Available online at www.sciencedirect.com

ScienceDirect

IFAC-PapersOnLine 48-23 (2015) 507–512

# MPC with State Window Target Control in Linear Impulsive Systems

**Pablo S. Rivadeneira** * **Antonio Ferramosca** ** **Alejandro H. González** **

* *'Nonlinear System Group', INTEC-Facultad de Ingeniería Química (UNL-CONICET), Güemes 3450, 3000 Santa Fe, Argentina. (e-mail: psrivade@santafe-conicet.gov.ar)*

** *'Laboratory of Process Control', INTEC-Facultad de Ingeniería Química (UNL-CONICET), Güemes 3450, 3000 Santa Fe, Argentina. (e-mail: ferramosca@santafe-conicet.gov.ar, alejgon@santafe-conicet.gov.ar.)*

**Abstract:** In this paper a zone MPC controller is proposed to deal with the tracking problem of linear impulsive control systems. The control strategy is based on the analysis of some system equilibrium generalizations, which are characterized by means of two underlying discrete-time systems. First, it is shown that the impulsive system has a kind of orbits in the state space, passing trough the equilibrium points of the underlying systems, and then, these geometric equilibrium entities (the orbits) are used as possible targets for a zone control system. Based on this new description, an efficient MPC algorithm is designed to steer the system to a set - usually associated to a "therapeutic window" in drug administration problems - that includes a previously defined family of orbits. The strategy is tested by controlling an impulsive model of an intravenous bolus administration of Lithium ions system.



*Keywords:* Impulsive Systems, tracking, model predictive control, stability, drug administration.

## 1. INTRODUCTION

In the past decade, impulsive control systems (ICS) have received a great attention in the engineering community because of very interesting applications, specially in the field of biomedical research. There, one central problem has been the drug administration in the treatment of severe infections as the human immunodeficiency virus (HIV) (Chang et al. (2014); Rivadeneira and Moog (2012)), or in the management of insulin-therapies for diabetic type 1 patients as it has recently shown in Huang et al. (2012).

The impulsive control of biomedical problems related to drug administration has been analyzed and settled as a new challenge in control systems theory in several papers Bellman (1971); Ehrlich et al. (1980); Pierce and Schumitzky (1976). Indeed, the short time of action of the manipulated variable against the evolution of the dynamics suggests that the most suitable way to represent such behaviors is by using ICS. Some control strategies have already been applied to this kind of problems, for instance, optimal control was designed in Pierce and Schumitzky (1976), and recently, a version of model predictive control (MPC) has been developed in Sopasakis et al. (2015) for the problem of dosing a intravenous bolus of Lithium ions described in Ehrlich et al. (1980).

Sopasakis et al. (2015) studies the problem of steering the system to a state target set (named therapeutic window), which could not contain the origin in its interior. Invariant control sets in open loop and closed loop are then defined and some criteria to compute them are given. Finally, based on these sets, a MPC strategy is derived by minimizing the evolution against the therapeutic window set. In this context, however, the calculation of the invariant sets is not a trivial task and it could be difficult to do in many applications. Besides, the computational effort appears to be high - depending on the prediction horizon, which in general must be settled so large as to obtain a large domain of attraction.

Zone control MPC (Ferramosca et al. (2010); Gonzalez and Odloak (2009)) is an advanced MPC strategy in which 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 intermediary variables that are forced to lie in the equilibrium space, this kind of controllers has an enlarged domain of attraction, depending on the controllable set to the entire equilibrium space, instead of the controllable set to a given point or invariant set.

The contributions of this paper are three-fold: first, an extended characterization of dynamical properties of LICS is developed, where non-zero impulsive equilibrium generalizations are analyzed and described through two underlying linear discrete time systems. Second, based on that novel description, a zone control MPC is developed to guarantee stability and convergence to a state window

2405-8963 © 2015, IFAC (International Federation of Automatic Control) Hosting by Elsevier Ltd. All rights reserved.
Peer review under responsibility of International Federation of Automatic Control.
10.1016/j.ifacol.2015.11.329

target set. Finally, the performance of the strategy is illustrated in an interesting biomedical application related to the central problem of drug administration.

## 2. PRELIMINARIES

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

$$\begin{cases} \dot{x}(t) \;=\; A_c x(t), \quad x(0) = x_0, \; t \neq \tau_k, \\ x(\tau_k^+) \;=\; A_d x(\tau_k) + Bu(\tau_k), \quad k \in \mathbb{N}, \end{cases} \tag{1}$$

where the independent variable $t \in \mathbb{R}$ denotes time, the state $x \in \mathcal{X} \subseteq \mathbb{R}^n$, and the inputs $u \in \mathcal{U} \subseteq \mathbb{R}^m$ denotes impulsive controls. Both, $\mathcal{X}$ and $\mathcal{U}$ are compact sets and contain the origin in their interior. Matrices $A_c \in \mathbb{R}^{n\times n}$, $A_d \in \mathbb{R}^{n\times n}$ are the continuous and discrete transition matrices, respectively, and $B \in \mathbb{R}^{n\times m}$. Notice that when $A_d = I$, there are not discontinuities of the first kind in the state variables, and they only are due to the controls $u(\tau_k)$. Furthermore, as part of the system description, the target state set $\mathcal{X}^T \subset \mathcal{X}$ is defined as the zone state where it is desired to remain.

Let us denote the initial time as $t_0 = 0$ and the set of time instants as $\mathcal{T} = \{0, \tau_1, \cdots, \tau_k, \cdots\}$, with $\delta_i$ being $\delta_i = \tau_{i+1} - \tau_i$. The state response for these systems can be generated as follows:

- In $t = 0$, there is no control applied. So, in the interval $0 \leq t \leq \tau_1$, the state response is $x(t) = \Phi(t, 0)x_0 = e^{A_c t}x_0$. Particularly, $x(\tau_1) = e^{A_c\delta_0}x_0$.
- In $t = \tau_1^+$, $x(\tau_1^+) = A_d x(\tau_1) + Bu(\tau_1) = A_d e^{A_c\delta_0}x_0 + Bu(\tau_1)$. Defining $T_i \triangleq A_d e^{A_c\delta_i}$, for $i = 0, 1, 2, ...$, the jump of the state is given by $x(\tau_1^+) = T_0 x_0 + Bu(\tau_1)$.
- In the interval $\tau_1 < t \leq \tau_2$, the state response with one impulse applied to the system becomes $x(t) = e^{A_c(t-\tau_1)}(T_0 x_0 + Bu(\tau_1)) = \Phi(t, 0)x_0 + \Phi(t, \tau_1)Bu(\tau_1)$. Particularly, $x(\tau_2) = e^{A_c\delta_1}x(\tau_1^+)$.
- In $t = \tau_2^+$, $x(\tau_2^+) = A_d x(\tau_2) + Bu(\tau_2) = T_1 T_0 x_0 + T_1 Bu(\tau_1) + Bu(\tau_2)$.
- In the interval $\tau_2 < t \leq \tau_3$,

$$\begin{aligned} x(t) &= e^{A_c(t-\tau_2)}(A_d x(\tau_2) + Bu(\tau_2)) = \\ &= e^{A_c(t-\tau_2)}(T_1 T_0 x_0 + T_1 Bu(\tau_1) + Bu(\tau_2)), \\ &= \Phi(t, 0)x_0 + \Phi(t, \tau_1)Bu(\tau_1) + \Phi(t, \tau_2)Bu(\tau_2). \end{aligned}$$

By repeating this procedure, the state transition matrix of Eq. (1) is deduced for a general interval $\tau_k < t \leq \tau_{k+1}$, with $k$ impulses applied to the system, and it is given by

$$\Phi(t, 0) = e^{A_c(t-\tau_k)} \prod_{i=1}^{k} T_{k-i}. \tag{2}$$

The state transition matrix is invertible for all $t \in [0, \infty)$ if and only if the matrix $A_d$ is invertible, and in this case, $\Phi(0, t) = \Phi^{-1}(t, 0)$. The state response of system (1) for $\tau_k < t \leq \tau_{k+1}$, with $k$ impulses applied to the system, is

$$x(t) = \Phi(t, 0)x_0 + \sum_{j=1}^{k} \Phi(t, \tau_j)Bu(\tau_j). \tag{3}$$

Notice that if $B = 0$ and $A_d = I$, the state transition matrix for linear time invariant (LTI) systems is recovered,

w

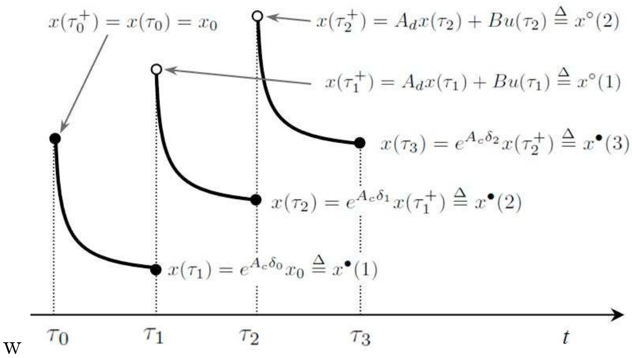


Fig. 1. Typical state system evolution

that is, $\Phi(t, 0) = e^{A_c t}$ and the state response is just $x(t) = e^{A_c t}x_0$. The state at times $\tau_k$ is given by

$$x(\tau_k^+) = \left(\prod_{i=1}^{k} T_{k-i}\right) x_0 + \sum_{j=1}^{k} \left(\prod_{i=1}^{k-j} T_{k-j-i}\right) Bu(\tau_j). \tag{4}$$

Now, if $B \neq 0$ but $A_d = I$, the state response equation becomes

$$x(t) = e^{A_c t}\left(x_0 + \sum_{j=1}^{k} e^{-A_c\tau_j}Bu(\tau_j)\right), \tag{5}$$

which agrees with the results in Yang (2001).

## 3. DYNAMICAL CHARACTERIZATION

### 3.1 Underlying discrete time systems

The impulsive control system given by Eq. (1) is a hybrid system characterized by an autonomous and continuous part (the differential equation), and by a discrete sequence, which describe the discontinuities of the first kind in the state. This discrete sequence is represented by the 'algebraic equation' in (1), and relates the state at time $\tau_k^+$ with the state and the impulsive input at times $\tau_k$. However, it is possible to expand this characterization adding two discrete time systems, which can be obtained by sampling the state at $\tau_k$ and $\tau_k^+$, for $k = 1, 2, \cdots$, respectively. This way, the first discrete system results

$$x(\tau_k) = e^{A_c\tau_k}[x(\tau_{k-1}) + Bu(\tau_{k-1})] \tag{6}$$

$$= T_{k-1}^* x(\tau_{k-1}) + e^{A_c\delta_{k-1}}Bu(\tau_{k-1}). \tag{7}$$

while the second one is

$$x(\tau_k^+) = A_d e^{A_c\delta_{k-1}}x(\tau_{k-1}^+) + Bu(\tau_k), \tag{8}$$

$$= T_{k-1}x(\tau_{k-1}^+) + Bu(\tau_k), \tag{9}$$

where $T_i^* = e^{A_c\delta_i}A_d$, $i = 0, 1, \cdots$. Notice that the inputs $u(\tau_k)$ are already known at time instants $\tau_k^+$. These two discrete systems are linear but with time-variant matrices due to $\delta_i$ is not necessarily equidistant. Here, it is assumed that $\delta_i = \delta$, then $T_i = T$, $T_i^* = T^*$, for $i = 0, 1, \cdots$, and the systems become

$$\begin{aligned} x^\bullet(j+1) &= T^* x^\bullet(j) + e^{A_c\delta}Bu^\bullet(j) \\ &= A^\bullet x^\bullet(j) + B^\bullet u^\bullet(j), \quad x^\bullet(0) = x_0, \end{aligned} \tag{10}$$

and

$$x^\circ(j+1) = Tx^\circ(j) + Bu^\circ(j) \qquad (11)$$
$$= A^\circ x^\circ(j) + B^\circ u^\circ(j), \quad x^\circ(0) = x_0,$$

where $A^\circ = T = A_d e^{A_c\delta}$, $A^\bullet = T^* = e^{A_c\delta}A_d$, $B^\circ = B$, $B^\bullet = e^{A_c\delta}B$, and $u^\circ(j+1) = u^\bullet(j)$, for $j \geq 0$. These two discrete time systems describe the original system (1) at the impulsive times, $\tau_i$, and an instant after this time, when the jump has already occurred, $\tau_i^+$. So, these two discrete time systems are part of system (1), and this is why (11) and (10) are called here as the **underlying discrete time systems** of the linear ICS (1). Notice that there is only one input $u$ (shifted one time instant) for both discrete time systems.

### *3.2 Impulsive equilibriums*

The only equilibrium of the impulsive system (1) is given by $(u_s, x_s) = (0, 0)$, which is the only pair verifying $\dot{x} = 0$ and $x(\tau_k^+) = x(\tau_k) = 0$. However, it is possible to define equilibrium points for the underlying discrete-time systems defined above, that are closely related to the impulsive system behavior. As it is known, equilibrium points of discrete time systems are pairs $(u_s, x_s)$ such that if the system is placed at $x_s$, then, the injection of $u_s$ to the system makes that it remains in $x_s$.

In fact, both discrete time systems (11) and (10) are part of an unique system, then

*Definition 1.* **(Extended equilibrium of an impulsive system)** An extended equilibrium of an impulsive system $(u_s, x_s^\circ, x_s^\bullet)$ is a triplet such that if the impulsive system starts in $x_s^\circ$, and the input $u_s$ is successively injected to the system with same amplitude at time instants $\tau_k$, then the impulsive system will describe an orbit that goes from $x_s^\circ$ to $x_s^\bullet$, and then back to $x_s^\circ$, indefinitely.

The equilibrium triplets will be given by $(u_s, x_s^\circ, x_s^\bullet) = (u_s, G^\circ u_s, G^\bullet u_s)$, where $G^\circ \triangleq (I_n - A^\circ)^{-1}B^\circ$, and $G^\bullet \triangleq (I_n - A^\bullet)^{-1}B^\bullet$. Notice that two equations relate $x_s^\bullet$ with $x_s^\circ$: the jump produced by input $u_s$, $A_d x_s^\bullet + Bu_s = x_s^\circ$, and the free response $e^{A_c\delta}x_s^\circ = x_s^\bullet$. In fact, this kind of systems has no equilibrium points, but equilibrium orbits:

*Definition 2.* **(State equilibrium orbit)** For a given extended equilibrium $(u_s, x_s^\circ, x_s^\bullet)$, the **state equilibrium orbit** of an impulsive systems, $o_s$, is described by $x(t) = e^{A_c t}x_s^\circ$, for $0 < t \leq \delta$, and particularly $x(\delta) = e^{A_c\delta}x_s^\circ = x_s^\bullet$, where the final state $x_s^\bullet$ is given by $x_s^\bullet = A_d x_s^\circ + Bu_s$.

See Fig. 2 for a schematic plot of some equilibrium orbits.

*Remark 1.* Orbits $o_s$ are not in general control invariants for the impulsive system (1). However, if the case where the time interval $\delta$ is not constant is considered, it can be shown that once the state $x(t)$ is in $o_s$, at a given time $\hat{t}$, then always there is a control sequence $\mathbf{u} = \{u(\tau_j), u(\tau_{j+1}), \cdots\}$, with $\tau_j \geq \hat{t}$, and a sequence of time intervals $\{\delta_j, \delta_{j+1}, \cdots\}$ such that $x(t) \in o_s$ for $t \geq \hat{t}$.

The extended equilibrium and the equilibrium orbit defined before play 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 in which each elements is an equilibrium) [1]. That is

*Definition 3.* **(Control equilibrium sets for the underlying discrete time systems)** The control equilibrium sets for the systems (11) and (10) are given by:

$$\mathcal{X}_s^\circ \triangleq \{x \in \mathcal{X} : x = G^\circ u, \quad \text{for some} \quad u \in \mathcal{U}\} \qquad (12)$$
$$\mathcal{X}_s^\bullet \triangleq \{x \in \mathcal{X} : x = G^\bullet u, \quad \text{for some} \quad u \in \mathcal{U}\}, \qquad (13)$$

respectively. These sets implicitly generates the **input equilibrium set**:

$$\mathcal{U}_s \triangleq \{u \in \mathcal{U} : (G^\circ u, \quad G^\bullet u) \in \mathcal{X}_s^\circ \times \mathcal{X}_s^\bullet\}. \qquad (14)$$

The control equilibrium sets defined before have the following intuitive property:

*Property 1.* Consider that the impulsive system (1) is placed at a given state $x_s$ which belongs to $\mathcal{X}_s^\circ$ (or $\mathcal{X}_s^\bullet$), at time instant $\tau_i$. Then, there is a control impulsive sequence $\mathbf{u} = \{u(\tau_i), u(\tau_{i+1}), \cdots)\}$ in $\mathcal{U}_s$, that keeps the system (11) in $x_s$ (or the system (10) in $x_s$), for all $j \geq i$, which implies that the impulsive system (1) is kept in the orbit $o_s$ defined by $x_s$, for all $t \geq \tau_i$.

**Proof.** If $x_s \in \mathcal{X}_s^\circ$, then the control impulsive sequence $\mathbf{u} = \{0, u_s, u_s, \cdots)\}$, where $u_s \in \mathcal{U}_s$ is the input such that $x_s = G^\circ u_s$, makes that the impulsive system (1) keeps in the orbit $o_s$. On the other hand, if $x_s \in \mathcal{X}_s^\bullet$, then the control impulsive sequence $\mathbf{u} = \{u_s, u_s, u_s, \cdots)\}$, where $u_s \in \mathcal{U}_s$ is the input such that $x_s = G^\bullet u_s$, makes that the impulsive system (1) keeps in the orbit $o_s$.

Notice that $\mathcal{X}_s^\circ$ and $\mathcal{X}_s^\bullet$ lie in subspaces of dimension $m$ of $\mathbb{R}^n$. Given that $\mathcal{X}$, which contains the origin in its interior, the sets $\mathcal{X}_s^\circ$ and $\mathcal{X}_s^\bullet$ generate a **cone** in $\mathcal{X}$, which is in a subspace of dimension $2m$ of $\mathbb{R}^n$.

*Definition 4.* **(Control equilibrium set for the impulsive system)** Given an input equilibrium set $\mathcal{U}_s$, and a particular value of $\delta > 0$, the control equilibrium set of the impulsive systems (1) is given by:

$$\mathcal{X}_s = \{x \in \mathcal{X} : x = \alpha x_s^\circ + \beta x_s^\bullet\} \qquad (15)$$

where $x_s^\circ \in \mathcal{X}_s^\circ$, $x_s^\bullet \in \mathcal{X}_s^\bullet$ and $\alpha, \beta \geq 0$ or $\alpha, \beta \leq 0$.

*Remark 2.* The angle between $\mathcal{X}_s^\circ$ and $\mathcal{X}_s^\bullet$ is defined by $\delta$, in such a way that for larger values of $\delta$ the angle increases, and particularly, for $\delta \to 0$ both sets coincide because the impulsive input becomes a continuous one.

*Property 2.* Consider that the complete impulsive system (1) is placed at a given state $x_s \in \mathcal{X}_s$, at time instant $\tau_i$. Then, there exists a control impulsive sequence $\mathbf{u} = \{u(\tau_i), u(\tau_{i+1}), \cdots\}$ in $\mathcal{U}_s$, that keeps the system (11) in $x_s$ (or the system (10) in $x_s$), for all $j \geq i$, which implies that the complete impulsive system (1) is kept in the orbit $o_s$ defined by $x_s$, for all $t \geq \tau_i$. This means that, although $\mathcal{X}_s$ is not a strict control invariant set for the impulsive system (given that the orbits do not necessary belong to $\mathcal{X}_s$), this set is in fact a control invariant set for the discrete time underlying systems.

**Proof.** The proof follows the same steps than the proof of Property 1, if $x_s \in \mathcal{X}_s^\circ$ or $x_s \in \mathcal{X}_s^\bullet$. In addition, if $x_s$ is in the strict interior of $\mathcal{X}_s$, then there is an input

[1] A further generalization of the equilibrium set is the invariant set, which also includes transient evolution of the system. However, in this work it is not necessary to define such a sets for the proposed control objectives.

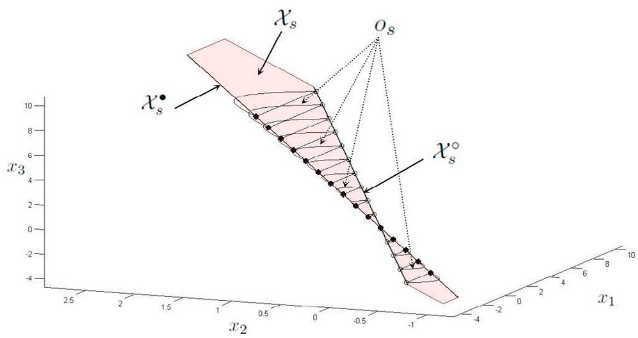


Fig. 2. Cone $\mathcal{X}_s$ into a subspace of dimension 2 in $\mathbb{R}^3$, sets $\mathcal{X}_s^\circ$ and $\mathcal{X}_s^\bullet$, and equilibrium orbits $o_s$ of a simulated impulsive system.

$\tilde{u} \in \mathcal{U}_s$, such that $A_d x_s + B\tilde{u} = x_s^\circ = G^\circ u_s$. This is so, because of linearity of the jump map. Then, the input sequence $\mathbf{u} = \{\tilde{u}, 0, u_s, u_s, \cdots\}$, which is in $\mathcal{U}_s$, makes that the impulsive system (1) holds in the orbit $o_s$.

*Definition 5.* **(State equilibrium orbit set)** Given the following equilibrium triplets $(u_{s,min}, x_{s,min}^\circ, x_{s,min}^\bullet)$ and $(u_{s,max}, x_{s,max}^\circ, x_{s,max}^\bullet)$, a State equilibrium orbit set of an impulsive system, $\mathcal{O}_s$, is the set of equilibrium orbits $o_s$ defined by all the triplets $(u_{s,i}, x_{s,i}^\circ, x_{s,i}^\bullet)$, such that $(u_{s,min}, x_{s,min}^\circ, x_{s,min}^\bullet) \preceq (u_{s,i}, x_{s,i}^\circ, x_{s,i}^\bullet) \preceq (u_{s,max}, x_{s,max}^\circ, x_{s,max}^\bullet)$.

See Fig. 2 and Fig. 3 for a schematic plot of the cone defining the control equilibrium set and an equilibrium orbit set, respectively.

### *3.3 Target equilibrium sets for control purposes*

The control goal is to steer the ICS (1) to an arbitrary target set $\mathcal{X}^T$, and once the system reaches this set, to keep it there indefinitely. To accomplish that, it is necessary to find an equilibrium set, included in $\mathcal{X}^T$, to be used as a target equilibrium set in a tracking control strategy.

So, the objective now is to find two **control equilibrium target sets for (11) and (10)**, $\mathcal{X}_s^{\circ T} \subset \mathcal{X}^T$ and $\mathcal{X}_s^{\bullet T} \subset \mathcal{X}^T$, such that the orbit set $\mathcal{O}_s$, associated to $\mathcal{X}_s^{\circ T}$ and $\mathcal{X}_s^{\bullet T}$, called as $\mathcal{O}_s^T$, is contained in $\mathcal{X}^T$. Equivalently, it is possible to define a **control equilibrium target set for the impulsive system (1)**, $\mathcal{X}_s^T$, by considering the convex hull of $\mathcal{X}_s^{\circ T}$ and $\mathcal{X}_s^{\bullet T}$.

Notice that the time interval $\delta$ is the parameter which decides if there are two sets $\mathcal{X}_s^{\circ T}$ and $\mathcal{X}_s^{\bullet T}$ inside a given target set $\mathcal{X}^T$, and such that the orbit set $\mathcal{O}_s^T$ associated to them is contained in $\mathcal{X}^T$. Given a non-empty set $\mathcal{X}^T$, there is a maximal $\delta$ such that the later conditions hold. According to this requirement, the maximum value of $\delta$, $\delta_{max}$, that the problem permits is defined. The minimum value, $\delta_{min}$, is given by practical restrictions (since maximal frequency of impulses is always determined by the control problem itself).

The suggested procedure to compute $\mathcal{X}_s^{\circ T}$ and $\mathcal{X}_s^{\bullet T}$ and to find $\delta_{max}$ is as follows:

(1) Compute $\mathcal{X}_s$, for $\delta = \delta_{min}$ ($\delta_{min}$ is assumed to be given), and compute $\mathcal{X}_s^\circ$ and $\mathcal{X}_s^\bullet$.

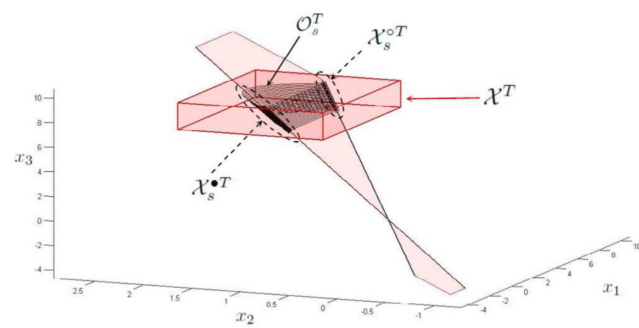


Fig. 3. State equilibrium orbit set, $\mathcal{O}_s^T$, state target set, $\mathcal{X}^T$, and state equilibrium sets for the underlying discrete systems $\mathcal{X}_s^{\circ T}$ and $\mathcal{X}_s^{\bullet T}$.

(2) Compute $\mathcal{X}_s^{\circ T} \triangleq \mathcal{X}_s^\circ \cap \mathcal{X}^T$ and $\mathcal{X}_s^{\bullet T} \triangleq \mathcal{X}_s^\bullet \cap \mathcal{X}^T$. If $\mathcal{X}_s^{\circ T}$ or $\mathcal{X}_s^{\bullet T}$ is empty, then, the control problem is not properly formulated, and the target set $\mathcal{X}^T$ must be increased or $\delta_{min}$ reduced. If $\mathcal{X}_s^{\circ T}$ and $\mathcal{X}_s^{\bullet T}$ are non-empty, then increase $\delta$ up to a value in which one of these sets is empty. This value defines $\delta_{max}$.
(3) Select a $\delta$ such that $\delta_{min} < \delta < \delta_{max}$. Check if the orbits set $\mathcal{O}_s^T$ is inside $\mathcal{X}^T$. Notice that $\mathcal{O}_s^T$ will be defined solely by $\delta$. So, if the extreme points of $\mathcal{X}_s^{\circ T}$ and $\mathcal{X}_s^{\bullet T}$ (together with the corresponding input $u_s$) generates (two) orbits inside $\mathcal{X}^T$, then, by continuity, $\mathcal{O}_s^T \subset \mathcal{X}^T$.
(4) If one of the extreme orbits is outside $\mathcal{X}^T$, reduce $\mathcal{X}_s^{\circ T}$ and $\mathcal{X}_s^{\bullet T}$ by scaling them: $\mathcal{X}_s^{\circ T} \leftarrow \lambda \mathcal{X}_s^{\circ T}$, $\mathcal{X}_s^{\bullet T} \leftarrow \lambda \mathcal{X}_s^{\bullet T}$, with $0 < \lambda < 1$ such that the extreme orbits associated to $\lambda \mathcal{X}_s^{\circ T}$ and $\lambda \mathcal{X}_s^{\bullet T}$ are inside $\mathcal{X}^T$.
(5) If this value of $\lambda$ does not exist, then, again, the control problem is not properly formulated, and this time $\mathcal{X}^T$ must be increased.

See Fig. 3 for an schematic plot of the state equilibrium orbit set, $\mathcal{O}_s^T$, the target set, $\mathcal{X}^T$, and state equilibrium set $\mathcal{X}_s^{\circ T}$, in $\mathbb{R}^3$.

## 4. PROPOSED MPC STRATEGY

This section is devoted to describe a zone MPC formulation which will steer the system from a given initial state $x_0$ to an equilibrium objective set defined by $\mathcal{X}_s^{\bullet T} \subset \mathcal{X}^T$. The cost of the optimization problem that the MPC solves on-line is given by:

$$V(x, p; \mathbf{u}, u_s, x_s) = V_{dyn}(x; \mathbf{u}, u_s, x_s) + V_{ter}(p; u_s, x_s) \quad (16)$$

where

$$V_{dyn}(x; \mathbf{u}, u_s, x_s) = \sum_{j=0}^{N-1} (x(j) - x_s)^T Q (x(j) - x_s) \quad (17)$$

$$+ (u(j) - u_s)^T R (u(j) - u_s), \quad (18)$$

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

$$V_{ter}(p; u_s, x_s) = p \left( dist(x_s, \mathcal{X}_s^{\bullet T}) + dist(u_s, \mathcal{U}_s^T) \right) \quad (19)$$

with $p > 0$, is the terminal term devoted to steer $x_s$ to $\mathcal{X}_s^{\bullet T}$ and $u_s$ to $\mathcal{U}_s^T$. Notice that in the later cost, the

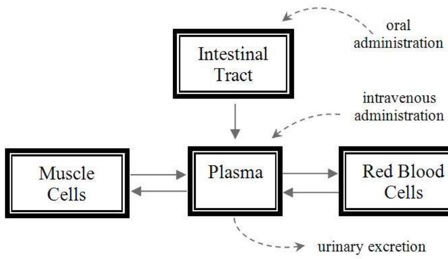


Fig. 4. Topology of the interconnected compartments of the PBPK model.

current state $x$ and the sets $\mathcal{X}_s^{\bullet T}$ and $\mathcal{U}_s^T$ are parameters, while $\mathbf{u} = \{u(0), u(1), \cdots, u(N-1)\}$, $u_s$ and $x_s$ are the optimization variables (being $N$ the control horizon).

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

$P_{MPC}$:

$$\begin{aligned}
\min_{\mathbf{u},u_s,x_s} \quad & V(x,p;\mathbf{u},u_s,x_s) \\
s.t. \quad & \\
& x(0) = x, \\
& x(j+1) = A^\bullet x(j) + B^\bullet u(j), \qquad j \in \mathbb{I}_{0:N-1} \\
& x(j) \in \mathcal{X},\ u(j) \in \mathcal{U}, \qquad j \in \mathbb{I}_{0:N-1} \\
& x(N) = x_s; \\
& x_s = G^\bullet u_s \quad ((u_s, x_s) \in \mathcal{X}_s^\bullet \times \mathcal{U}_s)
\end{aligned}$$

The constraint $x(N) = x_s$ is the terminal constraint that forces the final state (at the end of control horizon $N$) to reach the artificial equilibrium state $x_s$. Furthermore, the last constraint forces the artificial variable pair $(u_s, x_s)$ to be in $\mathcal{X}_s^\bullet \times \mathcal{U}_s$. This way, following a similar procedure as in Ferramosca et al. (2010); Gonzalez and Odloak (2009), it can be shown that this MPC formulation ensures the stability of the objective set $\mathcal{X}_s^{\bullet T}$, and furthermore, because of the use of the artificial variables $(u_s, x_s)$, the domain of attraction is given by the $N$-step controllable set to the equilibrium set $\mathcal{X}_s^\bullet$. Notice that otherwise, the domain of attraction is given by the $N$-step controllable set to the objective set $\mathcal{X}_s^{\bullet T}$, which is in general too small.

## 5. CASE STUDY

In Ehrlich et al. (1980) a physiological pharmacokinetic model based on experimental data which describes the distribution of Lithium ions in the human body upon intravenous administration is provided. The compartmental model is shown in Fig. 4. The state is given by $x(t) = [C_P(t)\ C_{RBC}(t)\ C_M(t)]^T$, where $C_P(t)$ is the concentration of plasma (P), $C_{RBC}(t)$ is the concentration of the red blood cells (RBC), and $C_M(t)$ is the concentration of muscle cells (M). All these concentrations are given in $nmol/L$. The input $u$ represents the amount of the dose, in $nmol$. The administration period is initially fixed in $T = 3\ hr$. The matrices that describe the impulsive control system are:

$$A_c = \begin{pmatrix} -0.6137 & 0.1835 & 0.2406 \\ 1.2644 & -0.8 & 0 \\ 0.2054 & 0 & -0.19 \end{pmatrix}, B = \begin{pmatrix} 10.9 \\ 0 \\ 0 \end{pmatrix}, \quad (20)$$

and $A_d = I_{2x2}$. The state and input constraints are imposed as $\mathcal{X} = \{x : [0\ 0\ 0]^T \preceq x \preceq [2\ 1.2\ 1.2]^T\}$ and $\mathcal{U} = \{u : 0 \leq u \leq 5.95\}$, respectively. The state window target is defined by $\mathcal{X}^T = \{x : [0.4\ 0.6\ 0.5]^T \preceq x \preceq [0.6\ 0.9\ 0.8]^T\}$. As it is described in Ehrlich et al. (1980); Sopasakis et al. (2015), this set is determined by the treating physician. The drug's concentration within the boundaries of $\mathcal{X}$ guarantees the effectiveness of the therapy.

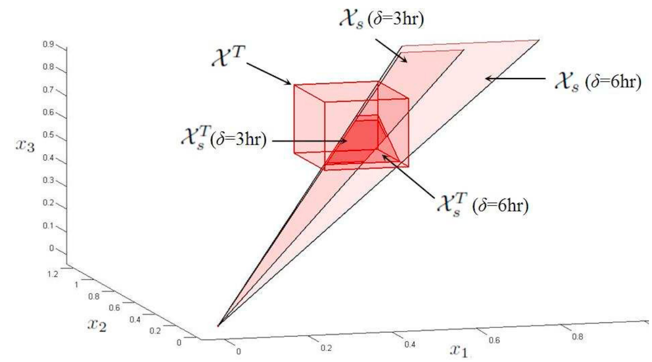


Fig. 5. State equilibrium set $\mathcal{X}_s^T$ for $\delta = 3\ hr$ and $\delta = 6\ hr$.

### 5.1 Equilibrium characterization

According to the description of the proposed methodology, the equilibrium set of the system is given by $(i)$ the (cone) set $\mathcal{X}_s$ calculated by Eq. (3.3), and $(ii)$ the set $\mathcal{X}_s^T$ and $\mathcal{U}_s^T$ computed as in Section 3.3. The input set is given by $\mathcal{U}_s^T = \{u : 0.83 \leq u \leq 0.93\}$. Fig. 5 shows the equilibrium set $\mathcal{X}_s^T$ (in dark blue) for the intake periods $\delta = 3\ hr$ and $\delta = 6\ hr$. As it can be seen, the maximum period for $\mathcal{X}_s^T$ to be contained in the 'therapeutic window' (or the state window target) $\mathcal{X}^T$ is precisely $T = 6\ hr$, since for large periods, there is not equilibrium pairs $(x_s^\circ, x_s^\bullet)$ entirely in $\mathcal{X}^T$. This provides a practical way to find the maximal value of $\delta$, according to control system specifications. However, remember that the minimum value of $\delta$ is generally decided by the physician experience. Furthermore, it will be shown later that the impulsive system response is entirely contained in $\mathcal{X}^T$ for any equilibrium pair $(x_{s,1}, x_{s,2})$ in $\mathcal{X}_s^T$. This means that the state equilibrium orbit set, $\mathcal{O}_s$, corresponding to $\mathcal{X}_s^T$ is in $\mathcal{X}^T$, as it is desired.

### 5.2 Control

The MPC controller is tuned as: $N = 4$, $Q = diag([1\ 1\ 1])$, $R = 2$ and $p = 100$. Notice that in contrast to the control horizon used in Sopasakis et al. (2015), which is $N = 15$, here it is used a reduced one, because of the enlarged domain of attraction.

Figs. 6 and 7 show the state and input time evolution, respectively. 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, remains constant at the desired equilibrium value $u_s$. Fig. 8 shows the portrait phase in the state space for the evolution of the figures above. As it can be seen, the state trajectory moves away from the cone $\mathcal{X}_s$ first, and then converges to $\mathcal{X}_s^T$ as it was designed. Notice that the state trajectory enters $\mathcal{X}_s^T$ from below, since the controller cost penalizes only the distance from the state trajectory to the

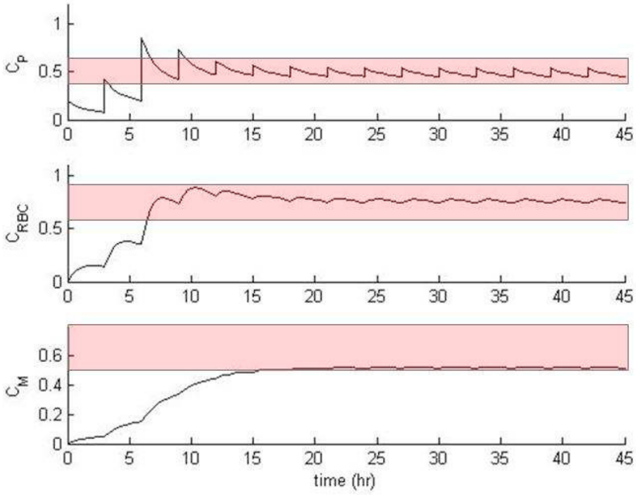


Fig. 6. State time evolution.

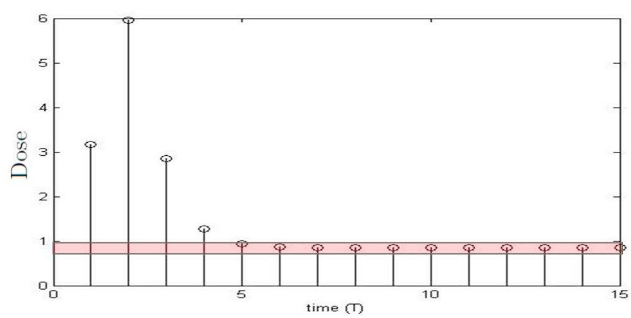


Fig. 7. Input time evolution.

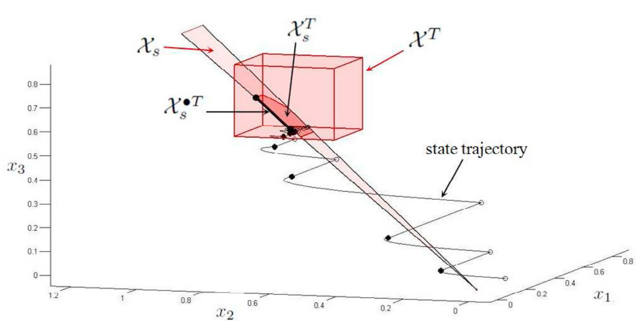


Fig. 8. State evolution in the state space.

entire set. In fact, no matter which state equilibrium pair $(x_s^\circ, x_s^\bullet) \in \mathcal{X}_s^T$ the system reaches, the controller objective will be null.

## 6. CONCLUSIONS

The tracking problem to steer a linear ICS from an arbitrary initial state to a state window target has been tackled in this paper. It has been shown that, although the only standard equilibrium (according to continuous systems) is the origin, other points and orbits can be seen as equilibriums of the LICS. Here, these equilibriums are characterized based on two underlying discrete time systems, which arise just by sampling the original system at times $\tau_k$ and $\tau_k^+$, respectively.

A case study coming from biomedical research, namely the pharmacokinetics dynamics of the distribution of Lithium ions in the human body by intravenous administration is analyzed. It was formerly studied in Sopasakis et al. (2015).

The MPC strategy proposed here with a state window target (accounting in the application for a **therapeutic window**) controls effectively the system, fulfilling hard constraints in the state and control. The main benefits of the proposed controller are listed next:

(1) A novel equilibrium characterization for impulsive systems is fully described, showing its useful in designing control strategies.
(2) The proposed strategy can steer the system to any feasible state window target, including those which does not contain the origin in its interior.
(3) The new control strategy does not need to compute invariant sets as target set as it was done in Sopasakis et al. (2015), which may be difficult in many cases. Instead, it uses an equilibrium set, which is easy to compute, and account for the 'state window target' requirements, leading to strategies with less computational effort.
(4) The proposed strategy has an enlarged domain of attraction, because of the use of artificial intermediary variables as proposed in Ferramosca et al. (2010); Gonzalez and Odloak (2009).

## REFERENCES

Bellman, R. (1971). Topics in pharmacokinetics, III: Repeated dosage and impulsive control. *Mathematical Biosciences*, 12(1-2), 1 – 5.

Chang, H., Astolfi, A., Moog, C.H., and Rivadeneira, P.S. (2014). A control systems analysis of HIV prevention model using impulsive input. *Biomedical Signal Processing and Control*, 13, 123 – 131.

Ehrlich, B.E., Clausen, C., and Diamond, J.M. (1980). Lithium pharmacokinetics: Single-dose experiments and analysis using a physiological model. *Journal of Pharmacokinetics and Biopharmaceutics*, 8(5), 439 – 461.

Ferramosca, A., Limon, D., González, A.H., Odloak, D., and Camacho, E.F. (2010). MPC for tracking zone regions. *Journal of Process Control*, 20(4), 506–516.

Gonzalez, A.H. and Odloak, D. (2009). A stable MPC with zone control. *Journal of Process Control*, 19(1), 110–122.

Huang, M., Li, J., Song, X., and Guo, H. (2012). Modeling impulsive injections of insulin: Towards artificial pancreas. *SIAM Journal on Applied Mathematics*, 72(5), 1524?1548.

Pierce, J.G. and Schumitzky, A. (1976). Optimal impulsive control of compartment models, i: Qualitative aspects. *Journal of Optimization Theory and Applications*, 18, 537–554.

Rivadeneira, P.S. and Moog, C.H. (2012). Impulsive control of single-input nonlinear systems with application to HIV dynamics. *Applied Mathematics and Computation*, 218(17), 8462–8474.

Sopasakis, P., Patrinos, P., Sarimveis, H., and Bemporad, A. (2015). Model predictive control for linear impulsive systems. *IEEE Transactions on Automatic Control*. doi: 10.1109/TAC.2014.2380672.

Yang, T. (2001). *Impulsive Control Theory*. LNCIS. Springer-Verlag Berlin Heidelberg, 1 edition.