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Robust Lyapunov Functions for Complex Reaction Networks: An Uncertain System Framework

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***Abstract*—We present a framework to transform the problem of finding a Lyapunov function for a Complex Reaction Network (CRN) in concentration coordinates with arbitrary monotone kinetics into finding a common Lyapunov function for a linear parameter varying system in reaction coordinates. This is applied to reinterpret previous results on Piecewise Linear in Rates Lyapunov function, and to introduce Piecewise Quadratic in Rates Lyapunov functions for CRNs. The results are illustrated by an example.**

***Index Terms*—Lyapunov stability, Linear Parameter Varying Systems, Biochemical Networks.**

I. INTRODUCTION

Complex (or Chemical) Reaction Networks (CRNs) is a multi-disciplinary area of research connecting engineering, mathematics, physics and systems biology. Despite diverse applications in engineering and science, the recent interest in CRNs is mainly due to the emergence of *systems biology*.

In the context of systems biology, CRNs are key to understand complex biological systems at the cellular level by explicitly taking into account the sophisticated network of chemical interactions that regulate cell life. This is because all major biochemical networks such as signalling pathways, gene-regulatory networks, and metabolic networks are naturally cast in the framework of CRNs.

A major obstacle in biochemical networks is the very large degree of uncertainty inherent in their modeling. Thus, a useful analysis of this networks shall be *robust* with respect to arbitrary variations in the values of parameters. In other words, it is needed to provide nontrivial conclusions based solely on the structural properties of the network. However, it is natural to expect that this is not always possible, since dynamics may be subject to bifurcations which are entirely dependent on parameter values. Fortunately, many results [1], [2], [3] [4] identified wide classes of CRNs in which such analysis is indeed possible, where it has been shown that some major dynamical properties such as stability, persistence, monotonicity, etc can be determined based on structural information only, and regardless of the parameters involved.

Early work [1], [3] studied Lyapunov stability for weakly reversible networks which meet a certain graphical condition known as the zero deficiency property. It was shown that for this class of networks with mass-action kinetics, there exists a unique equilibrium in the interior of each invariant manifold, which is locally asymptotically stable regardless of the constants involved. In addition, the absence of boundary equilibria implies global asymptotic stability [5]. Nevertheless, the general result is still an open problem.

A more recent approach for the stability problem utilized monotonicity [4] . If a derived system from the CRN is shown to be monotone, stability theorems for monotone systems can be used. ℓ_1-norm Lyapunov functions has been used for specific CRNs in [6].

In a previous work [7], [8], a more direct approach was proposed for the problem, where Piecewise-Linear in Rates (PWLR) Lyapunov functions were introduced. In addition to their simple structure, these functions are robust with respect to kinetic constants, and require mild assumptions on the rates; mass-action is a special case.

In this paper, we generalize this approach by transforming the problem of finding a Lyapunov function in concentration coordinates with arbitrary monotone kinetics into finding a common Lyapunov function for a linear parameter varying system in reaction coordinates. Furthermore, several related Lyapunov functions are presented. As a result, we link the PWLR Lyapunov functions introduced in [7] with results known in literature for piecewise linear Lyapunov functions [9], [10], [11]. Also, the new framework allows us to use Piecewise Quadratic in Rates (PWQR) Lyapunov functions for CRNs, where we provide a construction algorithm.

The paper is organized as follows. In Section 2, we present the backround and assumptions. Section 3 defines what we mean by a Robust Lyapunov function, and introduces the uncertain systems framework. PWLR Lyapunov functions are introduced in Section 4, while PWQR Lyapunov functions are discussed in Section 5. The results are illustrated by an example in Section 6, and Section 7 contains the conclusion. For space limitations, the proofs are presented in [12].

Notation: Let $A \subset \mathbb{R}^n$ be a set, then $A^\circ, \bar{A}, \partial A$ denote its interior, closure, and boundary, respectively. Let $x \in \mathbb{R}^n$ be a vector, then its ℓ_∞-norm is $\|x\|_\infty = \max_{1 \le i \le n} |x_i|$. The inequalities $x \ge 0$, $x > 0$, $x \gg 0$ denote elementwise nonnegativity, elementwise nonnegativity with at least one positive element, and elementwise positivity, respectively. A is a signature matrix if $A \in \{\pm 1\}^{n \times n}$ and A is diagonal. Let $A \in \mathbb{R}^{n \times \nu}$, then $\ker(A)$ denotes the kernel or null-space of A, while $\mathrm{Im}(A)$ denotes the image space of A. $A \in \mathbb{R}^{n \times n}$ is Metzler if all off-diagonal elements are nonnegative. The set of $n \times n$ real symmetric matrices is denoted by $\mathbb{S}^n$. Let $A \in \mathbb{S}^n$, then $A \ge (>) 0$ denotes A being positive semi-definite

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(definite), respectively. $A \succeq 0$ denotes A being nonnegative. The all-ones vector is denoted by $\mathbf{1}$, where its dimension can be inferred from the context. Let $\{X_i\}_{i=1}^k \subset \mathbb{R}^{n\times m}$, its conic hull denotes the set $\{\sum_{i=1}^k \lambda_i X_i : \lambda_i \in \bar{\mathbb{R}}_+\}$. Let $V : D \to \mathbb{R}$, then the kernel of V is $\ker(V) = V^{-1}(0)$.

II. Background on Complex Reaction Networks

We summarize in this section main definitions and notions of CRNs [7], [8].

A. Ordinary Differential Equations Formulation

A Complex (or Chemical) Reaction Network (CRN) is defined by a set of species $\mathscr{S} = \{X_1, .., X_n\}$, and set of reactions $\mathscr{R} = \{\mathrm{R}_1, ..., \mathrm{R}_\nu\}$. Each reaction is denoted as:

$$\mathrm{R}_j : \quad \sum_{i=1}^n \alpha_{ij} X_i \longrightarrow \sum_{i=1}^n \beta_{ij} X_i, \; j = 1, .., \nu, \qquad (1)$$

where α_{ij}, β_{ij} are nonnegative integers called *stoichiometry coefficients*. The expression on the left-hand side is called the *reactant complex*, while the one on the right-hand side is called the *product complex*. The forward arrow refers to the idea that the transformation of reactant into product is only occurring in the direction of the arrow. If it occurs in the opposite direction also, the reaction is said to be *reversible* and it is listed as a separate reaction. The reactant or product complex can be empty, though not simultaneously, which is used to model external inflows and outflows of the CRN.

A nonnegative concentration x_i is associated to each species X_i. Each chemical reaction R_j is specified by $R_j : \bar{\mathbb{R}}_+^n \to \bar{\mathbb{R}}_+$ which is assumed to satisfy the following:

A1. it is a $\mathscr{C}^1$ function, i.e. continuously differentiable;
A2. $x_i = 0 \Rightarrow R_j(x) = 0$, for all i and j such that $\alpha_{ij} > 0$;
A3. it is nondecreasing with respect to its reactants, i.e

$$\frac{\partial R_j}{\partial x_i}(x) \begin{cases} \geq 0 & : \alpha_{ij} > 0 \\ = 0 & : \alpha_{ij} = 0 \end{cases}. \qquad (2)$$

A4. The inequality in (2) holds strictly for all $x \in \mathbb{R}_+^n$.

A widely-used expression for the reaction rate function is the *Mass-Action* which is given by the formula: $R_j(x) = k_j \prod_{i=1}^n x_i^{\alpha_{ij}}$, with the convention $0^0 = 1$.

The stoichiometry coefficients are arranged in an $n \times \nu$ matrix $\Gamma = [\gamma_1 \, .. \gamma_n]^T$ called the *stoichiometry matrix*, which is defined element-wise as: $[\Gamma]_{ij} = \beta_{ij} - \alpha_{ij}$.

Therefore, the dynamics of a CRN with n species and ν reactions is described by a system of ordinary differential equations (ODEs) as:

$$\dot{x}(t) = \Gamma R(x(t)), \; x_\circ := x(0) \in \bar{\mathbb{R}}_+^n \qquad (3)$$

where $x(t)$ is the concentration vector evolving in the nonnegative orthant $\bar{\mathbb{R}}_+^n$, $\Gamma \in \mathbb{R}^{n\times\nu}$ is the stoichiometry matrix, $R(x(t)) \in \bar{\mathbb{R}}_+^\nu$ is the reaction rates vector.

Note that (3) belongs to the class of *nonnegative systems*, i.e, $\bar{\mathbb{R}}_+^n$ is forward invariant. In addition, the manifold $\mathscr{C}_{x_\circ} := (\{x_\circ\} + \mathrm{Im}(\Gamma)) \cap \bar{\mathbb{R}}_+^n$ is forward invariant, and it is called *the stoichiometric compatibility class* associated with $x_\circ$.

Furthermore, we assume the following:

A6. There are no autocatalytic reactions, i.e., $\alpha_{ij}\beta_{ij} = 0$ for all $i = 1, .., n, j = 1, .., \nu$.
A7. There exists $v \in \ker \Gamma$ such that $v \gg 0$. This condition is necessary for the existence of equilibria in the interior of stoichiometric compatibility classes.

The set of reaction rate functions, i.e. kinetics, satisfying A1-A4 for a given Γ satisfying A6-A7 is denoted by $\mathscr{K}_\Gamma$. A CRN family $\mathscr{N}_\Gamma$ is the triple $(\mathscr{S}, \mathscr{R}, \mathscr{K}_\Gamma)$.

B. Graphical Representation

A CRN can be represented via a bipartite weighted directed graph given by the quadruple (V_S, V_R, E, W), where V_S is a set of nodes associated with species, and V_R is associated with reactions.

The edge set $E \subset V \times V$ is defined as follows. Whenever a certain reaction R_j given by (1), then $(X_i, \mathrm{R}_j) \in E$ for all X_i's such that $\alpha_{ij} > 0$. That is, $(X_i, \mathrm{R}_j) \in E$ iff $\alpha_{ij} > 0$, and we say in this case that R_j is an *output reaction* for X_i. Similarly, we draw an edge from $\mathrm{R}_j \in V_R$ to every $X_i \in V_S$ such that $\beta_{ij} > 0$. That is, $(\mathrm{R}_j, X_i) \in E$ whenever $\beta_{ij} > 0$, and we say in this case that R_j is an *input reaction* for X_i. Note that there are no edges connecting two reactions or two species. The weight function $W : E \to \mathbb{N}$ assigns to each edge a positive integer as $W(X_i, \mathrm{R}_j) = \alpha_{ij}$, and $W(\mathrm{R}_j, X_i) = \beta_{ij}$. Hence, the stoichiometry matrix Γ becomes the *incidence matrix* of the graph.

III. Robust Lyapunov Functions and Uncertain Systems Framework

A. Robust Lyapunov Functions

In order for the stability analysis of CRNs to be independent of the specific kinetics, we aim at constructing Lyapunov functions which are dependent only on the graphical structure, and hence are valid for all reaction rate functions that belongs to $\mathscr{K}_\Gamma$. Therefore, we state the following definition:

Definition 1: Given (3). Let $\tilde{V} : \bar{\mathbb{R}}^q \to \bar{\mathbb{R}}_+$ be locally Lipschitz, and let $W_{R,x_e} : \mathbb{R}^n \to \mathbb{R}^q$ be a $\mathscr{C}^1$ function, where x_e is an equilibrium. Then, $(\tilde{V}, W_{R,x_e})$ is said to induce a *Robust Lyapunov Function* (RLF) with respect to the network family $\mathscr{N}_\Gamma$ if for any choice of $R \in \mathscr{K}_\Gamma, x_e \in \bar{\mathbb{R}}_+^n$ the following holds for $V = \tilde{V} \circ W_{R,x_e}$,

1) *Positive-Definite*: $V(x) \geq 0$, and $V(x) = 0$ if and only if $R(x) \in \ker \Gamma$.
2) *Nonincreasing*: $\dot{V}(x) \leq 0$ for all $x \in \mathscr{C}_{x_e}$.

Remark 1: As will be seen afterwards, the function $\tilde{V}$ in decomposition of the Lyapunov function is invariant with respect the to particular network realization in $\mathscr{K}_\Gamma$, while the function $W_{R,x_\circ}$ is allowed to depend on the kinetic details of the network. Two main examples of the function $W_{R,x_\circ}$ are $W_{R,x_\circ}(x) = R(x)$, and $W_{R,x_\circ}(x) = x - x_e$.

As an abuse of notation, we will call the parametrized Lyapunov function $V_{R,x_\circ}$ an RLF.

Remark 2: The time-derivative in the definition above is the upper right Dini's derivative [13]:

$$\dot{V}(x) := \limsup_{h\to 0^+} \frac{V(x + h\Gamma R(x)) - V(x)}{h}, \qquad (4)$$

which is finite for all x since V is locally Lipschitz.

Since the RLF defined above is not strict, we need the following definition:

Definition 2: An RLF V_{R,x_e} for $\mathscr{N}_\Gamma$ is said to satisfy *LaSalle's condition* if for all solutions $\tilde{x}(t), x(0) \in \mathscr{C}_{x_e}$ of (3) with $\tilde{x}(t) \in \ker \dot{V} \cap \mathscr{C}_{x_0}$ for all $t \geq 0$, we have $\tilde{x}(t) \in E_{x_\circ}$ for all $t \geq 0$, where $E_{x_\circ} \subset \mathscr{C}_{x_\circ}$ be the set of equilibria for (3).

The following theorem adapts Lyapunov's second method [13], [8] to our context.

Theorem 1 (Lyapunov's Second Method): Given (3) with initial condition $x_\circ \in \mathbb{R}_+^n$, and let $\mathscr{C}_{x_\circ}$ as the associated stoichiometric compatibility class. Assume there exists an RLF Lyapunov function. and suppose that $x(t)$ is bounded,

1) then the equilibrium set $E_{x_\circ}$ is Lyapunov stable.
2) If, in addition, V satisfies the LaSalle's Condition, then $x(t) \to E_{x_\circ}$ as $t \to \infty$ (i.e., the point to set distance of $x(t)$ to $E_{x_\circ}$ tends to 0). Furthermore, any isolated equilibrium relative to $\mathscr{C}_{x_\circ}$ is asymptotically stable.
3) If V satisfies the LaSalle's condition, and all the trajectories are bounded, then: If there exists $x^* \in E_{x_\circ}$, which is isolated relative to $\mathscr{C}_{x_\circ}$ then it is unique, i.e., $E_{x_\circ} = \{x^*\}$. Furthermore, it is globally asymptotically stable equilibrium relative to $\mathscr{C}_{x_\circ}$.

Remark 3: Note that the PWLR Lyapunov function considered can not be used to establish boundedness, as it may fail to be proper. Therefore, we need to resort to other methods so that the boundedness of solutions can be guaranteed. For instance, if the network is conservative, i.e the exists $w \in \mathbb{R}_+^n$ such that $w^T\Gamma = 0$, which ensures the compactness of $\mathscr{C}_{x_\circ}$.

B. Uncertain Systems Framework

As arbitrary monotone kinetics are allowed in our formulation of the CRN family $\mathscr{N}_\Gamma$, the system (3) with kinetics $\mathscr{K}_\Gamma$ can be viewed as an uncertain system. However, this system does not fit directly to the traditional types of uncertainties (e.g parameter uncertainty) known in the literature. In this subsection, we show that shifting the analysis of the system to reaction coordinates enables us to view it as a *linear parameter varying* (LPV) system where the existence of a common Lyapunov function for the LPV system implies the existence of a robust Lyapunov function for the CRN.

Let $r(t) := R(x(t))$, then we have:

$$\dot{r}(t) = \frac{\partial R}{\partial x}(x(t))\Gamma r(t) = \rho(t)\Gamma r(t), \tag{5}$$

where $\rho(t) := \frac{\partial R}{\partial x}(x(t))$. We can write $\rho(t)$ as a conic combination of individual partial derivatives as follows:

$$\rho(t) = \sum_{i,j:\alpha_{ij}>0} \rho_{ji}(t)E_{ji}, \tag{6}$$

where $[\rho(t)]_{ji} = \rho_{ji}(t)$, and $[E_{ji}]_{j'i'} = 1$ if $(j', i') = (j, i)$ and zero otherwise.

Let s denote the number of elements in the support of $\partial R/\partial x$, and let $\kappa : \{1, .., s\} \to \{(i, j) : \alpha_{ij} > 0\}$ be an indexing map. Then, we can write (5) as:

$$\dot{r} = \sum_{i,j:\alpha_{ij}>0} \rho_{ji}(t)E_{ji}\Gamma r = \sum_{\ell=1}^{s} \rho^\ell(t)\Gamma^\ell r, \tag{7}$$

where $\Gamma^\ell = e_j\gamma_i^T$, $\rho^\ell(t) = \rho_{ji}(t)$, with $(i, j) = \kappa(\ell)$, and $\{e_j\}_{j=1}^{\nu}$ denotes the canonical basis of $\mathbb{R}^\nu$. Hence, eq. (7) represents a linear parameter-varying system which has s nonnegative time-varying parameters $\{\rho^1(t), .., \rho^s(t)\}$ where the system matrix belongs to the conic hull of the set of matrices $\{\Gamma^1, ..., \Gamma^s\}$.

Hence, we have the following definition:

Definition 3: A function $\tilde{V} : \bar{\mathbb{R}}_+^\nu \to \bar{\mathbb{R}}_+$ is said to be a Lyapunov function for the linear system $\dot{r} = \Gamma^\ell r$ if it is locally Lipschitz, nonnegative, has a negative semi-definite time-derivative, and $\ker \tilde{V} \subset \ker \Gamma^\ell$. Furthermore, $\tilde{V}$ is said to be a *common Lyapunov function* for the set of linear systems $\{\dot{r} = \Gamma^1 r, ..., \dot{r} = \Gamma^s r\}$ if it is a Lyapunov function for each of them, and $\ker \tilde{V} = \bigcap_{\ell=1}^{s} \ker \Gamma^\ell$.

Hence, we are ready to state the following result:

Theorem 2: Given Γ. Assume that there exists a common Lyapunov function $\tilde{V} : \bar{\mathbb{R}}_+^\nu \to \bar{\mathbb{R}}_+$ for the set of linear systems $\{\dot{r} = \Gamma^1 r, ..., \dot{r} = \Gamma^s r\}$. Then, $(\tilde{V}, R)$ induces the Robust Lyapunov function parameterized as $V_R(x) = \tilde{V}(R(x))$ for the CRN family $\mathscr{N}_\Gamma$.

Remark 4: Since the zero matrix belongs to the conic hull of $\{\Gamma^1, ..., \Gamma^s\}$, asymptotic stability can't be established by the mere existence of the common Lyapunov function. A LaSalle's argument is needed as will be mentioned in the following section.

C. Dual Robust Lyapunov Function

The RLF introduced in the previous subsection was a function of $R(x)$. We show now that if $\tilde{V}$ can be written as a certain composition, then the Lyapunov function of the form $\hat{V}(x - x_e)$ can be used, where x_e is an equilibrium point for (3).

Theorem 3: Let $V_1(x) = \tilde{V}(R(x))$ be representing an RLF for the network family $\mathscr{N}_\Gamma$. If there exists $\hat{V} : \mathbb{R}_+^n \to \bar{\mathbb{R}}_+$ such that for all r:

$$\tilde{V}(r) = \hat{V}(\Gamma r), \tag{8}$$

then $V_2(x) = \hat{V}(x - x_e)$ represents an RLF for the network family $\mathscr{N}_\Gamma$, where x_e is an equilibrium point for (3).

In order to present the next theorem, we need some notation. Recall that the extent of reaction [2] is defined as: $\xi(t) = \int_0^t R(x(\tau))d\tau + \xi(0)$. If $x(t) \in \mathscr{C}_{x_e}$, then $\exists \xi^* \geq 0$ such that $x_e - x_\circ = \Gamma\xi^*$. We set $\xi(0) := \xi^*$. Hence, we can write:

$$\Gamma\xi(t) = x(t) - x_e, \tag{9}$$

and

$$\dot{\xi} = R(x_e + \Gamma\xi), \xi(0) := \xi^*. \tag{10}$$

Let D^T be a matrix which its columns are basis vectors of $\ker \Gamma^T$, and denote $z(t) = \dot{x}(t)$. Then, we can write:

$$\dot{z} = \Gamma \frac{\partial R(x)}{\partial x} z, Dz(0) = 0. \quad (11)$$

Therefore, we state the following result without proof for the sake of space:

Theorem 4: Given Γ. Let $\tilde{V} : \bar{\mathbb{R}}_+^{\nu} \to \bar{\mathbb{R}}_+$. Assume there exists $\hat{V} : \mathbb{R}_+^n \to \bar{\mathbb{R}}_+$ such that for all r, $\tilde{V}(r) = \hat{V}(\Gamma r)$. If $\tilde{V}$ is a common Lyapunov function for $\{\dot{r} = e_{j_1}\gamma_{i_1}^T r, ..., \dot{r} = e_{j_s}\gamma_{i_s}^T r\}$ where $(i_\ell, j_\ell) = \kappa(\ell)$. Then,

1) $(\tilde{V}, R)$ induces an RLF parameterized as $\tilde{V}(R(x))$ for $\dot{x} = \Gamma R(x)$.
2) $(\hat{V}, W)$, $W(x) = x - x_e$ induces an RLF parameterized as $\hat{V}(x - x_e)$ for $\dot{x} = \Gamma R(x)$.
3) $\tilde{V}(\xi)$ is nonnegative, and nonincreasing along the trajectories of $\dot{\xi} = R(x_e + \Gamma\xi)$.
4) $\hat{V}(z)$ is common Lyapunov function for the set of linear systems $\{\dot{z} = (\gamma_{i_1} e_{j_1}^T)z, ..., \dot{z} = (\gamma_{i_s} e_{j_s}^T)z\}$, with the constraint $Dz(0) = 0$ for each of them.

IV. Application to Piecewise Linear in Rates Lyapunov Functions

A. Relationship to Previous Results

In [7], the concept of Piecewise Linear in Rate (PWLR) Lyapunov functions has been introduced based on a direct analysis of the CRN. Such functions satisfy the conditions of Definition 1, and hence they are Robust Lyapunov functions. In this subsection, we show that those results can be interpreted in the uncertain systems framework introduced above. This also allows us to provide alternative algorithms for the existence and construction of PWLR functions.

For a given stoichiometry matrix $\Gamma \in \mathbb{R}^{n\times r}$, a partitioning matrix $H \in \mathbb{R}^{p\times r}$ is given such that $\ker H = \ker \Gamma$. PWLR Lyapunov functions are piecewise linear in rates, i.e. they have the form: $V(x) = \tilde{V}(R(x))$, where $\tilde{V} : \mathbb{R}^{\nu} \to \mathbb{R}$ is a continuous PWL function given as

$$\tilde{V}(r) = |c_k^T r|, \; r \in \pm\mathcal{W}_k, k = 1, .., m/2, \quad (12)$$

where $\mathcal{W}_k = \{r \in \mathbb{R}^{\nu} : \Sigma_k H r \geq 0\}, k = 1, .., m$ form a proper conic partition of $\mathbb{R}^{\nu}$ and $\{\Sigma_k\}_{k=1}^m$ are signature matrices with the property $\Sigma_k = -\Sigma_{m+1-k}, k = 1, .., m/2$. Further details on how H, C are defined and constructed are available in [8].

In [7], a procedure has been provided for checking candidate PWLR functions based on direct analysis. We state here an equivalent formulation of those conditions.

Proposition 5: Given Γ and H. Let $V = \tilde{V} \circ R$ be the candidate continuous nonnegative PWLR with $C = [c_1 \; ... \; c_{\frac{m}{2}}]^T \in \mathbb{R}^{\frac{m}{2}\times r}$. Then $\tilde{V}$ is a RLF if and and only if:

1) $\ker C = \ker \Gamma$, and
2) there exists $\{\Lambda^\ell\}_{\ell=1}^s \subset \mathbb{R}^{\frac{m}{2}\times\frac{m}{2}}$ such that

$$\Lambda^\ell H = C\Gamma^\ell, \quad (13)$$

and $\lambda_k^\ell \Sigma_k > 0$, where $\Lambda^\ell = [\lambda_1^{\ell\,T} ... \lambda_{m/2}^{\ell\;\,T}]^T$.

If $\tilde{V}$ is convex, then the second condition can be replaced with,

2) there exists $\{\Lambda^\ell\}_{\ell=1}^s \subset \mathbb{R}^{m\times m}$ Metzler matrices such that

$$\Lambda^\ell \tilde{C} = \tilde{C}\Gamma^\ell, \quad (14)$$

and $\Lambda^\ell \mathbf{1} = 0$ for all $\ell = 1, .., s$, where $\tilde{C} = [C^T - C^T]^T$.

The proof can be carried out by performing elementary algebraic manipulations on the results of [7]. The details are omitted for brevity.

Remark 5: Note that eq. (14) resembles the standard result on the existence of a convex PWL Lyapunov function for a linear system [9], [10]. This shows that Theorem 2 provides us with the framework to utilize the existing linear stability analysis techniques in the literature to construct robust Lyapunov functions for nonlinear systems such as CRNs.

Before proceeding, we need to introduce the concept of a neighbor to a region. Fix $k \in \{1, .., m/2\}$. Consider H: for any pair of linearly dependent rows $h_{i_1}^T, h_{i_2}^T$ eliminate $h_{i_2}^T$. Denote the resulting matrix by $\tilde{H} \in \mathbb{R}^{\tilde{p}\times\nu}$, and let $\tilde{\Sigma}_1, .., \tilde{\Sigma}_m$ the corresponding signature matrices. Therefore, the region can be represented as $\mathcal{W}_k = \{r | \tilde{\Sigma}_k \tilde{H} r \geq 0\}$. The *distance* d_r between two regions $\mathcal{W}_k, \mathcal{W}_j$ is defined to be the *Hamming distance* between $\tilde{\Sigma}_k, \tilde{\Sigma}_j$. Hence, the set of neighbors of a region $\mathcal{W}_k$ are defined as:

$$\mathcal{N}_k = \{j | d_r(\mathcal{W}_j, \mathcal{W}_k) = 1, j = 1, .., m\},$$

Equivalently, note that a neighboring region to $\mathcal{W}_k$ is one which differs only by the switching of one inequality. Denote the index of the switched inequality by the map $s_k(.) : \mathcal{N}_k \to \{1, .., p\}$. For simplicity, we use the notation $s_{k\ell} := s_k(\ell)$.

We use Theorem 2 to show that the problem of constructing a PWLR Lyapunv function over a given partition, i.e. a given H, can be solved via linear programming. However, instead of encoding the nondecreasingness condition into precomputed sign patterns as in [7], we use here an alternative conditions which are stated in the following proposition, where the proof is omitted for brevity:

Proposition 6: Given a stoichiometry matrix Γ and a partitioning matrix $H \in \mathbb{R}^{p\times r}$. Consider the following linear program:

$$\begin{aligned} \text{Find} \quad & c_k, \xi_k, \zeta_k \in \mathbb{R}^{\nu}, \Lambda^\ell \in \mathbb{R}^{m\times m}, \eta_{kj} \in \mathbb{R}, \\ & k = 1, .., \tfrac{m}{2}; j \in \mathcal{N}_k, \ell = 1, .., s, \\ \text{subject to} \quad & c_k^T = \xi_k^T \Sigma_k H, \\ & C\Gamma^\ell = \Lambda^\ell H, \lambda_k^\ell \Sigma_k \geq 0, \\ & c_k - c_j = \eta_{kj} \sigma_{k s_{kj}} h_{s_{kj}}, \\ & \xi_k \geq 0, \mathbf{1}^T \xi_k > 0, \Lambda^\ell \geq 0. \end{aligned}$$

Remark 6: The LaSalle's condition can be verified via a graphical algorithm described in [8].

B. The Dual PWL Lyapunov Function

In §III-C, it was shown that if there exists $\hat{V}$ such that $\tilde{V}(r) = \hat{V}(\Gamma r)$, then there exists a dual RLF for the same network family. In the case of PWLR Lyapunov functions, condition 1 in Proposition 5 implies that this is always possible. Hence, consider a PWLR Lyapunov function defined with a partitioning matrix H as in (12). By Proposition 5 and the assumption that $\ker H = \ker \Gamma$, there exists $G \in \mathbb{R}^{p\times n}, B \in \mathbb{R}^{\frac{m}{2}\times n}$ such that $H = G\Gamma, C = B\Gamma$. Similar to $\{\mathcal{W}\}_{k=1}^m$, we can define the following regions:

$$\mathcal{V}_k = \{z | \Sigma_k G z \geq 0\}, k = 1, .., m,$$

where it can be seen that $\mathcal{V}_k$ has nonempty interior iff $\mathcal{W}_k$ has nonempty interior.
Therefore, as the pair (C, H) specify the PWLR function fully, also the pair (B, G) specifies the following function:

$$\hat{V}(z) = b_k^T z, \text{ when } \Sigma_k G z \geq 0,$$

where $B = [b_1, ..., b_{\frac{m}{2}}]^T$. If $\tilde{V}$ is convex, then it can be written in the form: $V_1(x) = \|CR(x)\|_\infty$. Similarly, the convexity of $\hat{V}$ implies that $V_2(x) = \|B(x - x_e)\|_\infty$.

Theorem 3 established that if $\tilde{V}(R(x))$ is an RLF, then $\hat{V}(x - x_e)$ is an RLF also. The following theorem shows that converse holds also.

Theorem 7: Given Γ, Then, if there exists $G \in \mathbb{R}^{p\times n}, B \in \mathbb{R}^{\frac{m}{2}\times n}$ such that:

1) $(B\Gamma, G\Gamma)$ defines a PWLR RLF, then (B, G) defines a dual PWL RLF.
2) (B, G) defines a dual PWL RLF, then $(B\Gamma, G\Gamma)$ defines a PWLR RLF.

V. PIECEWISE QUADRATIC IN RATES LYAPUNOV FUNCTIONS

The most widely used class of Lyapunov functions in the literature is the class of quadratic functions. However, as it has been known that this class functions is insufficient for uncertain system stability analysis, convex piecewise linear [14], [11] and convex piecewise quadratic [14] counterparts have been proposed. More recently, piecewise quadratic Lyapuonv functions were used for piecewise affine and hybrid systems [15]. In this section, we use Theorem 2 to cast a semi-definite program (SDP) for constructing Piecewise Quadratic in Rates (PWQR) Lyapunov function over a given polyhedral conic partition defined as in the previous section. Furthermore, we show that the existence of a PWLR Lyapunov function implies automatically that our PWQR SDP is feasible over the same partition. Thus, the class of PWQR Lyapunov functions is potentially more general the PWLR functions over a fixed partition.

However, a major disadvantage of PWQR Lyapuonv functions defined on polyhedral partitions is the absence of tight tools for checking positive definiteness such as the Farkas Lemma. The corresponding concept here is the concept of *copositive matrices*. A matrix $A \in \mathbb{R}^{n\times n}$ is said to be *copositive* if $x^T A x \geq 0$ for all $x \geq 0$. The class of optimization problems that involves copositive constraints is termed *copositive programming*. Although copositive programs are convex, solving them generally is shown to be NP-hard [16]. Therefore, several semi-definite relaxations of copositive constraints have been proposed [16]. A simple relaxation method (an S-procedure type) relies on the observation that the class of copositive matrices encompasses the classes of positive semi-definite matrices, and nonnegative matrices. Therefore, copositive constraints can be relaxed to a sum of a nonnegative and semi-definite matrices. This relaxation is exact only for $n \leq 4$, i.e there exists copositive matrices with $n > 4$ that can not be written as a sum of positive semi-definite and nonnegative matrices.

We are ready now to define PWQR functions over a conic polyhederal partition:

Definition 4: Let H be given. A function V is a PWQR function if it has the representation $V = \tilde{V} \circ R$, where $\tilde{V} : \bar{\mathbb{R}}_+^\nu \to \bar{\mathbb{R}}_+$ is a continuous nonnegative PWQ function which has the form:

$$\tilde{V}(r) = r^T P_k r + 2c_k^T r = \begin{bmatrix} r \\ 1 \end{bmatrix}^T \begin{bmatrix} P_k & c_k^T \\ c_k & 0 \end{bmatrix} \begin{bmatrix} r \\ 1 \end{bmatrix}, \text{ if } r \in \mathcal{W}_k, \tag{15}$$

for some matrices $\{P_k\}_{k=1}^m \subset \mathbb{R}^{\nu\times\nu}, \{c_k\}_{k=1}^m \subset \mathbb{R}^\nu$, with $P_k = P_{m+1-k}, c_k = -c_{m+1-k}$, for $k = 1, .., \frac{m}{2}$.

In order to construct such functions, we need to ensure that V and $-\dot{V}$ are nonnegative over the interior of partition regions. This amounts to add a constraint of nonnegativity of a quadratic form over a polyhedral region. Hence, our problem is essentially a copositive programming problem, which we will relax it to semi-definite programming as in the following theorem:

Theorem 8: Given a stoichiometry matrix Γ and a partitioning matrix $H \in \mathbb{R}^{p\times r}$. Consider the following semi-definite program:

Find $P_k \in \mathbb{S}^r, c_k \in \mathbb{R}^\nu, A_k^1, A_k^2, B_{k\ell}^1, B_{k\ell}^2 \in \mathbb{S}^p, \xi_k, \zeta_k \in \mathbb{R}^p,$
$\lambda_{kj} \in \mathbb{R}^r, \eta_{kj} \in \mathbb{R}, k = 1, .., \frac{m}{2}, \ell = 1, .., s, j \in \mathcal{N}_k$

subject to

$$\begin{bmatrix} P_k & c_k^T \\ c_k & 0 \end{bmatrix} \geq \begin{bmatrix} (\Sigma_k H)^T (A_k^1 + A_k^2)(\Sigma_k H) & \xi_k^T \Sigma_k H \\ (\xi_k^T \Sigma_k H)^T & 0 \end{bmatrix}, \tag{16}$$

$$\begin{bmatrix} \Gamma^{\ell^T} P_k + P_k \Gamma^\ell + (\Sigma_k H)^T (B_{k\ell}^1 + B_{k\ell}^2)(\Sigma_k H) & c_k^T \Gamma^\ell + \zeta_k \Sigma_k H \\ (c_k^T \Gamma^\ell + \zeta_k \Sigma_k H)^T & 0 \end{bmatrix} \leq 0, \tag{17}$$

$$P_k - P_j = \lambda_{kj} h_{s_{kj}}^T + h_{s_{kj}} \lambda_{kj}^T, c_k - c_j = \eta_{kj} h_{s_{kj}}, \tag{18}$$

$$P_k U = 0, c_k^T U = 0, \tag{19}$$

$$A_k^1, B_{k\ell}^1 \succeq 0, A_k^2, B_{k\ell}^2 \geq 0, \xi_k \geq 0, \zeta_{kj} \geq 0.$$

If the SDP is feasible , then $V = \tilde{V} \circ R$ with $\tilde{V}$ as defined in (15) is a Robust Lyapunov function for the network family $\mathscr{N}_\Gamma$ if $\ker \tilde{V} = \ker \Gamma$.

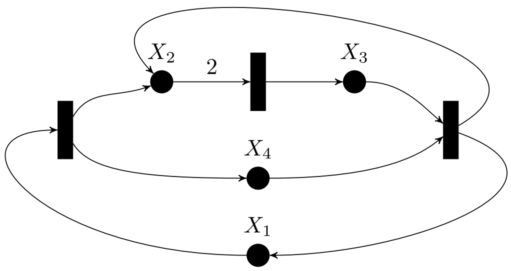

Fig. 1. Example of a CRN.

Remark 7: The linear term in (15) can be set to zero, which simplifies that SDP in Theorem 8. In this case, if compare with the linear program for constructing PWLR Lyapunov functions on a given partiton as in Proposition 6, we note that Theorem 8 gives sufficient conditions only due to the relaxation of copositive constraints to semi-define counterparts. Nevertheless, it can be seen as easily that whenever a PWLR Lyapunov function exists over a particular partition, then the simplified SDP is feasible. Therefore, the class of feasbile solutions to the simplified SDP in Theorem 8 is potentially larger than PWLR counterparts. This can be stated as follows:

Corollary 9: Given Γ. If there exists a PWLR Lyapunov function $V(x)$ with a partition matrix H, then the SDP problem in Theorem 8 with the linear terms constrained to be zeros is feasible. In particular, $P_k = c_k c_k^T, k = 1, .., m$ is a feasible solution.

VI. Example

Consider the following CRN depicted in Figure 1:

$$\begin{aligned} X_1 &\longrightarrow X_2 + X_4, \\ 2X_2 &\longrightarrow X_3, \\ X_3 + X_4 &\longrightarrow X_1 + X_2. \end{aligned}$$

Despite its simplicity, its stability can not be established via previous results in the literature [3], [4], [17] even for the Mass-Action case. However, if we apply Proposition 6, Theorem 3, and Theorem 8 we get the following matrices:

$$C = \begin{bmatrix} 3 & 10 & -13 \\ 10 & -10 & 0 \\ 10 & -4 & -6 \end{bmatrix}, B = \begin{bmatrix} 3 & 0 & -10 & 0 \\ 10 & 0 & 10 & 0 \\ 10 & 0 & 4 & 0 \end{bmatrix}$$
$$P_1 = \begin{bmatrix} -1 & 2 & -1 \\ 2 & 0 & -2 \\ -1 & -2 & 3 \end{bmatrix}, P_2 = \begin{bmatrix} 2 & -2 & 0 \\ -2 & 2 & 0 \\ 0 & 0 & 0 \end{bmatrix}, P_3 = \begin{bmatrix} 2 & 0 & -2 \\ 0 & -4 & 4 \\ -2 & 4 & -2 \end{bmatrix},$$

such that $V(x) = \|CR(x)\|_\infty$, $V(x) = \|B(x - x_e)\|_\infty$, and $V(x) = R^T(x) P_k R(x)$ for $R(x) \in \pm\mathcal{W}_k, k = 1, .., 3$, are RLFs for netwrok family $\mathscr{K}_\Gamma$. The LaSalle's condition can be checked via the algorithm described in [8] to show asymptotic stability.

VII. Conclusion

A framework is presented to transform the problem of finding a Lyapunov function for a Complex Reaction Network (CRN) in concentration coordinates with arbitrary monotone kinetics into finding a common Lyapunov function for a linear parameter varying system in reaction coordinates. Dual Lyapunov functions are presented also. We applied this to reinterpret previous results on Piecewise Linear in Rates Lyapunov function, and to introduce Piecewise Quadratic in Rates Lyapunov functions.

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