

Polyhedral Lyapunov functions for structural stability of biochemical systems in concentration and reaction coordinates

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Abstract—*Structural* properties, independent of specific parameter values, can explain the robustness of biochemical systems. In this paper we consider the framework previously proposed by the authors to assess structural stability of biochemical reaction networks with monotone reaction rates, which considers systems in *concentration coordinates*, and we show that the results can be applied to systems in *reaction coordinates* (whose stability was first investigated by Al-Radhawi and Angeli): the same numerical test can be employed to find a polyhedral Lyapunov function and thus certify stability. Under suitable assumptions on the rank of structural matrices, we prove the equivalence between the test performed for the system in concentration coordinates and in reaction coordinates. We finally illustrate the approach by examples.

I. INTRODUCTION

Structural investigation is a powerful tool to understand how and why biological systems are able to perform their specific task in completely different conditions, although affected by the intrinsic uncertainty and variability in the parameter values [1], [2]. A *structural* property is satisfied by all the systems belonging to a class, characterized by a structure, *regardless of parameter values* [3], [4]. This is a more demanding requirement than robustness [5], [6]: to be *robust*, a property just needs to be preserved under *large parameter variations*. Structural analysis of chemical reaction networks [7], [8], [9] has been providing fundamental results, such as the zero-deficiency theorem and the one-deficiency theorem in [10], [11], [12] and a lot of subsequent work [13], [14], [15], [16], [17]. The zero-deficiency theorem gives a criterion to assess structural stability of reaction networks, provided that reaction kinetics are of the mass action type (hence polynomial, although a generalization is proposed in [18]). Yet this assumption is not necessarily satisfied.

Structural stability is investigated in [19] for a wide class of (bio)chemical reaction networks, under the sole requirement of monotone reaction rates. The nonlinear system equations are absorbed in a linear differential inclusion and then a piecewise linear (*i.e.*, polyhedral) Lyapunov function [20] is sought, based on the network structure only: the existence of a polyhedral Lyapunov function is shown to be equivalent to the stability of a suitable discrete difference inclusion, and a numerical recursive procedure is proposed to generate the unit ball of the polyhedral norm. Whenever a polyhedral Lyapunov function is found, the proposed procedure structurally certifies the stability of the system *for any choice* of monotone reaction rate functions.

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Polyhedral Lyapunov functions were previously adopted in [4] for the analysis of specific biochemical networks. Piecewise linear in rate Lyapunov functions have been recently considered in [21], [22], [23] for the stability analysis of chemical reaction networks; in this paper we recast the methods in [19] to the framework proposed by Al-Radhawi and Angeli, in which the system variables are reaction rates, instead of species concentrations.

The main contributions of the paper are the following.

- We show that, since the system in reaction coordinates has the same structure as the differential inclusion considered in concentration coordinates, all the results provided in [19], including the computational procedure, apply in the reaction-coordinates setup as well.
- Under suitable assumptions on the rank of structural matrices, the stability of the system in reaction coordinates is equivalent to the stability of the corresponding differential inclusion in concentration coordinates. For a particular class of networks, which we name *unitary*, this means that the proposed computational procedure converges in the former case iff it converges in the latter.

To illustrate the approach, we finally apply the procedure to some biochemical networks, analyzed both in concentration and in reaction coordinates.

II. PIECEWISE LINEAR LYAPUNOV FUNCTIONS IN CONCENTRATION COORDINATES

In this section we summarize the framework introduced in [19] to find polyhedral Lyapunov functions in concentration coordinates. Chemical species are denoted by uppercase letters, their concentrations by the corresponding lowercase letter. We consider reaction networks of the form

$$\dot{x} = Sg(x) + g_0, \quad (1)$$

where $x \in \mathbb{R}_+^n$ is the species concentrations vector (mol/L), $g(x) \in \mathbb{R}^m$ is the reaction rates vector (mol/L/s) and $g_0 \geq 0$ is a vector of constant influxes; $S \in \mathbb{Z}^{n \times m}$ is the stoichiometric matrix of the system, whose entries s_{ij} represent the net amount of the i th species produced or consumed by the j th reaction, excluding the contribution of constant influxes.

We make the following standing assumptions.

Assumption 1: All the component functions of vector $g(x)$ are non-negative and continuously differentiable, with positive partial derivatives in the positive orthant.

Assumption 2: Each component function of vector $g(x)$ is zero if and only if at least one of its arguments is zero. Moreover, if $s_{ij} < 0$, then g_j must depend on x_i .

Thus, (1) is a positive system: for $x_i = 0$, we have $\dot{x}_i \geq 0$.

Assumption 3: Functions $g_j(\cdot)$ with all arguments depending on a single variable x_i are admitted if, for each argument, $s_{ij}\partial g_j/\partial x_i < 0$. Functions having as an argument the sum or difference of more variables, such as $g_j(\pm x_i \pm x_k)$, are admitted if they appear in a single equation, $\dot{x}_k = \dots$ (relative to a variable of the combination), and $s_{kj}\partial g_j/\partial x_k < 0$.

This means that the diagonal entries of the Jacobian of $Sg(x)$ are negative: no autocatalytic reactions are considered.

Biochemical networks admit a graph representation (see e.g. Fig. 3): nodes are associated with species, arcs with interactions among them. Fig. 1 reports possible reactions, together with the corresponding terms in the proper equations and the corresponding arcs in the graph.

Example 1: The reaction network associated with the graph named Frescobaldi3 in Fig. 3 has equations

$$\begin{aligned}\dot{a} &= a_0 - g_a(a) - g_{ac}(a, c) \\ \dot{b} &= g_a(a) - g_{bc}(b, c) \\ \dot{c} &= g_a(a) - g_{ac}(a, c) - g_{bc}(b, c)\end{aligned}\quad (2)$$

corresponding to the general model (1) with $x = [a \ b \ c]^\top$,

$$S = \begin{bmatrix} -1 & -1 & 0 \\ 1 & 0 & -1 \\ 1 & -1 & -1 \end{bmatrix}, \quad g(x) = \begin{bmatrix} g_a(a) \\ g_{ac}(a, c) \\ g_{bc}(b, c) \end{bmatrix}, \quad g_0 = \begin{bmatrix} a_0 \\ 0 \\ 0 \end{bmatrix}.$$

Networks composed of reactions in Fig. 1 are a subset of those satisfying Assumption 3, and are *unitary*.

Definition 1: The network is *unitary* if $s_{ij} \in \{-1, 0, 1\}$.

Remark 1: The presented theory works in general, but the computational procedure might not converge for non-unitary networks. However, any multimolecular reaction can be plausibly expressed as a cascade of bimolecular reactions [24], [25], which are unitary.

For a structural analysis, consider the ε -modified system

$$\dot{x}(t) = -\varepsilon x(t) + Sg(x(t)) + g_0, \quad (3)$$

with $\varepsilon > 0$ arbitrarily small (infinitesimal degradation).

Definition 2: System (1) is

- *structurally stable* if any equilibrium \bar{x} of the system with $g_0 = 0$ is Lyapunov stable: a continuous, strictly increasing and unbounded function $\omega : \mathbb{R}_+ \rightarrow \mathbb{R}_+$ exists, with $\omega(0) = 0$, s. t. $\|x(t) - \bar{x}\| \leq \omega(\|x(0) - \bar{x}\|)$;
- *structurally convergent* if it is structurally stable and, for any $\varepsilon > 0$ and $g_0 \geq 0$, the perturbed system (3) has globally bounded solutions and admits an equilibrium that is globally asymptotically stable in \mathbb{R}_+^n .

In general, to assess asymptotic stability, we need to consider a natural degradation of each species, represented by $\varepsilon > 0$ in (3), which is necessary for the system to tolerate persistent positive inputs. Considering a spontaneous degradation is reasonable in biochemical systems and, in practice, introducing ε cannot produce a wrong stability certificate for unstable systems.

We now absorb the system in a differential inclusion. Assume that an equilibrium $\bar{x} = \bar{x}(\varepsilon)$ exists $\forall \varepsilon > 0$.¹ Denote

¹An equilibrium does actually exist if the system passes the computational test in [19].

$z \doteq x - \bar{x}$. Since $0 = Sg(\bar{x}) - \varepsilon\bar{x} + g_0$, we have

$$\dot{z}(t) = S[g(z(t) + \bar{x}) - g(\bar{x})] - \varepsilon z(t). \quad (4)$$

System (4) is equivalent to

$$\dot{z}(t) = BD(x(t))Cz(t) - \varepsilon z(t), \quad (5)$$

where $B \in \mathbb{Z}^{n \times q}$ is formed by columns s_k of S , each repeated a number of times equal to the number of arguments of $g_k(\cdot)$, $D(x) = \text{diag}\{d_1, \dots, d_q\}$ is a diagonal matrix with non-negative diagonal entries, corresponding to all the nonzero partial derivatives $\partial g_j/\partial x_i$ with respect to all arguments, $C \in \mathbb{Z}^{q \times n}$ is such that $|c_{ki}| = 1$ if the derivative d_k is computed with respect to x_i , 0 otherwise.

Example 2: For system (2) in Example 1, let $\alpha = \partial g_a(a)/\partial a$, $\beta = \partial g_{ac}(a, c)/\partial a$, $\gamma = \partial g_{ac}(a, c)/\partial c$, $\delta = \partial g_{bc}(b, c)/\partial b$ and $\epsilon = \partial g_{bc}(b, c)/\partial c$ be positive parameters. Then $D = \text{diag}(\alpha, \beta, \gamma, \delta, \epsilon)$,

$$B = \begin{bmatrix} -1 & -1 & -1 & 0 & 0 \\ 1 & 0 & 0 & -1 & -1 \\ 1 & -1 & -1 & -1 & -1 \end{bmatrix}, \quad C = \begin{bmatrix} 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 1 \end{bmatrix}^\top.$$

Theorem 1: [19] Consider the linear differential inclusion

$$\dot{z}(t) = [-\varepsilon I + BD(t)C]z(t), \quad z(0) = z_0, \quad (6)$$

where $D(t) = \text{diag}\{d_1(t), \dots, d_q(t)\}$ and $d_i(t)$, $1, \dots, q$, are arbitrary non-negative scalar piecewise continuous functions. Then:

- stability of (6) for $\varepsilon = 0$ implies structural stability of any equilibrium of (1);
- asymptotic stability of (6) for $\varepsilon > 0$ implies structural convergence of (1).

□

If the differential inclusion (6) is asymptotically stable, then (3) admits an equilibrium. Moreover, stability of (6) for $\varepsilon = 0$ is equivalent to its asymptotic stability for $\varepsilon > 0$. Hence, the two claims of Theorem 1 can only be verified together. The stability of the differential inclusion (6) with $\varepsilon = 0$ can be analyzed by considering a discrete-time difference inclusion [19].

Theorem 2: Robust stability of the differential inclusion

$$\dot{z}(t) = BD(t)Cz(t), \quad d_i(t) \geq 0 \quad (7)$$

is equivalent to robust stability of the difference inclusion

$$y_{k+1} = \Phi(k)y_k, \quad \Phi(k) \in \mathcal{F}, \quad (8)$$

where \mathcal{F} is the family of matrices

$$\mathcal{F} = \left\{ \Phi_i \doteq \left[I - \frac{b_i c_i^\top}{c_i^\top b_i} \right], \quad i = 1, \dots, q \right\}, \quad (9)$$

b_i denotes the i th column of B and c_i^\top the i th row of C . □

Given a full row rank matrix $X \in \mathbb{R}^{n \times s}$,

$$V_X(x) = \inf\{\|w\|_1 : Xw = x, w \in \mathbb{R}^s\}$$

is a polyhedral norm. The vertices of its unit ball are the columns of matrix X and their opposites. Given a full column rank matrix $M \in \mathbb{R}^{s \times n}$, we have the dual function

$$V^M(x) = \|Mx\|_\infty.$$

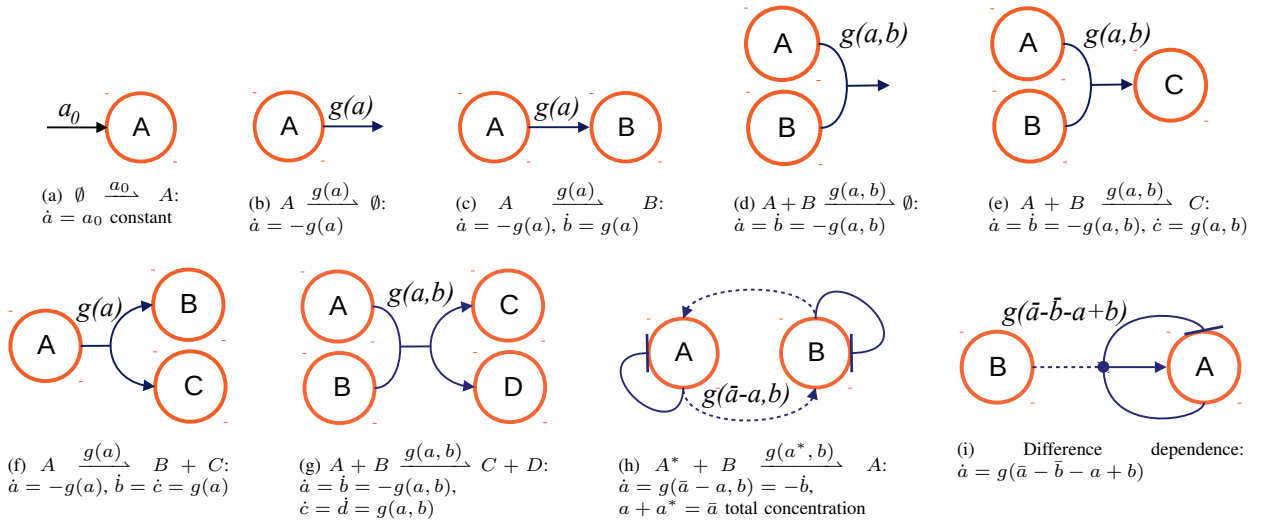


Fig. 1: Graph representations of biochemical reactions.

Denoting by M^k the k th row of M , the facets of the unit ball are on the planes $M^k x = 1$ or $M^k x = -1$. The positive definite function $V_X(x)$ ($V^M(x)$) is a weak Lyapunov function if it is non-increasing along all possible system trajectories. System (8) is marginally stable and has a weak polyhedral Lyapunov function if and only if (7) is marginally stable and has the same weak Lyapunov function.

Theorem 3: [19] If (8) admits a weak Lyapunov function,

- (6) is stable for $\varepsilon = 0$;
- (6) is asymptotically stable for $\varepsilon > 0$;
- (1) is structurally convergent. \square

The unit ball of a polyhedral Lyapunov function for (8) can be computed as follows. Given matrix X , let $Y = \text{mr}(X)$ be the minimal polytopic representation, achieved by removing all redundant vertices. Define the following iterate in the set of polyhedra:

$$X^{k+1} = \Psi(X^k), \quad (10)$$

where $\Psi(X) = \text{mr}[X \quad \Phi_1 X \quad \dots \quad \Phi_q X]$. System (8) admits a polyhedral Lyapunov function if and only if Ψ has a fixed point $\Psi(X) = X$ [26].

Procedure.

- 1) Fix $\nu > 1$, integer. Let $X^0 := [-I \ I]$.
- 2) Compute the sequence (10), until either
 Successful stop: $X^k = X^{k-1}$,
 Unsuccessful stop: $\max_{ij} |X^k|_{ij} > \nu$.

Remark 2: The quantity ν represents the maximum “tolerated escape”. For instance, the unsuccessful stop due to violation for $\nu = 10$ means that a trajectory has gone far away 10 times with respect the initial ball size. Moreover, it can be shown that, if the convex hull of X includes the convex hull of X^0 in its interior, then the difference inclusion is unstable, hence no Lyapunov function exists.

A dual procedure can be considered, in which iterations are applied to the dual system $x_{k+1} = \Phi(k)^\top x_k$, whose stability is equivalent to stability of the primal [20]; hence, the dual procedure converges iff the primal does. In case of convergence to a matrix \bar{X} , the primal system admits the polyhedral Lyapunov function $V^M(x) = \|\bar{X}^\top x\|_\infty$.

For unitary networks we have $c_i^\top b_i = -1 \ \forall i$ and the computation is particularly efficient [19].

We finally report the next equivalence result.

Theorem 4: [19] System (1), admitting a steady state \bar{x} , is stable with a polyhedral Lyapunov function $V(x - \bar{x})$, for any possible choice of functions g satisfying our assumptions, if and only if $V(z)$ is a Lyapunov function for (6) $\forall \varepsilon \geq 0$. \square

III. PIECEWISE LINEAR LYAPUNOV FUNCTIONS IN REACTION COORDINATES

Inspired by the concept of piecewise linear in rate Lyapunov functions [21], [22], [23], we now show that the results in the previous section hold for systems in reaction coordinates as well. First, to ensure that an equilibrium exists for the system in reaction coordinates iff it exists for the system in concentration coordinates, we consider *regular* chemical reaction networks, according to the next definition.

Definition 3: System (1) is *regular* if (i) it admits an equilibrium point \bar{x} , and (ii) $g(\cdot)$ is left invertible (injective), so that, given $\bar{g} = g(\bar{x})$, \bar{x} is unique.

Define the new variable $r \doteq g(x) - \bar{g}$, which can be thought of as a “relative” reaction rate, such that $r \rightarrow 0$ iff $x \rightarrow \bar{x}$ (due to the regularity assumption). The corresponding dynamics are

$$\dot{r} = \left[\frac{\partial g}{\partial x} \right] [Sg(x) + g_0] = \left[\frac{\partial g}{\partial x} \right] S r. \quad (11)$$

Remark 3: In general, reaction and concentration representations are both valid, but may lead to different conclusions. For instance, the non-regular system $\dot{a} = -g(a, b) + a_0$ and $\dot{b} = -g(a, b) + b_0$ converges in the reaction variable $r = g(a, b)$, but not in the concentration variables if $b_0 \neq a_0$.

Proposition 1: System (11) can be equivalently written as

$$\dot{r}(t) = ED(x(t))F r(t), \quad (12)$$

where $E \in \mathbb{Z}^{m \times q}$, $F \in \mathbb{Z}^{q \times m}$ is formed by rows of S , while q and D are as in (5). \square

Proof: Matrix $[\partial g / \partial x] S$ can be equivalently expressed as the product EDF , where the diagonal entries d_j of D are

the partial derivatives $\partial g_k / \partial x_h$, the entries of E are $|e_{ij}| = 1$ if g_k in d_j appears in the i th equation, 0 otherwise, and the j th row of F is the h th row of S if the derivative in d_j is with respect to x_h (or also a sum or difference of more rows of S , if the function has as an argument a sum or difference of more variables, see Assumption 3). ■

Remark 4: $D(x(t))$ is a matrix of partial derivatives, as in (5), but it is not the same matrix. Consider $\dot{x} = g(x) + g_0$, with steady state $0 = g(\bar{x}) + g_0$, and let $z = x - \bar{x}$. Then $\dot{z} = g(z + \bar{x}) - g(\bar{x}) = g'(\bar{x})z$, for some \bar{x} . Conversely, if $r = g(x) - g(\bar{x})$, then $\dot{r} = g'(x)\dot{x} = g'(x)r$. In principle we should write $D_{BC}(x(t))$ and $D_{EF}(x(t))$, but there is no point in doing this, since we will use the structural property that D has non-negative diagonal entries, only.

Example 3: For system (2) in Examples 1 and 2, $r = [g_a(a) - g_a(\bar{a}) \quad g_{ac}(a, c) - g_{ac}(\bar{a}, \bar{c}) \quad g_{bc}(b, c) - g_{bc}(\bar{b}, \bar{c})]^\top$. Let the partial derivatives and matrix D be defined as in Example 2. The system in reaction coordinates is

$$\dot{r} = \begin{bmatrix} \alpha & 0 & 0 \\ \beta & 0 & \gamma \\ 0 & \delta & \epsilon \end{bmatrix} Sr = EDFr,$$

where

$$E = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 \end{bmatrix}, \quad F = \begin{bmatrix} -1 & -1 & 1 & 1 & 1 \\ -1 & -1 & -1 & 0 & -1 \\ 0 & 0 & -1 & -1 & -1 \end{bmatrix}^\top.$$

Note that system

$$\dot{r}(t) = ED(t)Fr(t), \quad d_i(t) \geq 0, \quad (13)$$

has the same *structure* as system (7). Again, a spontaneous ε -degradation must be added to assess asymptotic stability; we can rewrite the system as

$$\dot{r}(t) = [-\varepsilon I + ED(t)F]r(t), \quad r(0) = r_0, \quad (14)$$

which has the same *structure* as system (6). Hence, all the reasoning and the results reported in Section II still hold in the new reaction coordinates framework. Then, the numerical procedure based on iterates (10) in the set of polyhedra can be employed to find a polyhedral Lyapunov function, thus ensuring stability of the system in reaction coordinates.

There are strong analogies between the two formulations, as we show next.

Proposition 2: Given a reaction network, consider the corresponding matrices B and C as in (5), and the corresponding matrices E and F as in (12). Then, we have the equality $CB = FE$. □

Proof: Denote by s_i the i th column and by s^i the i th row of the stoichiometric matrix S , and by \vec{e}_i the column vector having the i th element equal to 1, and all other elements equal to 0. Matrix B is composed by columns of S , $B = [s_{j_1} \quad s_{j_2} \quad \dots \quad s_{j_q}]$, while F by rows of S , $F = [(s^{i_1})^\top \quad (s^{i_2})^\top \quad \dots \quad (s^{i_q})^\top]^\top$; the rows of C are vectors, $C = [\vec{e}_{i_1} \quad \vec{e}_{i_2} \quad \dots \quad \vec{e}_{i_q}]^\top$, while the columns of E are vectors, $E = [\vec{e}_{j_1} \quad \vec{e}_{j_2} \quad \dots \quad \vec{e}_{j_q}]$. We can always order the columns of B and of E (and the rows of C and F accordingly) so that the order of the indices $\{j_k\}$ (respectively, $\{i_k\}$) is the same.

More in general, a row of F could be a sum or difference of more rows of S ; in this case, the corresponding row of C would be the same sum or difference of the corresponding vectors (e.g., if $f_k^\top = s^1 - s^2$, then $c_k^\top = \vec{e}_1^\top - \vec{e}_2^\top$). Then we consider the two matrix products and we observe that, if the entry $[CB]_{uv} = \vec{e}_{i_h}^\top s_{j_l}$, the corresponding entry $[FE]_{uv} = s^{i_h} \vec{e}_{j_l}$ (and analogously for the case of linear combinations). In the former case, we are selecting the i_h th element of the j_l th column of S ; in the latter case, the j_l th element of the i_h th row of S , which is clearly the same. Hence, the equality $CB = FE$ holds. ■

The following (immediate) corollary tells us that the same computational benefits are guaranteed when applying the numerical procedure to the system in reaction coordinates.

Corollary 1: A network is unitary in reaction coordinates iff it is unitary in concentration coordinates. □

Proof: In view of the equality $CB = FE$, $c_i^\top b_i = -1$ for all i iff $f_i^\top e_i = -1$ for all i . ■

We are now concerned with the connection between robust stability of the differential inclusion in concentration coordinates

$$\dot{z}(t) = [-\varepsilon I + BD(t)C]z(t), \quad d_i(t) \geq 0, \quad (15)$$

and robust stability of the system in reaction coordinates,

$$\dot{r}(t) = [-\varepsilon I + ED(t)F]r(t), \quad d_i(t) \geq 0. \quad (16)$$

As we have seen, in both cases the existence of a polyhedral Lyapunov function ensures asymptotic stability of the system. For unitary networks, for which $c_i^\top b_i = -1$ (resp. $f_i^\top e_i = -1$), stability of (6) (resp. of (14)) is *equivalent* to the existence of a polyhedral Lyapunov function [19]. Once we have shown stability of the system in one of the two frameworks, because the numerical procedure converges and generates the unit ball of the corresponding polyhedral Lyapunov function, what can we infer about stability of the system in the other framework?

Let $\eta(t) \doteq Cz(t)$ and $\xi(t) \doteq Fr(t)$. Consider the systems

$$\dot{\eta}(t) = [-\varepsilon I + CBD(t)]\eta(t), \quad d_i(t) \geq 0, \quad (17)$$

$$\dot{\xi}(t) = [-\varepsilon I + FED(t)]\xi(t), \quad d_i(t) \geq 0, \quad (18)$$

and the following definition.

Definition 4: System (18) (resp. (17)) is F -stable (C -stable) if the subspace $\text{span}[F]$ ($\text{span}[C]$)² is invariant and all the trajectories starting from that subspace converge to zero for any $D(t)$.

Note that, for a fixed $D(t)$, $FED = CBD$ in view of Proposition 2. We have the following results.

Lemma 1: If system (16) (resp. (15)) is asymptotically stable for any $D(t)$, then system (18) is F -stable (resp. (17) is C -stable). □

Proof: Fix a matrix $D(t)$. Given the solution $r(t)$ of (16) for initial conditions $r(0)$, $\xi(t) = Fr(t)$ is the solution of (18) for initial conditions $\xi(0) = Fr(0)$. If $r(t) \rightarrow 0$, then also $\xi(t) = Fr(t) \rightarrow 0$. ■

²We denote by $\text{span}[A]$ the column space of matrix A .

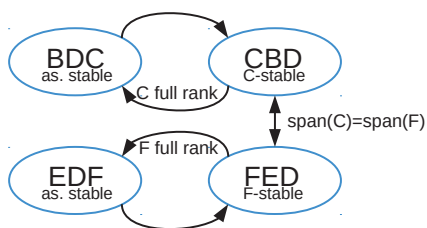


Fig. 2: The connection between stability properties.

Lemma 2: Assume $\text{span}(F) = \text{span}(C)$.³ If (16) (resp. (15)) is asymptotically stable for any $D(t)$, then (17) is C -stable (resp. (18) is F -stable). \square

Proof: Since $FE = CB$, under our assumptions C -stability of (17) is equivalent to F -stability of (18), which is guaranteed by Lemma 1. Hence, starting from initial conditions of the form $\xi(0) = Cz(0)$, the solution $\xi(t) = Cz(t) \rightarrow 0$, where $z(t)$ is the solution of system (15). \blacksquare

Lemma 3: If C (resp. F) has full column rank and system (17) is C -stable (resp. system (18) is F -stable), then system (15) (resp. (16)) is asymptotically stable. \square

Proof: Obviously, $\eta(t) = Cz(t) \rightarrow 0$ implies $z(t) \rightarrow 0$ if C has full column rank. The full rank assumption is fundamental; otherwise $Cz(t)$ may converge to zero, but $z(t)$ may diverge in the kernel of C . \blacksquare

The connection between stability properties of the four systems is summarized in Fig. 2 and leads to our main result.

Theorem 5: Assume that:

- (i) both F and C have full column rank;
- (ii) $\text{span}(F) = \text{span}(C)$.

Then the stability of system (15), in concentration coordinates, is equivalent to the stability of system (16), in reaction coordinates. \square

For unitary networks, as we have mentioned, stability is equivalent to the existence of a polyhedral Lyapunov function; therefore, under the assumptions of Theorem 5, the outcome of the computational procedure must be the same.

Remark 5: The injectivity assumption typically requires $m \geq n$ (the number of reactions is greater or equal to the number of species), while matrix F having full column rank typically requires $n \geq m$. Hence, the result in Theorem 5 particularly applies to the case $n = m$.

IV. EXAMPLES

We consider the systems corresponding to the graphs in Fig. 3, already considered in [19], which we now analyze both in concentration (z) and in reaction (r) coordinates. Each chemical reaction network is named after a musician and labeled with a number corresponding to the order of the system. Test results are reported in Table I. Column $\text{CV}_{z/r}$ shows whether the procedure converges (Yes/No) in concentration/reaction coordinates. Whenever the polyhedral function is found, the number of vertices and the number of facets of its unit ball are shown in the columns labeled as n_v and n_f respectively. The primal and dual procedure always provide the same answer on the existence of the function,

³This means that $\text{rank}([F \ C]) = \text{rank}(F) = \text{rank}(C)$.

TABLE I

Network	CV_z	n_v	n_f	CV_r	n_v	n_f
Buxtehude3	No	-	-	No	-	-
Corelli3	Yes	6	6	Yes	6	6
Frescobaldi3	No	-	-	No	-	-
Telemann3	Yes	10	12	Yes	8	6
Boccherini4	No	-	-	No	-	-
Čajkovskij4	No	-	-	No	-	-
Gounod4	No	-	-	No	-	-
Offenbach4	No	-	-	No	-	-
Paganini4	Yes	14	18	Yes	12	8
Grieg5	Yes	22	68	Yes	52	22
Liszt5	Yes	28	66	Yes	52	22
Martucci5	No	-	-	No	-	-
Mahler6	Yes	12	62	No	-	-

CV = Convergence (Yes/No);
 n_v = number of vertices (primal procedure);
 n_f = number of facets (dual procedure);

of course; yet n_v and n_f may be quite different. However, both n_v and n_f are surprisingly small (in general, polyhedral Lyapunov functions can be extremely complex [20]). All the networks in Fig. 3 correspond to regular systems. For all of them, apart from Mahler6, the assumptions of Theorem 5 hold: as expected, the outcome of the computational procedure, in terms of convergence, is the same in the two cases. For the network named Mahler6, the procedure converges in concentration coordinates, but not in reaction coordinates; as can be verified, matrix F does not have full (column) rank.

The network named Telemann3, *e.g.*, admits in concentration coordinates the polyhedral Lyapunov function with

$$X = \begin{bmatrix} 1 & 0 & 0 & 0 & -1 \\ 0 & 1 & 0 & 1 & 1 \\ 0 & 0 & 1 & 1 & 0 \end{bmatrix},$$

whose unit ball is shown in Fig. 4 (a), and its dual with

$$M = \begin{bmatrix} 0 & 1 & 1 & -1 & 1 & 0 \\ 1 & 1 & 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 1 & -1 & -1 \end{bmatrix}^T,$$

having the unit ball shown in Fig. 4 (b); in reaction coordinates, it admits the polyhedral Lyapunov function with

$$X = \begin{bmatrix} -1 & 1 & -1 & -1 \\ -1 & 1 & 1 & 1 \\ 1 & 1 & 1 & -1 \end{bmatrix},$$

whose unit ball is the cube of side 2, centered in the origin, and the dual function with $M = I$, the identity matrix, corresponding to the unit ball of the 1-norm (diamond).

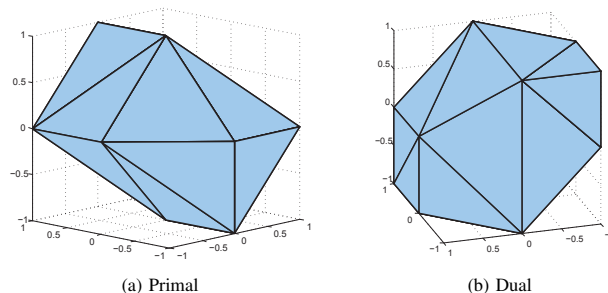


Fig. 4: Unit ball of the polyhedral Lyapunov functions in concentration coordinates, associated with the network named Telemann3 in Fig. 3.

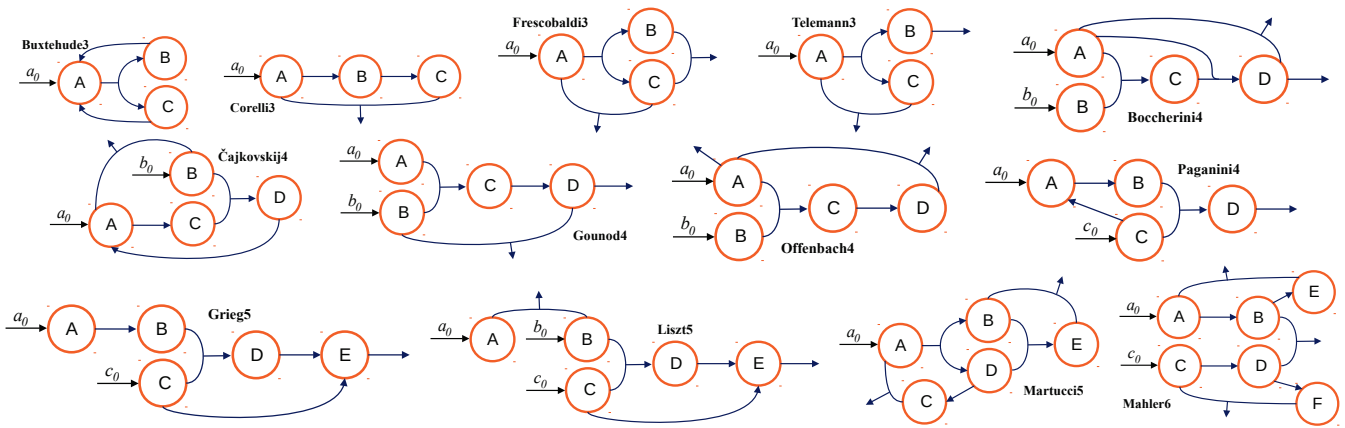


Fig. 3: Graphs corresponding to the biochemical networks tested in Section IV.

V. CONCLUDING REMARKS

An approach has been recently proposed [19] to assess the *structural* stability of a biochemical network by absorbing it in a linear differential inclusion, along with a numerical procedure for determining a polyhedral Lyapunov function for the system in concentration coordinates. In this paper, we have shown that this procedure can be applied to determine polyhedral functions for the system in reaction coordinates, as proposed in [21], [22], [23]. Under some full rank conditions, for unitary networks, the procedure converges when applied to the system in concentration coordinates iff it converges when applied to the system in reaction coordinates. Numerical experiments have shown how the procedure performs for some biochemical networks.

Further work along this direction may include the investigation of the case in which the full rank condition is not verified. Another intriguing direction concerns the global stability property that, so far, we can establish under the assumption of ε -degradation only. In [19] it is shown that, without any ε -degradation assumption, the existence of a polyhedral Lyapunov function in concentration coordinates assures local stability of the equilibrium (if any), provided that matrix BDC is robustly non-singular; hence, it can be inferred that a similar property holds for polyhedral Lyapunov functions in reaction coordinates. We believe that, under appropriate conditions, the assumption of ε -degradation can be removed, still ensuring global stability.

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