof of Theorem 2:

Proof: 1) Given that any state $x \in \mathcal{X}_N^{\bullet}$ could be steered to $\mathcal{X}_s^{\bullet}$, fulfilling every constraint in the path, it is possible to follow the usual steps to show feasibility in MPC. That is, a feasible input sequence could be constructed for the optimization problem at time step $k+1$, by shifting the optimal solution to the same problem at time step k, and adding at the end the artificial input value (see [3]).

2) Assume that the ICS is placed at $x_s^\bullet \in \mathcal{X}_s^{\bullet Tar} \subseteq \mathcal{X}_s^\bullet$, at $k = 0$. Then, the feasible input sequence $\hat{\mathbf{u}} = \{u(0), \ldots, u(N-1)\}$, with $u(j) = u_s = \left((I_n - A^\bullet)^{-1} B^\bullet x_s^\bullet\right) \in \mathcal{U}_s^{Tar}$, for $j \in \mathbb{I}_{0:N-1}$, produces a sequence of states $x^\bullet(k) = x_s^\bullet$, for $k \geq 1$, which clearly remain in $\mathcal{X}_s^{\bullet Tar}$. Furthermore, by the MPC cost function definition (12), this input sequence, together with the artificial variables $u_a = u_s$ and $x_a = x_s^\bullet$, are the optimal solution to MPC optimization problem, since they produce a null dynamic and terminal cost (notice that any input sequence $\hat{\mathbf{u}}$ with $u(j) \neq u_s$ for some $j \in \mathbb{I}_{0:N-1}$, produces a positive cost). Finally, given that $u(0) = u_s$ is injected to the ICS, system (5) will remains at $x_s^\bullet$, indefinitely.

3) Assume that the ICS is placed at $x_s^\bullet \in \mathcal{X}_s^{\bullet Tar} \subseteq \mathcal{X}^{Tar}$, at $k = 0$. According to the latter item, the MPC control law will keep the discrete-time system (5) at $x_s^\bullet$, indefinitely. Furthermore, since $x_s^\bullet$ is a generalized equilibrium, this implies that the ICS (1) will remain in the equilibrium orbits, o_s, defined by $u_s, x_s^\bullet, x_s^\circ$, where u_s fulfill $(I_n - A^\bullet)x_s^\bullet + B^\bullet u_s = 0$ and $(I_n - A^\circ)x_s^\circ + B^\circ u_s = 0$. So, $x(\tau_k) \in \mathcal{X}^{Tar}$, $0 \leq t \leq T$.

4) Following the usual steps of the artificial-variable MPC ([3], [4]), it can be shown that the optimal cost function V_N^0 is a decreasing function, whose decreasing steps, $V_N^0(x^+) - V_N^0(x)$, are bounded from above by the stage cost $-\left\|x^0(0;x) - x_a^0(x)\right\|_Q^2 - \left\|u^0(0;x) - u_a^0\right\|_R^2$. Since the stage cost is a positive definite function, by definition, the last inequality implies that $x^0(0;x)$ tends to $x_a^0(x)$ and $u^0(0;x)$ tends to $u_a^0(x)$ as $k \to \infty$. Then, by Lemma 1, this implies that $x^0(0;x)$ tends to $\mathcal{X}_s^{\bullet Tar}$ and $u^0(0;x)$ tends to $\mathcal{U}_s^{Tar}$ as $k \to \infty$, which means that $\mathcal{X}_s^{\bullet Tar}$ is an attractive set for the UDS (5), controlled by the MPC and so, by Theorem 1, $\mathcal{X}_s^{\bullet Tar}$ is weakly attractive for the ICS (1) controlled by the MPC. ■

Lemma 1 (Convergence to $\mathcal{X}_s^{\bullet Tar}$): Consider the closed-loop system obtained by applying the MPC control law, κ_{MPC}. The solution of Problem $P_{MPC}(x, \mathcal{X}_s^{\bullet Tar}, \mathcal{U}_s^{Tar})$, at a time step k, provides an input and a state, given by the pair $z(k) \triangleq (u(k), x(k))$, where, $u(k) \triangleq u^0(0;x)$ and $x(k) \triangleq x^0(0;x) = x$, respectively. Furthermore, the same problem solution provides an input and a state artificial variable pair, $z_a(k) \triangleq (u_a(k), x_a(k))$, where $u_a(k) \triangleq u_a^0(x)$ and $x_a(k) \triangleq x_a^0(x)$, respectively. Then, if $\lim_{k\to\infty} \|z(k) - z_a(k)\|_S^2 = 0$, with $S > 0$, then $\lim_{k\to\infty} \mathrm{dist}_{\mathcal{X}_s^{\bullet Tar}}(x(k)) = 0$ and $\lim_{k\to\infty} \mathrm{dist}_{\mathcal{U}_s^{Tar}}(u(k)) = 0$.

Proof: The elements of the sequence $z(k) \triangleq (u(k), x(k))$, for $k \geq 0$, are given by the system open-loop evolution, $x(k+1) = A^\bullet x(k) + B^\bullet u(k)$. On the other hand, elements of the sequence $z_a(k) \triangleq (u_a(k), x_a(k))$ are forced to be in $\mathcal{Z}_s \triangleq \mathcal{U}_s \times \mathcal{X}_s^\bullet$, for $k \geq 0$, by means of the last constraint in P_{MPC}. Once $z(k)$ reaches $z_a(k)$, for a large enough value of k, then both, $z(k)$ and $z(k+1)$ must be in $\mathcal{Z}_s$, i.e., $z(k)$ and $z(k+1)$ are both equilibrium pairs. This means that

$$x(k) = A^\bullet x(k) + B^\bullet u(k), \quad \text{and} \tag{18}$$

$$x(k+1) = A^\bullet x(k+1) + B^\bullet u(k+1). \tag{19}$$

But, by the open-loop system evolution, is $x(k+1) = A^\bullet x(k) + B^\bullet u(k)$, which means that $x(k+1) = x(k)$. Replacing $x(k+1)$ by $x(k)$ in Eq. (19), it follows that

$$x(k) = A^\bullet x(k) + B^\bullet u(k+1), \tag{20}$$

and by the equilibrium condition of $z(k)$, we have

$$x(k) = A^\bullet x(k) + B^\bullet u(k) \tag{21}$$

Then subtracting (21) from (20) we have $B^\bullet(u(k) - u(k+1)) = 0$, and assuming that $rank(B^\bullet) = nu$, this implies that $u(k+1) = u(k)$, and so $z(k+1) = z(k)$. This implies that $z(k)$ reaches $z_a(k)$ only at an equilibrium of the closed-loop system. Finally, it can be shown that every closed-loop equilibrium pair $(u(k), x(k))$ of $x(k+1) = A^\bullet x(k) + B^\bullet u(k)$, with $u(k) = \kappa_{MPC} x(k)$, is in $\mathcal{Z}_s^{Tar} \triangleq \mathcal{U}_s^{Tar} \times \mathcal{X}_s^{\bullet Tar}$. This means that $\lim_{k\to\infty} \mathrm{dist}_{\mathcal{X}_s^{\bullet Tar}}(x(k)) = 0$ and $\lim_{k\to\infty} \mathrm{dist}_{\mathcal{U}_s^{Tar}}(u(k)) = 0$. ■

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