Interplay between Contractivity and Monotonicity for Reaction Networks

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Abstract

This work studies relationships between monotonicity and contractivity, and applies the results to establish that many reaction networks are weakly contractive, and thus, under appropriate compactness conditions, globally convergent to equilibria. Verification of these properties is achieved through a novel algorithm that can be used to generate cones for monotone systems. The results given here allow a unified proof of global convergence for several classes of networks that had been previously studied in the literature.

1 Introduction

Formal models known as reaction networks provide good descriptions of certain processes (such as, but not limited to, in the fields of biology and chemistry). Various specific examples include modeling PCR kinetics [1], futile cycles in molecular systems biology [2], the Extracellular Regulated Kinase signaling pathway [3], and post-translational modification cycles [4]. For general introductions to the field see for instance [5] or [6].

A natural problem arising from these models is to predict their qualitative behavior. Significant effort has gone into developing the mathematics for reaction networks and various theorems describing the qualitative behavior of reaction networks. Some examples include deficiency theory for stability and uniqueness of equilibria [6], conditions relating to multistationarity for reaction networks [7], and conditions related to the existence of bifurcations [8]. Whether or not reaction networks converge to an equilibrium point, and whether that equilibrium point is unique, is of particular interest. This paper focuses on two properties closely related to the convergence to equilibrium points: contractivity and monotonicity.

A dynamical system is contractive when there exists a norm on the system's state space such that for every pair of points in the state space, these two points converge exponentially quickly to each other in the norm. We define weak contractivity in our paper to simply mean that the norm distance between the two points is always decreasing (not necessarily exponentially). A dynamical system is monotone if there exists a partial ordering on the state space that is preserved as the system evolves forward in time. Often times these partial orderings are induced by convex cones, where we say for two points x, y in the system's state space that $x \leq y$ if and only if $y - x \in K$, where K is some pointed cone.

Both contractivity and monotonicity each have their own extensive body of literature [9] [10] [11] [12] with applications to Riemannian geometry [13], safety constraints [14], network systems [15], excitatory Hopfield neural networks [16], and biological networks [17]. Both these methods have also been used (separately) in the literature to establish conclusions about the dynamics of reaction networks, for example in [18],[2],[19], [20], and [21]. Contractivity methods have been used in reaction networks before, such as in [18] where it is shown that a certain class of networks has a negative logarithmic norm, and thus contractive properties. In the papers [2], [19] and [20] various monotonicity methods are used to prove the convergence properties of certain reaction networks. Contractivity has also been shown to have connections to Lyapunov functions. In the work in [22] algorithms are provided for constructing piecewise linear Lyapunov functions for reaction networks, and in later work these functions are connected to contractivity [17].

In our work, we demonstrate a connection between monotonicity and contractivity and use this to establish weak contractivity of a class of networks via monotonicity. Our main results pertain to establishing the weak contractivity of reaction networks. We produce an algorithm (Algorithm 1) to produce the vertices that define the unit ball for a norm for which our system is weakly contractive. In

particular, we establish weak contractivity for three new classes of reaction networks. These include the globally convergent networks considered in [20], [19], and [2]. We also note in the appendix that our results can be extended to irreversible networks, thus also generalizing results contained in [23].

Weak contractivity is important since it limits the possible dynamics of our system. In particular, if our weakly contractive system has a compact state space, it must converge to a unique equilibrium.

Below we state one of our core theorems, which generalizes several older results. First, we will need a few definitions. Let S be the set of matrices of any dimensions where each entry is either -1, 0, or 1, and each matrix has at most 2 nonzero entries in each column. Let S^t be the set of matrices such that $A \in S^t$ iff $A^t \in S$ (here A^t is the transpose of A), and let $\mathcal{N} = S \cup S^t$. Let \mathcal{P} be the set of matrices that have at most one nonzero entry in each row, and no column of zeroes. Let \mathcal{D} be the set of square matrices with a nonzero diagonal, and zeros elsewhere. Lastly, we say a reaction network is non-catalytic if no species appears on both sides of a reaction. (Undefined terms are introduced in Section 2.)

Theorem 1. If a reversible non-catalytic reaction network has a stoichiometric matrix of the form PND where $P \in \mathcal{P}$, $N \in \mathcal{N}$, and $D \in \mathcal{D}$, and the dimensions are such that we can multiply out the matrices in PND, then its corresponding system is weakly contractive.

This theorem contains all the explicit classes of networks that we consider in this paper. One advantageous aspect to this theorem is that for many networks, it can be simple to tell via inspection of the reaction network whether or not the theorem applies.

Our work is organized as follows. In Section 2 we establish our background and notation. In Section 3 we establish some preliminary lemmas to allow us to establish the monotonicity of a system. In Section 4 we establish a connection between monotonicity and contractivity, allowing us to go between the two properties. In Section 5 we establish an algorithm, which in some cases can be used to establish that a system is contractive/monotone. In Section 6 we give some examples meant to help further explain some of our constructions. Sections 7 and 8 use our methods to explicitly show certain classes of reaction networks are contractive with respect to certain norms. Finally, Section 9 brings multiple parts together to establish Theorem 1. Section 10 provides further examples.

2 Background and Notation

Our objects of study in this paper will be reaction networks (defined below) and their corresponding differential equations. Throughout the paper fix a positive integer n.

For a vector $x \in \mathbb{R}^n$ we indicate the *i*'th coordinate as $(x)_i$, and if I contains multiple indices then $(x)_I$ is the ordered set of values with these indices. As an example, if we take $I = \{1, 2, 4\}$ and x = [2, 3, 4, 5, 6], then we have $(x)_I = [2, 3, 5]$. The support of a vector x is the set of indices I such that if $i \in I$ then $(x)_i \neq 0$. We indicate the usual Euclidean inner product by $\langle x, y \rangle$. We use the word cone for a convex cone (i.e., closed under multiplication by nonnegative reals, and closed under addition). For a cone $K \subseteq \mathbb{R}^n$ we indicate its dual cone by $K^* \subseteq \mathbb{R}^n$. Recall that if we have a cone $K \subseteq \mathbb{R}^n$ the dual cone is $K^* = \{x \in \mathbb{R}^n | \langle x, y \rangle \ge 0 \forall y \in K\}$. We indicate the Jacobian of a function f by \mathcal{J}_f . We indicate the boundary of an arbitrary set B by ∂B . We indicate the interior by Int(B). Let \mathbb{R}_{\geq} be the set of nonnegative real numbers.

For a subspace L we indicate the orthogonal subspace by L^{\perp} . In general, for a vector v we indicate by $v^* = v^{\perp} \cap K^*$ the vector space orthogonal to v intersected with the cone K^* (K^* is the dual of a cone K, where the definition of K should be clear from context). For a face of a cone F we define $F^* =$ $(\operatorname{span} F)^{\perp} \cap K^*$. In particular, if we have an extremal $v = k_1 \in K$ then k_1^* is a face of K^* called the dual face. The affine hull of a set $M \subseteq \mathbb{R}^n$ is AffHul $(M) = \left\{ \sum_{i=1}^k \alpha_i x_i | x_i \in M, k > 0, \alpha_i \in \mathbb{R}, \sum_{i=1}^k \alpha_i = 1 \right\}$. By the dimension of a set, we mean the dimension of the affine hull of the set. In general, when we consider the interior or boundary of a set M, we consider these operations with respect to the subspace topology of AffHul(M). We sometimes use the phrase 'relative interior' or 'relative boundary' when using the interior or boundary operations in this sense. A cone K is defined to be pointed if $K \cap -K = \emptyset$. The state space of a system is simply a forward invariant set for the system.

Definition 1. A reaction network with m reactions is a set of m column vectors each containing n entries, where each column vector is a reaction vector (or reaction). We will sometimes organize the set of reaction vectors into a matrix Γ , called the stoichiometric matrix, where the reaction vectors are the columns of Γ (the ordering is chosen arbitrarily and will not impact our results). The stoichiometric compatibility classes are the sets $\{S_0 + \Gamma x | S_0 \in \mathbb{R}^n_{>0}, x \in \mathbb{R}^m\}$.

We will sometimes refer to the reaction network as the matrix Γ .

Definition 2. The species of a reaction network are the coordinates of the space \mathbb{R}^n (that the reaction vectors are assumed to reside in).

Definition 3. Suppose we have two vectors v_1 and v_2 such that intersection of their support is the set of indices I. We say the two vectors v_1 and v_2 are **matched** if either $I = \emptyset$ or

$$\dim(\operatorname{span}((v_1)_I, (v_2)_I)) = 1.$$

We say they are **unmatched** otherwise. We say a matrix is **matched** if every two of its column vectors are matched, and we say a reaction network is **matched** if its stoichiometric matrix Γ is matched.

Definition 4. We say two vectors v_1 and v_2 are sign coordinated if $(v_1)_i(v_2)_i(v_1)_j(v_2)_j \ge 0 \forall 1 \le i, j \le n$.

For example, the two vectors [1, 0, 1, 1, -1] and [0, -1, 1, 1, 0] are sign coordinated, while the vectors [1, 0, 1, 1, -1] and [0, -1, 1, -1, 0] are not.

Definition 5. Suppose we have two reaction vectors v_1 and v_2 . We say these reactions **share species** i if both $(v_1)_i$ and $(v_2)_i$ are nonzero. We say the reactions **share species** I if for each species $i \in I$, v_1 and v_2 share species i. We say the reactions **share species** if there exists an i such that they share species i.

Definition 6. The reaction graph or R-graph is the graph whose nodes correspond to the reaction vectors in our graph, and we draw an edge between two nodes corresponding to reactions R_i and R_j iff the reactions share species. We say an edge is **positive** if all the coordinates they share have the same sign, and **negative** if all the coordinates they share have different signs. Otherwise, the edge has no sign.

When referring to the nodes of an R-graph we use the term node and reaction interchangeably. When we say reaction in this context we are referring to the corresponding node in the R-graph. We assume throughout the paper the R-graphs for all our networks are connected. For networks with disconnected R-graphs, one can simply apply our results to each component of the R-graph (for example, if each component has a corresponding decreasing norm, the max norm of all such norms is also decreasing for the entire network).

We deviate somewhat from the reaction graph definition in [2]. In the definition in [2], there is a positive edge between every two reactions that share a species with opposite signs, and a negative edge between two reactions that share a species with the same sign. Thus in the original definition signs are reversed, and one can have multiple edges between two reactions.

2.1 Reaction Network Kinetics

Given a reaction network Γ it induces a system of ordinary differential equations, which we now describe. Our differential equations are of the form

$$\dot{x} = \Gamma R(x).$$

Here $x \in \mathbb{R}^n$ is a column vector with n entries, or equivalently, a column vector of the amount of each species that is present. The column vector R(x) is a function of x and describes the kinetics of our reactions, for which we provide only a few simple restrictions (described below). We will refer to the *i*'th entry of R(x) as $R_i(x)$. Each $R_i(x)$ is a function from \mathbb{R}^n_{\geq} to \mathbb{R} . The entry $R_i(x)$ corresponds to the "reaction rate" of the *i*'th reaction, i.e., the *i*'th column in Γ , which we will refer to as Γ_i . We refer to the positive entries of Γ_i as the **products** and the negative entries as **reactants**. We say all species from a set I are present if $(x)_I > 0$ entrywise. Each function $R_i(x)$ satisfies:

- 1. $R_i(x)$ is C^1 (continuously differentiable).
- 2. We have that

$$R_i(x) \begin{cases} \ge 0 & \text{if not all products are present} \\ \le 0 & \text{if not all reactants are present} \end{cases}$$

3. We have that

$$\frac{\partial R_i(x)}{\partial x_j} \begin{cases} \ge 0 & \text{if } x_j \text{ is a reactant} \\ \le 0 & \text{if } x_j \text{ is a product} \\ = 0 & \text{otherwise} \end{cases}$$

4. We have that

 $\frac{\partial R_i(x)}{\partial x_j} \begin{cases} > 0 & \text{if } x_j \text{ is a reactant and all the reactants are present} \\ < 0 & \text{if } x_j \text{ is a product and all the products are present} \end{cases}$

These conditions define the class of differential equations we will be examining. Going forward, all dynamical systems of the form $\dot{x} = f(x)$ will be assumed to satisfy $f \in C^1$.

2.2 Monotonicity

Informally, a dynamical system is monotone if its evolution preserves a partial ordering on its state space. More precisely, suppose we have a dynamical system with an invariant state space $\mathbb{X} \subseteq \mathbb{R}^n$ (i.e., invariant under time evolution) and with evolution operator $\phi_t : \mathbb{X} \to \mathbb{X}$, defined for each $0 \leq t \leq T$ for some T > 0. Suppose we have a partial ordering of \mathbb{X} which we will indicate by \leq . Then our dynamical system is **monotone** iff for all $x, y \in \mathbb{X}$ we have that $x \leq y$ implies that $\phi_t(x) \leq \phi_t(y)$ for all $t \in [0, T)$. If we have a system of ordinary differential equations $\dot{x} = f(x)$, then due to our assumption that $f \in C^1$ we have a canonical operator ϕ_t which we can use in our definition of monotonicity for differential equations.

In this paper, we will be interested only in partial orderings induced by cones. Suppose we have an affine space $\mathbb{A} \subset \mathbb{X}$ and a pointed cone K such that there exists $j \in \mathbb{X}$ such that $j + K \subset \mathbb{A}$. Then we can define a partial ordering on \mathbb{A} by $x \leq y$ iff $y - x \in K$.

One more term we will define is that of strong monotonicity, which will involve our cone orderings. A system $\dot{x} = f(x)$ with an invariant affine space A is **strongly monotone** with respect to a cone K if for every two trajectories x(t) and y(t), if $y(0) - x(0) \in \partial K$ (recall we consider the boundary of K in the subspace topology of AffHull(K)), then we have that $y(t) - x(t) \in \text{Int}(K)$ for all $t \in [0, T)$ (i.e., they move to the relative interior of our cone).

3 Conditions for Monotonicity and Strong Monotonicity

To determine whether a network is monotone we will rely on Proposition 1.5 in [24]. Let $\mathcal{J}_f(x)$ be the Jacobian of a C^1 function f(x) evaluated at a point x. We have

Theorem 2. [24] A system $\dot{x} = f(x)$ with forward invariant state space \mathbb{X} is monotone with respect to a proper, pointed and convex cone K iff for all $x \in \mathbb{X}$ and for all $k_1 \in \partial K$ and $k_2 \in K^*$ such that $\langle k_1, k_2 \rangle = 0$ we have that $\langle \mathcal{J}_f(x)k_1, k_2 \rangle \geq 0$.

By restricting to an invariant subspace, we can relax the requirement that the cone be proper. If a system $\dot{x} = f(x)$ has an invariant subspace S, then we define the restricted system to have its state space be S, and every point in S is evolving in time according to $\dot{x} = f(x)$. Thus we will only need the cone to be proper in an invariant subspace. In particular, we have:

Corollary 1. Suppose our system has an invariant linear subspace S, and, for all $j \in \mathbb{R}^n$, that S + j is also an invariant space. Suppose we have a cone K such that K has the same dimension as S and $K \subset S$. Suppose also that K satisfies that for all $x \in S + j$ and for all $k_1 \in K$ and $k_2 \in K^*$ such that $\langle k_1, k_2 \rangle = 0$ we have that $\langle \mathcal{J}_f(x)k_1, k_2 \rangle \geq 0$. Then our system restricted to S + j is monotone with respect to K. In particular, the system is monotone when restricted to S.

Proof. Note that since $\operatorname{Im}(\mathcal{J}_f) \subset S$ we have that $\langle \mathcal{J}_f(x)k_1, k_2 \rangle = \langle \mathcal{J}_f(x)k_1, \pi(k_2) \rangle$ where $\pi(k_2)$ is the projection of k_2 onto S. Thus we can consider $k_2 \in S \cap K^*$ instead of $k_2 \in K^*$ without any issue. Now Theorem 2 can be used and so the system must be monotone on S + j, and in particular S.

In the sequel we will write \mathcal{J}_f instead of $\mathcal{J}_f(x)$, where it is to be understood that statements involving \mathcal{J}_f are to hold for all x in our system's state space. We can manipulate the expression in Theorem 2 to get a more geometric statement, specifically for reaction networks. First, we will define a few regions:

Definition 7. Given a vector $v \in \mathbb{R}^n$ we define $Q_1(v) = \{x \in \mathbb{R}^n | (x)_i(v)_i \ge 0 \ \forall \ 1 \le i \le n \}$. We define $Q_1^+(v) = Q_1(v) \setminus Q_1(-v), \ Q_1^-(v) = Q_1(-v) \setminus Q_1(v) \text{ and } Q_2(v) = Q_1(v) \cap Q_1(-v)$

For example, take the vector v = [1, 2, 0, -1, -2, 0]. Then we have that $Q_1(v)$ consists of all vectors with sign pattern $[\geq, \geq, *, \leq, \leq, *]$ (here \geq indicates nonnegative and \leq nonpositive, and * can be anything). We have that $Q_2(v)$ consists of all vectors with sign pattern [0, 0, *, 0, 0, *]. Lastly, we have that $Q_1^+(v)$ contains vectors of the form $[\geq, \geq, *, \leq, \leq, *]$, but at least one of the non-star entries must be nonzero, such as [1, 0, 0, 0, 0, 0] but not [0, 0, 1, 0, 0, 0]. Note we have some simple properties such as $Q_1^+(-v) = Q_1^-(v)$ and $Q_2(v) = Q_2(-v)$. We also have that $Q_1(v) \cup Q_1(-v) = Q_1^-(v) \cup Q_2(v) \cup Q_1^+(v)$. One last observation we will note is that v and v' are matched vectors if and only if $v \in Q_1(v') \cup Q_1(-v')$.

Intuitively, this means that $Q_1(\Gamma_i)$ consists of vectors in which we do not care about the species that do not participate in reaction *i*, for all reactants the corresponding entry should be nonpositive, and for all products the corresponding entry should be nonnegative. On the other hand, if $v \in Q_1^+(\Gamma_i)$, this means that there is a nonzero entry in at least one of the species that participates in reaction Γ_i . If $v \in Q_2(\Gamma_i)$ this means that the only nonzero entries are the species that do not participate in the reaction Γ_i , and the entries corresponding to every reaction or product have to be 0.

We will need a way to determine strong monotonicity from [25] (Theorem 3.6).

Theorem 3. [25] Suppose we have a system $\dot{x} = f(x)$ and a proper, pointed and cone K. Suppose also that $\langle \mathcal{J}_f k_1, k_2 \rangle \geq 0$ for all $k_1 \in \partial K$ and $k_2 \in K^*$ such that $\langle k_1, k_2 \rangle = 0$. Suppose for each $k_1 \in \partial K$ we can find a $k_2 \in K^*$ such that $\langle k_1, k_2 \rangle = 0$ and

$$\langle \mathcal{J}_f k_1, k_2 \rangle > 0 \tag{1}$$

Then our system is strongly monotone with respect to K.

Lemma 1. Suppose we have a reaction network with only one reaction Γ_1 and the corresponding system $\dot{x} = \Gamma_1 R(x)$. Then the network is monotone with respect to a cone K iff all the following conditions hold:

- 1. For all extremal $k \in K$ we have that $k \in Q_1(\Gamma_1) \cup Q_1(-\Gamma_1)$.
- 2. When $k \in Q_1^+(\Gamma_1)$ then for all $k' \in k^*$ we have that $\langle \Gamma_1, k' \rangle \leq 0$.
- 3. When $k \in Q_1^-(\Gamma_1)$ then for all $k' \in k^*$ we have that $\langle \Gamma_1, k' \rangle \ge 0$.

Proof. First suppose our network is monotone with respect to a cone K. Note for one reaction we have that $\mathcal{J}_f = \Gamma_1 \partial R_1$ where $\partial R_1 = [\partial_1 R_1, \partial_2 R_1, ..., \partial_n R_1]$. By Theorem 2 the system is monotone with respect to K iff $\langle \mathcal{J}_f k_1, k_2 \rangle \geq 0$ whenever $k_2 \in k_1^*$. We have that

$$\langle \mathcal{J}_f k_1, k_2 \rangle = \langle \Gamma_1 \partial R_1 k_1, k_2 \rangle = \langle \Gamma_1, k_2 \rangle \langle \partial R_1, k_1 \rangle \ge 0.$$

Suppose $k_1 \notin Q_1(\Gamma_1) \cup Q_1(-\Gamma_1)$. Then we can pick reaction rates such that $\langle \partial R_1, k_1 \rangle$ can be as positive or negative as we want. This forces $\langle \Gamma_1, k_2 \rangle = 0$ for all $k_2 \in k_1^*$, and since k_1^* is an n-1 dimensional face we must have Γ_1 is perpendicular to k_1^* and so Γ_1 is a multiple of k_1 , which forces $k_1 \in Q_1(\Gamma_1) \cup Q_1(-\Gamma_1)$; a contradiction. Thus condition 1 of the lemma must hold.

Now back to the inequality

$$\langle \Gamma_1, k_2 \rangle \langle \partial R_1, k_1 \rangle \ge 0,$$

for $k_1 \in Q_1^+(\Gamma_1)$ we have that $\langle \partial R_1, k_1 \rangle < 0$. Thus we must have $\langle \Gamma_1, k_2 \rangle \leq 0$ in this case for the inequality to hold. Thus condition 2 of the lemma must also hold. For $k_1 \in Q_1^-(\Gamma_1)$ similarly we have $\langle \Gamma_1, k_2 \rangle \geq 0$, and so condition 3 of the lemma holds.

Now suppose the three conditions of the lemma hold. Then we have that $\langle \mathcal{J}_f k_1, k_2 \rangle = \langle \Gamma_1, k_2 \rangle \langle \partial R_1, k_1 \rangle$. If $\langle \partial R_1, k_1 \rangle < 0$ then $k_1 \in Q_1^+(\Gamma_1)$ and so $\langle \Gamma_1, k_2 \rangle \leq 0$ and so $\langle \mathcal{J}_f k_1, k_2 \rangle \geq 0$. A similar argument holds for $\langle \partial R_1, k_1 \rangle > 0$. Thus by Theorem 2 the reaction network is monotone with respect to K.

Corollary 2. Suppose we have a network consisting of one reaction vector Γ_1 which is also an extremal of our cone K. Then the network is monotone with respect to K iff our one reaction vector is the only extremal in $Q_1^+(\Gamma_1)$.

Proof. Suppose Γ_1 is a positive linear multiple of an extremal vector in our cone. Then $\operatorname{span}(\Gamma_1^*)$ supports the dual cone and in particular intersects K^* in an (n-1)-dimensional face Γ_i^* . Note this implies $\langle \Gamma_1, k' \rangle \geq 0$ for all $k' \in K^*$, and $\langle \Gamma_1, k' \rangle > 0$ for vectors in the relative interior of faces other than Γ_1^* . Thus, by Lemma 1, for all extremals $k \in K$ not equal to Γ_1 , we must have $k \in Q_1(-\Gamma_1)$ for all the extremals $k \neq \Gamma_1$.

Definition 8. We say a face F of a cone is a mixed face for Γ_i (or just a mixed face if it is clear from the context what Γ_i is) if F contains extremal vectors from both $Q_1^+(\Gamma_i)$ and $Q_1^-(\Gamma_i)$.

Lemma 2. Suppose that Γ_i is monotone with respect to a cone K. If $F \subseteq K$ is a mixed face for Γ_i , then $\Gamma_i \in span(F)$.

Proof. Suppose that $k \in Q_1^+(\Gamma_i) \cap F$ and $k' \in Q_1^-(\Gamma_i) \cap F$, where k, k' are both extremals. If $k_2 \in F^*$ then this implies that $k_2 \in k^* \cap k'^*$. Lemma 1 then implies that for all $k_2 \in F^*$ that both $\langle \Gamma_i, k_2 \rangle \geq 0$ and $\langle \Gamma_i, k_2 \rangle \leq 0$. This implies that $\langle \Gamma_i, k_2 \rangle = 0$ for all $k_2 \in F^*$. Thus we must have Γ_i in the space perpendicular to F^* , or $\Gamma_i \in \text{span}(F)$.

Lemma 3. Suppose we have a reaction network \mathcal{N} . Then

- 1. The network \mathcal{N} is monotone with respect to a cone K iff each individual reaction is monotone with respect to K.
- 2. Assuming the reaction network \mathcal{N} is monotone, we have that $\langle \mathcal{J}_{f}k_{1}, k_{2} \rangle > 0$ (as in Equation (1) in Theorem 3, assuming the same conditions on k_{1} and k_{2}), iff $\langle \mathcal{J}_{f^{*}}k_{1}, k_{2} \rangle > 0$ is true for a reaction network consisting of one reaction vector Γ_{i} from \mathcal{N} (where the system $\dot{x} = f^{*}(x)$ determines the dynamics of a network consisting of only Γ_{i}).

Proof. Consider the first statement. Suppose our network \mathcal{N} consists of reaction vectors $\{\Gamma_i\}_{i=1}^n$. We have that $\mathcal{J}_f k_1 = \sum_{i=1}^n \Gamma_i \partial R_i$. Clearly $\langle \mathcal{J}_f k_1, k_2 \rangle = \langle \sum_{i=1}^n \Gamma_i \partial R_i k_1, k_2 \rangle \geq 0$ is true if and only if it is true for each individual summand, i.e., reaction. If a system consisting of one reaction vector is not monotone, we could set the other reaction rate derivatives to arbitrarily small values, to get that $\langle \sum_{i=1}^n \Gamma_i \partial R_i k_1, k_2 \rangle < 0$; a contradiction. If all the reactions are monotone with respect to a cone K, then we simply have a sum of nonnegative terms, which must be nonnegative.

then we simply have a sum of nonnegative terms, which must be nonnegative. Consider the second statement. Note if $\langle \sum_{i=1}^{n} \Gamma_i \partial R_i k_1, k_2 \rangle = \sum_{i=1}^{n} \langle \Gamma_i \partial R_i k_1, k_2 \rangle > 0$ then the inequality must be true for at least one of the summands (in our sum of nonnegative terms). If one of the summands is strictly positive for each of our possible choices of k_1, k_2 , then we would have $\langle \sum_{i=1}^{n} \Gamma_i \partial R_i k_1, k_2 \rangle > 0$ (since, due to monotonicity, each summand is nonnegative) and can apply Theorem 3.

Lemma 4. Suppose we are given a polyhedral cone K and a reaction network consisting of a single reaction vector Γ_1 . Suppose that the following properties hold:

- 1. $k \in Q_1(\Gamma_1) \cup Q_1(-\Gamma_1)$ for all extremals $k \in K$.
- 2. For all extremals $k \in Q_1^+(\Gamma_1)$ we can find a vector $k' \in Q_1(-\Gamma_1) \cap K$ such that $\Gamma_1 = k k'$.
- 3. For all extremals $k \in Q_1^-(\Gamma_1)$ we can find a vector $k' \in Q_1(\Gamma_1) \cap K$ such that $\Gamma_1 = k' k$.

Then our network is monotone with respect to K.

Proof. Take an arbitrary extremal $k \in Q_1^+(\Gamma_1) \cap K$, and find k' such that $\Gamma_1 = k - k'$ where $k' \in Q_1(-\Gamma_1) \cap K$. Now for $k_2 \in k^*$ we have that $\langle \Gamma_1, k_2 \rangle = \langle -k', k_2 \rangle \leq 0$ (since in general $\langle a, b \rangle \geq 0$ for a in a cone and b in its dual cone). A similar argument applies for $k \in Q_1^-(\Gamma_1)$. Thus our reaction vector Γ_1 satisfies the condition of Lemma 1, and so our reaction network is montone with respect to K.

Starting with this lemma, we can begin to deduce the properties of concrete networks. Take as an example the network

$$\Gamma_{ex} = \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

and the cone generated by the column vectors of

$$\alpha = \begin{bmatrix} -1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 & 1 \\ 1 & 1 & 1 & 1 & 1 & 1 & 1 \end{bmatrix}.$$

We will indicate column vector i by α_i or $(\Gamma_{ex})_i$. Note the network satisfies all three conditions of Lemma 4. For example, we have $\alpha_1 \in Q_1^+((\Gamma_{ex})_1)$ and $(\Gamma_{ex})_1 = \alpha_1 - \alpha_3$ and we also have $\alpha_2 \in Q_1^-((\Gamma_{ex})_1)$ and $(\Gamma_{ex})_1 = \alpha_4 - \alpha_2$. We will use this network Γ_{ex} as a running example throughout the paper.

Lemma 5. Suppose we have a polytope P with a set of vertices $V = \{k_j | 1 \le j \le n\}$. For each $k_i \in V$ and each k in the interior of P we can write $k = \sum_{j=1}^n \alpha_j k_j$ where $\sum_{j=1}^n \alpha_j = 1$, $\alpha_j \ge 0$ for all j, and $\alpha_i \ne 0$.

Proof. Select an arbitrary vertex k_i and arbitrary k in the interior of P. Consider a line between these two points, and note that this line must leave our convex figure at precisely two points, one point being k_i . Label the point where the line exits the polytope (which is not k_i) as k_e . Then k is a convex combination of k_i and k_e , and k_e is a convex combination of some of the vertices, and so we are done.

Lemma 6. Suppose we have a network \mathcal{N} and a cone K such that each individual reaction of \mathcal{N} satisfies the conditions in Lemma 4. Suppose also for each face in $F \subseteq K$ we can find three vectors $\Gamma_i \in \mathcal{N}, k \in F$, and $k_i \in K$ such that

- 1. k is an extremal and satisfies $k \notin Q_2(\Gamma_i)$.
- 2. $k_i \notin F$.
- 3. There exists $j \in \{0,1\}$ such that $\Gamma_i = (-1)^j (k k_i)$.

Then the network \mathcal{N} is strongly monotone with respect to the cone.

Proof. For arbitrary $k' \in \partial K$, let F be the minimal face (with respect to inclusion) in which k' is contained (thus k' is in F's relative interior). Without loss of generality, let $\Gamma_i = k - k_i$ (we are given such as expression from the assumptions) where $k \in F$ is an extremal and $k_i \notin F$. Suppose we could not find $k_2 \in F^*$ such that $\langle k_2, \Gamma_i \rangle = \langle k_2, -k_i \rangle \neq 0$. Then we would have that $\langle k_2, -k_i \rangle = 0$ for all $k_2 \in F^*$. This implies $k_i \in F$, a contradiction. Thus we can find a vector $k_2 \in F^* \subset K^*$ such that

$$\langle \Gamma_i, k_2 \rangle = \langle -k_i, k_2 \rangle \neq 0$$

Note that $\langle \partial R_i, k' \rangle \neq 0$ since k' can be written as a convex sum of some extremals including k (here we use Lemma 5, which applies to cross sections of our cone), and if say $k \in Q_1^+(\Gamma_i)$ (without loss of generality) then we must have all the other extremals of F also be in $Q_1(\Gamma_i)$, which would force $k' \in Q_1^+(\Gamma_i)$. Otherwise, F would be a mixed face for Γ_i which would force $\Gamma_i \in \text{span}(F)$ (we use here Lemma 2) which would imply $k_i \in F$, a contradiction. So we have that for $f = \sum_i \Gamma_i R_i$ that

$$\langle \mathcal{J}_f k', k_2 \rangle \geq \langle \mathcal{J}_{\Gamma_i R_i} k', k_2 \rangle = \langle \Gamma_i, k_2 \rangle \langle \partial R_i, k' \rangle > 0.$$

From Lemma 4 we know that $\langle \Gamma_i, k_2 \rangle \langle \partial R_i, k' \rangle \geq 0$, and that they are nonzero from previous observations. Thus the system corresponding to the network \mathcal{N} satisfies the conditions for Theorem 3.

Returning to our example, take as our face the face generated by extremals $\alpha_1, \alpha_3, \alpha_5$. The set $\{(\Gamma_{ex})_4, \alpha_1, \alpha_8\}$ satisfies the conditions in Lemma 6.

4 A Connection between Monotonicity and Contractivity

First, we will need two definitions.

Definition 9. We say a system $\dot{x} = f(x)$ is weakly contractive with respect to a norm ||.|| if for any two trajectories x(t) and y(t) such that $x(0) \neq y(0)$ and all numbers t_1 and t_2 such that $t_2 > t_1$ we have that $||x(t_2) - y(t_2)|| < ||x(t_1) - y(t_1)||$ for all t > 0. We say the system is **nonexpansive** with respect to the given norm if for trajectories x(t) and y(t) and $t_2 > t_1$ we have that $||x(t_2) - y(t_2)|| \le ||x(t_1) - y(t_1)||$ for all t > 0.

Here we will show how we can go from a weakly contractive system to a monotone system, and vice versa. Suppose we have a system $\dot{x} = f(x)$ where $x \in \mathbb{R}^n$, and which we know to be weakly contractive with respect to some norm $\|.\|$. Consider the closed unit ball $B_1(0) = \{x \in \mathbb{R}^n | \|x\| \le 1\}$. We will "lift" this unit ball to obtain a non-expansive system.

Consider now the system $\dot{z} = g(z)$ where $z \in \mathbb{R}^{n+1}$ and $z = [x, x_{n+1}]^t = [x_1, x_2, x_3, ..., x_{n+1}]$ and g(z) = [f(x), 0]. We call this system the **lift** of the system $\dot{x} = f(x)$. This new system is just many copies of our old system, along with the new coordinate x_{n+1} . Lastly define the set $B'_1(0) = [B_1(0), 1] = B_1(0) \times \{1\} \in \mathbb{R}^{n+1}$, this is the "lift" of our closed ball. Define $K \subset \mathbb{R}^{n+1}$ to be the cone generated by $B'_1(0)$ (i.e., it is the smallest cone containing $B'_1(0)$), where by smallest we mean contained in every other cone containing $B'_1(0)$. See Figure 1 for a visualization of this procedure.



Figure 1: An example of producing a cone by lifting a set of vectors. If our set of vectors is the circle in \mathbb{R}^2 , then our lifted cone has the cross section of a circle.

Definition 10. We call a vector v' the lift of v if we can obtain v' by appending a 1 to the end of v. We call a cone K the lift of a set of vectors $\{v\}$ if we K is generated by the lift of each vector in the set $\{v\}$.

A useful property of lifted cones is that they are always pointed:

Lemma 7. The cone generated by a lift of an arbitrary set of vectors $\{v_i\}$ is always pointed.

Proof. Suppose our lifted cone is K. Note that for all $v \in K$ we can find a set of positive integers A and nonnegative real numbers $\{\alpha_i\}$ such that v satisfies $v = \sum_{i \in A} \alpha_i v_i$. Thus the appended last coordinate (created by lifting) is always nonnegative for v, and is only 0 when $\alpha_i = 0 \forall i$ or v = 0. Thus if $v \in K$ and $v \neq 0$ then $-v \notin K$, and so K is pointed.

Definition 11. For a given system $\dot{x} = f(x)$ and a norm $\|.\|$, the **cone constructed from the norm** $\|.\|$, or equivalently **associated to the norm** $\|.\|$, is the cone K, as constructed above. In other words, the cone K is the smallest cone containing the set $[B_1(0), 1]$ where $B_1(0) = \{x \in \mathbb{R}^n | \|x\| \le 1\}$.

Lemma 8. For a given system $\dot{x} = f(x)$ and a norm ||.||, the cone K constructed from the norm ||.|| is always pointed, proper, and convex.

Proof. First note the ball $B_1(0) = \{x \in \mathbb{R}^n | ||x|| \le 1\}$ always has nonempty interior and is convex. Thus since K has as generators the convex set $B'_1(0) = [B_1(0), 1]$, it must also be convex. It is pointed since if $x \in K$ and $x \ne 0$ then -x would have a negative last coordinate and so $-x \notin K$. It is proper since $[B_1(0), 1]$ contains some relatively open set $U \subseteq [B_1(0), 1] \subseteq \mathbb{R}^{n+1}$, and $(1/2, 3/2) * U = \{y \in \mathbb{R}^{n+1} | y = ru, r \in (1/2, 3/2), u \in U\}$ is an open set contained in K.

Theorem 4. Suppose we are given a system $\dot{x} = f(x)$ which we assume has complete dynamics (i.e. has a solution for all $t \ge 0$), a norm $\|.\|$ and a cone K constructed from the norm. The system is weakly contractive with respect to the norm iff the system $\dot{z} = g(z)$ is strongly monotone with respect to the cone K. If we replace "weakly contractive" with "non-expansive" and "strongly monotone" with "monotone" the result is still true.

Proof. Assume that $\dot{x} = f(x)$ is weakly contractive. Define $B_d(0) = \{x \in \mathbb{R}^n : ||x|| \le d\}$ for all $d \ge 0$. Going forward, assume we choose a fixed and arbitrary $d \ge 0$. For $x, y \in \mathbb{R}^{n+1}$, if $y - x \in K$ and $y_{n+1} - x_{n+1} = d > 0$, then $[y_1 - x_1, ..., y_n - x_n] \in B_d(0)$. Define F_t to be the evolution function of the system $\dot{x} = f(x)$, which moves our system forward t > 0 units in time. By abuse of notation, we will also use F_t as the evolution function for $\dot{z} = g(z)$, since it is identical except for its action on the last coordinate, which always stays constant. Note under the flow of our system $\dot{z} = g(z)$ the last coordinate does not change, and for the first n coordinates since $\dot{x} = f(x)$ is weakly contractive we have that $[F_t(y_1) - F_t(x_1), ..., F_t(y_n) - F_t(x_n)] \in Int(B_d(0))$. Thus we see that

$$F_t(y) - F_t(x) = [F_t(y_1) - F_t(x_1), ..., F_t(y_n) - F_t(x_n), d] \in Int(K).$$

Thus this system is strongly monotone. If our system is non-expansive then the lifted system is just monotone by similar arguments.

If our system $\dot{z} = g(z)$ is strongly monotone with respect to K, then for $y - x \in K$ such that $y - x \in [B_d(0), d]$ we have that if $[y_1, y_2, ..., y_n] - [x_1, x_2, ..., x_n]$ is on the boundary of $B_d(0)$ then $[F_t(y_1), F_t(y_2), ..., F_t(y_n)] - [F_t(x_1), F_t(x_2), ..., F_t(x_n)]$ will be in the interior of $B_d(0)$ (by strong monotonicity), which is all we need for weak contractivity. If we have only monotonicity, we still know $[F_t(y_1), F_t(y_2), ..., F_t(y_n)] - [F_t(x_1), F_t(x_2), ..., F_t(x_n)]$ will always remain in $B_d(0)$ for $t \ge 0$, and so our system is non-expansive.

Definition 12. Given a reaction network, its **lift** is the reaction network including an extra species, which participates in no reactions.

Corollary 3. Given a reaction network \mathcal{N} , the following are equivalent:

- 1. The network is weakly contractive (respectively non-expansive) with respect to a norm $\|.\|$.
- 2. The lifted network is strongly monotone (respectively monotone) with respect to a cone associated with the norm $\|.\|$.

If we have a set β and a positive real number r then we define $r\beta = \{y \in \mathbb{R}^n | y = rx, x \in \beta\}$. Next we will discuss a way to go between sets and norms.

Definition 13. A set $\beta \subseteq \mathbb{R}^n$ is called **absorbing** if for every $x \in \mathbb{R}^n$ we can find r > 0 such that $x \in r\beta$. A set β is symmetric if whenever $x \in \beta$ then $-x \in \beta$. A set is good whenever it is symmetric, compact, convex, and absorbing.

Lemma 9. If we have a good set β then the function $||x|| = \inf\{t > 0 | x \in t\beta\}$ is a norm on \mathbb{R}^n .

Proof. This follows from general theory about Minkowski functionals, for example, Theorem 1.35 in [26]. In the terminology of this paper, this theorem states that if we have a good set β then our function $||x|| = \inf\{t > 0 | \frac{x}{t} \in \beta\}$ is a seminorm. We also have that ||x|| = 0 iff x = 0, due to the compactness of β . Thus this defines a norm.

Corollary 4. Suppose the lift of a system $\dot{x} = f(x)$ is strongly monotone with respect to the lift of a good set β . Then it is weakly contractive with respect to the norm determined by β .

Proof. This follows immediately from Theorem 4 since our good set induces a norm by Lemma 9. The dynamical system takes us into the interior of the set β , which implies that the norm β induces is decreasing in time.

There is a more general theorem, showing a strongly monotone lift is also sufficient for weak contractivity.

Theorem 5. If the lift of a system $\dot{x} = f(x)$ is strongly monotone with respect to the lift of some bounded set of vectors $\{v_i\}$ whose convex closure has nonempty interior, then the original system is weakly contractive with respect to a norm.

Proof. Suppose the convex closure of $\{v_i\}$ is P and the cone generated by the lift of P is K. For $v \in \mathbb{R}^n$ and r > 0 define $v + rP = \{x \in \mathbb{R}^n | \exists y \in P, x = v + ry\}$, and define the function

$$||x|| = \min(\{r > 0 | \exists v \in \mathbb{R}^n, \{0, x\} \subseteq v + rP\}).$$
(2)

We will show that a closed unit ball of this function is a good set when restricted to an arbitrary invariant subspace of our system which $\{v_i\}$ spans. Note that being strongly monotone with respect to the lift of $\{v_i\}$ implies that the components of f(x) which are orthogonal to this span must be constant.

The unit ball $B_1(0) = B_1 = \{x \mid ||x|| \le 1\}$ of the defined function is compact. Since P is convex and compact with nonempty relative interior in the span of $\{v_i\}$, this implies the function is continuous. Thus the set of points B_1 is closed. It is also bounded due to P having nonempty relative interior, and so it is compact. The unit ball is convex since if $x, y \in B_1$, $\{0, x\} \subset v_1 + r_1P$ and $\{0, y\} \subset v_2 + r_2P$ then $\{0, \lambda x + (1-\lambda)y\} \subset \lambda v_1 + (1-\lambda)v_2 + (\lambda r_1 + (1-\lambda)r_2)P$. The set B_1 is absorbing since P has nonempty relative interior and so B_1 contains the interior of P translated to contain the origin. The set B_1 is symmetric since if $x \in B_1$ then we have that there exist v and $r \leq 1$ such that $\{0, x\} \subseteq v + rP$, but then this implies $\{-x, 0\} \subseteq (v - x) + rP$. Thus $-x \in B_1$ as well. Thus the closed unit ball of the function is in fact a good set. This also establishes that our function is in fact our norm, by using Lemma 9.

Note that for all $x, y \in \mathbb{R}^n$ such that $x, y \in \partial (v + r(-1)^j P)$ for some v, r and j, where r is minimal, we can prove these two points are moving into the interior of $v + r(-1)^j P$, and thus ||x - y|| is strictly decreasing. Indeed, taking the same x, y, note that $v \leq x$ and $v \leq y$ (considering now the lifted space). The points x, y are on the boundary of our cone at height r, and so we know they are moving to the interior of our cone. Thus we can shrink the cross-section rP while still containing the point $\phi_t(x)$ and $\phi_t(y)$ for some t > 0, and so our system is weakly contractive with respect to our norm.



Figure 2: An example of the construction from Theorem 5 with a triangle. To construct the hexagon, we can imagine we have an unmovable point (in this case it will be the center of the hexagon), and we trace out a shape by moving our triangle around this unmovable point. The blue triangles we arrive at by trying to move our triangle as far as we can in some direction, we end up with a vertex of our triangle being at the same location as the unmovable point.

See Figure 2 for a visual example of the construction in Theorem 5. Here is an explicit example to help elucidate the above construction: Take P to be the convex closure of the columns of $\begin{bmatrix} 1 & 0 & 1 \\ 0 & 1 & 1 \end{bmatrix}$. Then we have B_1 is the convex closure of the columns of $\begin{bmatrix} 1 & 0 & -1 & 0 & 1 & -1 \\ 0 & 1 & 0 & -1 & -1 & 1 \end{bmatrix}$. To see this, note this is precisely the set of all points $H = \{x \in \mathbb{R}^2 | \exists v \in \mathbb{R}^2, \{0, x\} \subseteq v + P\}$. This is because H is precisely the convex closure of the vectors produced by taking the differences of each pair of vertices in the set P. Note that this is also how the hexagon in Figure 2 can be constructed.

4.1 Dynamical Conclusions

If we can establish that our system always reduces a norm distance between points, then we will want to be able to make dynamical conclusions from this property. Essentially, we can show all orbits are either unbounded or all converge to one fixed point. For the following assume our system $\dot{x} = f(x)$ is weakly contractive with respect to some norm ||x|| and has state space X. In the following we use the notation $B_{\delta}(x) = \{y \in \mathbb{X} \mid ||x - y|| \leq \delta\}$ and $N_{\delta}(x) = \partial B_{\delta}(x)$. Thus $B_{\delta}(x)$ is the closed ball of radius δ centered at x, and $N_{\delta}(x)$ is its boundary. Note that $N_{\delta}(x)$ is a compact set.

Lemma 10. Suppose our weakly contractive system $\dot{x} = f(x)$ has a forward invariant convex and compact set A. For every point $a \in A$ and every $x \in \mathbb{X}$ we have that $||\phi_t(a) - \phi_t(x)|| \to 0$ as $t \to \infty$.

Proof. For each t > 0 define

$$M_{\delta,t} = \inf\{||a - x|| - ||\phi_t(a) - \phi_t(x)|| \mid a \in A, x \in N_{\delta}(a)\}.$$

Note that since A and $N_{\delta}(a)$ are compact, we achieve the infimum for some choices of a and x. Note also that $M_{\delta,t}$ is continuous in δ for $\delta > 0$ since $||a - x|| - ||\phi_t(a) - \phi_t(x)||$ is continuous in a and x. Note that $M_{\delta,t} > 0$ for $\delta > 0$ and t > 0. From this follows that for each a > 0 we have that $\inf_{\delta \geq a} M_{\delta,t} = m > 0$. Thus if ||a - x|| > a we have that every application of ϕ_t to the two points reduces the norm of their difference by at least m. After finitely many applications of ϕ_t the norm must go below a. Thus $||\phi_t^n(a) - \phi_t^n(x)||$ (here ϕ_t^n is ϕ_t composed n times) must decrease to 0 as $n \to \infty$. We in general have $||\phi_t(a) - \phi_t(x)||$ is nonincreasing as $t \to \infty$ since our system is nonexpansive, so if some points on the trajectories become arbitrarily close, all the points forward in time must also be arbitrarily close. \Box

In particular, our system must be globally convergent if the previous lemma holds.

Corollary 5. If the conditions of Lemma 10 holds, then there exists a point $p \in \mathbb{X}$ such that p is a fixed point of ϕ_t for all $t \ge 0$, and $\lim_{t\to\infty} \|\phi_t(x) - p\| \to 0$ for all $x \in \mathbb{X}$.

Proof. First note by Brouwer's Fixed Point Theorem there must exist a fixed point p for ϕ_t for every choice of t > 0. Applying ϕ_t repeatedly we see that every point becomes arbitrarily close to this point. Note that for $\phi_{t/n}$, where $n \in \mathbb{N}$, we must have p again be a fixed point, since otherwise we would have two different points we repeatedly visit which is impossible. We also have for $m \in \mathbb{Z}$ that $\phi_{mt/n}$ has p as a fixed point. By continuity, we have p must be a fixed point for all $t \geq 0$. Thus all our points must converge to p by Lemma 10.

Definition 14. We say a dynamical system is **globally convergent** if every point in the state space X converges to a unique point p, i.e., if the conclusion of Corollary 5 holds.

5 An Algorithm to Generate Cones

Here we outline a general procedure to generate valid cones for some reaction networks. We initially make the following assumptions for the stoichiometric matrices Γ (these will be loosened later):

- 1. There exists a diagonal matrix D with positive diagonal entries such that ΓD has each entry be either 0, 1 or -1.
- 2. Every two reaction vectors have at most one common coordinate both with the same sign and at most one common coordinate with different signs.
- 3. For each reaction vector at most one nonzero coordinate is zero for all other reaction vectors.

Definition 15. A matrix that satisfies the above conditions is called an **aligned** matrix.

While the results in this section are not necessarily specific to aligned matrices, one can show that aligned matrices can produce especially nice results. Thus we will assume for the rest of this section, up to Theorem 8, that all stoichiometric matrices we consider are aligned. Next, we define a few terms indicating which steps we take in the algorithm, and when the algorithm yields a legitimate cone.

Definition 16. Suppose we have a stoichiometric matrix Γ , and that we have a column vector $v \in \mathbb{R}^n$. We say that the operation of subtracting(adding) a reaction vector Γ_i from v is **permissible** if $v \notin Q_2(\Gamma_i)$ and $v - \Gamma_i$ $(v + \Gamma_i)$ yields another vector with only 0's,1's, and -1's. We say a vector v' is **permissible** if for each reaction vector Γ_i in our network we have that $v' \in Q_1(\Gamma_i) \cup Q_1(-\Gamma_i)$, and v' consists of only 0's, 1's, and -1's. We say a cone is **permissible** if all its extremal vectors are permissible.

Now our algorithm is simply to start with a permissible vector and carry out as many permissible steps to obtain as many permissible vectors as we can. The details of the algorithm are in Algorithm 1.

Algorithm 1 An algorithm to produce co	one extremals
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Require: Permissible vector v and stoichiometric matrix Γ $M \leftarrow v$ while $\exists \Gamma_i$ and $v' \in M$ such that forming $v' - \Gamma_i$ or $v' + \Gamma_i$ is a permissible operation, and not both are in M do if $v' - \Gamma_i$ is a permissible vector and $v' - \Gamma_i \notin M$ then $M \leftarrow M \cup \{v' - \Gamma_i\}$ else if $v' + \Gamma_i$ is a permissible vector and $v' + \Gamma_i \notin M$ then $M \leftarrow M \cup \{v' + \Gamma_i\}$ end if end while return M

Definition 17. We say a set of vectors $A = \{v_1, v_2, ..., v_n\}$ is closed, if it satisfies the following conditions:

- 1. Whenever we have $v' \in A$ and there exists i such that $v' \notin Q_2(\Gamma_i)$ for a vector Γ_i in our network then either forming $v' \Gamma_i$ or $v' + \Gamma_i$ is a permissible operation.
- 2. All permissible operations produce vectors already contained in A.

Definition 18. We say a set of permissible vectors is viable if it satisfies the following:

- 1. The set is closed.
- 2. For each reaction vector Γ_i there is at least one extremal $k \in K$ such that $k \in Q_1(\Gamma_i) \cup Q_1(-\Gamma_i)$.

We can show an example of carrying out our algorithm on Γ_{ex} , where we start with just one of the vectors from α (currently we do not have a general procedure for choosing the starting vector, though in certain special cases we can show some particular choices work well). We will show the set of vectors as it grows, we have:

The lift of this final matrix β is the same as α , up to permutations of the columns. We see our procedure is finished since the columns vectors form a closed set.

We always need our cones to be proper with respect to the invariant subspace we want to draw conclusions about, so we need the following lemma:

Lemma 11. The affine hull of a viable output M of Algorithm 1 always has the same dimension as the stoichiometric compatibility classes. The affine hull is a translation of every stoichiometric compatibility class.

Proof. If we initiate algorithm 1 with vector v, then we can show AffHul $(M) = v + \operatorname{Im}(\Gamma)$. To see this, note that because M is viable, at some point for some $v \in M$ we form either $v - \Gamma_i$ or $v + \Gamma_i$. Assume without loss of generality that we form $v - \Gamma_i$, and so $v' = v - \Gamma_i \in M$. Note that for all $v'' \in \operatorname{AffHul}(M)$ and for all $\alpha \in \mathbb{R}$ we must also have $v'' + \alpha(v - v') = v'' + \alpha\Gamma_i \in \operatorname{AffHul}(M)$. Since this is true for all Γ_i we must have $v + \operatorname{Im}(\Gamma) \subseteq \operatorname{AffHul}(M)$. Note also that every vector in M is produced by a permissible operation, and so for $v, v' \in M$ we always have $v - v' \in \operatorname{Im}(\Gamma)$ and so we are done. \Box As an example, the matrix β from our previous computation has a column rank of 4, which is the same as the column rank of Γ_{ex} .

Theorem 6. Suppose we have a viable set of vectors. If we define our cone K to be the lift of this set, then our system is monotone with respect to K.

Proof. In this case, we will check that we satisfy the conditions for Lemma 4 and so that the system is monotone. To check that all the vectors are in $Q_1(\Gamma_1) \cup Q_1(-\Gamma_1)$ we simply need to note that this is part of Definition 18 for the set to be viable.

If we have a permissible vector $k \in Q_1^+(\Gamma_i)$, then by the closed condition this implies $k - \Gamma_i \in Q_1(-\Gamma_i)$ is also a member of our set (note that $k + \Gamma_i$ could no longer be a permissible vector, since both vector share at least one specie with the same sign). Similar reasoning applies for $k \in Q_1^-(\Gamma_i)$, and so our system must be monotone for each individual reaction, and thus the whole network as well by Lemma 3.

We are also interested in when our systems are strongly monotone. Assume that we have a set of vectors M that is viable.

Theorem 7. Assume every species partakes in at least one reaction of our network \mathcal{N} with stoichiometric matrix Γ . Take the convex hull of our viable set of vectors M, then take the extreme points of this convex closure, and label this new set of extreme points as M'. If M' contains no 0 vectors, then the lift of our network \mathcal{N} is strongly monotone with respect to the lift of M', which we will call K'.

Proof. Note that M' consists of points from our original set M due to Lemma 18. To prove our theorem we will verify Lemma 6. In the following, we will abuse notation slightly. A vector v can either refer to itself or its lifted version. If v is in a cone we are referring to its lifted version.

Consider an arbitrary proper face $F \subseteq K'$. Let $M' = \{v_1, ..., v_n\}$, let $m = \{v_1, v_2, ..., v_k\} \subseteq M'$ be the set of vectors $v \in M'$ such that the lift of v is in F. Let $L = \{\Gamma_{i_1}, \Gamma_{i_2}, ..., \Gamma_{i_k}\}$ be the set of vectors such that $\Gamma_{i_j} \in \mathcal{N}$; for each $\Gamma_{i_j} \in L$ we can find $v_1, v_2 \in F$ and $k \in \{0, 1\}$ such that $\Gamma_{i_j} = (-1)^k (v_1 - v_2)$. This is not all our reaction vectors, since otherwise this face would have the same dimension as our stoichiometric compatibility class, and so would not be proper.

Note that for all $\Gamma_i \in \mathcal{N}$ if we have $\Gamma_i \in \operatorname{span}(F)$ implies there exists $v' \in m$ such that $v' \notin Q_2(\Gamma_i)$. This is because if all $v' \in m$ also satisfy $v' \in Q_2(\Gamma_i)$ then this would imply $\operatorname{span}(F) \subseteq Q_2(\Gamma_i)$, contradicting that $\Gamma_i \in \operatorname{span}(F)$.

Consider the R-graph for \mathcal{N} . For the set of nodes corresponding to L, find one node (call this node Γ_j) adjacent to a node in L (call this node Γ_i) but $\Gamma_j \notin L$ (pick a node that shares coordinates with a vector in m if L is empty). Now in F, for every coordinate g for which $(\Gamma_i)_g \neq 0$, we can find $v' \in m$ such that $(v')_g \neq 0$. This is since if $(v')_g = 0$ for all $v' \in m$, then since $\Gamma_i \in \text{span}(F)$ we must have $(\Gamma_i)_g = 0$, a contradiction. If L is empty we simply already picked Γ_j such that it shares coordinates with some vector $v' \in F$.

Thus since Γ_j shares some coordinates with Γ_i (or directly with $v \in F$) we can find a vector $k \in m$ such that Γ_j and k share species. Thus we can form $k_i = \Gamma_j \pm k$ (whichever is permissible) to get another vector contained in M. Since $\Gamma_j \notin L$ we must have $k_i \notin F$, and since F is arbitrary for the lift K' we will satisfy the conditions for Lemma 6 (where we use k and k_i defined here also for the lemma).

Lemma 12. Suppose we have a finite set of vectors $S = \{v_i\}$ where each vector in S is permissible with respect to a stoichiometric matrix Γ , and the set S is closed. Then initiating Algorithm 1 with any vector $v_j \in S$, such that there exists at least one reaction Γ_k where $v_j \notin Q_2(\Gamma_k)$, will give us a viable set of vectors (we will call the lift of this set K).

Proof. Clearly, if we start with some vector $v_j \in S$, each permissible operation will give us another permissible vector in the set S, since it is closed under permissible operations. We terminate after finitely many procedures since S is finite.

Since we always assume the reaction graph of our network is connected, we must also have that for each reaction vector Γ_i , there is at least one extremal $k \in K$ such that $k \notin Q_2(\Gamma_i)$. We will show this via contradiction.

First assume that in our reaction graph we have a set of nodes A (i.e., a set of reaction vectors) such that every node that shares species with some of the vectors in S is in A. If A contains all our reaction vectors we are done, so suppose it does not contain all vectors.

Suppose $\Gamma_i \in A$ is adjacent to $\Gamma_j \notin A$. Since $\Gamma_i \in A$ we can find vectors $k \in K$ such that $k \notin Q_2(\Gamma_i)$ which implies by closedness that (without loss of generality we use addition) $k + \Gamma_i \in K$. Between these two vectors, each species in the support of Γ_i is shared with at least one of k or $k + \Gamma_i$. Since Γ_j shares a species with Γ_i , we can conclude Γ_j also shares a species with a vector in S. We must then have that every reaction vector adjacent to a member of A also shares a specie with at least one member of S. Thus, our set A must also contain all nodes adjacent to it, and so must contain all nodes, contradicting our premise that it does not contain all nodes. Our set then satisfies all the conditions we need to be viable.

Now we can relax our assumptions at the start slightly.

Theorem 8. Suppose we have an aligned matrix Γ for which Algorithm 1 produces a viable set of vectors. Let N be a matrix which has these vectors as columns. Suppose also that:

- 1. We have a matrix P which has no 0 columns, and for which each row has exactly 1 nonzero element.
- 2. The matrix Γ is strongly monotone (monotone) with respect to the cone generated by the lift of N.

Then the network $P\Gamma$ is strongly monotone (monotone) with respect to the lift of the column vectors of PN.

Proof. Assume that our system is strongly monotone with respect to the lift. Then the conditions of Lemma 6 are satisfied. Refer to the lift of N as K and the lift of PN as PK. Note there is a bijection between faces $F \subset K$ and faces $PF \subset PK$ obtained by sending F to $PF = \{x | \exists y \text{ such that } x = Py\}$. The matrix P has full column rank and thus is injective, but also surjective onto its image, and so we have a bijection between faces.

Now pick an arbitrary face PF. By the conditions in Lemma 6 we have that for $F \subset K$ we can find Γ_i, k, k_i satisfying the conditions in the Lemma. Now for PF the set $P\Gamma_i, Pk, Pk_i$ satisfy the conditions for Lemma 6. To see this, note that our transformation P has the general property that if $v \in Q_1^+(\Gamma_i)$ then $Pv \in Q_1^+(P\Gamma_i)$, if $v \in Q_1^-(\Gamma_i)$ then $Pv \in Q_1^-(P\Gamma_i)$, and if $v \in Q_2(\Gamma_i)$ then $Pv \in Q_2(P\Gamma_i)$. Thus we have that $\Gamma_i = (-1)^j (Pk - Pk_i)$, satisfying the third condition of Lemma 6, and the first two conditions are satisfied due to our having $Pk \notin Q_2(P\Gamma_i)$ and $Pk_i \notin PF$.

For the case that our system is monotone with respect to the lift, a similar argument applies. We can check that the conditions for Lemma 4 are kept upon transforming everything by the matrix P. Indeed, assume that Γ is monotone with respect to cone K and that we have a vector $k \in Q_1^+(\Gamma)$ and a vector $k' \in Q_1(-\Gamma) \cap K$ such that $\Gamma = k - k'$. Then it is true that $Pk \in Q_1^+(P\Gamma)$, $Pk' \in Q_1(-P\Gamma) \cap PK$ and that $P\Gamma = Pk - Pk'$. This verifies that Condition 2 of Lemma 4 continues to hold, and Condition 3 continues to hold as well due to similar reasoning. Condition 1 holds due to our observation about how P acts on different regions of note, i.e., if $v \in Q_1(\Gamma_i) \cup Q_1(-\Gamma_i)$ then $Pv \in Q_1(P\Gamma_i) \cup Q_1(-P\Gamma_i)$.

6 Explicit Constructions of the Norms

In this section we will explicitly construct norms for which certain reaction networks are weakly contractive, using our methods described above.

6.1 Example 1

Consider the reaction network

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

This reaction network is already known to be globally convergent(see, for example, [27]), and using our methods we can construct a norm for which it is weakly contractive. Starting with the vector $[1, 0, 0]^t$ and using our Algorithm 1, we will produce the set of vectors (listed as columns of a matrix)

$$C_1 = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}.$$

By Theorem 7 the lift of this network gives us a cone for which our system is strongly monotone. The convex closure of C_1 gives us a shape that we can use as in Theorem 5 to construct our norm explicitly.

Take a point x in a stoichiometric class S_0 . Now we will form the set

$$\{y \in \mathbb{R}^n | \exists v \in \mathbb{R}^n, \{x, y\} \subseteq v + C_1\}.$$

The set $\{y \in \mathbb{R}^n | \exists v \in \mathbb{R}^n, \{x, y\} \subseteq v + C_1\}$ is simply the x translate of the convex hull of the columns of

$$\beta = \operatorname{conv} \left(\begin{bmatrix} -1 & 0 & 1 & 1 & 0 & -1 \\ 1 & -1 & 0 & -1 & 1 & 0 \\ 0 & 1 & -1 & 0 & -1 & 1 \end{bmatrix} \right).$$

Thus the norm determined by the good set β as in Lemma 9 is the norm for which our system is weakly contractive.

6.2 Example 2

Consider our earlier example reaction network

$$\Gamma_{ex} = \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix}.$$

As shown earlier, using our Algorithm 1 we can generate the set

$$C_1 = \begin{bmatrix} -1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & -1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & -1 & 0 & 0 & 0 & 1 \end{bmatrix}.$$

To construct the set $\{y \in \mathbb{R}^n | \exists v \in \mathbb{R}^n, \{x, y\} \subseteq v + C_1\}$ we again use the x translate of the convex hull of the columns of

$$L = \operatorname{conv}\left(\begin{bmatrix} -2 & 0 & 0 & 0 & 2 & 0 & 0 & 0 \\ 0 & -2 & 0 & 0 & 0 & 2 & 0 & 0 \\ 0 & 0 & -2 & 0 & 0 & 0 & 2 & 0 \\ 0 & 0 & 0 & -2 & 0 & 0 & 0 & 2 \end{bmatrix} \right).$$

Thus the norm determined by the good set L as in Lemma 9 is a norm for which our system is weakly contractive.

7 Cross-Polytope Cones

We are now in a position to prove novel statements about the dynamics of a special class of networks. For one special case of our algorithm, we can produce cones with the structure of a cross-polytope for a special class of networks.

Definition 19. Let $e_i = (0, 0, ..., 0, 1, 0, ..., 0, 0)$ be the *i*'th standard basis vector, which has a 1 in the *i*'th place and 0's elsewhere. A standard simplex is the set $S = (\bigcup_i e_{j_i}) \cup (\bigcup_l - e_{k_l})$ such that there does not exist an *i* such that $\{e_i\} \cup \{-e_i\} \subset S$. By a simplicial cone we mean the lift of a standard simplex.

By a standard cross-polytope we mean the set $S = (\bigcup_i e_{j_i}) \cup (\bigcup_l - e_{k_l})$ such either $\{e_i\} \cup \{-e_i\} \subset S$ or $(\{e_i\} \cup \{-e_i\}) \cap S = \emptyset$. By a **cross-polytope cone** we mean the lift of a standard cross-polytope.

Definition 20. An aligned matrix is of type C if it satisfies the following properties:

- 1. Each entry is either -2, -1, 1, 2, or 0.
- 2. The l_1 norm of each column is 2.
- 3. It has no 0 rows.

Theorem 9. If our stoichiometric matrix Γ is of type C, then the corresponding reaction network is strongly monotone with respect to a cone with the poset structure of a cross-polytope or a simplex.

Proof. Initiate Algorithm 1 with an arbitrary standard basis vector that shares a coordinate with a column of Γ . For any permissible operation we perform, we will get another standard basis vector e_j , or possibly $-e_j$. To see this, note that in Γ we only really have 3 possible types of column vectors. Either a column vector has two 1 entries, one -1 and one 1 entry, or one entry with an absolute value of 2. Suppose one of our columns is of the first types, e.g., $\Gamma_i = [1, 1, 0, 0, ..., 0]^t$. Then if we performed the admissible operation $e_1 - \Gamma_i$ where $e_1 = [1, 0, 0, 0, ..., 0]$ we would get $e_1 - \Gamma_i = -e_2 = [0, -1, 0, 0, ..., 0]$, another standard basis vector. We have a similar computation for all our possible column vectors, and thus permissible operations simply produce more standard basis vectors.

Thus the algorithm must terminate after finitely many sets and produce a viable set (the second condition follows from the *R*-graph being connected). Refer to this set as *S*. Since the set $F = \{e_i\}_{i=1}^n \cup \{-e_i\}_{i=1}^n$ does not contain the 0 vector and our output must be contained in *F*, our set must also satisfy the conditions for Theorem 7 and thus is strongly monotone with respect to the lift of our cone. Indeed, we cannot have the 0 vector in our viable output as previously observed, and due to Γ having no 0 rows every specie participates in a reaction, and so our set satisfies all the necessary conditions.

Lastly, we can observe that our set of vertices $S \subseteq F$ either has the structure of a simplex or a cross-polytope. To see this, first assume there exists *i* such that $\{e_i\} \cup \{-e_i\} \subset F$. Now suppose reaction vector Γ_i has nonzero *i*'th component, assume without loss of generality its stoichiometric coefficient for the *i*'th specie is positive. Then by forming $e_i - \Gamma_i$ and $-e_i + \Gamma_i$, if it is nonzero of the *j*'th coordinate as well we will have that $\{e_j\} \cup \{-e_j\} \subset F$ as well. Thus we can repeat this procedure for all reaction vectors that have nonzero *j*'th coordinate. Due to the the *R*-graph being connected, eventually we will see that S = F, and thus our cone is a cross-polytope cone.

In the case that it is not true for any i that $\{e_i\} \cup \{-e_i\} \subset F$, then immediately we must have a simplicial cone.

We also have the following:

Corollary 6. Type C reaction networks are weakly contractive with respect to some norm.

Proof. By Theorem 5, the cone our system strongly monotone with respect to (from Theorem 9) implies we can construct a norm for which we are weakly contractive. We recall the norm is constructed as

$$||x|| = \min(\{r > 0 | \exists v \in \mathbb{R}^n, \{0, x\} \subseteq v + rP\}),$$

where P is the convex hull of the viable set Algorithm 1 outputs.

Corollary 7. If the stoichiometric compatibility class of a network of the form $\Gamma = PN$, where N is type C, is compact then the network converges globally to a unique fixed point on each stoichiometric compatibility class.

Proof. By Theorem 8, Lemma 10, Corollary 5, and Corollary 6 we obtain our result.

8 Additional Weakly Contractive Systems

Using our methods we can show that several constructions (as well as some new constructions) in the literature are special cases of Algorithm 1. We will first need an additional way to associate aligned matrices with stoichiometric matrices.

Definition 21. We say a stoichiometric matrix Γ is alignable if we can write it as PND where

- 1. N is an aligned matrix with -1, 0, or 1 entries.
- 2. P has no 0 columns or 0 rows and each row has exactly one nonzero entry.
- 3. D is a diagonal matrix with nonzero entries on its diagonal.

We call N in this factorization the alignment.

Definition 22. Suppose we have a matrix Γ . Define an equivalence relationship on the rows as follows: we say two rows i and j are related, written $i \sim j$, iff

- 1. For all columns $\Gamma_k \in \Gamma$, $(\Gamma_k)_i \neq 0$ iff $(\Gamma_k)_j \neq 0$.
- 2. For all columns $\Gamma_{k_1}, \Gamma_{k_2} \in \Gamma$, we have that $sign((\Gamma_{k_1})_i(\Gamma_{k_2})_j) = sign((\Gamma_{k_1})_i(\Gamma_{k_2})_j)$.

We define an equivalence relationship similarly for a set of vectors, viewing them as columns of a matrix. We call this equivalence relationship for sets of vectors or matrices the **coordinate equivalence**.

The main point of these definitions is that we can simplify certain reaction networks. If we can write $\Gamma = PND$, then for our purposes we can simplify and consider the reaction network $\Gamma' = N$ instead for our algorithm. In particular, we have

Corollary 8. Suppose we have an alignable stoichiometric matrix $\Gamma = PND$. Then if the stoichiometric matrix $\Gamma' = N$ is strongly monotone (monotone) with respect to a cone K, then Γ is strongly monotone (monotone) with respect to PK.

Proof. Note that multiplying by D^{-1} on the right gives us an equivalent reaction network so that $\Gamma = PND$ is strongly monotone (monotone) iff PN is strongly monotone (monotone). Here we can use Theorem 8 to see that if N is strongly monotone (monotone) then PN is strongly monotone (monotone), and so we are done.

Lemma 13. Suppose we have a matrix Γ that has at most two nonzero entries in each row and only consists of entries of -1, 0 or 1. Then Γ is alignable.

Proof. Suppose Γ has n rows. Form the coordinate equivalence classes of the rows of Γ . Let these classes by $[I]_{\nu}$ where $\nu \in \{1, 2, ..., n\}$. For each equivalence class $[I]_{\nu}$ pick a representative reaction vector Γ_{ν_i} such that Γ_{ν_i} is nonzero for each specie in $[I]_{\nu}$. Let P be a matrix with column i having a nonzero entry in row j if $j \in [I]_i$, and if the representative of $[I]_i$ is Γ_{ν_i} then we also have $P_{ij} = (\Gamma_{\nu_i})_j$. The matrix Pis 0 elsewhere. With this matrix P we can form the factorization $\Gamma = PN$ where N is an aligned matrix. Indeed, the matrix N will have for its i'th column a kind of 'reduced' version of the reaction vector Γ_i . It will have a 1, -1 or 0 in each row corresponding to whether Γ_i has the corresponding column in Pwith the same sign, opposite sign, or does not have overlapping support with the column, respectively. Every two columns of N will share at most two species, with opposite signs. Also, every column of Nwill have at most one nonzero entry in a row where every other column has a 0 entry. Each of these cases correspond to the different equivalence classes now laid out in P.

The claim in the proof of Lemma 13 that we can always perform the required factorization is best seen in an example. Consider the matrix

[1	-1	0	0	0	0		[1	0	0	0	0	0	0							
-1	1	0	0	0	0		-1	0	0	0	0	0	0							
1	1	0	0	0	0		0	1	0	0	0	0	0	[1	$^{-1}$	0	0	0	0	
-1	-1	0	0	0	0		0	-1	0	0	0	0	0	1	1	0	0	0	0	
0	0	1	1	0	0		0	0	1	0	0	0	0	0	0	1	1	0	0	
0	0	1	-1	0	0	=	0	0	0	1	0	0	0	0	0	1	$^{-1}$	0	0	
0	0	1	1	0	0		0	0	1	0	0	0	0	0	0	0	0	-1	-1	
0	0	0	0	$^{-1}$	-1		0	0	0	0	$^{-1}$	0	0	0	0	0	0	1	-1	
0	0	0	0	1	-1		0	0	0	0	0	1	0	1	0	0	0	0	0	
1	0	0	0	0	0		0	0	0	0	0	0	1	-					_	
1	0	0	0	0	0		0	0	0	0	0	0	1							

Note that the two matrices on the right-hand side are of the form PN, where N is aligned and P and disjoint columns.

8.1 Cubical Cones

Before examining the monotone systems in [19], we will describe a general cubical cone construction using 1.

Definition 23. We say an aligned network is cubical if it satisfies the following properties:

- 1. Each row contains at most two nonzero entries
- 2. The columns are linearly independent

Theorem 10. Cubical networks are monotone with respect to a cubical cone (i.e., a cone with the poset of a cube). Starting with one of the vectors from the cubical cone, Algorithm 1 will generate a viable set of vectors for the network (though it is not always cubical).

Proof. Pick as an initial vector v a vector with coordinate i equal to 1 if every reaction vector has nonnegative i'th coordinate, -1 if every reaction vector has nonpositive i'th coordinate, and 0 elsewhere (we carry out this procedure for all i). If we end up with the zero vector, multiply one of our reaction vectors by -1 and repeat the procedure to obtain a nonzero v. Note that this construction of v implies that $v \in Q_2(R_i) \cup Q_1^+(R_i)$ for all i. Indeed, the j'th coordinate of v is either 0 or is the same sign as the j'th coordinate of every reaction that is nonzero in this coordinate.

Suppose our reaction vectors are $\{R_i\}$. We have that $v \in Q_1(R_i)$ for all *i*. For every subset $J \subset \{1, 2, ..., n\}$ define the vector $v + \sum_{i \in J} (-1)^{k_i} R_i$ where $k_i = 0$ if $v \in Q_2(R_i)$ and $k_i = 1$ otherwise. Taking all these possible summands (produced by different J's) as vertices of our cube, we just need to verify these extremals indeed form a cube, and are all permissible for each reaction vector. Once we do this, by Theorem 6 our system is indeed monotone with respect to the lift of this set, which is a cubical cone.

To see that our set of vectors forms a cube, note that this follows from the fact that the vectors R_i are linearly independent. Indeed, an invertible linear transformation T defined such that $T(R_i) = e_i$, the *i*'th standard coordinate vector, sends our set of points to a standard cube (i.e., a cube with each edge parallel to one of the e_i). The set of vectors is sent to a set of points of the form $T(v) + \sum_{i \in J} (-1)^{k_i} e_i$, for all $J \subset \{1, 2, ..., n\}$, which forms a (possibly degenerate) cube.

Consider the vector R_i such that $v \in Q_2(R_i)$, and fix a specific summand (i.e., point of the form $v + \sum_{i \in J} (-1)^{k_i} R_i$). Note that if R_i is not in our given summand, then the specific vertex that corresponds to J must be in $Q_1(-R_i)$, and if it is included in the sum it must be in $Q_1(R_i)$. Indeed, if R_i is not included in the sum, for an arbitrary reaction vector R_j that shares support with R_i we will have that for all coordinates l that $(-1)^{k_i+k_j}(R_j)_l(R_i)_l \ge 0$. Thus including some such reaction vectors will create a sum in $Q_1(-R_i)$. If R_i is included in our sum, since our network is cubical adding other reactions will make each coordinate in the support of R_i no lower than 0.

If $v \in Q_1^+(R_i)$, then when R_i is not included the sum must be in $Q_1(R_i)$, when it is included the sum must be in $Q_1(-R_i)$. Indeed, this follows again from our network being cubical. Suppose j is in the support of v, let $L = v + \sum_{k \in J} (-1)^{k_i} R_k$, and assume without loss of generality that $(v)_j = 1$. Since each row has at most two nonzero entries, if $i \notin J$ and If there is no other vector R such that $(R)_j \neq 0$ then $(L)_j = 1$. If there is one other vector R such that $(R)_j \neq 0$ then we must have $(R)_j = 1$. Thus we could also possibly have $(L)_j = 1 - (R)_j = 0$. In either case, each coordinate will be such that our sum is contained in $Q_1(R_i)$. When R_i is included in the sum similar reasoning will lead to $(L)_j = 0$ or $(L)_j = -1$.

From these observations, we can conclude our set must be viable. Indeed, whenever $L = v + \sum_{i \in J} (-1)^{k_i} R_i$ does not contain a reaction vector R, then if $k_i = 1$ the $L \in Q_1(R)$ and if $k_i = 0$ we have $L \in Q_1(-R)$. Thus performing any permissible operations will give us vectors once again in our set of vectors (obtained by letting J vary). Also clearly we can always find a vector k for each R_i such that $k \in Q_1(R_i) \cup Q_1(-R_i)$ since k = v already satisfies this condition.

By Lemma 12 Algorithm 1 will produce a viable set, and by Theorem 6 the system of a cubical network is monotone with respect to the lift of this set.

We will call the cones from [19] **type S** cones, and the corresponding networks **type S** networks. The cones are of the form $\Lambda = c1^t + \Gamma B$ where c is some column vector, 1^t is the transpose of a vector of all 1's, Γ is some stoichiometric matrix, and B contains as columns the vertices of a cube, e.g., $B = \begin{bmatrix} 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 1 \end{bmatrix}$.

A type S network Γ satisfies the following:

- 1. Γ has linearly independent columns.
- 2. There exists a constant vector c such that $\Lambda = c1^t + \Gamma B$ satisfies:
 - (a) There exists a nonnegative matrix P such that $\Lambda P = I$.
 - (b) There exists a diagonal matrix D with positive entries such that $D\Lambda$ has entries only consisting of -1, 1 or 0.

Theorem 11. The type S networks are alignable. Their alignment is cubical.

Proof. First define $\Gamma' = D\Gamma$ and c' = Dc and $\Lambda' = D\Lambda' = c'1^t + \Gamma'B$ and we will work with the matrix Λ' instead, which has only entries of -1, 0 or 1. Defining $P' = PD^{-1}$, we see that we also have $\Lambda'P' = D\Lambda PD^{-1} = I$.

Note for Λ to only have entries in 0, 1, -1, the vector c' must also consist of -1, 0 or 1's. This is because the first column of $c'1^t + \Gamma'B$ consists simply of c'.

Note that Γ must have at most two nonzero entries in each row. To see this, first note that since Γ' can have at most 3 different values in each row, and that the same is true for $\Gamma'B$ (indeed, since Λ' has at most three different values -1, 0, 1 in each row, so does $\Lambda' - c'1^t = \Gamma'B$, and the first several columns of $\Gamma'B$ are the same as Γ'). Suppose that Γ had 3 nonzero entries in a given row, contained in columns i, j and k. Then among the columns in $\Gamma'B$ corresponding to i, j, k, i + j, j + k, k + i, i + j + k we have at least 3 different nonzero values, which along with the value of 0 gives us 4 different values in $\Gamma'B$. This is a contradiction and so Γ can have at most 2 nonzero entries in each row.

Now since $\Gamma' B = \Lambda' - c' 1^t$, by noting again that the first several columns of $\Gamma' B$ are the same as Γ' we see that Γ' can only have entries from $\{-2, -1, 0, 1, 2\}$. We also have that every two nonzero entries in a given row can be at most 2 units apart since this is true of Λ' and thus also $\Lambda' - c' = \Gamma' B$.

Suppose we also have that in a row l of Γ which has a nonzero entry a = 2 or -2 in column i. Then a can be the only nonzero entry in l. Suppose this was not true, and we have a column j with a nonzero entry b. Then among the 4 values 0, a, b, a + b we can always find 2 values more than 2 units apart, a contradiction.

Thus we can find an alignment of our matrix Γ' as follows: First pick a matrix D_a such that it is a diagonal matrix with the nonzero entry in column *i* equal to 1/2 if the *i*'th row of Γ contains an element with magnitude 2, and 1's elsewhere. Then $D_a\Gamma'$ has only -1, 0, and 1's everywhere and at most two nonzero entries in each row. Then use Lemma 13 to establish a factorization $D_a\Gamma' = P_aN$, where N is an aligned matrix, with linearly independent columns and at most two nonzero entries in each row. Thus $\Gamma = D^{-1}D_a^{-1}P_aN$ has a cubical alignment.

Theorem 12. Cubical networks, and in particular Type S networks, are weakly contractive.

Proof. First by Theorem 10 and Lemma 6 we know our system is monotone with respect to a cone. If we assume the cone from Theorem 10 has no 0 vectors, then our network also satisfies the conditions for Theorem 7 and are strongly monotone. Now we can use Theorem 5 and we are done.

Now assume our construction from Theorem 10 does have a 0 vector. By appending to our set of vectors $\{v\}$ all their negatives $\{-v\}$, we have a new set of vectors such that 0 is a convex combination of the other vectors. This set is viable since all permissible operations on a vector in both the new or old set gives us another vector in these sets (this is true for our original vectors, and thus also for their corresponding set of negative vectors). We also have that for each reaction vector Γ_i there is at least one extremal $k \in K$ such that $k \in Q_1(\Gamma_i) \cup Q_1(-\Gamma_i)$, since this is true for the set of vectors before we appended their negatives. Note also that the dimension of our new set is the same as the dimension of our old set. This is because each vector was contained in the affine span of the set (the affine span and span coincide when we have the 0 vector in our set).

Thus by Theorem 7 our system is strongly monotone with respect to the lifted cone. Thus our system is weakly contractive. $\hfill \Box$

8.2 Connection to a Class of Simplicial Cones

A class of networks monotone with respect to a class of simplicial cones is introduced in [20]. We will refer to these networks as **type I** networks. More precisely, we have the following definition (taken from [20]):

Definition 24. A type I network is a network satisfying the following conditions:

- 1. We can write $\Gamma = \Lambda \Theta$ where
 - (a) The matrix Λ has no 0 columns, and each row has exactly one nonzero entry.
 - (b) The matrix Θ satisfies that each column has at most 2 nonzero entries, and nonzero entries in the same column have opposite signs. Also, ker(Θ^t) is one-dimensional and contains a positive vector.

Lemma 14. All type I networks are alignable, and their alignment is type C.

Proof. Note from Condition 1b that the matrix Θ in $\Gamma = \Lambda \Theta$ must contain at most two nonzero entries of different sign in each column. Next factor $\Theta = D_1 \Theta'$ where D_1 is a diagonal matrix with entries the same as ker(Θ^t). Note by Condition 1b that each entry in a column of Θ' must now have the same magnitude, so we can write $\Theta' = \Theta'' D_2$ where D_2 is a diagonal matrix with positive entries, chosen so that Θ'' contains only -1, 1 or 0. Note that due to the kernel having a positive vector, each column contains 2 nonzero entries or is a zero column. Thus Θ'' is our desired alignment, satisfying the conditions to be type C.

Theorem 13. All type I networks are weakly contractive.

Proof. This follows immediately from Corollary 6.

8.3 Reaction Coordinates

Theorem 14. All the reaction networks that are monotone in reaction coordinates with respect to an orthant cone are monotone in species coordinates as well.

We will break proving this theorem into two parts. First, we assume our network has independent reaction vectors. We will need a graphical definition:

Definition 25. We say our *R*-graph satisfies the **signed loop** property if every edge in the graph has a sign, and every loop in the graph has an even number of positive edges.

It is shown in [2] that this is equivalent to being monotone with respect to an orthant cone in reaction coordinates. Our definition differs from [2] in that our usage of signs is switched and we do not allow multiple edges between our nodes (our edges without a sign correspond to nodes that would have had two edges between them, one positive and one negative, per the definition form [2]).

Lemma 15. Suppose we have a network monotone with respect to an orthant cone in reaction coordinates (i.e., satisfies the signed loop property). Then it is monotone with respect to a cone which has as extremals precisely the reaction vectors of our network.

Proof. We will systematically multiply our vectors by +1 or -1 until we arrive at a new set of vectors that make up our (equivalent) reaction network, such that for each i, Γ_i is the only vector in $Q_1^+(\Gamma_i)$. To prove that it is possible to do this, start by picking an arbitrary reaction vector in our graph, call it Γ_1 . For each reaction vector Γ_i adjacent to it (refer to the set of adjacent vectors as A_1) in the R-graph, multiply them by either +1 or -1 such that the edge between Γ_1 and Γ_i is now negative. Repeat this procedure for every reaction vector adjacent to Γ_1 . Note that this procedure does not impact whether our graph has the signed loop property. Note also that none of the reaction vectors adjacent to Γ_1 can have a positive edge between each other after multiplying, since otherwise, we would break the signed loop property.

Now we repeat this procedure with all vectors adjacent to a vector in A_1 ; call this set of new adjacent vectors A_2 . Select a vector $\Gamma_j \in A_2$ and note it must have either only positive edges with vectors in A_1 or only negative, to maintain the signed loop property. Thus we can multiply it by +1 or -1 such that all these edges are negative. We can repeat this procedure with the rest of A_2 . Now again we have all the vectors in A_2 must have negative edges between each other to maintain the positive loop property.

We can repeat this procedure until we end up with a graph of only negative edges. These new signadjusted vectors make up the extremals of our desired cone. This cone satisfies Corollary 2 for each reaction vector and so our system is monotone.

Note the cone from above might not always be pointed. We show that if the reaction vectors are linearly independent, the cone must always be pointed.

Corollary 9. Assume our reaction network from Lemma 15 has linearly independent reaction vectors. Then the cone produced from Lemma 15 is proper (restricted to the stoichiometric compatability class), convex, and pointed.

Proof. The cone K from Lemma 15 is generated by linearly independent vectors which also span their stoichiometric compatibility classes. We immediately know the cone is convex by the definition of it being generated by some vectors. We know it is proper since its dimension will be the same as the

number of linearly independent reaction vectors that span it. It is also pointed, since if $\pm x \in K$ then we have that

$$x = \sum_{i} a_{i} \Gamma_{i}$$
$$-x = \sum_{i} b_{i} \Gamma_{i}.$$
$$0 = \sum_{i} (a_{i} + b_{i}) \Gamma_{i}.$$

Since $a_i, b_i \ge 0$, with not all equal to 0, we see that the Γ_i are linearly dependent, a contradiction. Thus our cone must be pointed.

Next we assume our reaction network has linearly dependent reaction vectors:

Lemma 16. Suppose our reaction network is monotone in reaction coordinates and linearly dependent. Then we can multiply some of the columns of our reaction vector by nonzero real numbers to produce a stoichiometric matrix where each row has exactly two nonzero entries that sum to 0.

Proof. We can use the same process as in Lemma 15 to arrive at a similar set of vectors such that Γ_i is the only vector in $Q_1^+(\Gamma_i)$ (using the same notation as from the lemma). Note this implies that for each row, it can have at most two nonzero entries and they must have opposite signs. Indeed, if we had three nonzero entries in a row, then in our R-graph we would have a cycle with three edges going between the three reactions. Note that we can have all three reactions have positive edges between them, or one positive edge between two reaction vectors and the other edges being negative (corresponding to the cases where all three nonzero entries in the row have the same sign, or only two have the same sign). Both of these cases contradict the R-graph property.

For this set of vectors to be linearly dependent we must have a nontrivial sum of the form

$$\sum_{i=1}^{n} a_i \Gamma_i = 0,$$

where not all $a_i = 0$. Set $\Gamma'_i = \Gamma_i a_i$ to give us a new set of Γ'_i defining a new reaction network. Note now our sum is of the form

$$\sum_{i=1}^{n} \Gamma_i' = 0.$$

Note if at least one of the Γ'_i were the zero vector, say $\Gamma'_j = 0$, then every reaction vector sharing coordinates with Γ_j would also have to have a coefficient of 0, and we can continue in this manner until all coefficients have to be 0. Thus none of the Γ'_j can be equal to 0, and they must then all be equal to 1. Thus in fact our new network of Γ'_i is equivalent to our old network. Note this means each Γ'_j cannot have a nonzero coordinate which it does not share with every other reaction vector. Thus our network consisting of the reaction vectors Γ'_j must have each row consisting of two nonzero entries with opposite signs and the same magnitude.

Lemma 17. If our reaction network is linearly dependent and monotone in reaction coordinates, it is alignable.

Proof. Suppose the set of our reaction vectors is $\{r_i\}_{1 \le i \le n}$, with stoichiometric matrix Γ . Note for the system to be monotone in reaction coordinates, the R-graph condition must hold, and so each species appears at most two times. Suppose one species only appears one time for a reaction R_i . Then since our system is linearly dependent, a nontrivial sum of the reactions summing to 0 must not include R_i . But then since each species appears at most twice, each reaction that shares a species with R_i must also not show up in the sum, and so forth. Thus, assuming our reaction graph is connected, each species must appear either 0 or exactly 2 times. If a species appears 0 times we can ignore it; so we will assume all our species show up exactly two times.

Suppose we have our nontrivial sum $\sum_{i=1}^{n} a_i r_i$. We know by our previous observation that $a_i \neq 0$ always. Factor our matrix as $\Gamma = MD$ where D has as its diagonal the a_i entries. Then using Lemma 13 we have a factorization M = PN for an aligned matrix N, and so Γ is alignable.

Theorem 15. Suppose our reaction network is monotone in reaction coordinates and linearly dependent. Then the reaction network is weakly contractive.

Proof. Assume without loss of generality that our stoichiometric matrix is an aligned matrix with -1, 0, 1entries (if it was not, we could multiply it by a diagonal matrix D). Assume also that we use the procedure of Lemma 15 so that each row has exactly one positive and one negative element, or only zero elements. Suppose our reaction vectors are the set $\{r_i\}_{1 \le i \le n}$, and consider the set M of all possible 2^n summands of the r_i (e.g., $r_1 + r_2 + r_3$ or $r_1 + r_3$). Take the convex hull of M and let M' be the extreme points of the convex hull. Then M' is a viable set not containing 0. To see this, first note that since our matrix is alignable it only has -1, 0, 1 entries. Every member of M is either in $Q_1(r_i)$ or $Q_1(-r_i)$ for all i, and for an arbitrary sum $s = \sum_{j \in A} r_j$, we have that $s \in Q_1(r_i)$ if $r_i \in A$ and otherwise $s \in Q_1(-r_i)$. Every permissible operation will simply produce another summand, and thus this set is closed under permissible operations. Lastly note that if we take the complement of A, call it C(A), then we have that

$$\sum_{j \in A} r_j + \sum_{j \in C(A)} r_j = 0.$$

From this we see that 0 is not a vertex of our set.

Thus we can find a norm for which our system is weakly contractive by Theorem 7 and Theorem 5. By Corollary 8 and Lemma 17 our network is weakly contractive in general. \Box

This result is related to the results in [2] and [28]. This result also shows the global convergence of this class of networks in [2] using the results in [28]. One novel aspect of our result, however, is the establishment of a decreasing norm on the species space of our reaction network (note that in [28] they do establish a function which decreases along the trajectories, though it is constructed differently and only applied to reaction coordinates in [2]).

Lastly, we will note that if we combine these results with the results on cubical cones, we arrive at:

Theorem 16. Suppose we have an aligned matrix Γ which satisfies that each row has at most 2 nonzero entries. Then it is weakly contractive with respect to some norm.

Proof. If the columns of Γ are independent, then this is handled by Theorem 12. If they are dependent, then this is Theorem 15. Indeed, all aligned matrix with linearly dependent columns with at most 2 nonzero entries in each row must have either 0 or 2 nonzero entries. Assume without loss of generality that Γ always has two entries. We can multiply the columns by either +1 or -1 so that each row has exactly one +1 entry and one -1 entry. Now there are no positive edges so they automatically satisfy the *R*-graph property and so we can apply Theorem 15.

9 Proof of the Theorem 1

- 1. Let S be the set of matrices where each entry is either -1, 0, or 1, and it has at most 2 nonzero entries in each column (hence all matrices in S are alignable by Lemma 13).
- 2. Let S^t be the set of matrices such that $A \in S^t$ iff $A^t \in S$.
- 3. Let $\mathcal{N} = S \cup S^t$.
- 4. Let \mathcal{P} be the set of matrices that have at most one nonzero entry in each row, and no column of zeroes.
- 5. Let \mathcal{D} be the set of square matrices with a nonzero diagonal, and zeros elsewhere.

Now we prove our Theorem 1 (the following theorem is identical to Theorem 1):

Theorem 17. If a reversible reaction network has a stoichiometric matrix of the form PND where $P \in \mathcal{P}$ and $N \in \mathcal{N}$ and $D \in \mathcal{D}$, and dimensions such that we can multiply out the matrices in PND, then its corresponding system is weakly contractive.

Proof. Since multiplying our reversible reactions by a nonzero number does not impact any of our conclusions, clearly PN is weakly contractive if and only if PND is as well. Both these networks lead to exactly the same families of ordinary differential equations under our kinetics assumptions.

First, suppose we have a matrix of the form PN where $N \in S^t$. Then we can write PN = PP'N' by Lemma 13 (here P' is some matrix in \mathcal{P} , unrelated to P), then noting that $PP' \in \mathcal{P}$ our theorem for this case follows from Theorem 16 and Theorem 8.

Now assume that $N \in S$. Then we can find a matrix D such that ND is type C (simply multiply a column by 2 if it only has one nonzero entry). Then by Corollary 6 we have that PND is weakly contractive, and thus our theorem holds for this case and so we are done.

10 Examples

All the following examples can be shown to be weakly contractive via Theorem 1 (i.e., they all possess a factorization as described in this theorem). To check for a factorization of Γ , we can first check if we can factor Γ as PN', where P is constructed as in Lemma 13. We can then check if we can factor N'as N' = ND where D is a diagonal matrix. This is in general how we carried out our factorizations below. Note also that in our approach we do not require any graphical conditions to be checked, whereas results in the literature often require one to check some graphical conditions (e.g., Theorem 7 in [19] and Theorem 1 in [2])

10.1 Cubical Networks

10.1.1 Example 1

This is an example of a cubical network which is not a type S network (since type S matrices cannot have a row including entries with a ratio of 3:1, this follows from the proof of Theorem 11 since in the proof $\Gamma' = D\Gamma$ can only have entries of $\{-2, -1, 0, 1, 2\}$, from which it follows row entries of Γ cannot be 3:1), and thus the network is not one of those considered in [19]. As far as the authors are aware, this network is not contained in any previously known classes of globally convergent networks. Suppose we have the stoichiometric matrix and alignment matrix(Γ and N respectively)

$$\Gamma = \begin{bmatrix} -3 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 1 & 0 & -1 & 0 \\ 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & -1 \end{bmatrix}, N = \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 1 & 0 & -1 & 0 \\ 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & -1 \end{bmatrix}.$$

We can factor our matrix as:

$$\Gamma = PND = \begin{bmatrix} 3 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 3 \end{bmatrix} \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 1 & 0 & -1 & 0 \\ 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & -1 \end{bmatrix} \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1/3 \end{bmatrix}$$

Picking initial vector $v = [0, 0, 0, 1, -1]^t$ (we pick the vector as is done in the proof of Theorem 10) for Algorithm 1, we arrive at the set of vectors

After lifting the matrix $P\alpha$ we get that our cone is generated by the column extremals

	$\left[-3\right]$	0	0	-3	0	0	3	0	0	-3	3	3	-3	0	0	
	0	1	0	1	1	0	0	-1	0	1	0	-1	0	0	-1	
. /	1	0	$^{-1}$	1	1	0	0	0	1	0	-1	0	0	0	-1	
$\alpha =$	0	0	0	-1	-1	1	$^{-1}$	0	0	0	0	0	1	$^{-1}$	1	
	0	-3	0	0	-3	-3	-3	0	-3	0	-3	-3	0	0	0	
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	

This cone and the set of vectors it is lifted from tell us that the matrix N is weakly contractive with respect to the norm induced by α , and that Γ is strongly monotone in the lifted system with respect to

the cone generated by α' by Theorem 7, which agrees with Theorem 12. Since our system has compact compatibility classes, we can conclude our system converges globally on each compatibility class by Corollary 5.

For each of the following examples we follow the same procedure: We first factor our stoichiometric matrix as $\Gamma = PND$, give N to our algorithm to generate the output α , and then lift $P\alpha$ to create our cone.

10.1.2 Example 2

This is an example of a cubical network that is not a matched network (Definition 3). Suppose we have the stoichiometric and alignment matrices

$$\Gamma = \begin{bmatrix} -3 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 1 & 0 & 1 & 0 \\ 1 & 0 & -1 & 0 \\ 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & -1 \end{bmatrix}, N = \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 1 & 0 & 1 & 0 \\ 1 & 0 & -1 & 0 \\ 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & -1 \end{bmatrix}.$$

Picking as our initial vector $v = [0, 0, 1, 0, 1, -1]^t$ (we again pick the vector as is done in the proof of Theorem 10) we arrive at the matrix

	1	0	1	0	-1	1	-1	1	-1	0	0	0	-1	0	0	0	
	-1	0	0	1	1	0	0	-1	0	0	0	0	1	-1	-1	1	
~ -	0	0	0	1	1	-1	1	-1	0	0	-1	1	0	-1	0	0	
$\alpha =$	-1	1	-1	0	0	0	0	0	1	-1	0	0	1	0	-1	1	•
	1	0	0	0	0	-1	1	0	0	0	-1	1	-1	0	1	-1	
	[-1]	-1	-1	-1	0	-1	0	-1	0	0	0	-1	0	0	0	-1	

So our system is monotone with respect to the cone generated by the following column extremals:

	$\begin{bmatrix} 3 \\ -1 \end{bmatrix}$	$\begin{array}{c} 0\\ 0\end{array}$	$\frac{3}{0}$	0 1	$-3 \\ 1$	$\frac{3}{0}$	$-3 \\ 0$	3 - 1	$-3 \\ 0$	$\begin{array}{c} 0\\ 0\end{array}$	$\begin{array}{c} 0\\ 0\end{array}$	$\begin{array}{c} 0\\ 0\end{array}$	$-3 \\ 1$	$0 \\ -1$	0 -1	$\begin{bmatrix} 0\\1 \end{bmatrix}$	
	0	0	0	1	1	-1	1	-1^{-1}	0	0	-1	1	0	$^{-1}$	0	0	
$\alpha' =$	-1	1	-1	0	0	0	0	0	1	-1	0	0	1	0	-1	1	
	1	0	0	0	0	-1	1	0	0	0	-1	1	-1	0	1	-1	
	-3	-3	-3	-3	0	-3	0	-3	0	0	0	-3	0	0	0	-3	
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	

Again we have weak contractivity following from Theorem 7, which agrees with Theorem 12. Since the stoichiometric subspace of our network is compact our system is globally convergent on each stoichiometric compatibility class by Corollary 5.

10.2 Degenerate Cubical Cone

In the following, whenever we pick an initial vector for Algorithm 1 we simply pick one of the column vectors of Γ (it does not matter which one we pick). This is motivated by Theorem 15, where the construction of a viable set includes every reaction vector.

10.2.1 Example 3

The following is an example of a type of network considered in [2] (the network is monotone in reaction coordinates and has a nontrivial kernel). In addition to global convergence, our results show how this network also has monotone and contractive properties. Suppose we have the stoichiometric matrix

$$\Gamma = \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 1 & 0 & -1 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & -1 \end{bmatrix}.$$

This matrix is already aligned. Using initial vector $v = [-1, 1, 1, 0, 0]^t$ we arrive at

	0	0	$^{-1}$	$^{-1}$	0	0	1	0	$^{-1}$	1	0	1	0	1	-1]	1
	0	0	0	0	1	-1	0	$^{-1}$	1	0	0	$^{-1}$	1	-1	1	1
$\alpha =$	1	-1	1	0	1	0	0	-1	0	-1	0	$^{-1}$	0	0	1	•
	1	$^{-1}$	1	0	0	1	0	0	$^{-1}$	-1	0	0	-1	1	0	1
	-1	1	0	1	-1	0	-1	1	1	0	0	0	0	-1	0	I

Finally, the lifted network is monotone with respect to the cone generated by the following column extremals:

Since the extreme points of the convex hull of α do not contain the 0 vector, we can conclude by Theorem 7 that our system is in fact strongly monotone with respect to the cone generated by α' and thus weakly contractive, which agrees with Theorem 15. Since the stoichiometric subspace of our network is compact the network is globally convergent on each stoichiometric compatibility class by Corollary 5.

10.3 Type C Networks

For each example in the following section, the following conclusions hold: Since α does not contain the 0 vector, we can conclude our system is strongly monotone with respect to the cone generated by α' by Theorem 7 and Theorem 8, which agrees with Corollary 6. If the stoichiometric subspace of our network is compact it must be globally convergent on each stoichiometric compatibility class by Corollary 5.

We pick our starting vectors for Algorithm 1 as an arbitrary standard basis vector that shares a coordinate with a column of Γ , as described in Theorem 9. The examples below show how, despite their factoring as $\Gamma = PN$ where the factorization does not satisfy the conditions in Definition 24 (and thus neither the conditions in [20]), we can still apply our methods to conclude the network is weakly contractive. Examples 5 and 6 serve to show the various matrix factorizations we can have, and for Example 6, since the stoichiometric subspace is compact, the system must in fact be globally convergent.

10.3.1 Example 4

Suppose we have the stoichiometric matrix and alignment matrix

$$\Gamma = \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 2 & -2 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix}, \ N = \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix}$$

Thus we can write $\Gamma = PN$ where

$$P = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 2 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}.$$

Using the initial vector $[1, 0, 0, 0]^t$ in Algorithm 1 we get the matrix

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

After lifting the matrix $P\alpha$ we get that our system is monotone with respect to the cone generated by (the columns are the extremal vectors)

$$\alpha' = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 1 & -1 \\ 0 & 0 & -1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -2 & 0 & 2 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 1 & 1 & 1 & 1 & 1 \end{bmatrix}$$

10.3.2 Example 5

Suppose we have the stoichiometric matrix and alignment matrix

$$\Gamma = \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix}, \ N = \begin{bmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix}.$$

Picking as our initial vector $v = [1, 0, 0, 0]^t$ we arrive at the vectors

$$\alpha = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 1 & -1 \\ 0 & 0 & 0 & -1 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 & -1 & 0 & 0 & 0 \\ 1 & 0 & -1 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$
$$\alpha' = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 1 & -1 \\ 0 & 0 & 0 & -1 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 & -1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & -1 & 0 & 0 & 0 \\ 1 & 0 & -1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 1 & 1 & 1 & 1 & 1 \end{bmatrix}$$

10.3.3 Example 6

Suppose we have the stoichiometric matrix

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$$\Gamma = \begin{bmatrix} 1 & 1 & 0 & -1 \\ -1 & -1 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & 1 & -1 \end{bmatrix}, \quad N = \begin{bmatrix} -1 & -1 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & 1 & -1 \end{bmatrix}.$$

Picking $v = [0, 0, 0, 0, 1]^t$ as our initial vector we arrive at our lifted cone's extremals:

11 Discussion

We have produced new classes of monotone systems, as well as a new method to prove global convergence via contractivity. Typically the methods of monotonicity and contractivy are considered as two separate tools for examining the qualitative behavior, but in this paper, we observe that these two methods are intricately linked. Our algorithm shows how many results in the literature have a similar type of structure to them (i.e., they have the factorization decribed in Theorem 1). It is an interesting task for future work to determine exactly how many aligned matrices lead to weakly contractive systems.

A Appendix

A.1 Polytope Geometry

Here we lay out a few basic definitions related to polytopes and cones.

Definition 26. A polytope is the convex hull of a finite number of points in \mathbb{R}^n . A cone is a set of points in \mathbb{R}^n which is closed under addition and multiplication by nonnegative scalars.

Definition 27. The affine hull of a set $S \subset \mathbb{R}^n$ is the set $affHull(S) = \{\sum_i \alpha_i x_i | x_i \in S, \alpha_i \in \mathbb{R}, \sum_i \alpha_i = 1\}$. The dimension of a convex set is the dimension of its affine hull. The relative interior of a set S is its interior in the subspace topology of affHull(S).

A **ray** is a one-dimensional cone.

Definition 28. An extreme point of a polytope P is any point $x \in P$ that satisfies if there exists $y, z \in P$ and $0 \le \gamma \le 1$ such that $x = \gamma y + (1 - \gamma)z$, then x = y = z.

Definition 29. Suppose we have a cone K. An **extremal** k of K is a ray contained in K, satisfying the property that if $\exists x, y \in K$ and $0 \le \gamma \le 1$ such that $\gamma x + (1 - \gamma)y \in k$, then we must have $x, y \in k$.

Definition 30. A proper face of a polytope P is any set of the form $P \cap \mathcal{H}$, where \mathcal{H} is a hyperplane that does not intersect the relative interior of P. A proper face of a cone K is any set of the form $K \cap \mathcal{H}$, excluding the set consisting of only the origin, where \mathcal{H} is a hyperplane which does not intersect the relative interior of K.

Definition 31. We define a cube to be the set of 2^n vectors in \mathbb{R}^n consisting of every possible vector v_i such that for all $1 \leq j \leq n$ we have that $(v_i)_j \in \{0, 1\}$. Here n can be any positive integer.

Definition 32. We say a polytope $K \subseteq \mathbb{R}^k$ is **cubical** if there exists an injective affine transformation $T : \mathbb{R}^k \to \mathbb{R}^n$ such that T(K) is a cube.

Definition 33. A cubical cone is any pointed and polyhedral cone such that it has a cubical crosssection.

We will need a lemma to characterize a certain operation:

Lemma 18. The following two operations on a finite set of points $A = \{v_1, v_2, ..., v_n\} \subset \mathbb{R}^n$ are equivalent:

- 1. Repeatedly remove all points v_i that can be expressed as a convex combination of the other points (removing the points in an unspecified order).
- 2. Take the convex hull of A and then take the extreme points of this convex hull

Proof. To show that the set from 2 is contained in the set from 1, note that every point that is a convex combination of the other points cannot be an extreme point.

Next, we will show the set of points from 1 is contained in the set of points from 2 (no matter the order in which we remove points). Refer to the set of the remaining set of points as B. Note all the points in A were a convex combination of the points in B. This can be seen inductively: The last point to be removed was a convex combination of B, the second to last a convex combination of B and the last point, and so forth. Since the last point was a convex combination of B, the second to last is also a convex combination of B. Thus, by induction, every point is in the convex combination of B.

Every point remaining in B, after removing as many points as possible, cannot be a convex combination of the other vectors in A. If it were, then it would be a convex combination of points in B and we could remove it. Thus each point in B is not in the convex combination of the other points and is thus an extreme point in the convex hull of B. Since the convex hull of B is the same as that of A, each of these points is an extreme point. Thus the set from operation 1 is always contained in the set from operation 2, and so they are the same set.

Note since the second operation leads to a canonical set of points, so does the first operation, no matter how we remove the points.

A.2 Irreversible reactions

Our results can be extended to include reactions which are not reversible. Assume we have a reaction network Γ that possibly contains irreversible reactions. For an irreversible reaction Γ_1 with the reactant species indexed by I, define $Q_1(\Gamma_1) = \{x \in \mathbb{R}^n | (x)_i(v)_i \ge 0 \forall i \in I\}$. We define the other regions correspondingly, as in Definition 7. Note that the results of Section 3 still hold for irreversible reactions. We have that Theorem 6 also holds.

Definition 34. For a network Γ with irreversible reactions, the *R***-graph** is the same as the *R*-graph in the reversible case, but for an edge between two reaction Γ_i and Γ_j we have the edge directed from Γ_i to Γ_i if a product or reactant of Γ_i is a reactant of Γ_i .

Definition 35. A directed graph is **strongly connected** if we can reach each node via a directed path starting at any other node.

We will need to modify Theorem 7:

Theorem 18. Suppose we have a viable set M. Suppose that every species either participates in a reversible reaction, or is a reactant of an irreversible reaction. Suppose the R-graph is strongly connected. Suppose that 0 is a convex sum of at least two different points in M. Then Γ is strongly monotone with respect to the lift of M.

Proof. We follow a similar proof as the reversible case, where we will verify that the conditions for Lemma 6. The proof carries over almost verbatim, where we just need to note we use strong connectedness for the existence of the node Γ_j adjacent to L where $\Gamma_j \notin L$.

Now we can extend our main result to irreversible reactions:

Corollary 10. If a non-catalytic network with a strongly connected R-graph has a stoichiometric matrix of the form PND where $P \in \mathcal{P}$ and $N \in \mathcal{N}$ and $D \in \mathcal{D}$, then its corresponding system is weakly contractive.

Proof. All of our constructions for the different cases contained in Theorem 1 involve constructing viable set. Then we can use 18 to conclude our networks are strongly monotone with respect to the lifted cone, and thus weakly contractive with respect to the norm determined by the viable set. \Box

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References

- Jana L. Gevertz, Stanley M. Dunn, and Charles M. Roth. Mathematical model of real-time PCR kinetics. *Biotechnology and Bioengineering*, 92(3):346–355, 2005.
- [2] David Angeli, Patrick De Leenheer, and Eduardo Sontag. Graph-theoretic characterizations of monotonicity of chemical networks in reaction coordinates. *Journal of Mathematical Biology*, 61(4):581– 616, October 2010.
- [3] Muhammad Ali Al-Radhawi, David Angeli, and Eduardo D. Sontag. A computational framework for a Lyapunov-enabled analysis of biochemical reaction networks. *PLOS Computational Biology*, 16(2):1–37, 02 2020.
- [4] Muhammad Ali Al-Radhawi. Graphical characterizations of robust stability in biological interaction networks. *Mathematics of Control, Signals, and Systems*, 35(3):585–617, 2023.
- [5] Péter Érdi and János Tóth. Mathematical Models of Chemical Reactions: Theory and Applications of Deterministic and Stochastic Models. Nonlinear science : theory and applications. Manchester University Press, 1989.
- [6] Martin Feinberg. Foundations of Chemical Reaction Network Theory, volume 202 of Applied Mathematical Sciences. Springer, 1 edition, 2019.

- [7] Murad Banaji and Casian Pantea. Some results on injectivity and multistationarity in chemical reaction networks. SIAM Journal on Applied Dynamical Systems, 15(2):807–869, 2016.
- [8] Murad Banaji and Balázs Boros. The smallest bimolecular mass action reaction networks admitting Andronov–Hopf bifurcation. *Nonlinearity*, 36(2):1398, jan 2023.
- [9] Hal L. Smith. Monotone Dynamical Systems: An Introduction to the Theory of Competitive and Cooperative Systems. Mathematical surveys and monographs. American Mathematical Society, 2008.
- [10] Zahra Aminzare and Eduardo D. Sontag. Contraction methods for nonlinear systems: A brief introduction and some open problems. In 53rd IEEE Conference on Decision and Control, pages 3835–3847, 2014.
- [11] Winfried Lohmiller and Jean-Jacques E. Slotine. On contraction analysis for non-linear systems. Automatica, 34(6):683–696, 1998.
- [12] Alexander Davydov, Saber Jafarpour, and Francesco Bullo. Non-Euclidean contraction theory for robust nonlinear stability. *IEEE Transactions on Automatic Control*, 67(12):6667–6681, 2022.
- [13] John W. Simpson-Porco and Francesco Bullo. Contraction theory on Riemannian manifolds. Systems & Control Letters, 65:74–80, 2014.
- [14] Saber Jafarpour and Samuel Coogan. Monotonicity and contraction on polyhedral cones, 2023.
- [15] Saber Jafarpour, Pedro Cisneros-Velarde, and Francesco Bullo. Weak and semi-contraction for network systems and diffusively coupled oscillators. *IEEE Transactions on Automatic Control*, 67(3):1285–1300, 2022.
- [16] Saber Jafarpour, Alexander Davydov, and Francesco Bullo. Non-Euclidean contraction theory for monotone and positive systems. *IEEE Transactions on Automatic Control*, pages 1–8, 2022.
- [17] Muhammad Ali Al-Radhawi, David Angeli, and Eduardo Sontag. On structural contraction of biological interaction networks, 2023.
- [18] Murad Banaji and Stephen Baigent. Electron transfer networks. J Math Chem, 43:1355–1370, 07 2007.
- [19] Murad Banaji and Janusz Mierczyński. Global convergence in systems of differential equations arising from chemical reaction networks. *Journal of Differential Equations*, 254(3):1359–1374, 2013.
- [20] Pete Donnell and Murad Banaji. Local and global stability of equilibria for a class of chemical reaction networks. *SIAM Journal on Applied Dynamical Systems*, 12(2):899–920, 2013.
- [21] Murad Banaji. Monotonicity in chemical reaction systems. Dynamical Systems, 24(1):1–30, 2009.
- [22] Muhammad Ali Al-Radhawi and David Angeli. New approach to the stability of chemical reaction networks: Piecewise linear in rates Lyapunov functions. *IEEE Transactions on Automatic Control*, 61(1):76–89, 2016.
- [23] Mitchell Eithun and Anne Shiu. An all-encompassing global convergence result for processive multisite phosphorylation systems. *Mathematical Biosciences*, 291:1–9, 2017.
- [24] Sebastian Walcher. On cooperative systems with respect to arbitrary orderings. Journal of Mathematical Analysis and Applications, 263(2):543–554, 2001.
- [25] Morris W. Hirsch and Hal Smith. Chapter 4 Monotone Dynamical Systems. In A. Cañada, P. Drábek, and A. Fonda, editors, Handbook of Differential Equations: Ordinary Differential Equations Volume 2, volume 2 of Handbook of Differential Equations: Ordinary Differential Equations, pages 239–357. North-Holland, 2006.
- [26] Walter Rudin. Functional Analysis. Higher mathematics series. McGraw-Hill, 1973.
- [27] Hajime Maeda, Shinzo Kodama, and Yoshito Ohta. Asymptotic behavior of nonlinear compartmental systems: Nonoscillation and stability. *IEEE Transactions on Circuits and Systems*, 25(6):372– 378, 1978.

[28] David Angeli and Eduardo D. Sontag. Translation-invariant monotone systems, and a global convergence result for enzymatic futile cycles. Nonlinear Analysis: Real World Applications, 9(1):128–140, 2008.