Systems & Control Letters 68 (2014) 9–19

Contents lists available at ScienceDirect

Systems & Control Letters

journal homepage: www.elsevier.com/locate/sysconle

A small-gain result for orthant-monotone systems under mixed feedback

David Angeli [a,b], Germán A. Enciso [c,*], Eduardo D. Sontag [d]

[a] Department of Electrical and Electronic Engineering, Imperial College London, UK

[b] Dip. Sistemi e Informatica, University of Firenze, Italy

[c] Department of Mathematics, University of California, Irvine, United States

[d] Department of Mathematics, Rutgers University, United States

ARTICLE INFO

Article history:
Received 26 June 2013
Received in revised form
5 March 2014
Accepted 7 March 2014

Keywords:
Systems biology
Monotone systems
Mixed feedback
Global asymptotic stability

ABSTRACT

This paper introduces a small-gain result for interconnected orthant-monotone systems for which no matching condition is required between the partial orders in input and output spaces. Previous results assumed that the partial orders adopted would be induced by positivity cones in input and output spaces and that such positivity cones should fulfill a compatibility rule: namely either be coincident or be opposite. Those two configurations correspond to positive feedback or negative feedback cases. We relax those results by allowing arbitrary orthant orders.

A linear example is provided showing that the small-gain iteration used for the negative feedback case is not sufficient for global attractivity under mixed feedback. An algebraic characterization is given of the new small-gain condition, generalizing a result known in the negative feedback case. An application is given to nonlinear protein networks with one positive and one negative feedback loop.

1. Introduction

Monotone dynamical systems [1] and monotone control systems [2] are important classes of models used in various applications, particularly in the emerging field of systems biology. The defining property is the preservation of a partial order for the solutions of the system (precise definitions to be given later). This property has rich consequences in terms of the possible dynamical behaviors that monotone systems may exhibit. For instance, according to the celebrated 'Generic Convergence Theorem' by Hirsch [1], under mild irreducibility assumptions the generic bounded solution of an autonomous monotone system converges towards the set of equilibria. In the case of nonlinear control models, perhaps the simplest example is that of a *cooperative* control system, defined by the equations

$$\dot{x} = f(x, u), \qquad y = h(x), \tag{1}$$

under the assumption that $\frac{\partial f_i}{\partial x_j}(x, u) \geq 0$, $\frac{\partial f_i}{\partial u_k}(x, u) \geq 0$ for every $i, j = 1, \ldots, n$, $i \neq j$, $k = 1, \ldots, m$, and every $x \in X \subseteq \mathbb{R}^n$, $u \in U \subseteq \mathbb{R}^m$. A more general definition of monotone systems will be discussed below, although in that case a change of variables can be used to bring the system into this form. Regarding the output function $h(x)$, assume that there exist $s_1, \ldots, s_m \in \{-1, 1\}$, such that for all $k = 1, \ldots, m$, $i = 1, \ldots, n$, and $x \in X$:

$$s_k \frac{\partial h_k}{\partial x_i}(x) \geq 0.$$

This last equation departs from established results in the literature of control monotone systems, which has been divided into two groups of results. Using the above notation, in *positive feedback* input–output (I/O) systems one assumes that $s_i = 1$, $i = 1, \ldots, m$ [3], whereas in *negative feedback* systems the assumption is that $s_i = -1$, $i = 1, \ldots, m$ [2]. Each of the two assumptions has led to a number of papers that determine the qualitative behavior of the closed loop system

$$\dot{x} = f(x, h(x)) \tag{2}$$

under specific circumstances (see below) as well as a number of applications e.g. [4–8]. For a system with m inputs and outputs, all 2^m combinations of orthant matches are allowed in our new *mixed feedback* framework, compared to the two special cases studied previously. The goal of this paper is to provide sufficient conditions

* Corresponding author. Tel.: +1 949 824 3727.
E-mail addresses: d.angeli@imperial.ac.uk (D. Angeli), enciso@uci.edu (G.A. Enciso), sontag@math.rutgers.edu (E.D. Sontag).

http://dx.doi.org/10.1016/j.sysconle.2014.03.002
0167-6911/

for the global asymptotic stability of (2) in the mixed feedback case, as well as for more general monotone systems.

As a general hypothesis, the system (1) is assumed to converge globally towards a unique steady state $\gamma^X(u)$ under any time-invariant input $u \in U$; the function $\gamma(u) = h(\gamma^X(u))$ is called the *steady-state I/O characteristic* of the system.

Under the negative feedback framework, if the discrete iteration induced by the map γ has a unique globally asymptotically stable fixed point, then (2) also has a globally asymptotically stable steady state. We refer to this theorem as a *small-gain theorem*, and the global convergence of the discrete iteration

$$u_{k+1} = \gamma(u_k) \tag{3}$$

towards a unique fixed point is called the *small-gain condition*. In the linear single-input, single-output case the small-gain condition is equivalent to $|\gamma'(0)| < 1$, hence the name of the theorem. The small-gain theorem allows to prove the global asymptotic stability of systems that are not themselves monotone but can be described as the interconnection of monotone systems. The small-gain condition is necessary as well as sufficient provided one is willing to allow for arbitrary delays in the feedback loop (see below). The result was first proved in [2] for one input, then generalized to systems with multiple inputs and outputs and reaction–diffusion systems [9], multi-valued I/O characteristics [10], and oscillatory systems [11]. See also [12,13].

In the positive feedback case, the main result can be described as establishing a bijection between the stable fixed points of the discrete iteration (3) and the stable steady states of (2) [3]. A generalization to multiple-input, multiple-output (MIMO) systems of the result concerning positive feedback interconnections can be found in [14]. In particular, if the small-gain condition holds, then there is a unique fixed point for the I/O characteristic map, and the closed loop interconnection has a unique globally asymptotically stable steady state. The positive feedback framework has also been generalized and applied to various specific models in [6,15], among others.

In the positive feedback case the function γ is monotonically increasing, that is, if $u \leq v$ (defined componentwise) then $\gamma(u) \leq \gamma(v)$. Similarly, the function $\gamma(\gamma(u))$ is monotonically increasing in the negative feedback case, and this fact is fundamental for the proof of the small-gain theorem. In the mixed feedback framework, it can be shown using the chain rule that $s_k \partial\gamma_k/\partial u_j \geq 0$ for every $k = 1, \ldots, m, j = 1, \ldots, m$. As a possible strategy for a proof in the mixed feedback case, one might think that γ^k is monotone increasing for sufficiently large k. As a simple counterexample, suppose that $\gamma(u) = Au$, where

$$A = \begin{pmatrix} 0.5 & 0.5 \\ -1 & -1 \end{pmatrix}.$$

This function can be the mixed feedback I/O characteristic of a system with $s_1 = 1, s_2 = -1$. However $A^q = (-0.5)^{q-1}A$ for every $q \in \mathbb{N}$, which is not monotonically increasing. Hence the argument used in the proof of the small-gain theorem cannot be simply generalized using higher powers in the mixed feedback case.

It should be stressed that the results presented here constitute a significant extension and unification of two lines of research. Results for monotone control systems under positive and negative feedback, while similar, have remained separate during the decade since the papers [2,3] were first published. The nature of the feedback (positive or negative) in general cannot be changed by carrying out simple coordinate transformations, and the proof of the stability results for positive and negative feedback use different techniques. The extension of the small-gain result to positive feedback systems, as well as to systems that have mixed feedback, can provide a framework for further integration of the two types of results.

Using a linear counterexample, it is shown that the original small-gain condition fails to imply the global attractivity of the closed loop system in the mixed feedback case (Section 8). On the other hand a different iteration is proposed here for the mixed feedback case, involving a *pair* of inputs and thus raising the dimensionality of the associated discrete system to $2m$. A new small-gain condition is proposed, namely that the iterations of this $2m$-dimensional map converge globally towards a single fixed point. An algebraic system of $2m$ equations is also derived and shown to be equivalent to the new small-gain condition. This algebraic system is a generalization of the results developed by Cosner [16] and later in [9] for the negative feedback case, which also convert the m-dimensional small-gain condition into a $2m$ dimensional system of equations.

The case of one positive and one negative input ($m = 2$) is considered as a special case, and the small-gain condition is reduced in that case to studying the iterations of a 1-dimensional, possibly multi-valued map. Lemma 2 and the main result, Theorem 1, together lead to a unified generalization of the SISO theorems proved in both original papers [2,3] for monotone systems under positive and negative feedback. An application is given to the double feedback loop with one positive and one negative cycle, in the context of protein networks with Hill function nonlinearities.

2. Problem formulation

Monotone control systems are usually defined on subsets of Euclidean space. Denote the state space by $X \subseteq \mathbb{R}^n$, the input space by $U \subseteq \mathbb{R}^m$ and the output space by $Y \subseteq \mathbb{R}^p$. Input signals are assumed to be measurable, locally essentially bounded functions of time $u : \mathbb{R}_0^+ \to U$, and $\mathcal{U}$ denotes the set of all such input signals. The set $\mathcal{Y}$ is similarly defined and consists of all continuous functions $y : \mathbb{R}_0^+ \to Y$. An *orthant set* is a subset of Euclidean space of the form $S = S_1 \times \cdots \times S_k$, where each S_i is either $\mathbb{R}_0^+$ or $\mathbb{R}_0^-$. Consider orthant sets $K_U \subseteq \mathbb{R}^m$, $K_X \subseteq \mathbb{R}^n$, and $K_Y \subseteq \mathbb{R}^p$. Partial orders can be defined on U, X and Y by letting for all $u_1, u_2 \in U$, $x_1, x_2 \in X$, $y_1, y_2 \in Y$:

$$u_1 \geq_{K_U} u_2 \Leftrightarrow u_1 - u_2 \in K_U$$
$$x_1 \geq_{K_X} x_2 \Leftrightarrow x_1 - x_2 \in K_X$$
$$y_1 \geq_{K_Y} y_2 \Leftrightarrow y_1 - y_2 \in K_Y.$$

To simplify notations we may omit the subscript $\geq_{\{K_U,K_X,K_Y\}}$ when clear from the context.

We define a (time-invariant) *I/O control system* in the usual way to be given by a state space X, a set of inputs $\mathcal{U}$, an output map $h : X \to Y$, and a function $\varphi : \mathbb{R}_{\geq 0} \times X \times \mathcal{U} \to X$ with the following properties:

1. $\varphi(0, x_0, u) = x_0$, for all $x_0 \in X$ and all $u \in \mathcal{U}$;
2. $\varphi(t_1, \varphi(t_2, x_0, u), \sigma_{t_2}u) = \varphi(t_1 + t_2, x_0, u)$, for all $t_1, t_2 \geq 0$, all $x_0 \in X$ and all $u \in \mathcal{U}$. The operator $\sigma_t : \mathcal{U} \to \mathcal{U}$ denotes the shift by t units backwards in time, that is $(\sigma_t u)(s) = u(s + t)$, and $\mathcal{U}$ is assumed to be closed under this operator.

One can think of $\varphi(t, x_0, u)$ as the solution of the system with initial condition x_0 and input u at time t, and of $h(x)$ as the readout of the system at state $x \in X$. Each initial condition x_0 and input $u \in \mathcal{U}$ produces an output function $y(t) = h(\varphi(t, x_0, u))$, and $y \in \mathcal{Y}$.

Definition 1. An I/O control system is *orthant-monotone with respect to the order sets* K_U, K_X, K_Y if for every $x_1, x_2 \in X$ and $u_1, u_2 \in \mathcal{U}$,

$$u_1(t) \geq_{K_U} u_2(t) \quad \forall\, t \geq 0, x_1 \geq_{K_X} x_2$$
$$\Rightarrow \varphi(t, x_1, u_1) \geq_{K_X} \varphi(t, x_2, u_2) \quad \forall\, t \geq 0. \tag{4}$$

It is also assumed that the map h is orthant-monotone, that is

$$x_1 \geq_{K_X} x_2 \Rightarrow h(x_1) \geq_{K_Y} h(x_2).$$

Notice that in this definition it is equivalent to write $u_1(t) \geq_{K_U} u_2(t)$ for almost every $t \geq 0$, since $u \in \mathcal{U}$ can be re-defined arbitrarily on a set of measure zero. By combining the two equations in this definition, if $u_1(t) \geq_{K_U} u_2(t)$ for (almost) all $t \geq 0$ and $x_1 \geq_{K_X} x_2$, it follows that $y_1(t) \geq_{K_Y} y_2(t)$ for every $t \geq 0$, where $y_i(t) = h(\varphi(t, x_i, u_i))$.

From now on we will restrict our attention to the special case of an I/O orthant-monotone control system arising from a forward-complete system of ordinary differential equations,

$$\dot{x} = f(x, u) \qquad y = h(x), \tag{5}$$

where $f : \tilde{X} \times U \to \mathbb{R}^n$ is defined in some open neighborhood $\tilde{X}$ of X and is locally Lipschitz continuous in x and jointly continuous in x and u, while $h : X \to Y$ is a continuous readout map. In this case $\varphi(t, x_0, u)$ is the solution of the system at time t with initial condition $x_0 \in X$ and input $u \in \mathcal{U}$. Let K_U, K_X, K_Y be orthant cones as before, and let $\alpha \in \{-1, 1\}^m$ be such that $K_U = \{u \in \mathbb{R}^m \mid \alpha_i u_i \geq 0, i = 1, \dots, m\}$. Let $\beta \in \{-1, 1\}^n$, $\delta \in \{-1, 1\}^p$ characterize K_X, K_Y respectively in the same way. It was proved in [2] that system (5) satisfies (4) if f is differentiable and its partial derivatives satisfy

$$\beta_i \beta_j \frac{\partial f_i}{\partial x_j}(x, u) \geq 0, \qquad \beta_i \alpha_k \frac{\partial f_i}{\partial u_k}(x, u) \geq 0, \tag{6}$$

for every $i, j = 1, \dots, n, i \neq j, k = 1, \dots, m, x \in X$, and $u \in U$. The monotonicity of a differentiable function h is equivalent to

$$\beta_i \delta_\ell \frac{\partial h_\ell}{\partial x_i}(x) \geq 0, \tag{7}$$

for all $i = 1, \dots, n$, $\ell = 1, \dots, p$, and $x \in X$. In fact, a change of variables can be carried out to bring the system into the cooperative form $\alpha_k = \beta_j = \delta_\ell = 1$, as described in [2]. However when dealing with non-monotone interaction networks as described below, it will be necessary to consider the more general case with negative interactions.

We are now ready to define the notion of steady-state I/O characteristic.

Definition 2. An I/O control system admits a steady-state I/O characteristic if, for each constant input signal $u \in \mathcal{U}$, there exists a unique $\bar{y} \in Y$, such that for every $x_0 \in X$ the output $y(t)$ satisfies

$$\lim_{t \to \infty} y(t) = \bar{y}.$$

Moreover the map $\gamma : U \to Y$ that to each input value u associates the corresponding asymptotic output value $\bar{y}$ is assumed to be continuous. This map γ is called the steady-state I/O characteristic of the system.

It is easy to prove that $\gamma(\cdot)$ is, for any I/O orthant-monotone system, an orthant-monotone map.

An I/O control system is said to admit an *input-state characteristic* if for every constant input signal $u \in \mathcal{U}$ and every $x_0 \in X$, the solution $x(t) = \varphi(t, x_0, u)$ converges towards a value $\gamma^X(u)$. It is also assumed that $\gamma^X : U \to X$ is a continuous function.

In the following we consider interconnected I/O orthant-monotone systems of the form

$$\begin{aligned} \dot{x}_1 &= f_1(x_1, u_1), \qquad h_1(x_1) = y_1 = u_2, \\ \dot{x}_2 &= f_2(x_2, u_2), \qquad h_2(x_2) = y_2 = u_1, \end{aligned} \tag{8}$$

where $X_1 \subseteq \mathbb{R}^{n_1}, U_1 \subseteq \mathbb{R}^{m_1}, Y_1 \subseteq \mathbb{R}^{p_1}$ and $X_2 \subseteq \mathbb{R}^{n_2}, U_2 \subseteq \mathbb{R}^{m_2}, Y_2 \subseteq \mathbb{R}^{p_2}$ respectively. Also, to make sense of (8) we assume that $Y_2 \subseteq U_1$, $Y_1 \subseteq U_2$, and that $p_2 = m_1$, $p_1 = m_2$. Together, this interconnection forms a single system of differential equations defined on $X_1 \times X_2$. Assume that f_1, f_2, h_1, h_2 are globally Lipschitz, and that X_i is forward invariant under $\dot{x}_i = f_i(x_i, u_0)$ for every constant input $u_0 \in U_i$. Then for every initial condition $(x_1(0), x_2(0))$ the system has a unique solution $(x_1(t), x_2(t))$ defined for all $t \geq 0$ [2]. The outputs $y_i(t) \in \mathcal{Y}_i$ are defined as before.

For technical reasons, which will become clear later, we ask that $U_1, X_1, Y_1, U_2, X_2, Y_2$ be closed boxes, that is cartesian products of possibly unbounded closed real intervals. If the variable x_i is defined on the interval $\mathbb{R}_0^-$, then a change of variable $\bar{x}_i = -x_i$ allows $\bar{x}_i$ to lie in the range $\mathbb{R}_0^+$. However it also changes the sign of all edges involving x_i in the network. Allowing for more general state spaces gives more flexibility to the resulting network.

We do not assume, however, that $K_{U_1} = \pm K_{Y_2}$ *nor that* $K_{U_2} = \pm K_{Y_1}$, and that is the main point of departure of the present paper with respect to previous small-gain results in the literature. We denote by Λ_{12} and Λ_{21}, diagonal matrices of suitable dimensions with diagonal entries in $\{-1, 1\}$ so that

$$K_{U_1} = \Lambda_{21} K_{Y_2}, \qquad K_{U_2} = \Lambda_{12} K_{Y_1}. \tag{9}$$

It is useful in the following developments to introduce the notion of interval for a partially ordered space. Given a partial order $\leq$, we define the set $[a, b] = \{x : a \leq x \leq b\}$, in analogy to intervals of the real line. As we will need more than one partial order even for the same underlying Euclidean space, it is convenient to specify as a subscript the order associated to a particular interval set. Accordingly we let $[a, b]_K$ denote the interval a, b as defined by considering the partial order induced by K.

An easy but essential step in the following developments is to realize that, for the case of orthant-induced orders, intervals are always closed boxes. Moreover, it is possible to express any given box as an interval regardless of the adopted partial order.

Lemma 1. *Let $K_1, K_2 \subset \mathbb{R}^m$ be orthants, and let the diagonal matrix Λ with entries in $\{-1, 1\}$ be such that $K_2 = \Lambda K_1$. Let $\Lambda_+ = \max\{\Lambda, 0\}$, interpreted coordinate-wise, and $\Lambda_- = -\min\{\Lambda, 0\} = I - \Lambda_+$. Then for $a \leq_{K_2} b$,*

$$[a, b]_{K_2} = [\Lambda_+ a + \Lambda_- b, \Lambda_+ b + \Lambda_- a]_{K_1}. \tag{10}$$

Proof. Suppose first that $K_1 = (\mathbb{R}_0^+)^m$, and set $s_1, \dots, s_m \in \{-1, 1\}$ such that $K_2 = \{u \in \mathbb{R}^m \, s_i x_i \geq 0\}$. Then also $\Lambda = \operatorname{diag}(s_1, \dots, s_m)$. One can think of $[a, b]_{K_2}$ as the set of points $u \in \mathbb{R}^m$ such that each u_i lies between a_i and b_i. That is,

$$\begin{aligned} [a, b]_{K_2} &= \{u \in \mathbb{R}^m \mid a_i \leq u_i \leq b_i \text{ if } s_i = 1, \; b_i \leq u_i \leq a_i \text{ if } s_i = -1\} \\ &= \{u \in \mathbb{R}^m \mid \Lambda_+ a + \Lambda_- b \leq_{K_1} u_i \leq_{K_1} \Lambda_+ b + \Lambda_- a\} \\ &= [\Lambda_+ a + \Lambda_- b, \Lambda_+ b + \Lambda_- a]_{K_1}. \end{aligned}$$

For the case of general K_1, suppose that M is a diagonal matrix with diagonal entries in $\{-1, 1\}$, such that $\overline{K}_1 := (\mathbb{R}_0^+)^m = MK_1$. Define $\overline{K}_2 = MK_2$. Then

$$\overline{K_2} = MK_2 = M\Lambda K_1 = M\Lambda M\overline{K}_1 = \Lambda \overline{K}_1.$$

For any $a \leq_{K_2} b$, it holds $Ma \leq_{\overline{K}_2} Mb$, and by the first part of the proof

$$[Ma, Mb]_{\overline{K}_2} = [\Lambda_+ Ma + \Lambda_- Mb, \Lambda_+ Mb + \Lambda_- Ma]_{\overline{K}_1}.$$

Notice that $M[u, v]_K = [Mu, Mv]_{MK}$ for any orthant K and any $u \leq_K v$. Multiplying the above equation by M, the result follows. □

Define the function $\eta : \mathbb{R}^{2m} \to \mathbb{R}^{2m}$, $\eta(a, b) := (\Lambda_+ a + \Lambda_- b, \Lambda_+ b + \Lambda_- a) = (\eta_1(a, b), \eta_2(a, b))$. In this way

$$[a, b]_{K_2} = [\eta_1(a, b), \eta_2(a, b)]_{K_1}. \tag{11}$$

It is worth pointing out that for symmetric intervals this takes the simpler form:

$$[-a, a]_{K_2} = [-\Lambda a, \Lambda a]_{K_1}. \tag{12}$$

Regarding the interconnection in (8) and using the notation in (9), define η^1 and η^2 using the matrices $\Lambda = \Lambda_{12}$ and $\Lambda = \Lambda_{21}$ respectively.

3. Main result

We are now ready to state our main result. We define a generalized discrete iteration analogous to the discrete iteration (3), and we assume as the new small-gain condition that the solutions of this iteration converge towards a unique fixed point of the associated discrete map.

Theorem 1. *Consider a well-posed feedback interconnection of I/O orthant-monotone systems (8), and assume that every solution $(x_1(t), x_2(t))$ is bounded. Suppose both I/O systems admit continuous steady-state I/O characteristics $\gamma^1 : U_1 \to Y_1$ and $\gamma^2 : U_2 \to Y_2$ as well as continuous input-state characteristics. Define the discrete iteration that given $u_1^-(0) \le_{K_{U_1}} u_1^+(0)$ in U_1 calculates input and output values for every $k = 0, 1, 2, \ldots$ as follows:*

$$\begin{aligned} &y_1^-(k) = \gamma^1(u_1^-(k)), \qquad y_1^+(k) = \gamma^1(u_1^+(k)),\\ &(u_2^-(k), u_2^+(k)) = \eta^1(y_1^-(k), y_1^+(k)),\\ &y_2^-(k) = \gamma^2(u_2^-(k)), \qquad y_2^+(k) = \gamma^2(u_2^+(k)),\\ &(u_1^-(k+1), u_1^+(k+1)) = \eta^2(y_2^-(k), y_2^+(k)). \end{aligned} \tag{13}$$

Here η_1, η_2 are as described in (11). Provided that for all initial conditions $u_1^-(0), u_1^+(0)$ the discrete iteration converges towards a unique fixed point $(\bar{u}, \bar{u})$, the closed-loop system is globally convergent. Namely, for every solution $(x_1(t), x_2(t))$ of (8), the functions $y_i(t) = h_i(x_i(t))$ fulfill

$$\lim_{t\to\infty} (y_1(t), y_2(t)) = (\gamma^1(\bar{u}), \bar{u}).$$

Also, every state solution $(x_1(t), x_2(t))$ converges towards a unique globally attractive steady state.

Notice that $u_1^-(k+1) \le_{K_{U_1}} u_1^+(k+1)$ according to this iteration. The proof of Theorem 1 will rely on two results. In the following, given a closed set B denote by $d(p, B) := \min_{s\in B} d(p, s)$, where $d(p, s)$ is the L^∞ metric in Euclidean space.

Remark 1. Small-gain theorems are a classical tool in the study of interconnected systems, [17]. A considerable body of literature has been developed around this theme, by exploiting the so called Input-to-State Stability framework. Two seminal contributions in this respect are [18,19], where the Small-Gain Theorem was first derived in a trajectory-based and Lyapunov-based formulation, respectively. More recently, a considerable effort has been devoted to generalizing these conditions to the case of multiple systems, see for instance [20–22], and/or to relaxing it to the case of integrally Input-to-State Stable subsystems, [23,24] as well as dealing with various ISS formulations, [25].

While the results in this paper only deal with the simple case of two subsystems, we believe that similar ideas could be extended to the case of multiple feedback loops. On the other hand, some peculiar advantages of focusing on monotone systems to state small-gain results are the following:

1. They can be formulated on spaces that are products of closed intervals and therefore not necessarily diffeomorphic to Euclidean space (this occurs rather frequently in biological systems).
2. Input–output gains are derived directly from steady-state Input–output characteristics, rather than from Lyapunov-like dissipation inequalities, removing the need to look for Lyapunov functions.
3. As a consequence, small-gain conditions tend to be tighter, and in fact become necessary if one is willing to allow for arbitrary delays in interconnections or in the case of positive feedback systems.
4. Gain functions are not necessarily symmetric with respect to the equilibrium of interest and small-gain conditions are formulated as nonlinear iterations rather than compositions of $\mathcal{K}^\infty$ functions.
5. Coping with uncertainty is somewhat easier as one may study convergence of the small-gain iteration without explicit knowledge of the fixed point this is converging to (in other words we avoid the usual assumption that the equilibrium should be at 0). For instance, if one of the systems is affected by uncertainty which potentially may shift the equilibrium position, this is only going to affect its own input–output steady state characteristic, and not the gains of both subsystems.

Lemma 2. *Suppose given an orthant-monotone system with continuous steady-state I/O characteristic γ. Let $u \in \mathcal{U}$ be such that $\lim_{t\to\infty} d(u(t), [u^-, u^+]_{K_U}) = 0$. Let $y(t) = h(\varphi(t, x, u))$, where $x \in X$ is an arbitrary initial condition. Then*

$$\lim_{t\to\infty} d(y(t), [\gamma(u^-), \gamma(u^+)]_{K_Y}) = 0. \tag{14}$$

Proof. Notice that if $B = B_1 \times \cdots B_k$ is a box set, $d(p, B) < \alpha$ if and only if $d(p_i, B_i) < \alpha$ for every $i = 1, \ldots, k$. Let $\varepsilon > 0$ be given, and let $\delta > 0$ be such that $d(v, u^\pm) < \delta$ implies $d(\gamma(v), \gamma(u^\pm)) < \varepsilon/2$, where $u^\pm = u^+, u^-$. Such δ exists by continuity of γ. Let w be in the interior of K_U such that $|w| < \delta$, and set $u^{--} = u^- - w$, $u^{++} = u^+ + w$. Thus $[u^-, u^+]_{K_U}$ is contained in the interior of $[u^{--}, u^{++}]_{K_U}$ and $d(u^{--}, u^-) < \delta$, $d(u^{++}, u^+) < \delta$. By assumption, there exists $t_1 > 0$ such that $t > t_1$ implies $u(t) \in [u^{--}, u^{++}]_{K_U}$.

Now define the new input $u_1 = \sigma_{t_1} u$, the state $x_1 = \varphi(t_1, x, u)$, and the output $y_1 = \sigma_{t_1} y(t) = h(\varphi(t, x_1, u_1))$. Also let $y^{--}(t) = h(\varphi(t, x_1, u^{--}))$, $y^{++}(t) = h(\varphi(t, x_1, u^{++}))$, where with a slight abuse of notation we have identified the input values u^{--} and u^{++} with the corresponding constant signals. By orthant-monotonicity,

$$y^{--}(t) \le_{K_Y} y_1(t) \le_{K_Y} y^{++}(t) \quad \forall\, t \ge 0. \tag{15}$$

By definition of steady-state I/O characteristic $y^{--}(t) \to \gamma(u^{--})$ and $y^{++}(t) \to \gamma(u^{++})$ as $t \to \infty$. Hence there exists t_2 such that

$$d(y_1(t), [\gamma(u^{--}), \gamma(u^{++})]_{K_Y}) \le \varepsilon/2 \quad \forall\, t \ge t_2.$$

On the other hand given that $d(\gamma(u^{\pm\pm}), \gamma(u^\pm)) < \varepsilon/2$,

$$d(y_1(t), [\gamma(u^-), \gamma(u^+)]_{K_Y}) \le \varepsilon \quad \forall\, t \ge t_2.$$

By definition of y_1, this is equivalent to the statement

$$d(y(t), [\gamma(u^-), \gamma(u^+)]_{K_Y}) \le \varepsilon \quad \forall\, t \ge t_1 + t_2. \quad \square$$

The following corollary is known as the *converging input, converging state* property for I/O monotone systems, and it is included here for completeness; see also [2,26].

Corollary 1. *Suppose that a given orthant-monotone system admits a continuous input-state characteristic γ^X. Let $u \in \mathcal{U}$ converge towards $\bar{u} \in U$. Then for every $x_0 \in X$, $x(t) = \varphi(t, x_0, u)$ converges towards $\gamma^X(\bar{u})$.*

Proof. Define the auxiliary output set $\tilde{Y} = X$ with the identity output function $\tilde{h}(x) = x$. Since $\gamma(u) = \gamma^X(u)$, this function is also continuous. Let $u^- = u^+ = \bar{u}$. By Lemma 2, $y(t)$ converges towards $\gamma(\bar{u})$. But $y(t) = \varphi(t, x_0, u) = x(t)$, so $x(t)$ converges towards $\gamma^X(\bar{u})$. $\square$

We are now ready to prove the main result.

Pick $x = (x_1, x_2) \in X_1 \times X_2$, and let $y(t) = (y_1(t), y_2(t))$ be the corresponding output response, with $y_1 \in \mathcal{Y}_1$ and $y_2 \in \mathcal{Y}_2$. By assumption y_1 and y_2 are defined for all $t \ge 0$ and bounded.

Given the interconnection rules, so are also u_1 and u_2. Hence, exploiting the fact that U_1 is a box, there exist $\underline{u}_1, \bar{u}_1$ such that $u_1(t) \in [\underline{u}_1, \bar{u}_1]_{K_{U_1}}$ for all $t \geq 0$.

Denote $\underline{y}_1 = \gamma^1(\underline{u}_1), \bar{y}_1 = \gamma^1(\bar{u}_1)$. By Lemma 2, $y_1(t) \to [\underline{y}_1, \bar{y}_1]_{K_{Y_1}}$ as $t \to \infty$. Set $(\underline{u}_2, \bar{u}_2) = \eta^1(\underline{y}_1, \bar{y}_1)$. Hence, by Lemma 1, $u_2(t) \to [\underline{u}_2, \bar{u}_2]_{K_{U_2}}$ as $t \to \infty$. By setting $\underline{y}_2 = \gamma^2(\underline{u}_2), \bar{y}_2 = \gamma^2(\bar{u}_2)$ and applying Lemma 2 once more we get $y_2(t) \to [\underline{y}_2, \bar{y}_2]_{K_{Y_2}}$ as $t \to \infty$. Defining $(\underline{u}_1', \bar{u}_1') = \eta^2(\underline{y}_2, \bar{y}_2)$, by Lemma 1 this is equivalent to $u_1(t) \to [\underline{u}_1', \bar{u}_1']_{K_{U_1}}$.

Denote $u_1^-(0) = \underline{u}_1, u_1^+(0) = \bar{u}_1$, so that $u_1^-(1) = \underline{u}_1', u_1^+(1) = \bar{u}_1'$ according to the iteration (13). By induction one can show that for any k, as t increases it holds that:

$$u_1(t) \to [u_1^-(k), u_1^+(k)]_{K_{U_1}}.$$

As by assumption the discrete iteration (13) converges to a fixed point $(\bar{u}, \bar{u})$ of its associated map, we have that for any $\varepsilon > 0$ it is possible to choose k large enough, so that $|u_1(t) - \bar{u}| \leq 2\varepsilon$ for all sufficiently large t. As $\varepsilon > 0$ is arbitrary, $u_1(t) \to \bar{u}$. This shows that $y_2(t) \to \bar{u}$. A similar argument can be employed to show that $y_1(t) \to \gamma^1(\bar{u})$. Notice that this argument in particular implies that $\gamma^2 \circ \gamma^1(\bar{u}) = \bar{u}$.

Finally, consider the state solution of the system given by $\dot{x}_i = f_i(x_i, u_i)$ with initial condition $x_i(0)$, for $i = 1, 2$. Since u_i are converging inputs, the state functions $x_1(t), x_2(t)$ are also convergent towards the unique states $\gamma^{1,X}(\bar{u})$ and $\gamma^{2,X}(\gamma^1(\bar{u}))$ respectively, by Corollary 1. □

It is worth pointing out that, unlike classical small-gain theorems such as [18], boundedness of solutions is assumed rather than being a consequence of the small-gain condition. This was remarked also in [2], where additional technical assumptions are provided to ensure boundedness for the case of monotone systems of differential equations in feedback.

Let us mention that the positive feedback case corresponds here to $\Lambda_{12} = I_{m_1}, \Lambda_{21} = I_{m_2}$. As $\eta^i(a, b) = (a, b), i = 1, 2$, the iteration (13) decouples into two identical and non-interacting subsystems. Instead, the negative feedback case amounts to $\Lambda_{12} = I_{m_1}$ and $\Lambda_{21} = -I_{m_2}$. In this case, $\eta^1(a, b) = (a, b)$ and $\eta^2(a, b) = (b, a)$. Iteration (13) looks coupled and seems to depart from the original criterion proposed in [2]. However, even iterates of (13) exhibit the desirable decoupled structure of two identical non-interacting subsystems. This allows one to reduce the dimension of the iteration from $2m_1$ to just m_1 and restate the results in terms of the iteration originally proposed in [2].

Remark 2. It is worth pointing out that an even more general class of systems fulfilling the small-gain theorem are those for which the properties expressed in Lemma 2 and Corollary 1 hold, regardless of any monotonicity assumptions.

Single interconnection. The same argument can be carried out for the interconnection of a single I/O orthant-monotone system under unity feedback rather than the interconnection of two separate systems in (8). Let $U \subseteq \mathbb{R}^m$ be a box set, $X \subseteq \mathbb{R}^n$ a state space, and $Y \subseteq U$. For orthant cones $K_U \subseteq \mathbb{R}^m, K_X \subseteq \mathbb{R}^n, K_Y \subseteq \mathbb{R}^m$, consider an I/O orthant-monotone system (5) closed under unity feedback, forming the closed loop interconnection

$$\dot{x} = f(x, u), \qquad h(x) = y = u. \tag{16}$$

Let Λ be a diagonal matrix such that $K_U = \Lambda K_Y$, and η defined as in (11) such that

$$[a, b]_{K_Y} = [\eta_1(a, b), \eta_2(a, b)]_{K_U}. \tag{17}$$

Suppose that the system has steady state I/O characteristic γ, and consider the discrete iteration that given $u^-(0) \leq_{K_U} u^+(0)$ calculates

$$\begin{aligned} &y^-(k) = \gamma(u^-(k)), \qquad y^+(k) = \gamma(u^+(k)), \\ &(u^-(k+1), u^+(k+1)) = \eta(y^-(k), y^+(k)). \end{aligned} \tag{18}$$

Proposition 1. *Given system (16) admitting bounded solutions, assume that the discrete iteration (18) converges towards a unique fixed point $(\bar{u}, \bar{u})$ of the associated discrete map. Then the solutions $x(t)$ of (16) are globally convergent towards a unique steady state, and $y(t) := h(x(t)) \to \bar{u}$ as $t \to \infty$.*

The proof of this proposition is analogous to that of Theorem 1. This simpler framework will be used in the next section for further analysis of the convergence of the iteration (18). It should be clear that $\bar{u}$ satisfies the fixed point properties $\bar{u} = \gamma(\bar{u})$ and $(\bar{u}, \bar{u}) = \eta(\gamma(\bar{u}), \gamma(\bar{u}))$.

Notice that the single interconnection case can also represent the original double interconnection system, by using u_1 as the input and defining a single orthant-monotone system as the cascade

$$\begin{aligned} &\dot{x}_1 = f_1(x_1, u_1), \qquad h_1(x_1) = y_1 = u_2, \\ &\dot{x}_2 = f_2(x_2, u_2), \qquad h_2(x_2) = y_2. \end{aligned}$$

However, this can only be done when the order in the output y_1 matches the order in the input u_2, i.e. if $K_{Y_1} = K_{U_2}$. If these two orders are incompatible, then the open loop cascade is not itself an orthant-monotone system. Also notice that in some exceptional scenarios it is possible for the overall system to be orthant-monotone even if both input and output orders are incompatible. As an example see the bipartite network discussed in Fig. 1 of [5].

In a similar way as in Proposition 1, longer interconnections of three or more I/O orthant-monotone systems forming a cycle can be shown to satisfy the same small-gain result.

4. Algebraic equivalence

The key hypothesis of our proposed small-gain results is the so-called small-gain condition, namely that the iterations of a certain discrete function converge globally towards a unique fixed point. In this section we introduce an algebraic system of equations, such that the small-gain condition holds if and only if the algebraic system has a unique solution. We carry out this analysis in the single interconnection framework of Proposition 1.

Let K_U, K_Y be two orthants of $\mathbb{R}^m$. Recall that $U \subseteq \mathbb{R}^m$ is a box set, and that $\gamma : U \to U$ is a continuous function such that $a \leq_{K_U} b$ implies $\gamma(a) \leq_{K_Y} \gamma(b)$, for any variables $a, b \in U$. Although γ is the steady-state I/O characteristic of an I/O orthant-monotone system, it can also be considered here abstractly.

We first cite without proof a result by Dancer [27] in the context of finite-dimensional orthant-monotone systems, which will be used shortly.

Lemma 3. *Let $K \subseteq \mathbb{R}^p$ be an orthant of $\mathbb{R}^p$, and $B \subseteq \mathbb{R}^p$ closed. Suppose that $T : B \to B$ is a continuous function such that $x \leq_K y$ implies $T(x) \leq_K T(y)$. Assume that the system $u_{n+1} = T(u_n)$ has bounded solutions, and that each omega limit set $\omega(x)$ can be K-bounded from below and above. Then for every $x \in B$ there exists a fixed point E of T such that $\omega(x) \leq_K E$.*

A symmetric statement also holds that for every $x \in B$ there is a fixed point E of T such that $\omega(x) \geq_K E$. In particular, if T has a unique fixed point E, then all solutions must converge towards it.

Recall that Λ is an $m \times m$ diagonal matrix with entries in $\{-1, 1\}$ on the diagonal, such that $K_Y = \Lambda K_U$. Define $\Lambda_+ = \max\{\Lambda, 0\}$, $\Lambda_- = -\min\{\Lambda, 0\}$, and $\eta_1(a, b) = \Lambda_+ a + \Lambda_- b$, $\eta_2(a, b) = \Lambda_+ b + \Lambda_- a$, as in Lemma 1. Define the function $F : U \times U \to U \times U$ by

$$F(a, b) := \eta(\gamma(a), \gamma(b)).$$

Notice that the induced discrete-time system

$$(a(k+1), b(k+1)) = F(a(k), b(k)) \tag{19}$$

corresponds to the iteration map in (18), involving the unit feedback interconnection of a single I/O system as described in the end of the previous section. Then we have the following result.

Proposition 2. *Suppose that γ has a unique fixed point e, and that every solution of the discrete system (19) is bounded. The following statements are equivalent:*

(1) *All solutions of (19) with initial condition $a(0) \leq_{K_U} b(0)$ converge towards (e, e).*
(2) *For every $a \leq_{K_U} b$,*

$$a = \Lambda_+\gamma(a) + \Lambda_-\gamma(b), \qquad b = \Lambda_+\gamma(b) + \Lambda_-\gamma(a)$$
$$\text{implies } a = b = e. \tag{20}$$

Proof. Define $A = \{(a, b) \in U \times U \mid a \leq_{K_U} b\}$. Then (2) can be rephrased as stating that the only fixed point of F in A is (e, e). It is clear in this way that (1) implies (2).

Let $a \leq_{K_U} b$. Then $\gamma(a) \leq_{K_Y} \gamma(b)$, and moreover $\eta_1(\gamma(a), \gamma(b)) \leq_{K_U} \eta_2(\gamma(a), \gamma(b))$ by Lemma 1. Therefore

$$a \leq_{K_U} b \quad \text{implies } F_1(a, b) \leq_{K_U} F_2(a, b), \tag{21}$$

where $F(a, b) = (F_1(a, b), F_2(a, b))$. The idea now is to identify a stronger monotonicity condition that is satisfied by the map F itself. For $(a, b), (c, d) \in A$, define a nonstandard orthant order on $\mathbb{R}^m \times \mathbb{R}^m$ using the cone $L = K_U \times (-K_U)$, that is $(a, b) \leq_L (c, d)$ if $a \leq_{K_U} c,\ d \leq_{K_U} b$.

Let $(a, b), (c, d) \in A$. We show that

$$(a, b) \leq_L (c, d) \quad \text{implies } F(a, b) \leq_L F(c, d).$$

In order to prove this, notice that $a \leq_{K_U} c \leq_{K_U} d \leq_{K_U} b$, so that $\gamma(a) \leq_{K_Y} \gamma(c) \leq_{K_Y} \gamma(d) \leq_{K_Y} \gamma(b)$. For every x such that $\gamma(c) \leq_{K_Y} x \leq_{K_Y} \gamma(d)$, it holds $\gamma(a) \leq_{K_Y} x \leq_{K_Y} \gamma(b)$, and therefore $F_1(a, b) \leq_{K_U} x \leq_{K_U} F_2(a, b)$ by Lemma 1. Since $x = F_1(c, d)$ and $x = F_2(c, d)$ satisfy this property, again by Lemma 1, it follows $F_1(a, b) \leq_{K_U} F_1(c, d) \leq_{K_U} F_2(c, d) \leq_{K_U} F_2(a, b)$. But this means $F(a, b) \leq_L F(c, d)$.

Another way to think about this monotonicity condition is to regard $F(a, b)$ as a transformation of order intervals, sending the order interval $[a, b]$ into the interval $[F_1(a, b), F_2(a, b)]$. The monotonicity condition essentially means that F preserves set inclusion, that is $[c, d] \subseteq [a, b]$ implies $[F_1(c, d), F_2(c, d)] \subseteq [F_1(a, b), F_2(a, b)]$.

Define the set $B_e := \{(a, b) \in U \times U | a \leq_{K_U} e \leq_{K_U} b\}$. Then B_e is invariant under F: if $a \leq_{K_U} e \leq_{K_U} b$, then $\gamma(a) \leq_{K_Y} e \leq_{K_Y} \gamma(b)$, and therefore $F_1(a, b) \leq e \leq F_2(a, b)$.

The convergence of the iterations of F towards the unique fixed point is an application of Lemma 3. First we prove that all iterations of F in B_e converge towards (e, e). The continuous map $F : B_e \to B_e$ has bounded solutions, preserves the order $\leq_L$ and has a unique fixed point by (2). If $C \subseteq B_e$ is a compact set, the Dancer lemma requires that C be bounded from above and below in B_e. Here C is $\leq_L$-bounded from above by (e, e). It is also $\leq_L$-bounded from below by $(\hat{a}, \hat{b})$, where $\hat{a} = \inf\{a \mid (a, b) \in C\}$, $\hat{b} = \sup\{b \mid (a, b) \in C\}$ are calculated using the order $\leq_{K_U}$. Both of these sets are compact by compactness of C, so that $\hat{a}, \hat{b}$ are both elements of the box U and $(\hat{a}, \hat{b}) \in B_e$. By the Dancer lemma, all the iterates with initial condition in B_e must converge towards (e, e).

Finally we prove the more general result that all iterations of F in A converge towards (e, e). Let $(c, d) \in A$, and let $(a, b) \in B_e$ such that $a \leq c \leq d \leq b$. Then the iterates $(a(k), b(k))$ of (a, b) converge towards (e, e) by the proposition above. Also, the iterates $(c(k), d(k))$ of (c, d) satisfy $a(k) \leq c(k) \leq d(k) \leq b(k)$ by the $\leq_L$-ordering property of F. The conclusion follows. □

This equivalence nicely generalizes that found by Cosner [16] and also in [9] for the negative feedback case, namely that the small-gain theorem is satisfied whenever there is a unique fixed point of γ and the equations $a = \gamma(b),\ b = \gamma(a)$ imply $a = b = e$. In the negative feedback case $\Lambda_- = I$ and $\Lambda_+ = 0$, so the two conditions are equivalent. The following result is cited without proof from [9], see Corollary 7 in that reference.

Lemma 4. *Suppose that $\dot{x} = f(x, u), y = h(x)$ is an I/O orthant-monotone system under negative feedback, for $U = [u_0, \infty)_{K_U} := \{u \in \mathbb{R}^m \mid u_0 \leq_{K_U} u\}$, and that the open loop system has input-state characteristic γ^X. Assume that there is no pair $u \leq_{K_U} v, u \neq v$, such that $\gamma(u) = v, \gamma(v) = u$. Let $X_0 = \bigcup_{u\in U}[\gamma^X(u_0), \gamma^X(u)]_{K_U}$. Then all solutions of the closed loop system with initial condition in X_0 converge towards a unique steady state $x_* \in X_0$.*

It is interesting to consider the special case of a linear function $\gamma : \mathbb{R}^m \to \mathbb{R}^m$, $e = 0$. In this case F is also a linear function, and the boundedness of solutions of (19) ensures that $\rho(F) \leq 1$, where ρ denotes the spectral radius. Condition (2) states that 1 is not an eigenvalue of F. Condition (1) states that $\rho(F) < 1$, or equivalently, that no eigenvalue λ has magnitude 1. The equivalence between (1) and (2) follows from the monotonicity condition on F using the Perron–Frobenius theorem.

5. The simple mixed feedback case

Since Theorem 1 and the closely related Proposition 1 generalize statements for positive and negative feedback systems, the simplest nontrivial special case must involve at least two inputs and outputs, one under positive feedback and one under negative feedback. This leads to the special case of a single feedback interconnection (16) with $m = 2$, $K_U = (\mathbb{R}_0^+)^2$, $K_Y = \mathbb{R}^- \times \mathbb{R}^+$. In this case we calculate

$$\Lambda = \begin{pmatrix} -1 & 0 \\ 0 & 1 \end{pmatrix}, \qquad \Lambda_+ = \begin{pmatrix} 0 & 0 \\ 0 & 1 \end{pmatrix}, \qquad \Lambda_- = \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix}.$$

Set $\gamma = (\gamma_1, \gamma_2)$, which is not to be confused with the steady-state I/O characteristic functions γ^1, γ^2 in Theorem 1. The left side of Eq. (20) can be written as

$$\begin{pmatrix} a_1 \\ a_2 \end{pmatrix} = \begin{pmatrix} 0 \\ \gamma_2(a) \end{pmatrix} + \begin{pmatrix} \gamma_1(b) \\ 0 \end{pmatrix},$$
$$\begin{pmatrix} b_1 \\ b_2 \end{pmatrix} = \begin{pmatrix} 0 \\ \gamma_2(b) \end{pmatrix} + \begin{pmatrix} \gamma_1(a) \\ 0 \end{pmatrix},$$

that is

$$\begin{aligned} a_1 &= \gamma_1(b_1, b_2) \qquad & b_1 &= \gamma_1(a_1, a_2) \\ a_2 &= \gamma_2(a_1, a_2) \qquad & b_2 &= \gamma_2(b_1, b_2). \end{aligned} \tag{22}$$

The same matrix Λ, and therefore the same Eq. (22), would be obtained if one had used instead $K_U = \mathbb{R}^- \times \mathbb{R}^+$, $K_Y = (\mathbb{R}_0^+)^2$. The current choice of the cones means that the real-valued function $\gamma_1(\cdot, \cdot)$ is decreasing on both its arguments while $\gamma_2(\cdot, \cdot)$ is increasing on both of them. In a sense this special case embodies the general case, since one can permute the coordinates as necessary and use vectors for the variables a_i, b_i. The following lemma offers a systematic way to solve the above nonlinear system of equations, assuming $u_2 = \gamma_2(u_1, u_2)$ has a unique solution for any given u_1.

Lemma 5. *Suppose $m = 2$, $K_U = (\mathbb{R}_0^+)^2$, $K_Y = \mathbb{R}^- \times \mathbb{R}^+$, the function $\gamma : U \to U$ is continuous and bounded, $a \leq b$ implies $\gamma(a) \leq_{K_Y} \gamma(b)$, and γ has a unique fixed point e. Assume that*

(i) *For every $u_1 \geq 0$, the equation $u_2 = \gamma_2(u_1, u_2)$ has a unique solution u_2 denoted by $\psi(u_1)$.*
(ii) *Using the notation $S(u_1) := \gamma_1(u_1, \psi(u_1))$, the equation $u_1 = S(S(u_1))$ has a unique solution.*

Then all solutions of the discrete iteration (19) converge towards (e, e).

Proof. The lemma is proved by verifying that Eq. (22) implies $a = b = e$ and using Proposition 2. First some comments regarding the fixed point e. Since $e_2 = \gamma_2(e_1, e_2)$, then $\psi(e_1) = e_2$. But then $e_1 = \gamma_1(e_1, e_2) = \gamma_1(e_1, \psi(e_1)) = S(e_1)$. In particular e_1 is the solution of $u_1 = S(S(u_1))$.

Now assume that $a, b \in U$ satisfy (22). Then one can solve the bottom two equations given a_1, b_1 i.e. $a_2 = \psi(a_1)$, $b_2 = \psi(b_1)$. Since

$$b_1 = \gamma_1(a_1, \psi(a_1)) = S(a_1), \qquad a_1 = \gamma_1(b_1, \psi(b_1)) = S(b_1),$$

it follows that $a_1 = S(S(a_1))$. By assumption (ii), $a_1 = e_1$. But then $b_1 = S(a_1) = e_1$, $a_2 = \psi(e_1) = e_2$, and $b_2 = \psi(e_1) = e_2$. Therefore $a = b = e$. $\square$

In the case that solutions of the equation $y = \gamma_2(x, y)$ are generally not unique, one can still carry out a similar argument using multi-functions. Denote $\psi(u_1)$ to be the set

$$\psi(u_1) := \{u_2 \mid u_2 = \gamma_2(u_1, u_2)\},$$

and similarly

$$S(u_1) := \{\gamma_1(u_1, u_2) \mid u_2 \in \psi(u_1)\}.$$

Lemma 6. *Suppose $m = 2$, $K_U = (\mathbb{R}_0^+)^2$, $K_Y = \mathbb{R}^- \times \mathbb{R}^+$, the function $\gamma : U \to U$ is continuous and bounded, $a \le b$ implies $\gamma(a) \le_{K_Y} \gamma(b)$, and γ has a unique fixed point e. Using the above multi-function notation, assume that*

(i) *$|\psi(e_1)| = 1$, i.e. the set $\psi(e_1)$ contains exactly one element.*
(ii) *The equation $u_1 \in S(S(u_1))$ has a unique solution.*

Then all solutions of the discrete iteration (19) converge towards (e, e).

Proof. The equation $u_1 \in S(S(u_1))$ is meant in the sense of multi-functions, i.e. it is satisfied if there exist u_1, u_2 such that $u_1 \in S(u_2)$, $u_2 \in S(u_1)$. Once again we first note that e_1 is a solution of this equation. This is because $e_2 \in \psi(e_1)$ and $e_1 = \gamma_1(e_1, e_2) \in S(e_1)$.

Next assume Eq. (22). Then $b_1 \in S(a_1)$, $a_1 \in S(b_1)$, and so both a_1 and b_1 satisfy $u_1 \in S(S(u_1))$. Therefore by (ii), $a_1 = b_1 = e_1$. Now by (i), $u_2 = \gamma_2(e_1, u_2)$ must have the unique solution e_2. Therefore $a_2 = b_2 = e_2$, and $a = b = e$. $\square$

It is interesting to compare this result (and its implication using Proposition 1) with the existing work on SISO positive and negative feedback systems. In the negative feedback case this result implies a version of the SISO small-gain theorem using the so-called Cosner condition and studied in [9,16].

Corollary 2. *Consider a SISO orthant-monotone system $\dot{x}_1 = \bar{f}_1(x_1, u_1)$, $h(x_1) = y_1 = u_1$ under the negative feedback interconnection $\bar{K}_U = \mathbb{R}^+$, $\bar{K}_Y = \mathbb{R}^-$. Assume that the bounded I/O characteristic $\bar{\gamma}$ has a fixed point e_1 and that $u_1 = \bar{\gamma}(\bar{\gamma}(u_1))$ implies $u_1 = e_1$. Then all solutions of the system converge towards a steady state.*

Proof. One can trivially introduce an input u_2 into the system which does not actually influence the solutions, to create a new orthant-monotone system (16) with $m = 2$ as in Lemma 2. The new steady-state I/O characteristic has the form $\gamma_1(u_1, u_2) = \bar{\gamma}(u_1)$, $\gamma_2(u_1, u_2) = e_2$ for any fixed e_2. Assumption (i) is automatically satisfied, since in fact $\psi(u_1) \equiv e_2$ is a single-valued function. Clearly $S(u_1) = \bar{\gamma}(u_1)$, and assumption (ii) holds. By Lemma 2 the iterations of the extended small-gain function converge towards a unique fixed point. By Proposition 1, the result follows. $\square$

The same lemma also implies a special case of the positive feedback result for SISO orthant-monotone systems as described in [3]. For more work on multi-valued functions in the context of I/O monotone systems see the more recent papers [6,15].

Corollary 3. *Consider a SISO orthant-monotone system $\dot{x}_2 = \bar{f}_2(x_2, u_2)$, $h(x_2) = y_2 = u_2$ under positive feedback e.g. $\bar{K}_U = \mathbb{R}^+$, $\bar{K}_Y = \mathbb{R}^+$. Assume that the bounded I/O characteristic $\bar{\gamma}$ has a unique fixed point e_2. Then all solutions of the system converge towards a steady state.*

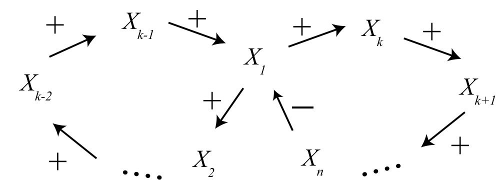

Fig. 1. The network topology of the system of differential equation (23)–(25).

Proof. Once again introduce a mute input u_1, to create a mixed feedback orthant-monotone system as in Lemma 2. Now the steady-state I/O characteristic satisfies $\gamma_1(u_1, u_2) = e_1$ for arbitrary fixed e_1, and $\gamma_2(u_1, u_2) = \bar{\gamma}(u_2)$. For any fixed u_1, $\psi(u_1) = \{u_2 \mid \bar{\gamma}(u_2) = u_2\} = \{e_2\}$, therefore assumption (i) is satisfied. Moreover $S(u_1) = \{e_1\}$ is constant, thus (ii) is also satisfied. By Lemma 2, the iterations of the extended small-gain function converge towards a unique steady state. By Proposition 1, once again the result follows. $\square$

6. Example: double loop network

Consider a system of n differential equations of the following form, which can represent a network of interacting proteins:

$$\dot{x}_1 = c_1 \frac{x_{k-1}^{h_1}}{x_{k-1}^{h_1} + Q_1^{h_1} + x_n^{h_1}} + \alpha_1 - d_1 x_1, \tag{23}$$

$$\dot{x}_k = c_k \frac{x_1^{h_k}}{x_1^{h_k} + Q_k^{h_k}} + \alpha_k - d_k x_k, \tag{24}$$

$$\dot{x}_i = c_i \frac{x_{i-1}^{h_i}}{x_{i-1}^{h_i} + Q_i^{h_i}} + \alpha_i - d_i x_i, \quad i \neq 1, k. \tag{25}$$

Here k is fixed, $1 < k < n$, and i varies between 2 and n, excluding k. This system consists of two feedback loops, one negative and one positive, as described in Fig. 1, where the node X_i represents the ith system. Both loops meet at the node X_1. All individual interactions are positive, except that x_n has an inhibitory effect on the rate of production of x_1 and it displayed in the figure using a blunt end.

There has been much interest in the mathematical biology literature regarding double loop protein regulatory systems with one positive and one negative cycle. While single negative feedback loop systems can present oscillations [28], an additional positive feedback loop provides desirable features such as robustness [29] and the ability to tune amplitude and frequency separately [30]. Positive–negative loops also underlie many excitable systems, for instance bacterial competence [31]. Hill function nonlinearities $x^h/(x^h + Q^h)$ are a function of choice for such systems since they saturate, allow to tune ultrasensitive behavior, and can be implemented through enzymatic reactions [32].

The open loop control system that we associate to the above network is

$$\dot{x}_1 = c_1 \frac{u_1^{h_1} u_2^{h_1}}{u_1^{h_1} u_2^{h_1} + Q_1^{h_1} u_1^{h_1} + 1} + \alpha_1 - d_1 x_1, \tag{26}$$

$$\dot{x}_k = c_k \frac{x_1^{h_k}}{x_1^{h_k} + Q_k^{h_k}} + \alpha_k - d_k x_k, \tag{27}$$

$$\dot{x}_i = c_i \frac{x_{i-1}^{h_i}}{x_{i-1}^{h_i} + Q_i^{h_i}} + \alpha_i - d_i x_i, \quad i \neq 1, k, \tag{28}$$

along with the output $h(x) = (1/x_n, x_{k-1})$ and the feedback interconnection $(u_1, u_2) = h(x)$. It is straightforward to verify that

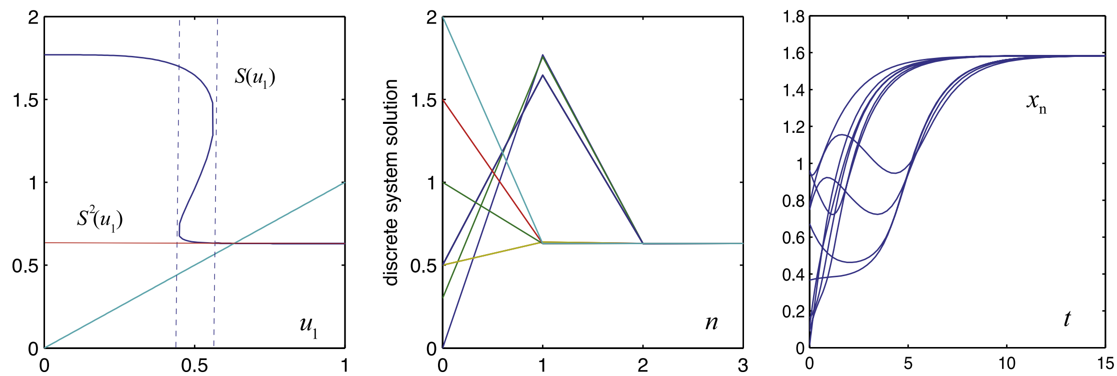

Fig. 2. Simulation of the system (23) using parameter values $n = 5$, $k = 4$, $c_i = 1$, $\alpha_i = 0.2$, $Q_i = 0.5$, $h_i = 4$, $d_i = 0.75$, for $i = 1, \ldots, n$. (a) Graph of the multi-valued function $S(u_1)$ as well as its composition $S^2(u_1) = S(S(u_1))$. (b) Several solutions of the 1D iterated inclusion $v_{q+1} \in S(v_q)$. (c) Several solutions of $x_n(t)$ given random initial conditions.

this system is I/O monotone with respect to the orthant cones $K_U = (\mathbb{R}_0^+)^2$, $K_X = (\mathbb{R}_0^+)^n$, $K_Y = \mathbb{R}^- \times \mathbb{R}^+$. Also, the closed loop of this system is the original double loop network.

Given fixed (u_1, u_2), it is clear that this system converges towards a single steady state, since the open system can be seen as a cascade of linear systems (with nonlinear interconnections). For instance, x_1 converges towards $x_1 = \frac{1}{d_1}(c_1 \frac{(u_1 u_2)^{h_1}}{(u_1 u_2)^{h_1} + (Q_1 u_1)^{h_1} + 1} + \alpha_1) =: r_1(u_1, u_2)$. Setting $r_i(z) := \frac{1}{d_i}(c_i \frac{z^{h_i}}{z^{h_i} + Q_i^{h_i}} + \alpha_i)$ for $i \neq 1$, at steady state

$$x_1 = r_1(u_1, u_2),$$
$$x_2 = r_2 \circ r_1(u_1, u_2), \ldots, x_{k-1} = r_{k-1} \circ \cdots \circ r_1(u_1, u_2) =: q(u_1, u_2).$$

Similarly $x_n = r_n \circ \ldots \circ r_k \circ r_1(u_1, u_2) =: p(u_1, u_2)$. The output of the system is

$$\gamma(u_1, u_2) = h(1/x_n, x_{k-1}) = (1/p(u_1, u_2), q(u_1, u_2)).$$

This function satisfies $a \leq b \rightarrow \gamma(a) \leq_{K_Y} \gamma(b)$ by the construction of the I/O orthant-monotone system.

Corollary 4. *Consider the double loop network described in (23)–(25). Suppose that the function $\gamma(u_1, u_2) = (1/p(u_1, u_2), q(u_1, u_2))$ has a fixed point e, and that the equation $u_2 = q(e_1, u_2)$ has a unique solution. Define the multi-function*

$$S(u_1) = \left\{ \frac{1}{p(u_1, u_2)} \middle| u_2 \text{ solution of } q(u_1, u_2) = u_2 \right\}.$$

If the inclusion $u_1 \in S(S(u_1))$ has a unique solution, then the double loop network is globally attractive towards a single steady state.

Proof. Once again, the inclusion $u_1 \in S(S(u_1))$ is meant to be satisfied if there exists u_2 such that $u_1 \in S(u_2)$, $u_2 \in S(u_1)$. The fact that the equation $u_2 = q(e_1, u_2)$ has a unique solution, together with the uniqueness of the inclusion $u_1 \in S(S(u_1))$ imply that the fixed point e is unique. Lemma 6 can be applied for this system, noting that $S(u_1)$ is as defined in that lemma and that γ is a bounded function. Therefore all solutions of the discrete iteration (13) converge towards (e, e).

Given the linear degradation terms and the bounded production rates for each variable, it is easy to see that the solutions of the closed loop (23)–(25) are uniformly bounded. By Theorem 1, this system is globally attractive towards a single steady state. □

In particular, if $S(u_1)$ is single-valued, the inclusion $u_1 \in S(S(u_1))$ becomes a standard equation $u_1 = S(S(u_1))$ as in Lemma 5. But even if the equation $u_2 = q(u_1 u_2)$ does not have a unique solution u_2 for all given u_1, one can still conclude the global attractivity of the system.

This reduces the analysis from an n-dimensional system of differential equations to a single one-dimensional (multi-)function. The analysis can be carried out computationally for a given set of parameters, or also analytically for systems of smaller size.

Notice that the two loops join at a single node x_1 in this system. This is mostly a notational convenience, and a similar result can be stated when the two loops have multiple variables in common. Also, the exact terms used are not overly relevant, for instance the first equation in the system could be e.g. of the form $\dot{x}_1 = p_1(x_{k-1}) + q_1(x_n) - d_1 x_1$, where p_1 and q_1 are increasing and decreasing functions respectively.

In Fig. 2 we illustrate this system with a numerical example. For $n = 5$ and $k = 4$, the positive and negative feedback loops have each length three. The function $S(u_1)$ is multi-valued in a range of values of u_1 (a), yet for $e_1 \approx 0.63$, it holds that $S(e_1)$ has a unique value and $S(e_1) = e_1$. Hence $q(e_1, u_2) = u_2$ has a unique solution e_2. Also, even though S is not constant, $S^2(u_1)$ is almost a constant function, and it has a unique fixed point. The diagonal line represents the identity function. In (b) several solutions of the inclusion map $v_{q+1} \in S(v_q)$ are displayed. Notice that for the same initial condition 0.5 there can be multiple values at $t = 1$. Corollary 4 shows that the solutions of the associated system must converge globally, as illustrated with several initial conditions in (c).

This analysis illustrates under what conditions the assumptions of Theorem 1 and Proposition 1 are satisfied. The application usually encountered is that of a closed loop system $\dot{z} = g(z)$ to be decomposed as the interconnection of I/O monotone systems, in a similar way as it was carried out above. The deletion of an edge on a negative (positive) feedback loop in the network will lead to a negative (positive) feedback interconnection. The fact that mixed feedback is allowed provides greater flexibility in the decomposition of the system. A flexible choice of edges to be cut can also make it easier for the resulting open loop system to have a steady-state I/O characteristic, which is another of the conditions of the theorem. The small-gain condition was reduced here to an algebraic condition (in the single interconnection case), which is easier to verify. Finally, the condition that the solutions of the system be bounded can be ensured in various ways, for instance by introducing bounded expression rates and linear degradation rates, as is often the case in gene regulatory networks.

7. Linear systems

The case of linear systems deserves special attention, as Theorem 1 is original, to the best of our knowledge, even in the case of finite dimensional orthant-monotone linear systems:

$$\dot{x} = Ax + Bu \qquad y = Cx. \tag{29}$$

To characterize the monotonicity property for a linear system one can use the same infinitesimal conditions described in Eqs. (6), (7), except that all partial derivatives in this case are constant. For example, this system is monotone with respect to the positive orthant orders if and only if all non diagonal entries of A are nonnegative and all entries of B, C are nonnegative.

The steady-state I/O characteristic $\gamma : U \to Y$ is trivially the map $\gamma(u) = \Gamma u$ with

$$\Gamma = -CA^{-1}B.$$

As a consequence of monotonicity $\Gamma K_U \subseteq K_Y$. It is clear from the proof of Theorem 1 that in the case of linear systems since U and Y are Euclidean spaces, it is possible to define iteration (13) by only considering symmetric intervals $[-a, a]$; in fact the iteration maps (for systems with odd characteristics) preserve symmetric intervals. Hence, exploiting the simpler formula (12) one may recast (13) as follows:

$$u(k+1) = \Lambda_{21}\Gamma_2\Lambda_{12}\Gamma_1 u(k),$$

where, for the sake of simplicity, we did not explicitly write the iteration for the interval $[-u(k), u(k)]$, but only for one of its extremes. Here $\Lambda_{12}, \Lambda_{21}$ are defined as in Eq. (9); see also Theorem 2 below for the definition of Γ_1, Γ_2. The condition that the latter be a converging iteration amounts to:

$$\rho(\Lambda_{21}\Gamma_2\Lambda_{12}\Gamma_1) < 1. \tag{30}$$

The following result holds for linear systems:

Theorem 2. *Consider the following interconnected systems:*

$$\begin{aligned} \dot{x}_1 &= A_1x_1 + B_1u_1 \qquad u_2 = y_1 = C_1x_1 \\ \dot{x}_2 &= A_2x_2 + B_2u_2 \qquad u_1 = y_2 = C_2x_2 \end{aligned} \tag{31}$$

with A_1 and A_2 Hurwitz matrices, whose exponentials preserve the cone K_{X_1} and K_{X_2}, respectively. Moreover, we assume that $B_1K_{U_1} \subset K_{X_1}$, $C_1K_{X_1} \subset K_{Y_1}$ and $B_2K_{U_2} \subset K_{X_2}$, $C_2K_{X_2} \subset K_{Y_2}$. Under such assumptions $\Gamma_1 = -C_1A_1^{-1}B_1$ and $\Gamma_2 = -C_2A_2^{-1}B_2$ define orthant-monotone maps, fulfilling $\Gamma_1K_{U_1} \subset K_{Y_1}$ and $\Gamma_2K_{U_2} \subset K_{Y_2}$. Then, provided condition (30) holds, the system (31) is asymptotically stable.

Let now define diagonal matrices $\Delta_1, \Delta_2, \Theta_1, \Theta_2$ with entries in $\{-1, +1\}$ such that $K_{U_1} = \Delta_1(\mathbb{R}_0^+)^{m_1}$, $K_{U_2} = \Delta_2(\mathbb{R}_0^+)^{m_2}$, $K_{Y_1} = \Theta_1(\mathbb{R}_0^+)^{p_1}$ and $K_{Y_2} = \Theta_2(\mathbb{R}_0^+)^{p_2}$. With the above notation $\Lambda_{12} = \Delta_2\Theta_1$ and $\Lambda_{21} = \Delta_1\Theta_2$. Notice moreover that $\Gamma_1K_{U_1} \subset K_{Y_1}$ implies $\Theta_1\Gamma_1K_{U_1} \subset (\mathbb{R}_0^+)^{p_1}$. Hence $\Theta_1\Gamma_1\Delta_1(\mathbb{R}_0^+)^{m_1} \subset (\mathbb{R}_0^+)^{p_1}$. This means that $\Theta_1\Gamma_1\Delta_1$ is a non-negative matrix, and in particular $\Theta_1\Gamma_1\Delta_1 = |\Gamma_1|$ (where $|\cdot|$ denotes componentwise absolute value). Similar considerations apply to $\Theta_2\Gamma_2\Delta_2 = |\Gamma_2|$. The small-gain condition (30) can be equivalently written as:

$$\begin{aligned} 1 &> \rho(\Lambda_{21}\Gamma_2\Lambda_{12}\Gamma_1) = \rho(\Delta_1\Theta_2\Gamma_2\Delta_2\Theta_1\Gamma_1) \\ &= \rho(\Theta_2\Gamma_2\Delta_2\Theta_1\Gamma_1\Delta_1) \\ &= \rho(|\Gamma_2||\Gamma_1|). \end{aligned} \tag{32}$$

Since for linear SISO orthant-monotone systems the impulse response is sign-definite, then the absolute value of the DC-gain equals the $\mathcal{L}_2$ (as well as the $\mathcal{L}_\infty$) induced gain [3]. Notice, then, that condition (32) can be interpreted as the spectral radius of the product of $\mathcal{L}_2$ induced gain matrices being less than one, which is a classical small-gain result for the case of linear systems (see for instance Theorem 7 in [33]).

8. Linear systems: an example

We show below by means of an example how the result can be used. We also point out that in general the absolute values $|\Gamma_2|$ and $|\Gamma_1|$ cannot be avoided, namely the condition that $\rho(\Gamma_2\Gamma_1) < 1$ is *not* enough to guarantee stability for the case of orthant-monotone systems in feedback. This may be counter-intuitive as for the positive feedback case (as well as for the negative feedback one) there is no need to introduce absolute values (indeed for positive feedback Γ_2 and Γ_1 can be taken to be both positive without loss of generality, whereas in the case of negative feedback Γ_1 and Γ_2 can be taken to be of opposite sign, but this is no concern as spectral radius is invariant with respect to sign inversions). Consider the following matrices:

$$A_1 = \begin{bmatrix} -1 & 0 & 1 & 0 \\ 0 & -1 & 0 & 1 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & -10 \end{bmatrix} \qquad B_1 = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 1 & 1 \\ 10 & 10 \end{bmatrix}$$

$$A_2 = \begin{bmatrix} -1 & 0 & 1 & 0 \\ 0 & -1 & 0 & 1 \\ 0 & 0 & -5 & 0 \\ 0 & 0 & 0 & -1 \end{bmatrix} \qquad B_2 = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 5 & 5 \\ -1 & -1 \end{bmatrix}$$

$$C_1 = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \end{bmatrix} \qquad C_2 = \gamma \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \end{bmatrix}$$

for some $\gamma \geq 0$. Notice that these matrices define monotone systems with respect to the partial orders induced by the following orthants: $K_{X_1} = (\mathbb{R}_0^+)^4$, $K_{X_2} = \mathbb{R}_0^+ \times \mathbb{R}_0^- \times \mathbb{R}^+ \times \mathbb{R}_0^-$, $K_{U_1} = K_{Y_1} = K_{U_2} = (\mathbb{R}_0^+)^2$, while $K_{Y_2} = \mathbb{R}^+ \times \mathbb{R}_0^-$. This can be verified using the infinitesimal characterizations for orthant-monotonicity. The DC-gain matrices are given by:

$$\Gamma_1 = \begin{bmatrix} 1 & 1 \\ 1 & 1 \end{bmatrix} \qquad \Gamma_2 = \gamma \begin{bmatrix} 1 & 1 \\ -1 & -1 \end{bmatrix}.$$

Computing the DC loop gain yields:

$$\Gamma_2\Gamma_1 = \gamma \begin{bmatrix} 2 & 2 \\ -2 & -2 \end{bmatrix}.$$

Notice that $\Gamma_2\Gamma_1$ is a nilpotent matrix regardless of γ, so that $\rho(\Gamma_2\Gamma_1) = 0$. If one could avoid using absolute values in expressing the small-gain condition (32), this would mean asymptotic stability of the interconnected system regardless of γ. The characteristic polynomial of the closed-loop system reads:

$$\begin{aligned} \chi(s) &= s^8 + 21\,s^7 + 155\,s^6 + 545\,s^5 \\ &\quad + (1065 - 44\,\gamma)\,s^4 + (1231 - 168\,\gamma)\,s^3 \\ &\quad + (841 - 204\,\gamma)\,s^2 + (315 - 80\,\gamma)\,s + 50 \end{aligned}$$

which according to the Routh–Hurwitz criterion is asymptotically stable (for non-negative γ) if and only if $\gamma \in [0, \gamma^\star)$ with $\gamma^\star \approx 1.9662$. According to criterion (32), instead:

$$|\Gamma_2| \cdot |\Gamma_1| = \gamma \begin{bmatrix} 2 & 2 \\ 2 & 2 \end{bmatrix},$$

which yields $\rho(|\Gamma_2| \cdot |\Gamma_1|) = 4\gamma$. Then, according to Theorem 2 asymptotic stability of (31) holds provided $|\gamma| < 1/4$. There is a significant gap between the value $1/4$ (provided by the small-gain theorem) and the true value $\gamma^\star$ which renders the interconnected system (31) unstable.

9. Time delays and the necessity of the small-gain condition

As highlighted in Section 8, stability intervals assessed by means of the small-gain criterion can be rather conservative. One situation in which the predictions of the small-gain theorem are much tighter is the case of a positive feedback interconnection. In that case the dynamics of the $2m$-dimensional discrete iteration is equivalent to that of the standard m-dimensional gain function. And as shown in [3,14], the stable steady states of the closed loop correspond to the stable fixed points of the gain function. If the small-gain condition fails, the gain function is likely to have multiple stable fixed points, which implies that the closed loop does not have a unique globally attractive steady state.

A similar scenario where the small-gain condition is necessary for global convergence of the closed loop can be found if delays are introduced in the system. An argument analogous to the proof of Theorem 1 applies when arbitrary time delays are considered in the system interconnections, namely if the following interconnected system is considered:

$$\begin{aligned} \dot{x}_1 &= f_1(x_1, u_1), & h_1(x_1) &= y_1, \\ \dot{x}_2 &= f_2(x_2, u_2), & h_2(x_2) &= y_2, \\ u_2(t) &= y_1(t - \tau_1), & u_1(t) &= y_2(t - \tau_2), \end{aligned} \tag{33}$$

for some nonnegative τ_1, τ_2.

Theorem 3. *Consider a delay system (33) with bounded solutions, interconnecting two I/O orthant-monotone systems. Assume that the continuous steady-state I/O characteristics are well defined, and consider the same iteration map (13) as in Theorem 1. If the iterations of this discrete map are globally attractive towards a unique fixed point, then every solution of (33) converges towards a unique steady state, regardless of the value of τ_1, τ_2.*

Proof. The underlying state space for this system is infinite dimensional, and it can be defined to include all continuous functions $\gamma : [-\tau_3, 0] \to X_1 \times X_2$, $\tau_3 = \max(\tau_1, \tau_2)$. The two I/O orthant-monotone subsystems do not contain any delays, and the theory previously developed applies to them.

Consider any solution $x_1(t), x_2(t)$, and its corresponding inputs and outputs $u_i(t), y_i(t)$. Define $\underline{u}_1$, $\bar{u}_1$, $\underline{y}_1$, $\bar{y}_1$ as in the proof of Theorem 1, and use Lemma 2 to prove that $y_1(t) \to [\underline{y}_1, \bar{y}_1]_{K_{Y_1}}$ as $t \to \infty$. Define $(\underline{u}_2, \bar{u}_2) = \eta^1(\underline{y}_1, \bar{y}_1)$. Even in the presence of a delay, Lemma 1 still applies to show that $u_2(t) \to [\underline{u}_2, \bar{u}_2]_{K_{U_2}}$ as $t \to \infty$. This process can be repeated iteratively in the same way as in Theorem 1 to obtain the result. □

See also [9] for a more detailed discussion of the delay case for the standard small-gain theorem.

We argue next that if one is willing to allow for arbitrary time-delays as in Theorem 3 in the loop, then the small-gain condition (30) is also necessary for stability. We prove the following proposition.

Proposition 3. *Consider the linear system:*

$$\begin{aligned} \dot{x}_1(t) &= A_1 x_1(t) + B_1 u_1(t), & y_1(t) &= C_1 x_1(t) \\ \dot{x}_2(t) &= A_2 x_2(t) + B_2 u_2(t), & y_2(t) &= C_2 x_2(t), \end{aligned} \tag{34}$$

where A_1, B_1, C_1 and A_2, B_2, C_2 are as in Theorem 2. We consider the following delayed interconnections, where u_j^i and y_j^i are the components of the vectors u_j and y_j respectively:

$$u_1^i(t) = y_2^i(t - \tau_1^i) \qquad u_2^k(t) = y_1^k(t - \tau_2^k) \tag{35}$$

with $i = 1, \dots, m_1$, $k = 1, \dots, m_2$ and τ_1^i, τ_2^k nonnegative reals. Assume that $\rho(\Lambda_{21}\Gamma_2\Lambda_{12}\Gamma_1) > 1$. Then there exist values of $\tau_1^i \geq 0$ and $\tau_2^k \geq 0$, and $T > 0$ such that the system (34) admits a periodic solution of period T.

Proof. Define $G_1(\omega) = C_1(j\omega - A_1)^{-1}B_1$ and $G_2(\omega) = C_2(j\omega - A_2)^{-1}B_2$. Notice that $G_1(\omega) \to 0$ as $\omega \to \infty$, and the same applies to $G_2(\omega)$. Clearly $G_1(0) = \Gamma_1$ and $G_2(0) = \Gamma_2$. By continuity of G_i, $i = 1, 2$ and of the spectral radius $\rho(\cdot)$, there exists $\bar{\omega} > 0$ such that:

$$\rho(\Lambda_{21}G_2(\bar{\omega})\Lambda_{12}G_1(\bar{\omega})) = 1. \tag{36}$$

Let $\lambda_{21}(\omega) = \mathrm{diag}[\dots e^{-j\omega\tau_1^i}\dots]$ for $i = 1, 2, \dots, m_1$ and $\lambda_{12}(\omega) = \mathrm{diag}[\dots e^{-j\omega\tau_2^k}\dots]$ for $k = 1, 2, \dots, m_2$. Clearly there exist nonnegative τ_1^i and τ_2^k so that $\lambda_{12}(\bar{\omega}) = \Lambda_{12}$ and $\lambda_{21}(\bar{\omega}) = \Lambda_{21}$. By definition of $\bar{\omega}$ in (36) we have:

$$\rho(\lambda_{21}(\bar{\omega})G_2(\bar{\omega})\lambda_{12}(\bar{\omega})G_1(\bar{\omega})) = 1.$$

Notice that $\lambda_{21}(\bar{\omega})G_2(\bar{\omega})\lambda_{12}(\bar{\omega})G_1(\bar{\omega})$ can be interpreted as the loop-gain transfer function of (34) with the delayed interconnection (35) evaluated for $s = j\bar{\omega}$. Hence, by standard arguments, the linear system (34), (35) admits a sinusoidal solution of period $1/(2\pi\bar{\omega})$. □

As already remarked, Theorem 2 and its generalization to the delay case are true for general linear systems provided the matrices $[\Gamma_1]_{ij}$ and $[\Gamma_2]_{ji}$ in condition (32) represent the $\mathcal{L}_2$ induced gains from input j to output i and from output i to input j respectively $j = 1, \dots, m_1$, $i = 1, \dots, m_2$. The necessity result stated in Proposition 3 is however new and in fact false for general linear systems even in the SISO case. To see this, consider the simple example described below.

Example 1. Consider the transfer functions given below:

$$G_1(s) = \frac{\gamma}{1+s} \qquad G_2(s) = \frac{1+s}{(1+0.1s)^2}$$

where γ is a positive parameter. We want to study stability of the following closed-loop transfer function:

$$\frac{1}{1 + G_1(s)G_2(s)e^{-s\tau}}$$

corresponding to an interconnection of G_1 and G_2 in closed loop, where τ indicates the sum of the delays at the loop interconnections. Notice that:

$$G_1(s)G_2(s) = \frac{\gamma}{(1+0.1s)^2}.$$

This is a low-pass filter, hence the $\mathcal{L}_2$ induced gain equals the DC gain γ. Asymptotic stability for arbitrary delays holds provided $\gamma < 1$. Let us now compute the stability estimates provided by the small-gain theorem. For $G_1(s)$ the $\mathcal{L}_2$-induced gain equals the DC gain γ. However, for the second transfer function, the maximum of $|G_2(j\omega)|$ is achieved at $\omega = 2\sqrt{2}$ and equals $|G_2(j2\sqrt{2})| = 5/3$. This means that the small-gain theorem only predicts stability up to $\gamma < 3/5$, giving a conservative estimate of the stability region under arbitrary delays. Of course there is no state-space realization of G_2 that satisfies the monotonicity conditions in Theorem 2.

10. Conclusion

We generalized existing small-gain theorems for orthant-monotone MIMO systems connected in feedback. The results improve on existing literature as they do not assume any compatibility between the orthant-induced orders pertaining to input and output spaces of interconnected components. Though the methods are new also for linear systems, in that they arise from a different point of view, the conditions achieved in this case boil down to classical L_2 or L_∞ small-gain results.

References

[1] M.W. Hirsch, H. Smith, Monotone dynamical systems, in: Handbook of Differential Equations: Ordinary Differential Equations, vol. 2, 2006, pp. 239–357.
[2] D. Angeli, E.D. Sontag, Monotone control systems, IEEE Trans. Automat. Control 48 (10) (2003) 1684–1698.
[3] D. Angeli, E.D. Sontag, Multi-stability in monotone input/output systems, Systems Control Lett. 51 (3–4) (2004) 185–202.
[4] M. Arcak, On biological pattern formation by contact inhibition, Amer. Control Conf. (2012) 3439–3444.
[5] M. Arcak, Pattern formation by lateral inhibition in large-scale networks of cells, IEEE Trans. Automat. Control 58 (5) (2013) 1250–1262.

[6] T. Gedeon, G. Hines, Multi-valued characteristics and Morse decompositions, J. Differential Equations 247 (4) (2009) 1013–1042.
[7] S.S. Ge, Z. Tian, T.H. Lee, Nonlinear control of a dynamic model of HIV-1, IEEE Trans. Biomed. Eng. 52 (2005) 353–361.
[8] N. Radde, N.S. Bar, M. Banaji, Graphical methods for analysing feedback in biological networks—a survey, Internat. J. Systems Sci. 41 (1) (2010) 35–46.
[9] G.A. Enciso, H.L. Smith, E.D. Sontag, Non-monotone systems decomposable into monotone systems with negative feedback, J. Differential Equations 224 (2006) 205–227.
[10] M. Malisoff, P. de Leenheer, A small-gain theorem for monotone systems with multivalued input-state characteristics, IEEE Trans. Automat. Control 51 (2) (2006) 287–292.
[11] T. Gedeon, Oscillations in monotone systems with negative feedback, SIAM Dyn. Syst. 9 (1) (2010).
[12] D. Angeli, E.D. Sontag, Oscillations in I/O monotone systems, IEEE Trans. Circuits Syst. 55 (2008) 166–176. Special Issue on Systems Biology.
[13] D. Angeli, E.D. Sontag, Interconnections of monotone systems with steady-state characteristics, in: Optimal Control, Stabilization and Nonsmooth Analysis, in: Lecture Notes in Control and Information Sciences, vol. 301, Springer, Berlin, 2004, pp. 135–154.
[14] G.A. Enciso, E.D. Sontag, Monotone systems under positive feedback: multistability and a reduction theorem, Systems Control Lett. 54 (2) (2005) 159–168.
[15] G. Enciso, E. Sontag, Monotone bifurcation graphs, J. Biol. Dyn. 2 (2) (2008) 121–139.
[16] C. Cosner, Comparison principles for systems that embed in cooperative systems, with applications to diffusive Lotka–Volterra models, Dyn. Contin. Discrete Impuls. Syst. 3 (1997) 283–303.
[17] M. Vidyasagar, Input–output analysis of large-scale interconnected systems, in: Lecture Notes in Control and Information Sciences, vol. 29, Springer, Berlin, 1981.
[18] Z.-P. Jiang, A. Teel, L. Praly, Small-gain theorem for ISS systems and applications, Math. Control Signals Systems 7 (1994) 95–120.
[19] Z.-P. Jiang, I.M.Y Mareels, Y. Wang, A Lyapunov formulation of the nonlinear small-gain theorem for interconnected ISS systems, Automatica 32 (8) (1996) 1211–1215.
[20] S. Dashkovskiy, B. Rüffer, F. Wirth, Small gain theorems for large scale systems and construction of ISS Lyapunov functions, SIAM J. Control Optim. 48 (6) (2010) 4089–4118.
[21] T. Liu, D. Hill, Z.-P. Jiang, Lyapunov formulation of ISS cyclic-small-gain in continuous-time dynamical networks, Automatica 47 (9) (2011) 2088–2093.
[22] S. Dashkovskiy, H. Ito, F. Wirth, On a small gain theorem for ISS networks in dissipative Lyapunov form, in: Proc. of the European Control Conference, Budapest, Hungary, 2009, pp. 1077–1082.
[23] D. Angeli, A. Astolfi, A tight small gain theorem for not necessarily ISS systems, Systems Control Lett. 56 (2007) 87–91.
[24] H. Ito, Zhong-Ping Jiang, Necessary and sufficient small gain conditions for integral input-to-state stable systems: a Lyapunov perspective, IEEE Trans. Automat. Control 54 (10) (2009) 2389–2404.
[25] S. Dashkovskiy, M. Kosmykov, F. Wirth, A small-gain condition for interconnections of ISS systems with mixed ISS characterizations, IEEE Trans. Automat. Control 56 (6) (2011) 1247–1258.
[26] G.A. Enciso, E.D. Sontag, Global attractivity, I/O monotone small-gain theorems, and biological delay systems, Discrete Contin. Dyn. Syst. 14 (3) (2006) 549–578.
[27] E.N. Dancer, Some remarks on a boundedness assumption for monotone dynamical systems, Proc. AMS 126 (1998) 801–807.
[28] M. Elowitz, S. Leibler, A synthetic oscillatory network of transcriptional regulators, Nature 403 (6767) (2000) 335–338.
[29] M.R. Atkinson, M.A. Savageau, J.T. Myers, A.J. Ninfa, Development of genetic circuitry exhibiting toggle switch or oscillatory behavior in *Escherichia coli*, Cell 113 (5) (2003) 597–607.
[30] T.Y. Tsai, Y.S. Choi, W. Ma, J.R. Pomerening, C. Tang, J.E. Ferrell Jr., Robust, tunable biological oscillations from interlinked positive and negative feedback loops, Science 321 (5885) (2008) 126–129.
[31] G.M. Suel, J. Garcia-Ojalvo, L.M. Liberman, M. Elowitz, An excitable gene regulatory circuit induces transient cellular differentiation, Nature 440 (23) (2006) 545–550.
[32] J. Keener, J. Sneyd, Mathematical Physiology I: Cellular Physiology, Springer Verlag, 2008.
[33] A.N. Michel, On the status of stability of interconnected systems, IEEE Trans. Automat. Control 28 (6) (1983).