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Piecewise Linear in Rates Lyapunov Functions for Complex Reaction Networks

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Abstract— **Piecewise-Linear in Rates (PWLR) Lyapunov functions are introduced for a class of Complex Reaction Networks (CRNs). In addition to their simple structure, these functions are robust with respect to arbitrary monotone reaction rates, of which mass-action is a special case. The existence of such functions ensures the convergence of trajectories towards equilibria, and guarantee their asymptotic stability with respect to the corresponding stoichiometric compatibility class. We give the definition of these Lyapunov functions, present their basic properties, and provide algorithms for constructing them. Examples are provided, relationship with consensus dynamics are discussed, and future directions are elaborated.**

I. INTRODUCTION

The study of the qualitative behavior of complex reaction networks is an area of growing interest, especially in the light of the recent challenges posed by molecular and systems biology. One of the main goals therein is the understanding of cell behavior and function at the level of chemical interactions, and, in particular, the characterization of qualitative features of dynamical behavior (stability, periodic orbits, chaos, etc.). However, a major difficulty in this field is the large degree of uncertainty inherent in models of cellular biochemical networks. Thus, it is imperative to develop tools that are "robust" in the sense of being able to provide useful conclusions based only upon information regarding the qualitative features of the network, and not the precise values of parameters or even the specific form of reaction kinetics. Of course, this goal is often unachievable, since dynamical behavior may be subject to bifurcation phenomena which are critically dependent on parameter values.

Nevertheless, research by many [1], [2], [3] has resulted in the identification of classes of chemical reaction networks for which it is possible to check important dynamical properties such as stability, monotonicity, persistence, etc based on structural information only, and regardless of the parameters involved. In this work, we follow this line of research by proving stability for a wide class of CRNs.

Earlier work regarding asymptotic stability has concentrated on weakly reversible mass-action networks with deficiency zero [1]. It was shown that for this class of networks there exists a unique equilibrium in the interior of each class, which is locally asymptotically stable regardless of the constants involved. Furthermore, the absence of boundary equilibria ensures global asymptotic stability [4], however, showing this generally remains elusive. Another approach for CRN stability is based on the notion of monotone systems [2] . Once monotonicity is established, convergence theorems for monotone systems can be applied.

We propose a more direct approach for the problem, where Piecewise-Linear in Rates (PWLR) Lyapunov functions are 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. The concept of utilizing convex piecewise linear functions as Lyapunov functions to establish the stability is not a new one. For instance, it has been used for special nonlinear systems [5], linear systems [6], [7], and consensus dynamics [8]. Maeda et al. [9] used a piecewise linear function in term of the time derivative of the states.

In this work, we extend this approach for classes of nonlinear systems which admit a graphical structure. By identifying nodes which are represented by nonlinear functions, Lyapunov functions which are piecewise linear in terms of the node functions can be used. We use this approach for CRNs where node functions are reaction rates.

The paper is organized as follows. In Section 2, we present the main definitions and assumptions. Section 3 includes the definition of PWLR Lyapunov function, and the algorithms for checking candidates. Various constructions of PWLR functions are introduced in Section 4, and relation to consensus dynamics is mentioned. In Section 5, we present some illustrative examples, and Section 6 contains the conclusion. For space limitations, the proofs are presented in [10].

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 $\|x\|_\infty = \max_{1 \le i \le n} |x_i|$, and its ℓ_1-norm is $\|x\|_1 = \sum_{i=1}^n |x_i|$. The support of x is defined as $\text{supp}(x) = \{i \in \{1,..,n\} | x_i \neq 0\}$. 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. Let $A \in \mathbb{R}^{n \times \nu}$, then $\ker(A)$ denotes the kernel or null-space of A, while $\text{Im}(A)$ denotes the image space of A. Let $V : D \to \mathbb{R}$, then the kernel of V is $\ker(V) = V^{-1}(0)$.

II. BACKGROUND ON COMPLEX REACTION NETWORKS

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

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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 $x \in \mathbb{R}_+^n$.

In addition, we sometimes require the following to hold:

A5. $\forall i \in \{1, .., n\}, \forall x_1, .., x_{i-1}, x_{i+1}, .., x_n \in \mathbb{R}_+, \alpha_{ij} > 0$, we have $\lim_{x_i \to \infty} R_j(x) = \infty$.

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 non-negative 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 network 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. PWLR Lyapunov Functions

A. Definition

Consider a continuous Piecewise Linear (PWL) function $\tilde{V}$ defined over a polyhedral conic partition of $\mathbb{R}^\nu$. The partition is generated by a matrix $H \in \mathbb{R}^{p \times \nu}$, which is assumed to have $\mu \in \ker H$ with $\mu \gg 0$, and does not have zero rows. Let $\Sigma_1, ..., \Sigma_{2^p}$ be the set of $p \times p$ signature matrices, i.e. all possible $\{\pm 1\}$-diagonal matrices of size $p \times p$. Define cones $\mathcal{W}_1, ..., \mathcal{W}_{2^p}$ as:

$$\mathcal{W}_k = \{r \in \mathbb{R}^\nu : \Sigma_k H r \geq 0\}. \qquad (4)$$

$\mathcal{W}_k$ can be seen as the intersection of half-spaces given by the inequalities $\sigma_{ki} h_i^T r \geq 0, i = 1, .., p$, where $H = [h_1^T \, ... \, h_p^T]^T$, $\Sigma_k = \mathrm{diag}[\sigma_{k1} ... \sigma_{kp}]$. Note that these cones are not pointed as $\ker H \subset \mathcal{W}_k, k = 1, .., 2^p$, which is nontrivial. As some of the intersections may have empty interiors, i.e., conflicting inequalities, we reorder the cones' indices such that first m cones are the nonempty-interior cones, i.e. $\mathcal{W}_k^\circ \neq \varnothing$ iff $k \in \{1, .., m\}$. Thus, we can state the following proposition which ensures the well-posedness of our subsequent definitions:

Proposition 1: Let H, and $\{\mathcal{W}_k\}_{k=1}^m$ be as above, then:

1) *Partitioning:* We have $\mathbb{R}^\nu = \bigcup_{k=1}^m \mathcal{W}_k$, and $\mathcal{W}_k \cap \mathcal{W}_j = \partial W_k \cap \partial \mathcal{W}_j$, for all $j, k = 1, .., m$.
2) *Positivity:* All the cones intersect the positive orthant nontrivially, i.e., $\mathcal{W}_k^\circ \cap \mathbb{R}_+^n \neq \varnothing, k = 1, ..., m$.
3) *Symmetry:* For each $1 \leq k_1 \leq m$, there exists $1 \leq k_2 \leq m$ such that $\Sigma_{k_1} = -\Sigma_{k_2}$. Hence, we can reorder the cones so that $\mathcal{W}_k = -\mathcal{W}_{m-k+1}, k = 1, .., m/2$.

After the defining the partition, we define the function:

Definition 1: Let H, and $\{\mathcal{W}_k\}_{k=1}^m$ be defined as above so that $\ker H = \ker \Gamma$, and assume that $C = [c_1^T \, .. \, c_{m/2}^T]^T \in \mathbb{R}^{m/2 \times \nu}$ be the *coefficients matrix*. Then, $V : \mathbb{R}^n \to \mathbb{R}$ is said to be a Piecewise Linear in Rates (PWLR) function if it admits the representation $V(x) = \tilde{V}(R(x))$, where $\tilde{V} : \mathbb{R}^\nu \to \mathbb{R}$ is a continuous PWL function given as

$$\tilde{V}(r) = |c_k^T r|, \; r \in \mathcal{W}_k \cap -\mathcal{W}_k, k = 1, .., m/2. \qquad (5)$$

Note that by definition, if $\tilde{V}(r) = c_k^T r$, then the function is defined over the *active region* $\mathcal{W}_k$, and if $\tilde{V}(r) = -c_k^T r$, then the active region is $\mathcal{W}_{-k} := \mathcal{W}_{m-k+1}$.

Within the class of PWLR functions, the subclass of *convex* PWLR functions admits a simpler representation:

Definition 2: Let $C = [c_1^T \, .. \, c_{m/2}^T]^T \in \mathbb{R}^{m/2 \times \nu}$ be given such that there exists $v \in \ker C$ with $v \gg 0$. Then, V :

$\mathbb{R}^n \to \mathbb{R}$ is said to be a convex PWLR function if it admits the representation $V(x) = \tilde{V}(R(x))$, where $\tilde{V} : \mathbb{R}^\nu \to \mathbb{R}$ is a a convex PWL given by

$$\tilde{V}(r) = \max_{1 \le k \le m/2} |c_k^T r| = \|Cr\|_\infty. \quad (6)$$

Remark 1: It can be shown that any convex PWL function which satisfies (5) can be represented using (6) [11], and vice versa. Furthermore, given a function (6), partition regions $\{\mathcal{W}_k\}_{k=1}^m$ and the matrix H can be computed.

B. Lyapunov Functions and Stability

The main theme of this paper is to introduce a new class of Lyapunov functions for CRNs (3) which are piecewise linear in terms of the reaction rates (PWLR). Therefore, the functions introduced in Definitions 1 and 2 will be candidate Lyapunov functions. Such functions need to be non increasing along system's trajectories. However, since PWLR functions are non-differentiable on regions' boundaries, we will use the following expression of the time derivative of V along the trajectories of (3):

$$\dot{V}(x) := \max_{k \in K_x} c_k^T \dot{R}(x), \quad (7)$$

where $K_x = \{k : c_k^T R(x) = V(x), 1 \le k \le m\}$, $c_k = -c_{m+1-k}, k = 1, .., \frac{m}{2}$, and $\dot{R}(x) = \frac{\partial R(x)}{\partial x} \Gamma R(x)$.
We define PWLR Lyapunov functions as follows:

Definition 3: Given (3) with initial condition $x_\circ \in \bar{\mathbb{R}}_+^n$. Let $V : \bar{\mathbb{R}}_+^n \to \bar{\mathbb{R}}_+$ be given as: $V(x) = \tilde{V}(R(x))$, where $\tilde{V}$ is the associated PWL function. Then V is said to be a *PWLR Lyapunov Function* if it satisfies the following for all $R \in \mathscr{K}_\Gamma$,

1) *Positive-Definite*: $V(x) \ge 0$ for all x, and $V(x) = 0$ if and only if $R(x) \in \ker \Gamma$.
2) *Nonincreasing*: $\dot{V}(x) \le 0$ for all x.

The set of networks for which there exists a PWLR Lyapunov function is denoted by $\mathscr{P}$.

Definition 4: A PWLR Lyapunov function for $\mathscr{N}_\Gamma$ is said to satisfy *the LaSalle's condition* for $x_\circ$ if for all solutions $\tilde{x}(t)$ of (3) with $\tilde{x}(t) \in \ker \dot{V} \cap \mathscr{C}_{x_0}$ for all $t \ge 0$, we have $\tilde{x}(t) \in E_{x_\circ}$ for all $t \ge 0$, where $E_{x_\circ} \subset \mathscr{C}_{x_\circ}$ be the set of equilibria for (3).

The following theorem adapts Lyapunov's second method [12] to our context.

Theorem 2 (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 a PWLR 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.

Remark 2: For a given Γ, the existence of a PWLR Lyapunov function establishes the stability of system with the network $\mathscr{N}_\Gamma$. Therefore, the Lyapunov function is robust to all kinetic details of the network, and depends only on its graphical structure. It might seem that it is difficult for such function to exist, however, we will describe construction algorithms for wide classes of networks.

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 $\mathscr{C}_{x_\circ}$.

Remark 4: The LaSalle's condition can be verified via a graphical algorithm to be described partially in §III-E.

If the boundedness of solution was known a priori, then Theorem 2 can be strengthened to the following:

Corollary 3 (Global Stability): Consider a CRN in $\mathscr{P}$ that satisfies the LaSalle condition with a given $x_\circ$. Assume that all the trajectories are bounded. 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 5: Corollary 3 implies that the existence of two or more isolated equilibria, even if the interior's equilibrium is unique, excludes the possibility of the existence of a PWLR Lyapunov function. This is to be contrasted with deficiency-zero theorem [1] where boundary equilibria can be accommodated.

C. Checking candidate PWLR functions

The first problem we shall tackle is that of checking that whether a PWLR function is a Lyapunov function for a network family $\mathscr{N}_\Gamma$ given by $\Gamma \in \mathbb{R}^{n \times \nu}$. In this subsection, we are given a candidate V which is represented by the pair $C \in \mathbb{R}^{m/2 \times \nu}, H \in \mathbb{R}^{p \times \nu}$ as in (5).

We need further notation. Fix $k \in \{1, .., m/2\}$. We claim that for checking the continuity of V, it is enough to check it between *neighbors*, which we define next. Consider H, and 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. Note that (4) can be written equivalently as $\mathcal{W}_k = \{r | \tilde{\Sigma}_k \tilde{H} r \ge 0\}$. The *distance* d_r between two regions $\mathcal{W}_k, \mathcal{W}_j$ is defined to be the *Hamming distance* between $\tilde{\Sigma}_k, \tilde{\Sigma}_j$, which is the number of differing entries between them. Hence, the set of neighbors of a region $\mathcal{W}_k$, and the set of neighbor pairs are defined as:

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

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 $s_{k\ell} := s_k(\ell)$.

Let $c_k^T = [c_{k1} \; .. \; c_{k\nu}]$, and let $J_k = \mathrm{supp}(c_k) \subset \{1, .., \nu\}$ be the set of indices of reactions appearing in c_k. Define the set of indices of reactants of J_k as follows

$$I_k = \{1 \le i \le n | \exists j \in J_k \,\text{such that}\, (X_i, \mathrm{R}_j) \in E\}. \quad (8)$$

Also, for all $i \in I_k$, define $J_{ki} = \{j \in J_k | (X_i, \mathrm{R}_j) \in E\}$.

We are now ready to state the following theorem:

Theorem 4: Let $\Gamma \in \mathbb{R}^{n\times\nu}$, and $C \in \mathbb{R}^{m/2\times\nu}$ be given, and let $\tilde{V}$ be given by (5). Then, $V(x) = \tilde{V}(R(x))$ is a PWLR Lyapunov function for the network family $\mathscr{N}_\Gamma$ if and only if the following conditions hold:

C1. $\ker C = \ker\Gamma$.

C2. For all $1 \le k \le m/2$, there exists $\xi_k \in \mathbb{R}^p$ with $\xi_k > 0$ such that $c_k^T = \xi_k^T \Sigma_k H$.

C3. For all $(k,j) \in \mathcal{N}$, $\exists \eta_{kj} \in \mathbb{R}$ such that
$$c_k - c_j = \eta_{kj} h_{s_{kj}}. \tag{9}$$

C4. For all $k = 1,..,m/2$, $i \in I_k$. We require $\operatorname{sgn}(c_{kj_1})\operatorname{sgn}(c_{kj_2}) \ge 0$ for every $j_1, j_2 \in J_{ki}$. Thus, denote $\nu_{ki} = \operatorname{sgn}(c_{kj}), j \in J_{ki}$. Then, there shall exist $\lambda^{(ki)} \in \mathbb{R}^p$, with $\lambda^{(ki)} \ge 0$ such that
$$-\nu_{ki}\gamma_i^T = {\lambda^{(ki)}}^T \Sigma_k H, \tag{10}$$
where $c_k := -c_{m+1-k}$ for $j = 1 + m/2,..,m$. Furthermore, if (10) is satisfied, we shall choose $\lambda^{(ki)}$ so that $\operatorname{supp}(\lambda^{(ki)}) \subset s_k(\mathcal{N}_k)$.

Moreover, $\tilde{V}$ is convex if and only if η_{kj}'s can be chosen so that $\eta_{kj}\sigma_{ks_{kj}} \ge 0$.

Remark 6: Note that C1 is a linear system, while C2-C4 are equivalent to linear programming feasibility problems.

D. Checking candidate convex PWLR functions

The conditions in the previous subsection will be simplified in the case of convex PWLR functions, as it can be noted that C2-3 are satisfied automatically.

Theorem 5: Let $\Gamma \in \mathbb{R}^{n\times\nu}$, and $C \in \mathbb{R}^{m/2\times\nu}$ be given. Then, $V(x) = \|CR(x)\|_\infty$ is a PWLR Lyapunov function for the network family $\mathscr{N}_\Gamma$ if and only if the following two conditions hold:

C1′. $\ker C = \ker\Gamma$.

C4′. For all $k = 1,..,m/2$, $i \in I_k$. We require $\operatorname{sgn}(c_{kj_1})\operatorname{sgn}(c_{kj_2}) \ge 0$ for every $j_1, j_2 \in J_{ki}$. Thus, denote $\nu_{ki} = \operatorname{sgn}(c_{kj}), j \in J_{ki}$. Then, there shall exist $\lambda^{(ki)} \in \mathbb{R}^m$, with $\lambda^{(ki)} \ge 0$ such that
$$-\nu_{ki}\gamma_i = \textstyle\sum_{\ell=1}^m \lambda_\ell^{(ki)}(c_k - c_\ell), \tag{11}$$
where $c_k := -c_{m+1-k}$ for $j = 1 + m/2,..,m$. Furthermore, if (10) is satisfied, we shall choose $\lambda^{(ki)}$ with minimal support.

E. Checking the LaSalle's Condition

Assume that a PWLR Lyapunov function exists. We use the same notation used in the previous two subsections. Consider (10) with $\lambda^{(ki)}$ chosen so that $\operatorname{supp}(\lambda^{(ki)}) \subset s_k(\mathcal{N}_k)$. Let $L_{ki} = s_k^{-1}(\operatorname{supp}(\lambda^{(ki)}))$, which is nonempty since the LHS in (10) is nonzero. Let $L_k = \bigcup_{i\in I_k} L_{ki}$, $I_k^{(0)} := I_k$, and $L_k^{(0)} := L_k$. Define the following nested sets iteratively:
$$I_k^{(i)} = \bigcup_{\ell\in L_k^{(i-1)}} I_\ell, \text{ and } L_k^{(i)} = \bigcup_{\ell\in L_k^{(i-1)}} L_\ell.$$
The iteration terminates when $L_k^{(i^*)} = L_k^{(i^*+1)}$. Denote $\bar{I}_k := I_k^{(i^*)}$. Using this notation, we state the following condition which we call the LaSalle interior condition:

C5i. For all $k \in \{1,..,m\}$, the following shall hold: $\bar{I}_k = \{1,..,n\}$.

If $\tilde{V}$ is convex also, then the LaSalle interior condition is:

C5′i. For all k, $c_k \in \operatorname{Im}(\Gamma_{\bar{I}_k}^T)$, where $\Gamma_{\bar{I}_k} = [\gamma_{i_1}^T .. \gamma_{i_{o_k}}^T]^T, \bar{I}_k = \{i_1,..,i_{o_k}\}$ for some o_k.

Remark 7: It can be shown that conditions C5i and C5′i imply the LaSalle condition provided that $\tilde{x}(0) \in \mathbb{R}_+^n$, which explains the name. The LaSalle Interior condition alone can only establish the asymptotic stability of isolated equilibria in the relative interior of $\mathscr{C}_{x_0}$. However, solutions can in principle approach the boundary, and global stability fails to hold. For space limitations, this issue is handled in [10] where the algorithm is extended to ensure global stability.

Remark 8: C5′i does not follow from C1′ and C4′. For example consider the following CRN
$$X_1 + X_2 \xrightarrow{R_1} 0 \xrightarrow{R_2} X_1, 0 \xrightarrow{R_3} X_2,$$
then $V(x) = |R_1(x) - R_2(x)| + |R_3(x) - R_2(x)| + |R_1(x) - R_2(x)|$ satisfies C1′ and C2′, but not C5′i. For this system, it can be shown that there does not exist any C satisfying the three conditions simultaneously, nor any pair (H, C) satisfying C1-4,5i.

IV. Construction of PWLR Lyapunov Functions

Eq. (9), (10), (11) are bilinear in the variables. Hence, it is difficult to characterize exactly the class $\mathscr{P}$. Therefore, we will provide necessary conditions, and several constructions.

A. Necessary Condition

As the PWLR Lyapunov functions is nondecreasing with arbitrary kinetics, we require sign-definiteness of every term in the expansion of $\dot{V}$. Hence, we partition $\mathbb{R}^\nu$ into *sign regions* within which $\dot{x}$ has a constant term-wise sign. By A7, we can define sign regions in an analogous way to §2.1, where we set $H = \Gamma$ and signature matrix σ_k indicates the sign in that region. Thus, we may write
$$\mathcal{S}_k = \{r \in \mathbb{R}^\nu : \Sigma_k \Gamma r \ge 0\}, k = 1,..,m. \tag{12}$$

To encode this, define the diagonal matrices $B_k = \operatorname{diag}[b_{k1} ... b_{k\nu}]$, $k = 1,..,m/2$, where:
$$b_{kj} = \begin{cases} 1, & \text{if } M_j = \varnothing \\ 0, & \text{if } \exists i_1, i_2 \in M_j \text{ such that } \sigma_{ki_1}\sigma_{ki_2} < 0, \\ -\sigma_{ji^*}, & \text{otherwise, for any } i^* \in M_j. \end{cases}$$
where $M_j = \{i | (X_i, \mathrm{R}_j) \in E, 1 \le i \le n\}$. Therefore, we state the following necessary condition which can be tested via linear programming:

Theorem 6: Given Γ. Consider the network family $\mathscr{N}_\Gamma$, with $\{B_k\}_{k=1}^m$ defined as above, and let U a matrix whose columns form a basis for $\ker\Gamma$. If $\mathscr{N}_\Gamma$ admits a PWLR Lyapunov function, then there exists $0 \ne \zeta_k \in \mathbb{R}^\nu, k = 1,..,m/2$ such that $\zeta_k^T B_k U = 0$, with $\zeta_{kj} \ge 0, j \in \{1,..,\nu\}\backslash\mathcal{I}$, where $\mathcal{I} = \{j | M_j = \varnothing, 1 \le j \le \nu\}$.

B. Construction of PWLR Lyapunov functions over a given partition

Assume that the partition generator $\hat{H}$ is fixed, hence $\{\hat{\mathcal{W}}_k\}_{k=1}^{m_h}$ is determined. Then, conditions C2-C3 are linear in C. Furthermore, the inclusion $\ker C \subset \ker\Gamma$ is implied by C2. The constraint (10), however, is nonconvex. Nevertheless, we shall rewrite it as a linear constraint.

Consider the sign regions $\{\mathcal{S}_k\}_{k=1}^{m_s}$ defined in (12). If we intersect the two partitions $\{\hat{\mathcal{W}}_k\}_{k=1}^{m_h}$, $\{\mathcal{S}_k\}_{k=1}^{m_s}$ with the corresponding c_k's inherited from $\{\hat{\mathcal{W}}_k\}$, the matrix generating the new partition will be $H = [\Gamma^T \hat{H}^T]^T$. Therefore, we may consider, w.l.o.g, partitions induced by matrices of the form $H = [\Gamma^T \hat{H}^T]^T$.Note that we can consider $\{\mathcal{W}_k\}_{k=1}^{m}$ as a refined partition of $\{\mathcal{S}_k\}_{k=1}^{m_s}$, hence we define the map $q(.) : k \mapsto \ell$ if $\mathcal{W}_k \subset \mathcal{S}_\ell$, and the notation $q(k) = q_k$ is used. Thus, we present the following:

Theorem 7: Consider the system (3), with $H = [\Gamma^T \hat{H}^T]^T$, $\{\Sigma_k\}_{k=1}^{m}$,$\{B_k\}_{k=1}^{m_s}$, q_k given as above. Consider the following linear program:

$$\begin{array}{ll} \text{Find} & c_k, \xi_k, \zeta_k \in \mathbb{R}^\nu, \eta_{kj} \in \mathbb{R}, k = 1,..,\frac{m}{2}; j \in \mathcal{N}_k, \\ \text{subject to} & c_k^T = \xi_k^T \Sigma_k H, \\ & c_k^T = \zeta_k^T B_{q_k}, \\ & c_k - c_j = \eta_{kj} \sigma_{k s_{kj}} h_{s_{kj}}, \\ & \xi_k \geq 0, \mathbf{1}^T \xi_k > 0, \zeta_{kj} \geq 0, j \in \{1,..,\nu\} \backslash \mathcal{I}. \end{array}$$

Then there exists a PWLR Lyapunov function with partitioning matrix H if and only if there exist feasible solution to the above linear program with C1 satisfied. Furthermore, the PWLR function can be made convex by adding the constraints $\eta_{kj} \geq 0$.

Remark 9: A natural candidate for the partition matrix is $H = \Gamma$. Hence, we can write

$$V(x) = c_k^T R(x) = \xi_k^T \Sigma_k \Gamma R(x) = \| \operatorname{diag}(\xi_k) \dot{x} \|_1, R(x) \in S_k.$$

If we impose the constraint that for all k, $\xi_k = \mathbf{1}$, then the Lyapunov function considered in [9], $V(x) = \|\dot{x}\|_1$, can be recovered as a special case. However, there are classes of networks for which $H = \Gamma$ does not induce a PWLR Lyapunov function, while there exists a partitioning matrix $\hat{H}$ which does. Understanding when this happens is a challenging open question.

C. Iterative Algorithm for Convex PWLR functions

In this subsection, we present an iterative algorithm for constructing convex PWLR Lyapunov functions. The idea is to start with an initial PWLR function, and aim for restricting the active region of each linear function $c_k^T R(x(t))$ to the region for which it is nonincreasing on it, i.e $c_k^T \dot{R}(x(t)) \leq 0$. This is accomplished by refining the partition as follows.
Let $C_0 = [c_1 \ ... \ c_{m_0}]^T \in \mathbb{R}^{m_0 \times \nu}$, with associated PWLR function. Define the *active region* of a vector c_k, $k = 1,..,m_0$, as:

$$\mathcal{W}_0(c_k) := \{r \in \mathbb{R}^\nu : c_k^T r \geq c_j^T r, -m_0 \leq k \leq m_0, k \neq 0\},$$

where $c_{-k} = -c_k$. Assume that the associated CRN is given by (3). We define *permissible region* of a linear component c_k to be the region for which it is nonincreasing. Hence,

$$\begin{aligned} \mathcal{P}(c_k) &:= \{r \in \mathbb{R}^\nu : \nu_{ki} \gamma_i^T r \leq 0, i \in I_k\} \quad (13) \\ &\subset \{\tilde{r} \in \mathbb{R}^\nu : \tilde{r} = R(x), c_k^T \tfrac{\partial R}{\partial x}(x) \Gamma R(x) \leq 0\}, \end{aligned}$$

where $\nu_{ki} = \operatorname{sgn}(c_{ki})$. Note that in general, $\mathcal{W}_0(c_k) \not\subset \mathcal{P}(c_k)$. Therefore, we need to define a new PWL function with matrix C_1 so that $\mathcal{W}_1(c_k) \subset \mathcal{P}(c_k)$. To achieve this, we augment new rows to C_0. The new rows are of the form

$$c_{m_0+i} := c_k + \nu_{ki} \gamma_i, i \in I_k. \quad (14)$$

Thus, $C_1^{'} := [C_0^T \ c_{m_0+1} \ ... \ c_{m_0+n}]^T$. Finally, C_1 is defined by eliminating linearly dependent pairs of rows from $C_1^{'}$.

Hence, Algorithm 1 can be described as:

1) Given $C_0 = [c_1 \ ... \ c_{m_0}]^T \in \mathbb{R}^{m_0/2 \times \nu}$, $k = 1,..,m_0/2$, and $\ker \Gamma \subset \ker C_0$. Set $k = 1$.
2) Define $C_k^{'} := [C_{k-1}^T \ c_{m_k+1} \ ... \ c_{m_k+n}]^T$, where $c_{m_k+i} := c_k + \nu_{ki} \gamma_i, i = 1,...,n$.
3) Define C_k as $C_k^{'}$ with linearly dependent pairs of rows eliminated.
4) If $C_k = C_{k-1}$ or $k > N$, stop.
5) Set $k := k + 1$, and go to step 2,

where N is the maximum number of iterations allowed.
If Algorithm 1 terminates then we state the following:

Theorem 8: Consider (3). If Algorithm 1 terminates after finite number of iterations with C1$'$ with satisfied, then the resulting function is a PWLR Lyapunov function for the network family $\mathscr{N}_\Gamma$.

Remark 10: The formula (14) is not the unique way for constructing new vectors. Indeed, one can replace the inequality $\nu_{ki} \gamma_i \leq 0$ with any system of inequalities covering the same region. For instance, the region defined by the inequality $R_1 - 2R_2 + R_3 \leq 0$ is a subset of the region defined by the pair $R_1 - R_2 \leq 0, -R_2 + R_3 \leq 0$. Therefore, the *standard settings* of Algorithm 1 are (14) with $C = \Gamma$.

D. Special Constructions and Consensus Dynamics Link

It is possible to construct PWLR Lyapunov functions for CRNs with specific structural properties. For example, our previous work [3] follows this direction, where the following theorem has been proven:

Theorem 9: Consider the network family $\mathscr{N}_\Gamma$. Suppose the following properties are satisfied:

1) $\dim(\ker \Gamma) = 1$,
2) $\forall X_i \in V_S$, there exists a unique output reaction,

Then, the following is a PWLR function for the family $\mathscr{N}_\Gamma$.

$$V(x) = \max_{1 \leq j \leq \nu} \frac{1}{v_j} R_j(x) - \min_{1 \leq j \leq \nu} \frac{1}{v_j} R_j(x), \quad (15)$$

where $v = [v_1 \ldots v_\nu]^T \in \ker(\Gamma), v \gg 0$.

Remark 11: The Lyapunov function (15) is similar to the one used in the consensus literature [8]. In fact, Theorem 9 applies to the standard consensus system $\dot{x} = -Lx$, where L is the Laplacian of the graph. Thus (15) reduces to $V(x) = \max\{x_1,..,x_n\} - \min\{x_1,..,x_n\}$. This shows that proposed methods can be used to study nonlinear consensus problems. This interesting link is further discussed in [10].

V. Examples

A. Illustrative Examples

We present examples to illustrate the presented theorems.

1) Consider the following network given in [1]:
$X_1 \rightleftharpoons 2X_2,\ X_1 + X_3 \rightleftharpoons X_4 \longrightarrow X_2 + X_5 \longrightarrow X_1 + X_3$
The network violates both necessary condition given by 6, therefore it does not admit a PWLR Lyapunov

function. However, the deficiency-zero theorem [1] can be applied with Mass-Action kinetics to show that the interior equilibrium is asymptotically stable despite the existence of boundary equilibria, a situation which is not allowed in our case by Theorem 3.

2) The following CRN illustrates the fact that the mere existence of the PWLR Lyapunov function does not guarantee the boundedness of the trajectories:
$$X_3 \xrightarrow{k_1} X_1,\ 0 \xrightarrow{k_2} X_2, X_1 + X_2 \xrightarrow{k_3} X_3,$$
The three constructions presented yield a Lyapunov function, in particular (15) is a valid one. However, consider the network with Mass-Action Kinetics, and let $A = x_2(0) + x_3(0)$ be the parameter corresponding to the stoichiometric compatibility class. If $A > \frac{k_2}{k_3}$, then the system trajectories are bounded and the unique equilibrium $\left(\frac{k_2 k_3}{k_3 A - k_2}, A - \frac{k_2}{k_3}, \frac{k_2}{k_3}\right)$ is globally asymptotically stable by Theorem 2. However, when $A \le \frac{k_2}{k_3}$, there are no equilibria in the nonnegative orthant, solutions are unbounded and approach the boundary.

3) Consider the following network:
$X_1 \xrightarrow{k_1} X_2,\ X_5 \xrightarrow{k_4} X_4,\ X_2 + X_4 \xrightarrow{k_2} X_4 \xrightarrow{k_3} X_1 + X_5$
The linear program in Theorem 7 with $H = \Gamma$ is infeasible, however, Theorem 4 and Theorem 9 give rise to the PWLR function (15) with $v = \mathbf{1}$. In fact, the use a partitioning matrix $\hat{H} = [1\,0\,0\ -1]$, will ensure the feasibility of the linear program in Theorem 7.

4) Consider the following network:
$2X_1 + 3X_3 \xrightarrow{k_1} 0 \xrightarrow{k_3} 3X_1 + X_2 + 2X_3,\ X_1 + X_2 \xrightarrow{k_2} X_3$
Theorem 9 does not apply. Algorithm 1 with standard settings does not terminate. However, Theorem 7 with $H = \Gamma$ gives the following convex PWLR Lyapunov function: $V(x) = \max\{|6R_1(x) + R_2(x) - 7R_3(x)|, |3R_2(x) - 3R_3(x)|, |6R_1(x) - 6R_3(x)|\}$.

B. Biochemical Example

Consider the following CRN which represents a double futile cycle with distinct enzymes [13]:

$$X_0 + E_0 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} E_0X_0 \xrightarrow{k_2} X_1 + E_0,$$

$$X_1 + E_1 \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} E_1X_1 \xrightarrow{k_4} X_0 + E_1,$$

$$X_1 + F_0 \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} F_0X_1 \xrightarrow{k_6} X_2 + F_0,$$

$$X_2 + F_1 \underset{k_{-7}}{\overset{k_7}{\rightleftharpoons}} F_1X_2 \xrightarrow{k_8} X_1 + F_1,$$

where the associated graph is depicted in Figure 1.

Both Theorems 7, 8 are applicable. The PWLR function constructed can be represented as: $V(x) = \|\operatorname{diag}(\xi)\dot{x}\|_1$, where $\xi = [2\,2\,2\,1\,1\,1\,1\,1\,1\,1\,1]$ and species are ordered as $X_0, X_1, X_2, \ldots, F_1X_2$. The network is injective by the work of [14], hence it can not have more than a single equilibrium state in the interior of each stoichiometric class. Furthermore, the results of [1], [2] are not applicable. However, Theorem 2 implies that a Lyapunov function exists and that the unique equilibrium is globally asymptotically stable.

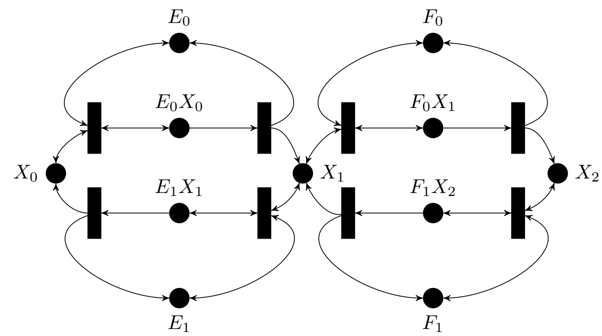

Fig. 1. Double Futile Cycle with distinct enzymes.

VI. Conclusions

A new type of Lyapunov functions have been introduced for network systems, and CRNs in particular. These functions are piecewise linear and possibly convex in terms of monotone reaction rates. We have provided methods for checking candidate PWLR Lyapunov functions. Several theorems were introduced for their construction. The authors are currently working on characterizing the class of CRNs that admit a PWLR Lyapunov function and methods to construct them.

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