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Control of Multi-Affine Systems on Rectangles with Applications to Hybrid Biomolecular Networks[1]

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Abstract

Given a multi-affine system on an N-dimensional rectangle, the problem of reaching a particular facet, using multi-affine state feedback is studied. Necessary conditions and sufficient conditions for the existence of a solution are derived in terms of linear inequalities on the input vectors at the vertices of the rectangle, and a method for constructing a multi-affine state feedback solution is presented. The technique is applied to the control of hybrid models of bioregulatory networks.

1 Introduction

This paper studies multi-affine dynamical systems evolving on rectangles and presents a controller design method for reachability of a facet. This problem is motivated by the control of multi-affine hybrid systems.

A hybrid system is a dynamic system that consists of discrete and continuous components with complex interactions [11]. The safety criticality of many embedded systems has resulted in significant research on computing reachable sets for hybrid systems.

Piece-wise linear hybrid systems have received great attention in the past years. This class of systems consists of automata for which each discrete state is an affine system on a polyhedral set [12]. Specialized tools like `HyTech` [8], `d/dt` [4], and `CheckMate` [3] have been developed for verification of such systems. (`CheckMate` can also handle low-dimensional nonlinear systems). A particular approach to the reachability problem was developed by van Schuppen in [13], which requires the solution of a facet reachability problem of an affine system on a polyhedral set, given in [5].

This paper extends the results derived for linear systems in [5, 7] to a class of non-linear dynamical systems. We determine necessary conditions and sufficient conditions for the existence of a multi-affine control such that, independent of the initial state, the trajectory of the closed loop system reaches a particular facet of a rectangle in finite time.

The main motivation for this work are hybrid models of bioregulatory networks, as the one described in [1, 2]. A bioregulatory network is an ensemble of genes, together with their products (mRNA and proteins), and other species affecting the expression of the genes. Traditionally, the level of gene transcription is modeled as a sigmoidal function of the concentration of the regulatory species. However, experimental data on numerous systems in biology suggests that regulation can be modeled as a piecewise constant function. If we consider all the genes in the network with all the corresponding levels of activation, we end up with a switched system with specific dynamics for each mode. The vector fields are multi-affine, because of the rate equations that describe chemical reactions among species. The invariants of the modes are rectangular and the facets correspond to genes being turned on or off. An important question is whether one can drive a genetic system from an arbitrary initial state to a final state so that some genes are turned on while others are not transcribed. To do this, the first problem to be solved is driving a system with multi-affine dynamics within rectangular regions so that some desired facet is hit in finite time. This is exactly the problem we formulate and solve in this work.

2 Problem formulation

For $N \in \mathbb{N}$, let R_N denote the N-dimensional rectangle described by:

$$R_N = \{x = (x_1, \dots x_N) \in \mathbb{R}^N \mid a_i \leq x_i \leq b_i\}$$

where $a_i, b_i \in \mathbb{R}$, $a_i < b_i$, $i = 1, \dots, N$. A multi-affine function $f : R_N \longrightarrow \mathbb{R}^m$ (with $m \in \mathbb{N}$) is a polynomial in the indeterminates $x_1, \dots, x_N$ with the property that the degree of f in any of the indeterminates $x_1, \dots, x_N$ is less than or equal to 1. Stated differently, f has the form

$$f(x_1, \dots, x_N) = \sum_{i_1, \dots, i_N \in \{0,1\}} c_{i_1, \dots, i_N} x_1^{i_1} \cdots x_N^{i_N}, \quad (1)$$

with $c_{i_1,\dots,i_N} \in \mathbb{R}^m$ for all $i_1, \dots, i_N \in \{0, 1\}$ and using the convention that if $i_k = 0$, then $x_k^{i_k} = 1$.

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Consider the following non-linear control system evolving in R_N:

$$\dot{x} = f(x) + Bu. \tag{2}$$

The drift term $f : R_N \to \mathbb{R}^N$ is a multi-affine function, $B \in \mathbb{R}^{N\times m}$ is a constant matrix whose columns give the directly controllable directions, and the input u is assumed to take values in a polyhedral set $U \subset \mathbb{R}^m$ only.

Problem 1. Consider the multi-affine system (2) on the rectangle R_N, and let F_j be a facet of R_N, with normal vector n_j pointing out of R_N. For any initial state $x_0 \in R_N$, we have to find a time instant $T_0 \geq 0$ and an input function $u : [0, T_0] \longrightarrow U$, such that

(i) $\forall t \in [0, T_0] : \; x(t) \in R_N$,

(ii) $x(T_0) \in F_j$, and T_0 is the smallest time-instant in the interval $[0, \infty)$ for which the state reaches the exit facet F_j,

(iii) $n_j^T \dot{x}(T_0) > 0$, i.e. the velocity vector $\dot{x}(T_0)$ at the point $x(T_0) \in F_j$ has a positive component in the direction of n_j. This implies that in the point $x(T_0)$, the velocity vector $\dot{x}(T_0)$ points out of the rectangle R_N.

Furthermore, this input function u should be realized by the application of a continuous feedback law

$$u(t) = k(x(t)), \tag{3}$$

with $k : R_N \longrightarrow U$ a continuous function, that is independent of the initial state x_0.

For the solution of Problem 1, we are particularly interested in multi-affine feedback laws $k(x)$. Note that if the feedback law $k(x)$ in (3) is multi-affine, the closed-loop system is also multi-affine:

$$\dot{x} = f(x) + Bk(x), \qquad x(0) = x_0. \tag{4}$$

To simplify the notation and without restricting the generality, we will solve the problem on the unit cube $K_N = [0,1]^N$ rather than on the arbitrary rectangle R_N. Indeed, by the affine coordinate transformation $z = S(x) = Ax + b$, with

$$A = \operatorname{diag}\left\{\frac{1}{b_1 - a_1}, \ldots, \frac{1}{b_N - a_N}\right\} \in \mathbb{R}^{N\times N},$$

$$b = \left[-\frac{a_1}{b_1 - a_1}, \ldots, -\frac{a_N}{b_N - a_N}\right]^T \in \mathbb{R}^N,$$

the problem is translated to the unit cube because S maps R_N to K_N in such a way that vertices are mapped to vertices, edges to edges, facets to facets etc. Moreover, since S simply consists of a translation and a scaling operation, the system remains multi-affine in the new z-coordinates. In the rest of the paper, when we refer to Problem 1, we assume that the rectangle R_N is the unit cube K_N.

3 Multi-affine functions on the unit cube

For any full-dimensional polytope P_N in $\mathbb{R}^N$, a *facet* of P_N is the intersection of P_N with one of its supporting hyperplanes. More generally, a *face* of P_N is the intersection of P_N with several of its supporting hyperplanes. If the dimension of the intersection is n (with $0 \leq n < N$) the face is called an *n-face*.

Let $(x_1, \ldots, x_N) \in [0,1]^N$ be a point in the unit cube K_N, and denote the 2^N vertices of K_N by $(i_1, \ldots, i_N)$, $i_1, \ldots, i_N \in \{0,1\}$. Let $m \in \mathbb{N}$ and $m < N$. Then every $N-m$-dimensional face F of the unit cube $K_N = \{(x_1, \ldots, x_N) \mid x_i \in [0,1], \; (i = 1, \ldots, N)\}$, characterized by m equations of the form

$$\begin{array}{rclcrcl} x_{i_1} & = & 0 & \text{or} & x_{i_1} & = & 1, \\ & \vdots & & & & \vdots & \\ x_{i_m} & = & 0 & \text{or} & x_{i_m} & = & 1, \end{array}$$

where $i_1, \ldots, i_m \in \{1, \ldots, N\}$ and $i_j \neq i_k$ for $j \neq k$, is isomorphic with the $N-m$ dimensional unit cube K_{N-m}. If $f : K_N \longrightarrow \mathbb{R}^m$ is a multi-affine function, and F is an $N-m$-dimensional face of K_N, then the restriction $f\,|_F$ of f to F is a multi-affine function on the $N-m$-dimensional unit cube K_{N-m}.

Lemma 1. *Let $f : K_N \longrightarrow \mathbb{R}^m$ be a multi-affine function, and assume that*

$$\forall (i_1, \ldots, i_N) \in \{0,1\}^N : \; f(i_1, \ldots, i_N) = 0. \tag{5}$$

Then $f \equiv 0$.

Proposition 1. *Let $N \in \mathbb{N}$, and consider 2^N fixed vectors $v_{i_1,\ldots,i_N} \in \mathbb{R}^m$, $((i_1, \ldots, i_N) \in \{0,1\}^N)$. Then there exists a unique multi-affine function $f : K_N \longrightarrow \mathbb{R}^m$ such that*

$$\forall (i_1, \ldots, i_N) \in \{0,1\}^N : \; f(i_1, \ldots, i_N) = v_{i_1,\ldots,i_N}, \tag{6}$$

which is given by

$$f(x_1, \ldots, x_N) = \sum_{i_1,\ldots,i_N \in \{0,1\}} \prod_{k=1}^{N} (1-x_k)^{1-i_k} x_k^{i_k} v_{i_1,\ldots,i_N}. \tag{7}$$

Proof. It is obvious that f defined in (7) is multi-affine. Moreover, for every $(i_1, \ldots, i_N) \in \{0,1\}^N$:

$$\prod_{k=1}^{N} (1 - x_k)^{1-i_k} x_k^{i_k} =$$

$$\begin{cases} 1 & \text{if} \quad (x_1, \ldots, x_N) = (i_1, \ldots, i_N), \\ 0 & \text{if} \quad (x_1, \ldots, x_N) \in \{0,1\}^N \setminus \{(i_1, \ldots, i_N)\}. \end{cases}$$

So indeed $f(i_1, \ldots, i_N) = v_{i_1,\ldots,i_N}$ for all $(i_1, \ldots, i_N) \in \{0,1\}^N$.

If $g : K_N \longrightarrow \mathbb{R}^m$ is a multi-affine function satisfying (6), then $h := f - g$ is multi-affine, and $h(i_1, \ldots, i_N) = 0$ for all $(i_1, \ldots, i_N) \in \{0,1\}^N$. By Lemma 1, $h \equiv 0$, hence f defined in (7) is unique. □

Proposition 2. *Let $f : K_N \longrightarrow \mathbb{R}^m$ be a multi-affine function, and let $(\lambda_1, \ldots, \lambda_N) \in [0,1]^N$. Then $f(\lambda_1, \ldots, \lambda_N)$ is a convex combination of $\{f(i_1, \ldots, i_N) \mid i_1, \ldots, i_N \in \{0,1\}\}$, i.e. $f(\lambda_1, \ldots, \lambda_N)$ is a convex combination of the values of f at the vertices of K_N.*

Proof. Let $(\lambda_1, \ldots, \lambda_N) \in [0,1]^N$. Since f is a multi-affine function, representation (7) is also valid for f, with $v_{i_1,\ldots,i_N} = f(i_1, \ldots, i_N)$ for all $(i_1, \ldots, i_N) \in \{0,1\}^N$. So, in the point $(\lambda_1, \ldots, \lambda_N)$ we have

$$f(\lambda_1, \ldots, \lambda_N) = \sum_{i_1,\ldots,i_N \in \{0,1\}} \prod_{k=1}^{N} (1-\lambda_k)^{1-i_k} \lambda_k^{i_k} f(i_1, \ldots, i_N). \tag{8}$$

Also the identity function $h \equiv 1$ is multi-affine. In this situation, representation (7) applies with $v_{i_1,\ldots,i_N} = 1$ for $(i_1, \ldots, i_N) \in \{0,1\}^N$. So in the point $(\lambda_1, \ldots, \lambda_N)$:

$$\sum_{i_1,\ldots,i_N \in \{0,1\}} \prod_{k=1}^{N} (1-\lambda_k)^{1-i_k} \lambda_k^{i_k} = 1. \tag{9}$$

Combining (8) and (9), it is apparent that (8) represents $f(\lambda_1, \ldots, \lambda_N)$ as a convex combination of the values of f at the vertices of K_N. □

Corollary 1. *Let $f : K_N \longrightarrow \mathbb{R}^m$ be a multi-affine function. Let $(\lambda_1, \ldots, \lambda_N) \in K_N$, and let F be the face of K_N of lowest dimension of which $(\lambda_1, \ldots, \lambda_N)$ is an element. Then $f(\lambda_1, \ldots, \lambda_N)$ is a convex combination of the values of f at the vertices of F.*

4 Necessary conditions for feedback control to a facet

Proposition 3. *Let P_N be a full-dimensional polytope in $\mathbb{R}^N$ with vertices $v_1, \ldots, v_M$, $(M \geq N+1)$. Let $F_1, \ldots, F_K$ denote the facets of P_N, with normal vectors $n_1, \ldots, n_K$, respectively, pointing out of the polytope P_N. For $i \in \{1, \ldots, K\}$, let $V_i \subset \{1, \ldots, M\}$ be the index set such that $\{v_j \mid j \in V_i\}$ is the set of vertices of the facet F_i. Conversely, for every $j \in \{1, \ldots, M\}$, the set $W_j \subset \{1, \ldots, K\}$ contains the indices of all facets of which v_j is a vertex. Consider the system*

$$\dot{x} = f(x) + G(x) \cdot u, \qquad x(0) = x_0, \tag{10}$$

on the polytope P_N, where $f : P_N \longrightarrow \mathbb{R}^N$ and $G : P_N \longrightarrow \mathbb{R}^{N \times m}$ are assumed to be Lipschitz-continuous functions. If there exists a feedback $u = k(x)$, with $k : P_N \longrightarrow U$ a Lipschitz-continuous function, that solves Control Problem 1 with exit facet F_1, then there exist inputs $u_1, \ldots, u_M \in U$ such that

(1) $\forall j \in V_1$:

(a) $n_1^T(f(v_j) + G(v_j)u_j) > 0$,
(b) $\forall i \in W_j \backslash \{1\} : n_i^T(f(v_j) + G(v_j)u_j) \leq 0$.

(2) $\forall j \in \{1, \ldots, M\} \backslash V_1$:

(a) $\forall i \in W_j : n_i^T(f(v_j) + G(v_j)u_j) \leq 0$,
(b) $\sum_{i \in W_j} n_i^T(f(v_j) + G(v_j)u_j) < 0$.

Idea of the proof: Suppose that the Lipschitz - continuous function $k : P_N \longrightarrow U$ generates a feedback law $u(t) = k(x(t))$, that solves Control Problem 1. Then the inputs $u_j = k(v_j) \in U$, $(j = 1, \ldots, M)$, obtained by applying feedback k to the vertices $v_1, \ldots, v_M$, satisfy (1) and (2). The proof of this claim is carried out in a similar way as for affine systems (see [6], proof of Proposition 3.1).

The necessary conditions stated in Proposition 3 consist of a set of strict and non-strict linear inequalities on the inputs to the system at the vertices of the polytope P_N. Since also the input set U is assumed to be polyhedral, the existence of a solution $u_1, \ldots, u_M \in U$ may be checked, using existing software for polyhedral sets, like e.g. [10, 14]. The computation is further facilitated by the fact that the inequalities for each input are completely decoupled. Note that the formulation in Proposition 3 is more general than needed in this paper; the claim is valid for arbitrary full-dimensional polytopes P_N and for systems described by Lipschitz-continuous dynamics.

5 Sufficient conditions for feedback control to a facet

In this section, first sufficient conditions for the solvability of Control Problem 1 are stated in terms of the feedback function k. These conditions have to be satisfied on the polytope P_N or its facets. For multi-affine systems on the N-dimensional unit cube, convexity properties are used to transform these conditions into requirements on the inputs to the system at the vertices of the cube K_N. These conditions turn out to be comparabe with the necessary conditions described in Proposition 3.

Theorem 1. *Let P_N be a full-dimensional polytope in $\mathbb{R}^N$ with facets $F_1, \ldots, F_K$, and let $n_1, \ldots, n_K$ denote the normal vectors of $F_1, \ldots, F_K$, respectively, pointing out of the polytope P_N. Consider the system*

$$\dot{x} = f(x) + G(x) \cdot u, \qquad x(0) = x_0,$$

on the polytope P_N, with f and G Lipschitz-continuous functions. If there exists a Lipschitz function $k : P_N \longrightarrow U$, such that

(i) $\forall x \in P_N : n_1^T(f(x) + G(x) \cdot k(x)) > 0$,

(ii) $\forall i \in \{2, \ldots, K\}$ $\forall x \in F_i : n_i^T(f(x) + G(x) \cdot k(x)) \leq 0$,

then the feedback law $u = k(x)$ solves Control Problem 1 with exit facet F_1.

Proof. If in condition *(ii)* the inequality is strict, then the proof is straightforward. Since the polytope P_N is compact, and the function $x \mapsto n_1^T(f(x)+G(x)\cdot k(x))$ is continuous, condition *(i)* implies that there exists a $c > 0$, such that for all $x \in P_N$: $n_1^T(f(x) + G(x) \cdot k(x)) \geq c$. So the closed-loop system will move in the direction of F_1 with a strictly positive speed of at least c, and the polytope P_N is left in finite time. Condition *(ii)* with strict inequality indicates that the state of the closed-loop system can not leave P_N through any of the facets $F_2, \ldots, F_K$. So the state of the closed-loop system will leave P_N through F_1 in finite time.

The extension of the proof to the non-strict inequality in *(ii)* may be carried out in a similar way as for affine systems (see [6]). □

Theorem 2. *Let K_N be the N-dimensional unit cube in $\mathbb{R}^N$, and consider the multi-affine system*

$$\dot{x} = f(x) + Bu, \qquad x(0) = x_0 \in K_N$$

on K_N, with $B \in \mathbb{R}^{N\times m}$, $f : K_N \longrightarrow \mathbb{R}^N$ multi-affine, and $u \in U$, with $U \subset \mathbb{R}^m$ a polyhedral set. Each vertex $(i_1, \ldots, i_N) \in \{0,1\}^N$ of K_N is also a vertex of the facets $x_k = i_k$, $(k = 1, \ldots, N)$, with normal vectors $(-1)^{i_k+1}e_k$, pointing out of K_N. Let $F_1 := K_N \cap \{x \in \mathbb{R}^N \mid x_1 = 1\}$ be the exit facet of K_N. Assume that in every vertex $(i_1, \ldots, i_N) \in \{0,1\}^N$ there exists an input $u_{i_1,\ldots,i_N}$ such that $\forall(i_1, \ldots, i_N) \in \{0,1\}^N$:

$$\begin{aligned} &(1) \quad e_1^T(f(i_1, \ldots, i_N) + Bu_{i_1,\ldots,i_N}) > 0, \\ &(2) \quad \forall k \in \{2, \ldots, N\} : \\ &\qquad (-1)^{i_k+1}e_k^T(f(i_1, \ldots, i_N) + Bu_{i_1,\ldots,i_N}) \leq 0. \end{aligned} \tag{11}$$

Let $k : K_N \longrightarrow U$ be the unique multi-affine function satisfying

$$\forall(i_1, \ldots, i_N) \in \{0,1\}^N : \ k(i_1, \ldots, i_N) = u_{i_1,\ldots,i_N},$$

that may be constructed using formula (7). Then the continuous multi-affine feedback law $u = k(x)$ solves Control Problem 1.

Proof. The closed-loop dynamics is described by the multi-affine function $f(x) + Bk(x)$. According to Proposition 2, for every $x \in K_N$, $f(x) + Bk(x)$ is a convex combination of $\{f(i_1, \ldots, i_N) + Bk(i_1, \ldots, i_N) \mid i_1, \ldots, i_N \in \{0,1\}\}$. Since by construction $k(i_1, \ldots, i_N) = u_{i_1,\ldots,i_N}$, condition (1) in (11) implies that

$$\forall x \in K_N : \ e_1^T(f(x) + Bk(x)) > 0,$$

and condition *(i)* of Theorem 1 is satisfied.

Similarly, if F_j is a facet of K_N, different from F_1, and if F_j is described by $x_j = i_j$ for a fixed $i_j \in \{0,1\}$, then Corollary 1 and the definition of k imply that for every $x \in F_j$, the value of $f(x) + Bk(x)$ is a convex combination of $\{f(i_1, \ldots, i_N) + Bu_{i_1,\ldots,i_N} \mid i_1, \ldots, i_{j-1}, i_{j+1}, \ldots, i_N \in \{0,1\}\}$. Hence condition (2) (in combination with condition (1)) of formula (11) implies that

$$\forall x \in F_j : \ (-1)^{i_j+1}e_j^T(f(x) + Bk(x)) \leq 0,$$

and condition *(ii)* of Theorem 1 is satisfied. □

For multi-affine systems on the unit cube the sufficient conditions stated in Theorem 2 differ only slightly from the necessary conditions in Proposition 3: for vertices $(0, i_2, \ldots, i_N)$ of the facet $x_1 = 0$ the necessary condition

$$\forall i_2, \ldots, i_N \in \{0,1\} :$$
$$e_1^T(f(0, i_2, \ldots, i_N) + Bu_{0,i_2,\ldots,i_N}) \geq 0,$$

is replaced by the strict inequality

$$\forall i_2, \ldots, i_N \in \{0,1\} :$$
$$e_1^T(f(0, i_2, \ldots, i_N) + Bu_{0,i_2,\ldots,i_N}) > 0,$$

to obtain a sufficient condition.

Checking the sufficient conditions in formula (11) of Theorem 2 requires the solution of 2^N systems of N linear inequalities in m unknowns: for each vertex of K_N, one system of N linear inequalities in the unknown $u \in \mathbb{R}^m$. If a solution exists, construction of a multi-affine feedback is immediate, using formula (7).

Remark 1. *Conditions (1) and (2) in formula (11) of Theorem 2 provide polyhedral sets $U_{i_1,\ldots,i_N}$ of controls at the vertices $(i_1, \ldots, i_N)$ that solve Problem 1. If all the sets $U_{i_1,\ldots,i_N}$ are non-empty, then one can choose a representant $u_{i_1,\ldots,i_N}$ from each set and construct the feedback control using formula (7). An interesting special case is when $\bigcap_{i_1,\ldots,i_N\in\{0,1\}} U_{i_1,\ldots,i_N} \neq \varnothing$. An element $\bar{u} \in \bigcap_{i_1,\ldots,i_N\in\{0,1\}} U_{i_1,\ldots,i_N}$ can be used as a constant (independent of the current state) control that solves Problem 1. Note that this is consistent with (7): if $u_{i_1,\ldots,i_N} = \bar{u}$ in all vertices of a cube, then $u(x) = \bar{u}$. This case might be extremely useful for practical situations when the state is not available for feedback.*

6 Case study: gene transcription control in *Vibrio fischeri*

Vibrio fischeri is a marine bacterium that can be found both as free-living organism and as a symbiont of some marine fish and squid. As a free-living organism, *V. fischeri* exists at low densities and appears to be non-luminescent. As a symbiont, the bacteria live at high densities and are, usually, luminescent.

The luminescence in *V. fischeri* is controlled by the transcriptional activation of the *lux* genes [9]. A detailed description and mathematical modeling is given in [2], where a conventional, highly non-linear, purely continuous model is compared to a lower dimensional, switched system with multi-affine dynamics in each mode.

Under reasonable assumptions, the system of differential equations describing the dynamics of one mode of the simplified hybrid model is three dimensional $x = [x_1\, x_2\, x_3]^T$ with two inputs $u = [u_1\, u_2]^T$ in the form given by (2) with

$$f(x) = \begin{bmatrix} k_2x_2 - k_1x_1x_3 \\ k_1x_1x_3 - k_2x_2 \\ k_2x_2 - k_1x_1x_3 - nx_3 \end{bmatrix}, \quad B = \begin{bmatrix} 1 & 0 \\ 0 & 0 \\ 0 & n \end{bmatrix}$$

The state variables represent cellular concentrations of different species and the parameters are binding, dissociation and diffusion rates:

$$\begin{array}{lcl} x_1 & = & \text{protein LuxR } (ml^{-3}) \\ x_2 & = & \text{complex Ai-LuxR } (ml^{-3}) \\ x_3 & = & \text{autoinducer Ai}(ml^{-3}) \\ k_1 & = & \text{binding rate constant } (30\, l^3m^{-1}t^{-1}) \\ k_2 & = & \text{dissociation rate constant } (10\, t^{-1}) \\ n & = & \text{diffusion constant } (10\, t^{-1}) \end{array}$$

where m, l, and t are units for mass, length, and time, respectively. The control variable u_1 could be physically represented by a plasmid producing protein LuxR, while u_2 is an external source of autoinducer. We want to design a multi-affine feedback control so that all states in the rectangle

$$R_3 = \{x = [x_1\, x_2\, x_3]^T \in \mathbb{R}^3 \mid 1 \leq x_i \leq 2,\ i = 1, 2, 3\}$$

are driven through the facet $x_2 = 2$. In the larger hybrid system, this could correspond to steering the system so that the lux gene is switched on. Also, the controls are supposed to be constrained in the rectangle

$$U = \{20 \leq u_1 \leq 60,\ 1 \leq u_2 \leq 10\}$$

The vector field of the uncontrolled system ($u = 0$) is plotted in Figure 1 (a). We can see that the vector field already has a positive component along e_2, as desired. On the other hand, the uncontrolled vector field would steer the system out of the rectangle through $x_1 = 1$ and $x_3 = 1$, which is not desired. So, in this problem, we expect the controls to solve the "stay inside" condition.

First, for simplicity, we change the coordinates so that the control problem is reduced to the unit cube K_3. In this particular case, this consists of translations $z_i = x_i - 1$. In the unit cube the dynamics are described by $\dot{z} = \tilde{f}(z) + Bu$, where

$$\bar{f}(z) = \begin{bmatrix} -k_1 + k_2 - k_1z_1 + k_2z_2 - k_1z_3 - k_1z_1z_3 \\ k_1 - k_2 + k_1z_1 - k_2z_2 + k_1z_3 + k_1z_1z_3 \\ -k_1 + k_2 - n - k_1z_1 + k_2z2 - k_1z_3 - nz_3 - k_1z_1z_3 \end{bmatrix}$$

It is easy to see that

$$e_2^T\dot{z}|_{(i_1,1,i_3)} > 0, \quad -e_2^T\dot{z}|_{(i_1,0,i_3)} < 0, \ i_1, i_3 \in \{0,1\},$$

mainly because the binding rate k_1 is significantly higher than the dissociation rate k_2. The two above conditions are equivalent to condition (1) in formula (11) of Theorem 2 and prove that the vector field has a positive component along e_2 everywhere in K_3, as observed at the beginning of this section.

To make sure that the system does not leave the rectangle through any facet different from $z_2 = 1$, we need to design controls. For facet $z_3 = 1$, we require $e_3^T\dot{z}\,|_{(i_1,i_2,1)} \leq 0$ which is equivalent to

$$u_2^{001} \leq 7, \ , u_2^{011} \leq 6, \ u_2^{101} \leq 13, \ u_2^{111} \leq 12 \qquad (12)$$

On the opposite facet $z_3 = 0$, the "stay inside" conditions $-e_3^T\dot{z}\,|_{(i_1,i_2,0)} \leq 0$ translate to

$$u_2^{000} \geq 3, \ , u_2^{010} \geq 2, \ u_2^{100} \geq 6, \ u_2^{110} \geq 5 \qquad (13)$$

For facet $z_1 = 1$, $e_1^T\dot{z}\,|_{(1,i_2,i_3)} \leq 0$ is equivalent to

$$u_1^{100} \leq 50, \ u_1^{101} \leq 110, \ u_1^{110} \leq 40, \ u_1^{111} \leq 100 \qquad (14)$$

Finally, for $z_1 = 0$, $-e_1^T\dot{z}\,|_{(0,i_2,i_3)} \leq 0$ become

$$u_1^{000} \geq 20, \ u_1^{001} \geq 50, \ u_1^{010} \geq 10, \ u_1^{011} \geq 40 \qquad (15)$$

According to the above conditions, we can choose the controls at the vertices:

$$u_{000} = \begin{bmatrix} 30 \\ 4 \end{bmatrix}, \ u_{001} = \begin{bmatrix} 60 \\ 6 \end{bmatrix}, \ u_{010} = \begin{bmatrix} 20 \\ 3 \end{bmatrix},$$

$$u_{011} = \begin{bmatrix} 50 \\ 5 \end{bmatrix}, \ u_{100} = \begin{bmatrix} 30 \\ 7 \end{bmatrix}, \ u_{101} = \begin{bmatrix} 50 \\ 10 \end{bmatrix},$$

$$u_{110} = \begin{bmatrix} 20 \\ 6 \end{bmatrix}, \ u_{111} = \begin{bmatrix} 40 \\ 10 \end{bmatrix}$$

Going back to the original coordinates, the multi-affine feedback control is given by $u(x) = [u_1(x), u_2(x)]^T$ with

$$\begin{aligned} u_1(x) &= -10(x_2 + x_1(-1 + x_3) - 4x_3), \\ u_2(x) &= x_1(3 + x_2(-1 + x_3)) - (-2 + x_2)x_3 \end{aligned} \qquad (16)$$

The controlled vector field is plotted in Figure 1 (b).

A careful examination of (12) and (13) shows that a constant $u_2 = 6$ solves the problem, according to Remark 1. We cannot say the same thing about u_1, because the intersection of the allowed controls u_1 at the vertices is empty, as it can be noticed from (14) and (15).

The controlled vector field with u_1 as in (16) and $u_2 = 6$ is given in Figure 1 (c).

7 Concluding remarks

For multi-affine systems on the N-dimensional unit cube, necessary conditions were derived for the existence of a

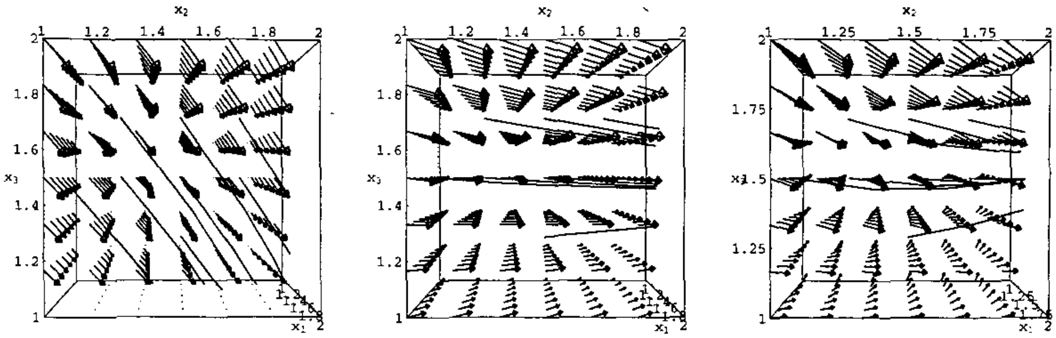

Figure 1: The orientation of the vector field in the rectangle $1 \leq x_i \leq 2$, $i = 1, 2, 3$ together with some trajectories originating within: (a) the uncontrolled case, (b) the controlled case using (16), and (c) the controlled case with $u_2 = 6$.

continuous feedback law, that realizes the control objective of steering the state in finite time to a particular facet of the cube. These conditions consist of linear inequalities on the inputs at the vertices of the cube. For the same control problem also a set of (slightly stronger) sufficient conditions in terms of linear inequalities was obtained, and a method for constructing a continuous multi-affine state feedback law solving the reachability problem under consideration was described. The method can be applied to the control of hybrid models of bioregulatory networks. A case study of gene transcription control for the bacterium Vibrio fischeri was presented. Such approaches may lead to novel methods for designing and engineering biological circuits.

References

[1] Alur, R., C. Belta, V. Kumar, M. Mintz, G. J. Pappas, H. Rubin, and J. Schug, "Modeling and analyzing biomolecular networks", *Computing in Science and Engineering*, January/February (2002), pp. 20–31.

[2] Belta, C., J. Schug, T. Dang, V. Kumar, G. J. Pappas, H. Rubin, and P. Dunlap, "Stability and reachability analysis of a hybrid model of luminescence in the marine bacterium v. fischeri", *40th IEEE Conference on Decision and Control*, Orlando, FL, 2001.

[3] Chutinam, A., and B. Krogh, "Verification of polyhedral-invariant hybrid automata using polygonal flow pipe approximations", In F. Vaandrager and J. H. van Schuppen, editors, *Hybrid Systems: Computation and Control*, volume 1569 of *Lecture Notes in Computer Science*. Springer-Verlag, Berlin, 1999.

[4] Dang, T., *Verification and Synthesis of Hybrid Systems*, PhD thesis, Institut National Polytechnique de Grenoble, Laboratoire Verimag, 2000.

[5] Habets, L.C.G.J.M., and J.H. van Schuppen, "Control of piecewise-linear hybrid systems on simplices and rectangles", In M.D. Di Benedetto and A.L. Sangiovanni-Vincentelli, editors, *Hybrid Systems: Computation and Control*, volume 2034 of *Lecture Notes in Computer Science*, Springer-Verlag, Berlin, 2001, pp. 261–274.

[6] Habets, L.C.G.J.M., and J.H. van Schuppen, "A control problem for affine dynamical systems on a full-dimensional polytope", *Technical report*, CWI, Amsterdam, 2001.

[7] Habets, L.C.G.J.M., and J.H. van Schuppen, "A controllability result for piecewise-linear hybrid systems", *Proc. European Control Conference (ECC 2001)*, Porto, 2001, pp. 3870–3873.

[8] Henzinger, T.A., P.-H. Ho, and H. Wong-Toi, "A user guide to HYTECH", In E. Brinksma, W.R. Cleaveland, K.G. Larsen, T. Margaria, and B. Steffen, editors, *TACAS 95: Tools and Algorithms for the Construction and Analysis of Systems*, volume 1019 of *Lecture Notes in Computer Science*, Springer-Verlag, Berlin, 1995, pp. 41–71.

[9] James, S., P. Nilsson, G. James, S. Kjelleberg, and T. Fagerstrom, "Luminescence control in the marine bacterium vibrio fischeri: an analysis of the dynamics of lux regulation", *Journal of molecular biology*, 2000, vol. 296, pp. 1127–1137.

[10] Jeannet, B., "Convex polyhedra library", *Technical report*, Verimag, Grenoble, 1999.

[11] Lynch, N., and B. H. Krogh, editors, *Hybrid Systems: Computation and Control*, volume 1790 of *Lecture Notes in Computer Science*, Springer-Verlag, Berlin, 2000.

[12] Sontag, E.D., "Nonlinear regulation: The piecewise linear approach", *IEEE Trans. Automatic Control*, vol. 26, 1981, pp. 346–358.

[13] van Schuppen, J.H., "A sufficient condition for controllability of a class of hybrid systems", In T. A. Henzinger and S. Sastry, editors, *Hybrid Systems: Computation and Control*, volume 1386 of *Lecture Notes in Computer Science*, pages 374–383. Springer-Verlag, Berlin, 1998.

[14] Wilde, D.K., "A library for doing polyhedral operations", *Technical report*, IRISA, Rennes, 1993, Publication Interne 785.