

# Decomposable and essentially univariate mass-action systems: Extensions of the deficiency one theorem

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## Abstract

The classical and extended deficiency one theorems by Feinberg apply to reaction networks with mass-action kinetics that have independent linkage classes or subnetworks, each with a deficiency of at most one and exactly one terminal strong component. The theorems assume the existence of a positive equilibrium and guarantee the existence of a unique positive equilibrium in every stoichiometric compatibility class.

In our work, we use the *monomial dependency* which extends the concept of deficiency. First, we provide a dependency one theorem for parametrized systems of polynomial equations that are essentially univariate and decomposable. As our main result, we present a corresponding theorem for mass-action systems, which permits subnetworks with arbitrary deficiency and arbitrary number of terminal strong components. Finally, to complete the picture, we derive the extended deficiency one theorem as a special case of our more general dependency one theorem.

**Keywords.** reaction networks, mass-action kinetics, existence of a unique positive equilibrium, parametrized systems of polynomial equations, monomial dependency, dependency one theorem.

**AMS subject classification.** 12D10, 26C10, 92C42

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# 1 Introduction

Many systems in chemistry and biology (particularly in ecology and epidemiology) and also in economics and engineering are modeled as polynomial or power-law dynamical systems. These models can be formulated as *reaction networks* with mass-action or generalized *mass-action kinetics*. They capture complex dynamic behaviors, such as multistationarity, oscillations, and chaos, and the corresponding bifurcations.

The most prominent results of (chemical) reaction network theory, as founded in the 1970's by Horn, Jackson, and Feinberg, are the *deficiency zero* and *one theorems* (for mass-action systems) [21, 20, 14, 15, 17]. In essence, the concept of deficiency captures affine dependencies between *complexes* (representing the left- and right-hand sides of the reactions). The deficiency zero theorem assumes *weak reversibility* (and deficiency zero) and guarantees the existence of a unique positive equilibrium in every *stoichiometric compatibility class* (invariant subspace) and for all *rate constants* (system parameters); moreover, it ensures the asymptotic stability of this equilibrium. The deficiency one theorem has several assumptions. It applies to mass-action systems with *independent linkage classes* or subnetworks, *each* with a deficiency of at most one and exactly one terminal strong component. Additionally, the theorem assumes the existence of a positive equilibrium (for given rate constants) and guarantees the existence of a unique positive equilibrium in every compatibility class (but does not address stability). Finally, weak reversibility ensures the existence of a positive equilibrium.

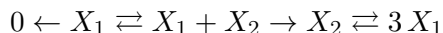
Both, the deficiency zero and one theorems, have been difficult to improve upon. Only after 2010, the deficiency zero theorem has been extended, namely from mass-action to *generalized* mass-action kinetics [25, 26, 23, 24, 12, 8, 30]. In this work, we will extend the deficiency one theorem, even in the setting of mass-action kinetics.

The deficiency one theorem was first fully stated in 1987 [15], but was not proved until 1995 [16]. Its extension from independent linkage classes to independent subnetworks was mentioned in [15], and a proof was outlined in [16]. Since then, the upper bound of one for both the deficiency and the number of terminal strong components (per independent linkage class or subnetwork) has not been addressed. Only the assumption of existence (of a positive equilibrium) has been investigated further [3, 4, 5, 6]. In [3, 4], Boros provides an equivalent condition for the existence of a positive equilibrium for reaction networks that satisfy the assumptions of the deficiency one theorem. In [5], he characterizes single linkage-class, deficiency one mass-action systems for which a positive equilibrium exists for all or some rate constants. Finally, in [6], Boros proves the existence of a positive equilibrium within every stoichiometric compatibility class for weakly reversible, deficiency one mass-action systems. Using different methods, this result can be further extended to weakly reversible (not necessarily deficiency one) mass-action systems [7].

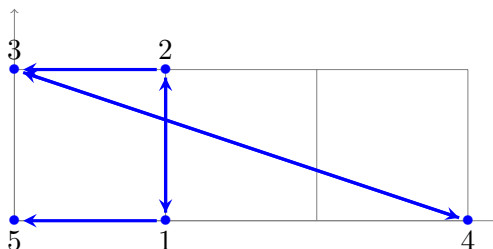
In this work, we extend the validity of the deficiency one theorem to a much broader class of mass-action systems. First, we consider independent subnetworks (instead of independent linkage classes) from the outset. Second, we do not assume that the sub-

networks have a deficiency of at most one. Instead, we use the *monomial dependency* which generalizes the concept of deficiency. Specifically, dependency accounts for the fact that non-source vertices in a reaction network do not contribute monomials to the polynomial equations for the equilibria. As a consequence, the dependency is often smaller than the deficiency. Third, we do not assume that the subnetworks have exactly one terminal strong linkage class. Instead, we bound only the number of terminal strong linkage classes that are not singletons.

We illustrate our results in a series of examples in Section 8. Here, we consider Example 2, given by the reaction network



or, equivalently, by the “embedded” graph

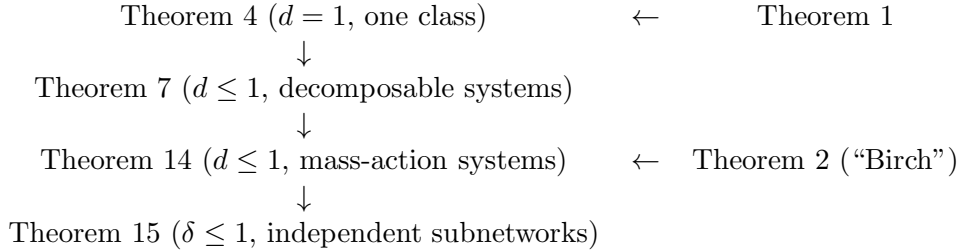


and assume mass-action kinetics. The network has one independent linkage class/subnetwork. Hence, its deficiency is  $\delta = |V| - 1 - \dim(S) = 5 - 1 - 2 = 2$ , where  $V$  is the set of vertices and  $S$  is the stoichiometric subspace (the linear span of the differences of complexes). However, its dependency is  $d = |V_s| - 1 - \dim(L) = 4 - 1 - 2 = 1$ , where  $V_s$  is the set of source vertices and  $L$  is the monomial difference subspace (the linear span of the differences of source complexes). Moreover, this network has two terminal strong components, one singleton (vertex 5 resp. complex 0) and one non-singleton (with vertices 3 and 4 resp. complexes  $X_2$  and  $3X_1$ ). Clearly, it does not satisfy the conditions of the deficiency one theorem. Still, our dependency one theorem for mass-action systems, Theorem 14, can be applied.

Technically, we treat positive equilibria of mass-action systems as *parametrized* systems of *polynomial equations* with *classes* and apply recent fundamental results for such systems [28]. Specifically, their solution set is essentially the solution set on the *coefficient polytope* (modulo an exponential fiber involving the *monomial difference subspace*  $L$ ). The assumption of independent subnetworks and mass-action kinetics makes the system *decomposable* (in the terminology of [28]), and the assumption of *monomial dependency* one (per class) makes the subsystems univariate. Finally, the assumption of  $L = S$  allows to apply Birch’s theorem.

We first provide a *dependency one theorem* for one class, Theorem 4, using the fundamental result from [28], Theorem 1. Next, we extend it to *decomposable systems* (with several classes) and obtain Theorem 7. By applying the latter to reaction networks

(and using Birch’s theorem), we arrive at a dependency one theorem for mass-action systems, Theorem 14. Finally, this allows us to provide a modular proof of the extended deficiency one theorem, Theorem 15, and hence of the classical deficiency one theorem.



### Organization of the work

In Section 2, we recall the relevant geometric objects corresponding to parametrized systems of generalized polynomial equations (with classes) including the coefficient polytope and the monomial dependency and difference subspaces. In Section 3, we provide sufficient conditions for the unique existence of a solution on the coefficient polytope, along with an equivalent condition for its existence. In Section 4, we introduce basic notions for reaction networks with mass-action kinetics, and in Section 5, we decompose a reaction network into subnetworks (as a pre-processing step) and finally into independent subnetworks. In Section 6, we present our main result, the dependency one theorem for mass-action systems, and in Section 7, we derive the extended deficiency one theorem as a special case.

Finally, in Section 8, we provide three examples where the conditions of the deficiency one theorem are not satisfied, but the dependency one theorem can be applied (to conclude the unique existence of a positive equilibrium within every stoichiometric compatibility class for some or all rate constants).

### Notation

For vectors  $x, y \in \mathbb{R}^n$ , we denote their scalar product by  $x \cdot y \in \mathbb{R}$  and their component-wise (Hadamard) product by  $x \circ y \in \mathbb{R}^n$ . We denote the vector with all entries equal to one by  $\mathbf{1}_n \in \mathbb{R}^n$  and the identity matrix by  $\text{Id}_n \in \mathbb{R}^{n \times n}$ .

We denote the positive (non-negative) real numbers by  $\mathbb{R}_{>} (\mathbb{R}_{\geq})$ . For  $x \in \mathbb{R}_{>}^n$  and  $y \in \mathbb{R}^n$ , we define the monomial  $x^y = \prod_{i=1}^n (x_i)^{y_i} \in \mathbb{R}_{>}$ ; and for  $Y = (y^1, \dots, y^m) \in \mathbb{R}^{n \times m}$ , we define the vector of monomials  $x^Y \in \mathbb{R}_{>}^m$  via  $(x^Y)_j = x^{y^j}$ .

For  $x \in \mathbb{R}^n$ , we define  $e^x = (e^{x_1}, e^{x_2}, \dots, e^{x_n})^\top \in \mathbb{R}_{>}^n$ ; and for  $x \in \mathbb{R}_{>}^n$ , we define  $\ln(x) = (\ln(x_1), \ln(x_2), \dots, \ln(x_n))^\top \in \mathbb{R}^n$ .

For  $x \in \mathbb{R}^n$ , we obtain its sign vector  $\text{sign}(x) \in \{-, 0, +\}^n$  by applying the sign function componentwise. For a subset  $S \subseteq \mathbb{R}^n$ ,  $\text{sign}(S) = \{\text{sign}(x) \mid x \in S\} \subseteq \{-, 0, +\}^n$ .

## 2 Previous results on parametrized systems of polynomial equations

In order to state Theorem 1 below for the parametrized system of generalized polynomial equations  $A(c \circ x^B) = 0$ , we introduce geometric objects and auxiliary matrices as defined in [28, 29].

- (i) We call  $C = \ker A \cap \mathbb{R}_{>}^m$  the *coefficient cone*. Its closure  $\overline{C} = \ker A \cap \mathbb{R}_{\geq}^m$  is a polyhedral cone, called an s-cone (subspace cone) in [27]. As a necessary condition for the existence of solutions,  $C$  must be non-empty.
- (ii) We assume that  $A = (A_1 \ \dots \ A_\ell) \in \mathbb{R}^{\ell \times m}$  with  $\ell \geq 1$  blocks  $A_j \in \mathbb{R}^{\ell \times m_j}$  (and hence  $m_1 + \dots + m_\ell = m$ ) such that the kernel of  $A$  is the direct product of the kernels of  $A_j$  that is,  $\ker A = \ker A_1 \times \dots \times \ker A_\ell$ . Accordingly,  $B = (B_1 \ \dots \ B_\ell) \in \mathbb{R}^{n \times m}$  with  $\ell$  blocks  $B_j \in \mathbb{R}^{n \times m_j}$  and  $c^\top = ((c^1)^\top \ \dots \ (c^\ell)^\top) \in \mathbb{R}_{>}^m$  with  $c^i \in \mathbb{R}_{>}^{m_j}$ .

The decomposition of  $\ker A$  induces a partition of the indices  $\{1, \dots, m\}$  into  $\ell$  *classes*. In particular, the columns of  $B = (b^1, \dots, b^m)$  and hence the monomials  $x^{b^j}$ ,  $j = 1, \dots, m$  are partitioned into classes.

- (iii) We introduce the direct product  $\Delta = \Delta_{m_1-1} \times \dots \times \Delta_{m_\ell-1}$  of the standard simplices  $\Delta_{m_j-1} = \{y \in \mathbb{R}_{\geq}^{m_j} \mid 1_{m_j} \cdot y = 1\}$  and define the bounded set  $P = C \cap \Delta$ .

Clearly,  $P = P_1 \times \dots \times P_\ell$  with  $P_j = C_j \cap \Delta_{m_j-1}$ .

We call  $P$  the *coefficient polytope*. In fact,  $P$  is a polytope without boundary. Strictly speaking, only its closure  $\overline{P}$  is a polytope.

- (iv) Let  $I_m = \begin{pmatrix} \text{Id}_{m-1} \\ -1_{m-1}^\top \end{pmatrix} \in \mathbb{R}^{m \times (m-1)}$ , which can be seen as the incidence matrix of a star shaped graph with vertices  $\{1, \dots, m\}$  and root  $m$ . We introduce the  $\ell \times \ell$  block-diagonal (incidence) matrix

$$I = \begin{pmatrix} I_{m_1} & & 0 \\ & \ddots & \\ 0 & & I_{m_\ell} \end{pmatrix} \in \mathbb{R}^{m \times (m-\ell)}$$

with blocks  $I_{m_j} \in \mathbb{R}^{m_j \times (m_j-1)}$  and the “monomial difference” matrix  $M = BI \in \mathbb{R}^{n \times (m-\ell)}$ . Clearly,  $M = (B_1 I_{m_1} \ \dots \ B_\ell I_{m_\ell})$  is generated by taking the differences between the first  $m_j - 1$  columns of  $B_j$  and its last column, for  $j = 1, \dots, \ell$ , and hence  $L = \text{im } M \subseteq \mathbb{R}^n$  is the sum of the linear subspaces associated with the affine spans of the columns of  $B$  in the  $\ell$  classes.

We call  $L$  the *monomial difference subspace*. Further, we call  $d = \dim(\ker M)$  the *monomial dependency*. It can be determined as  $d = m - \ell - \dim L$ , cf. [28, Proposition 1].

(v) We introduce the  $\ell \times \ell$  block-diagonal ‘‘Cayley’’ matrix

$$J = \begin{pmatrix} 1_{m_1}^\top & & 0 \\ & \ddots & \\ 0 & & 1_{m_\ell}^\top \end{pmatrix} \in \mathbb{R}^{\ell \times m}$$

with blocks  $1_{m_j}^\top \in \mathbb{R}^{1 \times m_j}$  and the matrix  $\mathcal{B} = \begin{pmatrix} B \\ J \end{pmatrix} \in \mathbb{R}^{(n+\ell) \times m}$ .

We call  $D = \ker \mathcal{B} \subset \mathbb{R}^m$  the *monomial dependency subspace*. It records affine dependencies between the columns of  $B$  within the  $\ell$  classes.

In fact,  $\dim D = d$ , cf. [28, Lemma 4].

(vi) Finally, we introduce the ‘‘exponentiation’’ matrix  $E = IM^* \in \mathbb{R}^{m \times n}$ , where  $M^* \in \mathbb{R}^{(m-1) \times n}$  is a generalized inverse of  $M$ .

We can now state the main result of our previous work (for equation systems) [29].

**Theorem 1** ([29], Theorem 1). *Consider the parametrized system of generalized polynomial equations  $A(c \circ x^B) = 0$ . The solution set  $Z_c = \{x \in \mathbb{R}_>^n \mid A(c \circ x^B) = 0\}$  can be written as*

$$Z_c = \{(y \circ c^{-1})^E \mid y \in Y_c\} \circ e^{L^\perp},$$

where

$$Y_c = \{y \in P \mid y^z = c^z \text{ for all } z \in D\}$$

is the solution set on the coefficient polytope  $P$ .

Theorem 1 can be read as follows: In order to determine the solution set  $Z_c$ , first determine the solution set on the coefficient polytope,  $Y_c$ . Recall that the coefficient polytope  $P$  is determined by the coefficient matrix  $A$ , and the dependency subspace  $D$  is determined by the exponent matrix  $B$  (and the classes). To a solution  $y \in Y_c$ , there corresponds the actual solution  $x = (y \circ c^{-1})^E \in Z_c$ . In fact, if (and only if)  $\dim L < n$ , then  $y \in Y_c$  corresponds to an exponential manifold of solutions,  $x \circ e^{L^\perp} \subset Z_c$ . Strictly speaking, existence of a unique solution corresponds to  $|Y_c| = 1$  and  $\dim L = n$  (that is,  $L^\perp = \{0\}$ ).

**Theorem 2** (Birch’s theorem). *Let  $x_0, x^* \in \mathbb{R}_>^n$  and let  $S \subseteq \mathbb{R}^n$  be a subspace. Then we have*

$$|(x_0 + S) \cap (x^* \circ S^\perp)| = 1.$$

Theorem 2 was originally proved by Birch in 1963 [2] and reproved by Horn and Jackson [21, Lemma 4B] in the context of reaction networks with mass-action kinetics. Motivated by applications, ‘‘Birch’s theorem’’ has been extended to cover generalized mass-action kinetics [24, 12].

### 3 Dependency one systems

First, we consider systems with one class, second, we consider decomposable systems.

#### 3.1 One class

For one class, we consider  $d = \dim P = 1$ . (The case  $d = \dim P = 0$  is trivial.)

**Definition 3.** For a parametrized system of generalized polynomial equations  $A(c \circ x^B) = 0$  with  $\ker A \cap \mathbb{R}_{>}^m \neq \emptyset$ , one class, one-dimensional coefficient polytope, and monomial dependency one, let  $y^1, y^2 \in (\ker A \cap \mathbb{R}_{\geq}^m)$  be the two vertices of the coefficient polytope, let  $q = (y^1 - y^2) \circ (y^1 + y^2)^{-1} \in \mathbb{R}^m$ , and assume that  $1 = q_1 \geq \dots \geq q_m = -1$  (after reordering of the index set  $\{1, \dots, m\}$ ). Further, let  $I_1, \dots, I_\omega \subset \{1, \dots, m\}$  be  $\omega$  equivalence classes corresponding to equal (consecutive) components of  $q$ , and let  $\tilde{q} \in \mathbb{R}^\omega$  with  $\tilde{q}_i = q_{i'}$  for  $i' \in I_i$  be the vector of different  $q$ 's. Finally, let  $b \in \mathbb{R}^m$  with  $\text{im } b = \ker(\mathcal{B})$ , and let  $\tilde{b} \in \mathbb{R}^\omega$  with  $\tilde{b}_i = \sum_{i' \in I_i} b_{i'}$  be the vector of lumped  $b$ 's.

**Theorem 4** ( $d = 1$ , one class). *Let  $A(c \circ x^B) = 0$  be a parametrized system of generalized polynomial equations with  $\ker A \cap \mathbb{R}_{>}^m \neq \emptyset$ , one class, one-dimensional coefficient polytope ( $\dim P = 1$ ), and monomial dependency one ( $d = 1$ ). Then,  $|Y_c| = 1$  for all  $c$  if*

$$\sum_{i'=1}^i \tilde{b}_{i'} \geq 0 \text{ for all } i = 1, \dots, \omega - 1 \text{ (or “}\leq 0\text{” for all } i) \text{ and } \tilde{b}_1 \cdot \tilde{b}_\omega < 0.$$

*Proof.* Let  $\hat{y} = \frac{y^1 - y^2}{2}$ ,  $\bar{y} = \frac{y^1 + y^2}{2} > 0$ , and hence  $q = \hat{y} \circ \bar{y}^{-1}$ . Every  $y \in P$  can be written as  $y = \bar{y} + t\hat{y}$  with  $t \in (-1, 1)$ , and the binomial condition  $y^b = c^b$  for  $y \in P$  can be written as  $(\bar{y} + t\hat{y})^b = c^b$  for  $t \in (-1, 1)$  or, after division by  $\bar{y}$ , as  $f(t) := (1 + tq)^b = c^b \bar{y}^{-b} =: c^*$ . After considering equal components of  $q$ ,

$$f(t) = \prod_{i=1}^m (1 + tq_i)^{b_i} = \prod_{i=1}^\omega (1 + t\tilde{q}_i)^{\tilde{b}_i}.$$

Now, let  $\tilde{b}_1 \cdot \tilde{b}_\omega < 0$ , in particular,  $\tilde{b}_1 > 0$  and  $\tilde{b}_\omega < 0$ . (The other case is analogous.) Clearly,  $\tilde{q}_1 = 1$  implies  $f(-1) \rightarrow 0$ , and  $\tilde{q}_\omega = -1$  implies  $f(1) \rightarrow \infty$ . By continuity, there is a solution to  $f(t) = c^*$  for all  $c^*$  and hence for all  $c$ . That is,  $|Y_c| \geq 1$  for all  $c$ .

Moreover,  $f'(t) = f(t)h(t)$  with

$$h(t) = \sum_{i=1}^\omega \tilde{b}_i \frac{\tilde{q}_i}{1 + t\tilde{q}_i} = \sum_{i=1}^{\omega-1} \left( \sum_{i'=1}^i \tilde{b}_{i'} \right) \underbrace{\left( \frac{\tilde{q}_i}{1 + t\tilde{q}_i} - \frac{\tilde{q}_{i+1}}{1 + t\tilde{q}_{i+1}} \right)}_{>0}.$$

Now, also let  $\sum_{i'=1}^i \tilde{b}_{i'} \geq 0$  for all  $i = 1, \dots, \omega - 1$  (or “ $\leq 0$ ” for all  $i$ ). Altogether, this implies  $f'(t) > 0$  (or  $f'(t) < 0$ ). That is,  $|Y_c| \leq 1$  for all  $c$ .  $\square$

Recently, unique existence of a positive solution to a parametrized system of generalized polynomial equations (with arbitrary dependency and using one class) has been characterized using Hadamard's Global Inversion Theorem [13].

For completeness, we state that existence (without uniqueness) on the coefficient polytope (for all parameters) can be characterized.

**Theorem 5.** *Let  $A(c \circ x^B) = 0$  be a parametrized system of generalized polynomial equations with  $\ker A \cap \mathbb{R}_{>}^m \neq \emptyset$ , one class, one-dimensional coefficient polytope, and monomial dependency one. The following statements are equivalent:*

1.  $|Y_c| \geq 1$  for all  $c$ .
2.  $\tilde{b}_1 \cdot \tilde{b}_\omega < 0$ .

*Proof.* See Appendix A. □

### 3.2 Decomposable systems

**Definition 6.** For a parametrized system of generalized polynomial equations  $A(c \circ x^B) = 0$  with  $\ker A \cap \mathbb{R}_{>}^m \neq \emptyset$  and  $\ell$  classes, let  $P_j$  be the coefficient polytope and  $d_j$  be the monomial dependency of the subsystem  $A_j(c^j \circ x^{B_j}) = 0$ ,  $j = 1, \dots, \ell$ . If  $\dim P_j = 1$ , let  $y^{j,1}, y^{j,2} \in (\ker A_j \cap \mathbb{R}_{\geq}^{m_j})$  be the two vertices of  $P_j$ , let  $q^j = (y^{j,1} - y^{j,2}) \circ (y^{j,1} + y^{j,2})^{-1} \in \mathbb{R}^{m_j}$ , and assume that  $1 = q_1^j \geq q_2^j \geq \dots \geq q_{m_j}^j = -1$  (after reordering of the index set  $\{1, \dots, m\}$ ). Further, let  $I_1^j, I_2^j, \dots, I_{\omega_j}^j \subset \{1, \dots, m_j\}$  be  $\omega_j$  equivalence classes corresponding to equal (consecutive) components of  $q^j$ . If  $d_j = 1$ , let  $b^j \in \mathbb{R}^{m_j}$  with  $\text{im } b^j = \ker(\mathcal{B}_j)$ , and let  $\tilde{b}^j \in \mathbb{R}^{\omega_j}$  with  $\tilde{b}_i^j = \sum_{i' \in I_i} b_{i'}^j$  be the vector of lumped  $b^j$ 's.

**Theorem 7** ( $d \leq 1$ ). *Let  $A(c \circ x^B) = 0$  be a parametrized system of generalized polynomial equations with  $\ell$  classes that fulfills the following conditions:*

- (i)  $\ker A \cap \mathbb{R}_{>}^m \neq \emptyset$ .
- (ii)  $d = d_1 + \dots + d_\ell$ .
- (iii) For every (class)  $j = 1, \dots, \ell$ ,
  - $d_j = \dim P_j \leq 1$ .
  - If  $d_j = 1$ , then
    - $\sum_{i'=1}^i \tilde{b}_{i'}^j \geq 0$  for all  $i = 1, 2, \dots, \omega_j - 1$  (or “ $\leq 0$ ” for all  $i$ )
    - $\tilde{b}_1^j \cdot \tilde{b}_{\omega_j}^j < 0$ .

Then,  $|Y_c| = 1$  for all  $c$ .



*Proof.* By (i), the coefficient polytope  $P = P_1 \times \cdots \times P_\ell$  is non-empty. By (ii) and [28, Fact 10], the system is decomposable. By [28, Proposition 10],  $Y_c = Y_{c,1} \times \cdots \times Y_{c,\ell}$ , that is, the solution set on the coefficient polytope is a direct product. In particular,  $|Y_c| = |Y_{c,1}| \times \cdots \times |Y_{c,\ell}|$ . By the first item in (iii),  $d_j = \dim P_j \leq 1$ .

Case  $d_j = \dim P_j = 0$ :  $P_j$  is a point, and there is no binomial condition on  $P_j$ . Hence,  $|Y_{c,j}| = 1$ .

Case  $d_j = \dim P_j = 1$ : By the second item in (iii),  $\sum_{i'=1}^i \tilde{b}_{i'}^j \geq 0$  for all  $i = 1, 2, \dots, \omega_j - 1$  (or “ $\leq 0$ ” for all  $i$ ) and  $\tilde{b}_1^j \cdot \tilde{b}_{\omega_j}^j < 0$ . By Theorem 4 for the subsystem  $A_j(c^j \circ x^{B_j}) = 0$ ,  $|Y_{c,j}| = 1$ .

Altogether,  $|Y_c| = |Y_{c,1}| \times \cdots \times |Y_{c,\ell}| = 1$ , and all implications hold for all  $c$ .  $\square$

## 4 Reaction networks

We recall basic notions for reaction networks with mass-action kinetics [1, 31, 32, 19] from [26]. See also [24, 25].

A reaction network  $(G, y)$  is given by a simple directed graph  $G = (V, E)$  and a map  $y: V \rightarrow \mathbb{R}^n$ . Every vertex  $i \in V$  is labeled with a (*stoichiometric*) *complex*  $y(i) \in \mathbb{R}^n$ , and every edge  $(i \rightarrow i') \in E$  represents a (*chemical*) *reaction*  $y(i) \rightarrow y(i')$ . If all components of the graph are strongly connected, the network is called *weakly reversible*.

**Remark.** In the classical definition of a reaction network, complexes (like reactions) are primary objects and correspond to the vertices of the induced complex-reaction graph. Such reaction networks can also be represented as Euclidean-embedded graphs [9]. See also [10, 11].

A *mass-action system*  $(G_k, y)$  is given by a reaction network  $(G, y)$  and positive edge labels  $k \in \mathbb{R}_{>}^E$ . Every edge/reaction  $(i \rightarrow i') \in E$  is labeled with a *rate constant*  $k_{i \rightarrow i'} > 0$ .

The associated ODE system for the positive *concentrations*  $x \in \mathbb{R}_{>}^n$  (of  $n$  chemical species) is given by

$$\frac{dx}{dt} = \sum_{(i \rightarrow i') \in E} k_{i \rightarrow i'} x^{y(i)} (y(i') - y(i)). \quad (1)$$

The sum ranges over all reactions, and every summand is a product of the *reaction rate*  $k_{i \rightarrow i'} x^{y(i)}$ , involving a monomial  $x^y = \prod_{j=1}^n (x_j)^{y_j}$  determined by the kinetic-order complex of the reactant, and the *reaction vector*  $y(i') - y(i)$  given by the stoichiometric complexes of product and reactant.

Let  $I_E \in \{-1, 0, 1\}^{V \times E}$  and  $I_{E,s} \in \{0, 1\}^{V_s \times E}$  be the incidence and source matrices of the digraph  $G$ , respectively, and  $R_k = I_E \text{diag}(k)(I_{E,s})^\top \in \mathbb{R}^{V \times V_s}$  be the rectangular “Laplacian matrix”. (For details on the index notation, see Appendix B.1.) Further, let  $Y \in \mathbb{R}^{n \times V}$  and  $Y_s \in \mathbb{R}^{n \times V_s}$  be the matrices of (source) complexes, and  $N = Y I_E \in \mathbb{R}^{n \times E}$  be the stoichiometric matrix. Then, the right-hand-side of (1) can be written in matrix

form and decomposed into stoichiometric, graphical, and kinetic-order contributions,

$$\frac{dx}{dt} = \underbrace{Y I_E}_N (k \circ x^{Y_s I_{E,s}}) = Y \underbrace{I_E \text{diag}(k)(I_{E,s})^\top}_{R_k} x^{Y_s}. \quad (2)$$

**Remark.** Traditionally, one uses the source matrix  $I'_{E,s} \in \{0, 1\}^{V \times E}$  which involves all vertices (not just the source vertices), and one obtains

$$\frac{dx}{dt} = Y I_E (k \circ x^{Y I'_{E,s}}) = Y \underbrace{I_E \text{diag}(k)(I'_{E,s})^\top}_{\mathcal{L}_k} x^Y$$

with the (square) Laplacian matrix  $\mathcal{L}_k \in \mathbb{R}^{V \times V}$ . This formulation can be misleading since columns of  $\mathcal{L}_k$  corresponding to non-source vertices are zero, and, after multiplication, non-source monomials do not appear in  $\frac{dx}{dt} = Y R_k x^Y$ . Indeed,  $R_k$  arises from  $\mathcal{L}_k$  by deleting zero columns, and  $\text{im } R_k = \text{im } \mathcal{L}_k$ .

The change over time lies in the *kinetic subspace*  $K = \text{im}(Y R_k)$  and further in the stoichiometric subspace *stoichiometric subspace*  $S = \text{im}(Y I_E)$ ,

$$\frac{dx}{dt} \in K \subseteq S.$$

Hence, trajectories are confined to cosets of  $K$  and  $S$ , respectively, that is,  $x(t) \in x(0) + K \subseteq x(0) + S$ . For positive  $x' \in \mathbb{R}_{>}^n$ , the sets  $(x' + K) \subseteq (x' + S) \cap \mathbb{R}_{>}^n$  are called *kinetic* and *stoichiometric compatibility classes*, respectively.

Finally, we introduce non-negative integer characteristics of a graph or a reaction network. In particular, let  $l$  be the number of *components* of  $G$  (not to be confused with  $\ell$  defined below), let  $t$  be the number of *terminal strong components*, and let  $t'$  be the number of terminal strong components that are not singletons (consisting of one non-source vertex). It is well known that

$$\dim(\ker I_E^\top) = l \quad \text{and} \quad \dim(\ker \mathcal{L}_k) = t,$$

which further implies

$$\dim(\text{im } I_E) = |V| - l \quad \text{and} \quad \dim(\text{im } R_k) = \dim(\text{im } \mathcal{L}_k) = |V| - t.$$

Analogously,

$$\dim(\ker R_k) = t'.$$

Most importantly, the (stoichiometric) *deficiency* is given by

$$\delta = \dim(\ker Y \cap \text{im } I_E) = |V| - l - \dim(S).$$

From the facts above, it can be easily shown that

$$t = l \quad \implies \quad K = S \quad \implies \quad \delta \geq t - l.$$

Mass-action systems with  $K \neq S$  can be “pathological”. The assumption  $t = l$  in the classical deficiency one theorem [15] rules out such systems. In the extended deficiency one theorem [16] (for independent subnetworks), this assumption is missing.

## 5 Network decomposition

First, we decompose a reaction network/mass-action system and the associated ODE. Then, in Subsection 5.1, we formulate the resulting polynomial equations for positive equilibria. Only in Subsection 5.2, we assume independent subnetworks (in the sense of [15]) and demonstrate the decomposability of the polynomial equations (in the sense of [28]).

In order to decompose the right-hand side of the ODE of a mass-action system,

$$\frac{dx}{dt} = Y I_E (k \circ x^{Y_s I_{E,s}}), \quad (3)$$

we proceed in three steps.

(i) We assume that the edge set is partitioned into  $\ell$  disjoint subsets,  $E = E^1 \dot{\cup} \dots \dot{\cup} E^\ell$ . (For the moment, the partition is arbitrary. In Subsection 5.2, it will arise from writing the kernel of  $N = Y I_E$  as a direct product.) The partition induces the subgraphs  $G^j = (V^j, E^j)$ ,  $j = 1, \dots, \ell$ , with vertex sets  $V^j$ , source vertex sets  $V_s^j$ , and non-source vertex sets  $V_{ns}^j$ . Note that the vertex sets need not be disjoint. Further note that  $t_j = t'_j + |V_{ns}^j|$ , where  $t_j$  denotes the number of terminal strong components (of the subgraph  $G^j$ ) and  $t'_j$  denotes the number of terminal strong components that are not singletons (consisting of one non-source vertex). The subgraph  $G^j$  has incidence matrix and source matrices

$$I_E^j \in \{-1, 0, 1\}^{V^j \times E^j}, \quad I_{E,s}^j \in \{0, 1\}^{V_s^j \times E^j}.$$

The corresponding subnetwork  $(G^j, y^j)$  has complex matrix  $Y^j \in \mathbb{R}^{n \times V^j}$  and source complex matrix  $Y_s^j \in \mathbb{R}^{n \times V_s^j}$ . (All matrices for a subgraph are submatrices of the corresponding matrices for the full graph.) Clearly,

$$Y I_E = (Y^1 I_E^1 \quad \dots \quad Y^\ell I_E^\ell) \quad \text{and} \quad Y_s I_{E,s} = (Y_s^1 I_{E,s}^1 \quad \dots \quad Y_s^\ell I_{E,s}^\ell).$$

The vector of parameters  $k \in \mathbb{R}_{>}^E$  is partitioned accordingly,

$$k = \begin{pmatrix} k^1 \\ \vdots \\ k^\ell \end{pmatrix}$$

with  $k^j \in \mathbb{R}_{>}^{E^j}$ , and the rectangular Laplacian matrix of the mass-action system  $(G_k^j, y^j)$  is given by

$$R_k^j = I_E^j \text{diag}(k^j) (I_{E,s}^j)^\top \in \mathbb{R}^{V^j \times V_s^j}.$$

(ii) In turn, we define “combined” block(-diagonal) matrices from the matrices of the subgraphs. Since the vertex sets need not be disjoint, we form the *disjoint unions* of

(source) vertex sets  $V^\sqcup = V^1 \sqcup \dots \sqcup V^\ell$  and  $V_s^\sqcup = V_s^1 \sqcup \dots \sqcup V_s^\ell$ . We introduce the combined incidence and source matrices

$$I_E^* = \begin{pmatrix} I_E^1 & & 0 \\ & \ddots & \\ 0 & & I_E^\ell \end{pmatrix} \in \{-1, 0, 1\}^{V^\sqcup \times E}, \quad I_{E,s}^* = \begin{pmatrix} I_{E,s}^1 & & 0 \\ & \ddots & \\ 0 & & I_{E,s}^\ell \end{pmatrix} \in \{0, 1\}^{V_s^\sqcup \times E}$$

and the combined rectangular Laplacian matrix

$$R_k^* = I_E^* \text{diag}(k) (I_{E,s}^*)^\top = \begin{pmatrix} R_k^1 & & 0 \\ & \ddots & \\ 0 & & R_k^\ell \end{pmatrix} \in \mathbb{R}^{V^\sqcup \times V_s^\sqcup}.$$

The (source) complex matrices can be combined accordingly,

$$Y^* = (Y^1 \quad \dots \quad Y^\ell) \in \mathbb{R}^{n \times V^\sqcup}, \quad Y_s^* = (Y_s^1 \quad \dots \quad Y_s^\ell) \in \mathbb{R}^{n \times V_s^\sqcup}.$$

On the one hand,  $Y^* I_E^* = Y I_E$ . On the other hand,  $Y_s^* = Y_s I_{V_s}^*$  with a matrix  $I_{V_s}^* \in \{0, 1\}^{V_s \times V_s^\sqcup}$  that assigns to every source vertex of a subgraph the corresponding source vertex of the full graph.

(iii) Now, we return to the ODE (3). Like the matrix  $Y I_E$ , the vector of monomials  $x^{Y_s I_{E,s}}$  in  $\mathbb{R}_{\geq}^E$  has  $\ell$  blocks and can be decomposed as

$$\begin{aligned} x^{Y_s I_{E,s}} &= \begin{pmatrix} x^{Y_s^1 I_{E,s}^1} \\ \vdots \\ x^{Y_s^\ell I_{E,s}^\ell} \end{pmatrix} = \begin{pmatrix} (I_{E,s}^1)^\top x^{Y_s^1} \\ \vdots \\ (I_{E,s}^\ell)^\top x^{Y_s^\ell} \end{pmatrix} \\ &= \begin{pmatrix} (I_{E,s}^1)^\top & & 0 \\ & \ddots & \\ 0 & & (I_{E,s}^\ell)^\top \end{pmatrix} \begin{pmatrix} x^{Y_s^1} \\ \vdots \\ x^{Y_s^\ell} \end{pmatrix} = (I_{E,s}^*)^\top x^{Y_s^*}. \end{aligned}$$

Using the definitions above, we decompose the right-hand side of the ODE as

$$\begin{aligned} \frac{dx}{dt} &= Y I_E (k \circ x^{Y_s I_{E,s}}) = Y I_E \text{diag}(k) x^{Y_s I_{E,s}} \\ &= Y^* I_E^* \text{diag}(k) (I_{E,s}^*)^\top x^{Y_s^*} = Y^* R_k^* x^{Y_s^*}. \end{aligned}$$

Finally, we introduce

$$\Gamma_k^j = Y^j R_k^j \in \mathbb{R}^{n \times V_s^j}, \quad j = 1, \dots, \ell,$$

and

$$\Gamma_k = Y^* R_k^* = (\Gamma_k^1 \quad \dots \quad \Gamma_k^\ell) = (Y^1 R_k^1 \quad \dots \quad Y^\ell R_k^\ell) \in \mathbb{R}^{n \times V_s^\sqcup}$$

and summarize the decomposition as

$$\frac{dx}{dt} = \Gamma_k x^{Y_s^*} = \sum_{j=1}^{\ell} \Gamma_k^j x^{Y_s^j}. \quad (4)$$

Before we proceed with the treatment of the resulting polynomial equations, we introduce linear subspaces associated with a subnetwork  $(G^j, y^j)$  or a mass-action system  $(G_k^j, y^j)$ ,  $j = 1, \dots, \ell$ . As above, we define the stoichiometric and kinetic subspaces  $S_j = \text{im}(Y^j I_E^j)$  and  $K_j = \text{im}(Y^j R_k^j)$ , where  $K_j \subseteq S_j$  since  $\text{im} R_k^j \subseteq \text{im} I_E^j$ . Clearly,  $S = \sum_{j=1}^{\ell} S_j$ . However, for  $K$ , there is only an inclusion.

**Proposition 8.**  $K \subseteq \sum_{j=1}^{\ell} K_j$ .

*Proof.* By definition,  $K = \text{im}(Y R_k)$  and  $\sum_j K_j = \sum_j \text{im}(Y^j R_k^j) = \text{im}(Y^* R_k^*)$ , where

$$Y R_k = Y I_E \text{diag}(k) (I_{E,s})^\top$$

and

$$Y^* R_k^* = Y^* I_E^* \text{diag}(k) (I_{E,s}^*)^\top.$$

Since  $Y I_E = Y^* I_E^*$  and  $\text{im}(I_{E,s})^\top \subseteq \text{im}(I_{E,s}^*)^\top$ ,  $\text{im}(Y R_k) \subseteq \text{im}(Y^* R_k^*)$ .  $\square$

## 5.1 Positive equilibria

Finally, we consider positive equilibria of the ODE (3), that is,  $x \in \mathbb{R}_{>}^n$  such that  $\frac{dx}{dt} = 0$ . Clearly, we can specify them in the form  $A(c \circ x^B) = 0$  as

$$N(k \circ x^{Y_s I_{E,s}}) = 0, \quad (5a)$$

that is, with  $A = N \in \mathbb{R}^{n \times E}$ ,  $c = k \in \mathbb{R}_{>}^E$ ,  $B = Y_s I_{E,s} \in \mathbb{R}^{n \times E}$ ; equivalently, using the decomposition (4), we can specify them as

$$\Gamma_k x^{Y_s^*} = 0, \quad (5b)$$

that is, with  $A = \Gamma_k \in \mathbb{R}^{n \times V_s^\cup}$ ,  $c = 1$ , and  $B = Y_s^* = Y_s I_{V,s}^* \in \mathbb{R}^{n \times V_s^\cup}$ .

In Equation (5a), the coefficient matrix  $A = N$  (and hence the classes determined by its kernel) do not depend on the parameters  $k$ . However, there may be repeated monomials (within classes) giving rise to trivial dependencies. In Equation (5b), the coefficient matrix  $A = \Gamma_k$  does depend on  $k$ , but repeated monomials are handled via the (rectangular) Laplacian matrix (which also eliminates non-source monomials). Hence, we will consider Equation (5b), but use classes arising from Equation (5a).

## 5.2 “Independent subnetworks” and “decomposability”

Let  $(G, y)$  be a reaction network. In the following, we assume that (i) the partition of the edge set arises from the finest *direct product* form of the kernel of the stoichiometric matrix (or, equivalently, from a *direct sum* form of the stoichiometric subspace). That is,

$$N = YI_E = (N^1 \quad \dots \quad N^\ell) = (Y^1 I_E^1 \quad \dots \quad Y^\ell I_E^\ell)$$

such that

$$\ker N = \ker N^1 \times \dots \times \ker N^\ell. \quad (6a)$$

Equivalently,

$$S = S_1 \oplus \dots \oplus S_\ell.$$

In the terminology of [15], the subnetworks  $(G^j, y^j)$  are *independent*. Moreover, we assume that (ii) the subgraphs  $G^j$  are *connected* (and say that the subnetworks are connected).

It is easy to see that (6a) implies

$$\ker \Gamma_k = \ker \Gamma_k^1 \times \dots \times \ker \Gamma_k^\ell \quad (6b)$$

for

$$\Gamma_k = Y^* R_k^* = (\Gamma_k^1 \quad \dots \quad \Gamma_k^\ell) = (Y^1 R_k^1 \quad \dots \quad Y^\ell R_k^\ell).$$

Just consider  $\xi \in \mathbb{R}^{V_s^\sqcup}$  with blocks  $\xi^j \in \mathbb{R}^{V_s^j}$ ,  $j = 1, \dots, \ell$ , and assume  $\Gamma_k \xi = \sum_{j=1}^\ell \Gamma_k^j \xi^j = 0$ . Now, introduce  $\alpha^j = \text{diag}(k^j)(I_{E,s}^j)^\top \xi^j \in \mathbb{R}^{E^j}$  with  $N^j \alpha^j = Y^j I_E^j \text{diag}(k^j)(I_{E,s}^j)^\top \xi^j = Y^j R_k^j \xi^j = \Gamma_k^j \xi^j$ . Hence,  $\sum_{j=1}^\ell N^j \alpha^j = 0$ . By (6a),  $N^j \alpha^j = \Gamma_k^j \xi^j = 0$ . That is, (6b).

In the terminology of [28] (for the polynomial equations  $\Gamma_k x^{Y_s^*} = 0$ ), the direct product form of  $\ker \Gamma_k \subseteq \mathbb{R}^{V_s^\sqcup}$  induces a partition of the source vertex set  $V_s^\sqcup = V_s^1 \sqcup \dots \sqcup V_s^\ell$  into the  $\ell$  *classes*  $V_s^j$ .

For the polynomial equations  $\Gamma_k x^{Y_s^*} = 0$ , the monomial dependency and difference subspaces,  $D$  and  $L$ , are defined in Section 2. For (the classes)  $j = 1, \dots, \ell$ , we introduce corresponding subspaces  $D_j$  and  $L_j$ . In particular,  $L_j = \text{im}(Y_s^j I_{\mathcal{E}_s}^j)$ , where  $I_{\mathcal{E}_s}^j \in \{-1, 0, 1\}^{V_s^j \times \mathcal{E}_s}$  is the incidence matrix of an auxiliary graph  $(V_s^j, \mathcal{E}_s)$  with  $|\mathcal{E}_s| = |V_s^j| - 1$ . (For details on auxiliary graphs, see Appendix B.2.) Now, let  $I_{\mathcal{E}}^j \in \{-1, 0, 1\}^{V^j \times \mathcal{E}}$  be the incidence matrix of another auxiliary graph  $(V^j, \mathcal{E})$  with  $|\mathcal{E}| = |V^j| - 1$ . Using connectedness and  $\text{im } I_{\mathcal{E}}^j = \text{im } I_E^j$ ,

$$L_j = \text{im}(Y_s^j I_{\mathcal{E}_s}^j) \subseteq \text{im}(Y^j I_{\mathcal{E}}^j) = \text{im}(Y^j I_E^j) = S_j.$$

By construction,  $L = L_1 + \dots + L_\ell$ .

As defined in [28], polynomial equations are *decomposable* if  $D$ , just as  $\ker \Gamma_k$ , has direct product form  $D = D_1 \times \dots \times D_\ell$  or, equivalently, if  $d = d_1 + \dots + d_\ell$ , where  $d_j = \dim D_j$ . For mass-action systems, the resulting polynomial equations are decomposable. (In general, this does not hold for generalized mass-action systems.)

**Proposition 9.** *Let  $\Gamma_k x^{Y_s^*} = 0$  have  $\ell$  classes (arising from  $\ell$  connected, independent subnetworks). Then  $d = d_1 + d_2 + \dots + d_\ell$ .*

*Proof.* First,  $V_s^\sqcup = V_s^1 \sqcup \dots \sqcup V_s^\ell$  implies  $|V_s^\sqcup| = |V_s^1| + \dots + |V_s^\ell|$ . Second,  $L_j \subseteq S_j$ ,  $L = L_1 + \dots + L_\ell$ , and  $S = S_1 \oplus \dots \oplus S_\ell$  imply  $L = L_1 \oplus \dots \oplus L_\ell$ . Hence,

$$d = |V_s^\sqcup| - \ell - \dim(L) = \sum_{j=1}^{\ell} |V_s^j| - 1 - \dim(L_j) = \sum_{j=1}^{\ell} d_j.$$

□

In the following, we consider dependencies, rather than deficiencies. Still, for completeness, we show that  $\delta = \delta_1 + \dots + \delta_\ell$  holds for a network decomposed into  $\ell$  connected, independent subnetworks.

Given the directed graph  $G = (V, E)$  of a network, we introduce the bipartite graph  $\mathcal{G} = (\mathcal{V}, \mathcal{W}, \mathcal{E})$  with the first vertex set  $\mathcal{V} = \{1, \dots, \ell\}$  representing subnetworks of  $G$ , the second vertex set  $\mathcal{W} \subseteq V$  representing “shared” vertices (appearing in more than one subnetwork), and the edge set  $\mathcal{E} = \{(j, i) \in \mathcal{V} \times \mathcal{W} \mid i \in V^j\}$ , connecting shared vertices with their subnetworks.

**Lemma 10.** *Let  $(G, y)$  be a reaction network decomposed into  $\ell$  connected, independent subnetworks. Then,  $|V^\sqcup| - |V| = \ell - l$ , that is,  $\ker I_E = \ker I_E^*$ .*

*Proof.* Since we assume that subgraphs are connected, all vertices of a given subgraph derive from only one component of the original graph, and we can consider the decomposition of  $l = 1$  component into  $\ell$  subgraphs. For the resulting bipartite graph  $\mathcal{G}$ ,  $|\mathcal{V}| = \ell$  and

$$|\mathcal{E}| = \sum_{i \in \mathcal{W}} \deg(i) = \sum_{i \in \mathcal{W}} (\deg(i) - 1 + 1) = V^\sqcup - V + |\mathcal{W}|.$$

Since  $\mathcal{G}$  is connected,  $|\mathcal{E}| \geq |\mathcal{V}| + |\mathcal{W}| - 1$ , that is,  $V^\sqcup - V \geq \ell - 1$ . For clarity, note that a “double edge”  $(ijj')$  indicates that the shared vertices  $i, i'$  reside in subgraph  $j$  and hence  $0 \neq y(i') - y(i) \in S_j$ . Now, assume  $V^\sqcup - V > \ell - 1$ . Then, there is a cycle of  $n \geq 2$  “double edges” with vertex sequence  $i_1 j_1 i_2 j_2 \dots i_n j_n i_{n+1}$ , where  $i_{n+1} = i_1$ ,  $i_* \in \mathcal{W} \subseteq V$ ,  $j_* \in \mathcal{V} = \{1, \dots, \ell\}$ . Hence,

$$\underbrace{y(i_2) - y(i_1)}_{\in S_{j_1}} + \dots + \underbrace{y(i_1) - y(i_n)}_{\in S_{j_n}} = 0,$$

contradicting  $S = S_1 \oplus \dots \oplus S_\ell$ . Hence,  $V^\sqcup - V = \ell - 1$ . By combining the arguments for the  $l$  components of the original graph,  $V^\sqcup - V = \ell - l$ .

Recall  $I_E \in \{-1, 0, 1\}^{V \times E}$  and  $I_E^* \in \{-1, 0, 1\}^{V^\sqcup \times E}$ . Obviously,  $\ker I_E \supseteq \ker I_E^*$ . By the rank-nullity theorem,  $\dim(\ker I_E) = |E| - \dim(\text{im } I_E) = |E| - \dim(\text{im } I_E^\top) = |E| - |V| + \dim(\ker I_E^\top) = |E| - |V| + l$  as well as  $\dim(\ker I_E^*) = |E| - |V^\sqcup| + \ell$ . Hence,  $\dim(\ker I_E) - \dim(\ker I_E^*) = |V^\sqcup| - |V| - (\ell - l) = 0$  and  $\ker I_E = \ker I_E^*$ . □

**Proposition 11.** *Let  $(G, y)$  be a reaction network decomposed into  $\ell$  connected subnetworks. The following statements are equivalent.*

1.  $S = S_1 \oplus \cdots \oplus S_\ell$ .
2.  $\delta = \delta_1 + \cdots + \delta_\ell$  and  $|V^\cup| - |V| = \ell - l$ .

*Proof.* 2  $\implies$  1. On the one hand,  $\delta = |V| - l - \dim S$ . On the other hand,  $\delta_j = |V^j| - 1 - \dim S_j$  and hence  $\sum_j \delta_j = |V^\cup| - \ell - \sum_j \dim S_j$ . Altogether,

$$\sum_j \dim S_j - \dim S = \delta - \sum_j \delta_j + |V^\cup| - |V| - (\ell - l).$$

1  $\implies$  2. By Lemma 10, if  $S = S_1 \oplus \cdots \oplus S_\ell$ , then  $|V^\cup| - |V| = \ell - l$ . By the displayed equation above, also  $\delta = \sum_j \delta_j$ .  $\square$

## 6 Dependency one mass-action systems

We present a *dependency* one theorem for mass-action systems, extending the deficiency one theorems by Feinberg [15, 16], cf. Theorem 15.

In Theorem 14 below, we neither assume  $\delta_i \leq 1$ ,  $t_i = 1$  nor  $K = S$ . In fact, for one class,  $K$  and  $L$  determine the desired equality of  $d$  and  $\dim P$ .

**Lemma 12.** *Let  $\Gamma_k x^{Y_s} = 0$  have one class and assume  $\ker \Gamma_k \cap \mathbb{R}_{>}^{V_s} \neq \emptyset$ . Then,*

$$\dim P = d \iff \dim K = \dim L.$$

*Proof.* On the one hand,  $\dim P + 1 = \dim C = \dim(\ker \Gamma_k) = \dim(\ker(YR_k)) = |V_s| - \dim(\text{im}(YR_k)) = |V_s| - \dim K$ . On the other hand,  $d + 1 = |V_s| - \dim L$ . Hence,  $\dim P = d$  if and only if  $\dim K = \dim L$ .  $\square$

Notably,  $\dim P \leq 1$  (an at most one-dimensional coefficient polytope) implies  $t' \leq 1$  (at most one terminal strong component that is not a singleton).

**Proposition 13.** *Let  $\Gamma_k x^{Y_s} = 0$  have one class and assume  $\ker \Gamma_k \cap \mathbb{R}_{>}^{V_s} \neq \emptyset$ . Then,*

$$\dim P \leq 1 \implies t' \leq 1.$$

*Proof.* Let  $\dim P \leq 1$ . Then,  $t' \leq 2$  since

$$\begin{aligned} \dim P + 1 &= \dim C = \dim(\ker \Gamma_k) = \dim(\ker(YR_k)) \\ &= \dim(\ker Y \cap \text{im } R_k) + \underbrace{\dim(\ker R_k)}_{t'}. \end{aligned}$$

However, if  $t' = 2$ , then  $\ker \Gamma_k = \ker(YR_k) = \ker R_k$  is generated by two nonnegative vectors with support on two (non-singleton) terminal strong components, contradicting  $\ker \Gamma_k \cap \mathbb{R}_{>}^{V_s} \neq \emptyset$ .  $\square$



**Theorem 14** ( $d \leq 1$ , mass-action systems). *Let  $(G_k, y)$  be a mass-action system with  $\ell$  classes that fulfills the following conditions:*

(I)  $\ker \Gamma_k \cap \mathbb{R}_{>}^{V_s^{\cup}} \neq \emptyset$ .

(IIa)  $K = L$  or (IIb)  $L = S$ .

(III) For every (class)  $j = 1, \dots, \ell$ ,

- $d_j \leq 1$  and  $K_j = L_j$ .

- If  $d_j = 1$ , then

- $\sum_{i'=1}^i \tilde{b}_{i'}^j \geq 0$  for all  $i = 1, 2, \dots, \omega_j - 1$  (or “ $\leq 0$ ” for all  $i$ )

- $\tilde{b}_1^j \cdot \tilde{b}_{\omega_j}^j < 0$ .

(The components of the (lumped) dependency vector  $\tilde{b}^j \in \mathbb{R}^{\omega_j}$  are ordered with respect to the vector  $\tilde{q}^j \in \mathbb{R}^{\omega_j}$  of the polytope  $P_j$ .)

Then, there exists a unique positive equilibrium within every (IIa) kinetic or (IIb) stoichiometric compatibility class.

*Proof.* The mass-action system  $(G_k, y)$  gives rise to the polynomial equations  $\Gamma_k x^{Y_s^*} = 0$  with  $\ell$  classes. In order to apply Theorem 7 for the polynomial equations  $A(c \circ x^B) = 0$ , we show that conditions (i), (ii), (iii) there follow from conditions (I), (II), (III) here.

(i) By (I) and  $A = \Gamma_k$ .

(ii) By Proposition 9.

(iii) By (III),  $K_j = L_j$ , and by Lemma 12,  $d_j = \dim P_j$  (for  $j = 1, \dots, \ell$ ). Regarding  $d_j = 1$ , (iii) and (III) are identical.

By Theorem 7, the solution set on the coefficient polytope is a singleton,  $|Y_c| = 1$ , and by Theorem 1, the solution set is an exponential fiber,  $Z_c = x^* \circ e^{L^\perp}$  with  $x^* \in \mathbb{R}_{>}^n$ .

The set of positive equilibria within the kinetic compatibility class given by  $x' \in \mathbb{R}_{>}^n$  is  $x^* \circ e^{L^\perp} \cap (x' + K)$ . By (IIa),  $K = L$ , and by Theorem 2, the intersection is a singleton.

The set of positive equilibria within the stoichiometric compatibility class given by  $x' \in \mathbb{R}_{>}^n$  is  $x^* \circ e^{L^\perp} \cap (x' + S)$ . By (IIb),  $L = S$ , and by Theorem 2, the intersection is a singleton.  $\square$

## 7 Deficiency one

We prove Theorem 15 below which already extends the “classical” deficiency one theorem [15, Theorem 6.2.1] from components (“linkage classes”) to independent subnetworks, cf. [15, Remark 6.2.D] and [16, Theorem A.1].

**Theorem 15** (deficiency one, independent subnetworks). *Let  $(G_k, y)$  be a mass-action system with  $\ell$  independent subnetworks that fulfills the following conditions:*

*For every (independent subnetwork)  $j = 1, \dots, \ell$ ,*

*(i)  $\delta_j \leq 1$  and*

*(ii)  $t_j = 1$ .*

*If (iii) there exists a positive equilibrium, then there exists a unique positive equilibrium within every stoichiometric compatibility class.*

*If the system is weakly reversible, then (iii) for all rate constants  $k$ .*

**Remark 16** (w.r.t. the statement). Note that in the deficiency one theorems, the existence of a positive equilibrium is assumed. In our dependency one theorem, we only assume the necessary condition  $\ker \Gamma_k \cap \mathbb{R}_{>}^{V_s^{\cup}} \neq \emptyset$ . Indeed, in this setting, the two conditions are equivalent. A different (more involved) equivalent condition for existence was given by Boros [6].

**Remark 17** (w.r.t. the proof). The proof of the classical theorem can be found in [16, Sections 5, 6, 7, 8, Appendix B]; it is quite lengthy (about 40 pages) and rather involved. For an outline of the proof of the extension (to independent subnetworks or “direct partitions”), see [16, Appendix A]. In [16, Sections 5, 6], Feinberg establishes that the set of positive equilibria has the form  $x^* \circ e^{S^\perp}$  (a particular solution  $x^*$  times the exponentiation of the orthogonal complement of the stoichiometric subspace  $S$ ), by rewriting the problem using a certain monotonic function. In contrast, we employ a geometric approach to parametrized systems of polynomial equations [28, 29] and establish the existence of a solution  $y^*$  on the coefficient polytope (with  $y^*$  corresponding to  $x^* \circ e^{S^\perp}$ ). As Feinberg, we use the “second salt theorem” (a network argument) and “Birch’s theorem”, but our proof fits within a few pages (see below). Notably, we replace Feinberg’s proof for the existence of a positive equilibrium in the case of weakly reversible networks [16, Section 8] with a one-paragraph, graph-theoretical argument.

We show that the deficiency one theorem easily follows from our more general dependency one result, Theorem 14. Indeed, we exhibit how the “network conditions” in Theorem 15 ensure the conditions in Theorem 14.

First, we consider one independent subnetwork with  $t = 1$  and assume  $\ker(YR_k) \cap \mathbb{R}_{>}^{V_s} \neq \emptyset$ . As one consequence of Lemma 18 below, the special case  $\delta = 1$  and  $t' = 0$  (one singleton terminal strong component) has  $d = 0$ .

**Lemma 18.** *Let  $(G_k, y)$  be a mass-action system with one independent subnetwork ( $G$  itself) and one terminal strong component ( $t = 1$ ), and assume  $C = \ker \Gamma_k \cap \mathbb{R}_{>}^{V_s} \neq \emptyset$ . Then,*

1.  $K = L = S$ .
2.  $d = \delta + t' - 1$ .

*Proof.* 1. Clearly,  $K = \text{im}(YR_k) = \text{im}(YI_E) = S$ , since  $l = t (= 1)$  and hence  $\text{im } R_k = \text{im } I_E$ . To show  $L = S$ , let  $(V, \mathcal{E})$  and  $(V_s, \mathcal{E}_s)$  be auxiliary graphs for  $G = (V, E)$  with incident matrices  $I_{\mathcal{E}}$  and  $I_{\mathcal{E}_s}$ , respectively. Then,  $L = \text{im}(Y_s I_{\mathcal{E}_s})$  and  $S = \text{im}(YI_E) = \text{im}(YI_{\mathcal{E}})$ , since  $\text{im}(I_{\mathcal{E}}) = \text{im}(I_E)$ . For  $V_s = V$ , also  $\mathcal{E}_s = \mathcal{E}$  and hence  $L = S$ . For  $V_s \subset V$ , let  $V = V_s \dot{\cup} \{i_*\}$  and  $E = E_s \dot{\cup} E_*$ , where  $E_s$  is the set of reactions between source vertices (and hence  $E_*$  is the set of reactions with target vertex  $i_*$ ). Now,  $\Gamma_k \xi = 0$  for  $\xi \in \mathbb{R}_{>}^{V_s}$  implies  $YI_E \alpha = 0$  with  $\alpha = \text{diag}(k)(I_{E,s})^\top \xi \in \mathbb{R}_{>}^E$ . That is,  $YI_{E_s} \alpha_{E_s} + YI_{E_*} \alpha_{E_*} = 0$ , using  $I_E = (I_{E_s} \ I_{E_*})$  and  $\alpha = \begin{pmatrix} \alpha_{E_s} \\ \alpha_{E_*} \end{pmatrix}$ . Since  $YI_{E_s} \alpha_{E_s} \in L$ , also  $YI_{E_*} \alpha_{E_*} \in L$ . Explicitly,

$$\begin{aligned} YI_{E_*} \alpha_{E_*} &= \sum_{(i \rightarrow i_*) \in E_*} (y(i_*) - y(i)) \alpha_{i \rightarrow i_*} \\ &= \bar{\alpha} \left( y(i_*) - \underbrace{\sum_{(i \rightarrow i_*) \in E_*} \beta_{i \rightarrow i_*} y(i)}_y \right) \\ &= \bar{\alpha} (y(i_*) - y), \end{aligned}$$

where  $\bar{\alpha} = \sum_{(i \rightarrow i_*) \in E_*} \alpha_{i \rightarrow i_*}$ ,  $\beta_{i \rightarrow i_*} = \alpha_{i \rightarrow i_*} / \bar{\alpha}$ ,  $\sum_{(i \rightarrow i_*) \in E_*} \beta_{i \rightarrow i_*} = 1$ , and hence  $y \in y(i) + L$  for (every)  $i \in V_s$ . That is, both  $y(i_*) - y \in L$  and  $y - y(i) \in L$  and hence  $y(i_*) - y(i) \in L$  for (every)  $i \in V_s$ . That is,  $S = L$ .

2. Recall  $d = |V_s| - 1 - \dim L$  and  $\delta = |V| - 1 - \dim S$ . By statement 1,  $L = S$  and hence  $d - \delta = |V_s| - |V|$ . Since  $t = 1$ ,  $|V| - |V_s| = 1 - t'$  and hence  $d = \delta + t' - 1$ .  $\square$

## The “second salt theorem”

We continue our study of one independent subnetwork (with  $\delta \leq 1$ ,  $t = 1$ , and  $\ker(YR_k) \cap \mathbb{R}_{>}^{V_s} \neq \emptyset$ ). By Lemma 12 and Lemma 18,  $d = \dim P \leq 1$ . We consider the nontrivial case  $d = \dim P = 1$  which has  $\delta = t' = 1$ , again by Lemma 18.

Let  $y^1, y^2 \in \ker(YR_k) \cap \mathbb{R}_{\geq}^{V_s}$  be the vertices of  $P$ . Since  $t' = 1$ , there is a nonnegative  $\hat{y} \in \bar{P}$  with  $R_k \hat{y} = 0$  and support on the (non-singleton) terminal strong component. (It lies in the interior of the coefficient polytope, if the network is weakly reversible, and on the boundary, otherwise.) Since  $\delta = 1$ , there is a positive  $\bar{y} \in P$  with  $R_k \bar{y} = \beta \in \mathbb{R}^V$  and  $\text{im } \beta = \ker Y \cap \text{im } R_k$ . (It lies in the interior, possibly after adding  $\hat{y}$ .) That is,

$$\begin{aligned} R_k \hat{y} &= 0, \\ R_k \bar{y} &= \beta. \end{aligned} \tag{7}$$

Without loss of generality, we assume that the vertices  $y^1, y^2$  of the coefficient polytope (a line segment) and the vectors  $\hat{y}, \bar{y}$  are ordered as  $y^1 \cdots \hat{y} \cdots \bar{y} \cdots y^2$ , where  $\hat{y} = y^1$  if the network is not weakly reversible. Now,  $\hat{y} = \hat{\lambda} y^1 + (1 - \hat{\lambda}) y^2$  for some  $\hat{\lambda} \in (0, 1]$  and  $\bar{y} = \bar{\lambda} y^1 + (1 - \bar{\lambda}) y^2$  for some  $\bar{\lambda} \in (0, 1)$ , where  $\hat{\lambda} > \bar{\lambda}$ . Let

$$\hat{q} = \hat{y} \circ (\bar{y})^{-1} = \left( \hat{\lambda} y^1 + (1 - \hat{\lambda}) y^2 \right) \circ \left( \bar{\lambda} y^1 + (1 - \bar{\lambda}) y^2 \right)^{-1}.$$

It is easy to see<sup>1</sup> that the order of the entries of  $\hat{q}$  agrees with the order of the entries of

$$q = (y^1 - y^2) \circ (y^1 + y^2)^{-1}$$

specified in Definition 3.

Finally, we introduce the scaled rectangular graph Laplacian

$$R_k \text{diag}(\bar{y}) = R_{\tilde{k}} \quad \text{with} \quad \tilde{k} = k \circ \bar{y},$$

and we rewrite Equations (7) as

$$\begin{aligned} R_{\tilde{k}} \hat{q} &= 0, \\ R_{\tilde{k}} 1_{V_s} &= \beta. \end{aligned} \tag{8}$$

Now, we state Feinberg's "second salt theorem" [18] for the rectangular (rather than the square) graph Laplacian. This is the only argument that we use from Feinberg's proof [16] (aside from "Birch's theorem" which is also used to prove the deficiency zero theorem).

**Lemma 19.** *Let  $G_k = (V, E, k)$  be a labeled simple digraph with one component. Let  $T = \{1, \dots, t\} \subseteq V = \{1, \dots, m\}$  be (the vertices of) a terminal strong component, let  $\hat{q} \in \mathbb{R}_{\geq}^{V_s}$  be the corresponding vector in the kernel of the rectangular graph Laplacian, that is,  $R_k \hat{q} = 0$  and  $\text{supp } \hat{q} = T$ , and assume  $\hat{q}_1 \geq \dots \geq \hat{q}_t > \hat{q}_{t+1} = \dots = \hat{q}_m = 0$ . Further, let  $\beta = R_k 1_{V_s} \in \mathbb{R}^V$ . Then,*

$$\sum_{i'=1}^i \beta_{i'} \geq 0, \quad \text{for } i \in T.$$

If  $i < t$  and  $\hat{q}_i > \hat{q}_{i+1}$ , then  $\sum_{i'=1}^i \beta_{i'} > 0$ . Finally,  $\sum_{i'=1}^t \beta_{i'} = 0$  if and only if  $T = V$ .

*Proof.* See Appendix B.3. □

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<sup>1</sup>For two vectors  $y^1, y^2 \in \mathbb{R}_{>}^m$  with  $y^1 + y^2, \bar{\lambda}y^1 + (1 - \bar{\lambda})y^2 \in \mathbb{R}_{>}^m$ , consider the maximal minors of the matrices  $(y^1 \ y^2)$ ,  $(y^1 - y^2 \ y^1 + y^2)$ ,  $(\hat{y} \ \bar{y}) \in \mathbb{R}^{m \times 2}$ . Explicitly, let

$$\begin{aligned} (y^1 \ y^2) &= \begin{pmatrix} a_1 & a_2 \\ b_1 & b_2 \\ \vdots & \vdots \end{pmatrix}, & (y^1 - y^2 \ y^1 + y^2) &= \begin{pmatrix} a_1 - a_2 & a_1 + a_2 \\ b_1 - b_2 & b_1 + b_2 \\ \vdots & \vdots \end{pmatrix}, \\ (\hat{y} \ \bar{y}) &= \begin{pmatrix} \hat{\lambda}a_1 + (1 - \hat{\lambda})a_2 & \bar{\lambda}a_1 + (1 - \bar{\lambda})a_2 \\ \hat{\lambda}b_1 + (1 - \hat{\lambda})b_2 & \bar{\lambda}b_1 + (1 - \bar{\lambda})b_2 \\ \vdots & \vdots \end{pmatrix}. \end{aligned}$$

If  $\hat{\lambda} > \bar{\lambda}$ , then

$$\text{sign} \left( \frac{\hat{\lambda}a_1 + (1 - \hat{\lambda})a_2}{\bar{\lambda}a_1 + (1 - \bar{\lambda})a_2} - \frac{\hat{\lambda}b_1 + (1 - \hat{\lambda})b_2}{\bar{\lambda}b_1 + (1 - \bar{\lambda})b_2} \right) = \text{sign} \left( \frac{a_1 - a_2}{a_1 + a_2} - \frac{b_1 - b_2}{b_1 + b_2} \right) = \text{sign} \begin{vmatrix} a_1 & a_2 \\ b_1 & b_2 \end{vmatrix}.$$

## Proof of the deficiency one theorem

*Proof of Theorem 15.* In order to apply Theorem 14, we show that conditions (I), (IIb), (III) there follow from conditions (i), (ii), (iii) here.

(I) Condition (iii), the existence of a positive equilibrium, that is, of  $x \in \mathbb{R}_{>}^n$  with  $\Gamma_k x^{Y_s^*} = 0$ , implies  $\ker \Gamma_k \cap \mathbb{R}_{>}^{V_s^{\sqcup}} \neq \emptyset$ .

This further implies  $\ker \Gamma_k^j \cap \mathbb{R}_{>}^{V_s^j} \neq \emptyset$  for the independent sub(mass-action) systems  $(G_k^j, y^k)$ ,  $j = 1, \dots, \ell$ , which have  $t_j = 1$  by condition (ii). Hence, Lemma 18 is applicable to the subsystems.

(IIb) By Lemma 18,  $L_j = S_j$ , for  $j = 1, \dots, \ell$ . Hence,  $L = L_1 + \dots + L_\ell = S = S_1 + \dots + S_\ell$ .

(III) By Lemma 18 and condition (i),  $d_j = \delta_j + t'_j - 1 \leq \delta_j \leq 1$  and  $L_j = K_j$ , for  $j = 1, \dots, \ell$ .

It remains to consider  $d_j = 1$  which implies  $\delta_j = 1$  and  $t'_j = 1$ , in particular, all vertices are source vertices, that is,  $V_s^j = V^j$ .

On the one hand, by the argument before the “second salt theorem” (Lemma 19), there are  $\beta \in \mathbb{R}^{V^j}$  with  $\text{im } \beta = \ker Y^j \cap \text{im } R_k^j$  and  $\hat{q} \in \mathbb{R}_{\geq}^{V_s^j}$  with  $R_k^j \hat{q} = 0$  and  $R_k^j \mathbf{1} = \beta$  (and  $\tilde{k} \in \mathbb{R}_{>}^{V_s^j}$ ), cf. Equation (8). In particular,  $\text{supp } \hat{q} = T$ , where  $T \subseteq V^j$  denotes (the vertices of) the terminal strong component. Let  $t = |T|$  and  $m = |V^j|$  and assume  $\hat{q}_1 \geq \dots \geq \hat{q}_t > \hat{q}_{t+1} = \dots = \hat{q}_m = 0$ . By Lemma 19,  $\sum_{i'=1}^i \beta_{i'} \geq 0$ , for  $i = 1, \dots, t$ . Further, if  $i < t$  and  $\hat{q}_i > \hat{q}_{i+1}$ , then  $\sum_{i'=1}^i \beta_{i'} > 0$ . Finally,  $\sum_{i'=1}^t \beta_{i'} = 0$  if and only if  $T = V$ .

On the other hand, writing the polynomial system  $\Gamma_k^j x^{Y_s^j} = 0$  as  $A(c \circ x^B) = 0$  with  $B = Y_s^j = Y^j$ , the dependency vector  $b \in \mathbb{R}^{V^j}$  in Theorem 14 is given by  $\text{im } b = D_k = \ker \begin{pmatrix} B \\ \mathbf{1}^\top \end{pmatrix} = \ker \begin{pmatrix} Y^j \\ \mathbf{1}^\top \end{pmatrix}$ . Since  $\text{im } R_k^j = \text{im } I_E^j = \ker \mathbf{1}^\top$ , equivalently  $\text{im } b = \ker Y^j \cap \text{im } R_k^j$ . That is, we can choose  $b = \beta$  and the (in)equalities for  $\beta$  guaranteed by Lemma 19 also hold for  $b$ .

Now, recall that  $I_1, \dots, I_\omega \subset V^j$  denote  $\omega$  equivalence classes corresponding to equal (consecutive) components of  $\hat{q}$  and that  $\tilde{b} \in \mathbb{R}^\omega$  with  $\tilde{b}_i = \sum_{i' \in I_i} b_{i'}$  is the vector of lumped  $b$ 's. Since  $\sum_{i'=1}^i b_{i'} \geq 0$  for  $i = 1, \dots, t$ , also  $\sum_{i'=1}^i \tilde{b}_{i'} \geq 0$  for  $i = 1, 2, \dots, \omega - 1$ . Further, since  $\hat{q}_i > \hat{q}_{i'}$  for  $i \in I_1$  and  $i' \in I_2$ , we get  $\tilde{b}_1 > 0$ . Finally, since  $\sum_{i=1}^\omega \tilde{b}_i = 0$ , we get  $\tilde{b}_\omega < 0$  and hence  $\tilde{b}_1 \cdot \tilde{b}_\omega < 0$ .

By Theorem 14, there exists a unique positive equilibrium within every stoichiometric compatibility class.

By Lemma 10,  $\ker I_E = \ker I_E^*$ , and hence the cycles of the graph  $G$  agree with the cycles of the subgraphs  $G^j$ ,  $j = 1, \dots, \ell$ . Hence, if  $G$  is weakly reversible, then every  $G^j$  is weakly reversible and hence  $\ker R_k^j \cap \mathbb{R}_{>}^{V_s^j} \neq \emptyset$ . Since  $\Gamma_k^j = Y^j R_k^j$ , also  $\ker \Gamma_k^j \cap \mathbb{R}_{>}^{V_s^j} \neq \emptyset$ , and since  $\Gamma_k = (\Gamma_k^1 \ \dots \ \Gamma_k^\ell)$ , also  $\ker \Gamma_k \cap \mathbb{R}_{>}^{V_s^{\sqcup}} \neq \emptyset$ . That is, condition (I) in

Theorem 14 follows from weak reversibility. (And conditions (IIb) and (III) follow from (i) and (ii), as above.)  $\square$

## 8 Examples

**Example 1: Deficiency two network with one (singleton) terminal strong component**

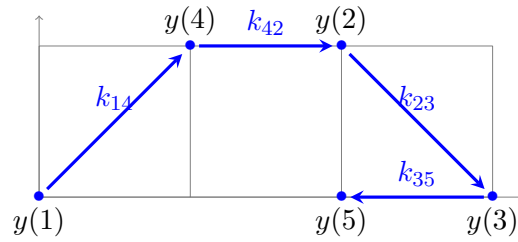


Figure 1: Mass-action system  $(G_k, y)$  with 5 vertices and 4 source vertices and hence  $\delta = 5 - 1 - 2 = 2$ , but  $d = 4 - 1 - 2 = 1$ .

The ODE associated with the mass-action system is given by

$$\begin{aligned}\frac{dx_1}{dt} &= k_{14} + k_{23} x_1^2 x_2 - k_{35} x_1^3 + k_{42} x_1 x_2, \\ \frac{dx_2}{dt} &= k_{14} - k_{23} x_1^2 x_2,\end{aligned}$$

and steady state can be written as  $\Gamma_k x^B = 0$  with  $\Gamma_k = \begin{pmatrix} k_{14} & k_{23} & -k_{35} & k_{42} \\ k_{14} & -k_{23} & 0 & 0 \end{pmatrix}$  and  $B = \begin{pmatrix} 0 & 2 & 3 & 1 \\ 0 & 1 & 0 & 1 \end{pmatrix}$ . We show that conditions (I), (IIb), and (III) of Theorem 14 are satisfied.

(I)  $\ker(\Gamma_k) \cap \mathbb{R}_{>0}^4$  is generated by  $y^1 = (\frac{1}{k_{14}}, \frac{1}{k_{23}}, \frac{2}{k_{35}}, 0)^\top$  and  $y^2 = (0, 0, \frac{1}{k_{35}}, \frac{1}{k_{42}})^\top$  and hence  $\ker(\Gamma_k) \cap \mathbb{R}_{>0}^4 \neq \emptyset$ . As a consequence,  $q = (1, 1, q_3, -1)^\top$  with  $q_3 \in (-1, 1)$ . (The vertices of the graph  $G$  have been labeled such that the components of  $q$  are ordered.)

(IIb) Since  $L = \mathbb{R}^2$  holds for the monomial difference subspace (and  $L \subseteq S$ ), we get  $L = S$ .

(III) Clearly,  $d = 4 - 1 - 2 = 1$ . Further, since  $\dim(K) = \dim(\text{im } \Gamma_k) = 2$ , we get  $K = L$ . Finally, the (lumped) dependency vectors are given by  $b = (1, 3, -1, -3)^\top$  and  $\tilde{b} = (4, -1, -3)^\top$  and hence  $\sum_{i'=1}^i \tilde{b}_{i'} \geq 0$  for  $i = 1, 2$  as well as  $\tilde{b}_1 \cdot \tilde{b}_3 = 4 \cdot (-3) < 0$ .

Using Theorem 14, we find that there exists a unique positive equilibrium in every stoichiometric compatibility class, for all rate constants.

**Example 2: Deficiency two network with one singleton and one non-singleton terminal strong components**

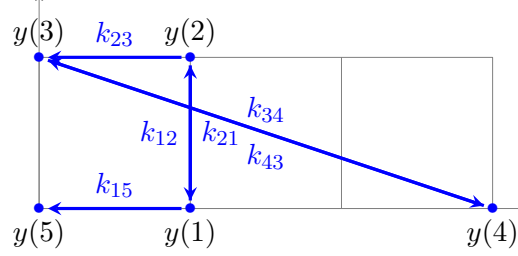


Figure 2: Mass-action system  $(G_k, y)$  with 5 vertices and 4 source vertices and hence  $\delta = 5 - 1 - 2 = 2$ , but  $d = 4 - 1 - 2 = 1$ .

The ODE associated with the mass-action system is given by

$$\begin{aligned}\frac{dx_1}{dt} &= -k_{15} x_1 - k_{23} x_1 x_2 + 3k_{34} x_2 - 3k_{43} x_1^3, \\ \frac{dx_2}{dt} &= +k_{12} x_1 - k_{21} x_1 x_2 - k_{34} x_2 + k_{43} x_1^3,\end{aligned}$$

and steady state can be written as  $\Gamma_k x^B = 0$  with  $\Gamma_k = \begin{pmatrix} -k_{15} & -k_{23} & 3k_{34} & -3k_{43} \\ k_{12} & -k_{21} & -k_{34} & k_{43} \end{pmatrix}$

and  $B = \begin{pmatrix} 1 & 1 & 0 & 3 \\ 0 & 1 & 1 & 0 \end{pmatrix}$ . We show that conditions (I), (IIb), and (III) of Theorem 14 are satisfied.

(I)  $\ker(\Gamma_k)$  is generated by  $y^1 = (3k_{21} + k_{23}, 3k_{12} - k_{15}, \frac{k_{12}k_{23} + k_{15}k_{21}}{k_{34}}, 0)^\top$  and  $y^2 = (0, 0, \frac{1}{k_{34}}, \frac{1}{k_{43}})^\top$  and hence  $\ker(\Gamma_k) \cap \mathbb{R}_{>0}^4 \neq \emptyset$  iff  $3k_{12} - k_{15} > 0$ . In this case,  $q = (1, 1, q_3, -1)^\top$  with  $q_3 \in (-1, 1)$ . (The vertices of the graph  $G$  have been labeled such that the components of  $q$  are ordered.)

(IIb) Since  $L = \mathbb{R}^2$  holds for the monomial difference subspace (and  $L \subseteq S$ ), we get  $L = S$ .

(III) Clearly,  $d = 4 - 1 - 2 = 1$ . Further, since  $\dim(K) = \dim(\text{im } \Gamma_k) = 2$ , we get  $K = L$ . Finally, the (lumped) dependency vectors are given by  $b = (1, 2, -2, -1)^\top$  and  $\tilde{b} = (3, -2, -1)^\top$  and hence  $\sum_{i'=1}^i \tilde{b}_{i'} \geq 0$  for  $i = 1, 2$  as well as  $\tilde{b}_1 \cdot \tilde{b}_3 = 3 \cdot (-1) < 0$ .

Using Theorem 14, we find that there exists a unique positive equilibrium in every stoichiometric compatibility class iff  $3k_{12} - k_{15} > 0$ .

**Example 3: Deficiency two network with two singleton terminal strong components**

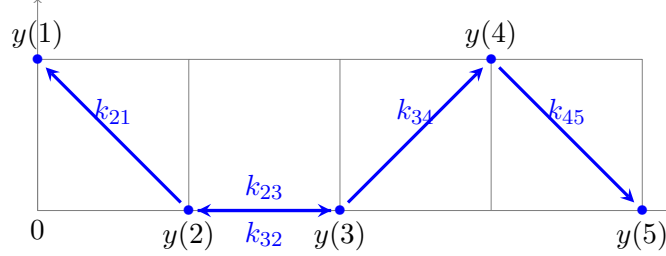


Figure 3: Mass-action system  $(G_k, y)$  with 5 vertices and 3 source vertices and hence  $\delta = 5 - 1 - 2 = 2$ , but  $d = 3 - 1 - 2 = 0$ .

The ODE associated with the mass-action system is given by

$$\begin{aligned}\frac{dx_1}{dt} &= (-k_{21} + k_{23})x_2 + (-k_{32} + k_{34})x_1^2 + k_{45}x_1^3x_2, \\ \frac{dx_2}{dt} &= k_{21}x_2 + k_{34}x_1^2 - k_{45}x_1^3x_2,\end{aligned}$$

and steady state can be written as  $\Gamma_k x^B = 0$  with  $\Gamma_k = \begin{pmatrix} -k_{21} + k_{23} & -k_{32} + k_{34} & k_{45} \\ k_{21} & k_{34} & -k_{45} \end{pmatrix}$

and  $B = \begin{pmatrix} 1 & 2 & 3 \\ 0 & 0 & 1 \end{pmatrix}$ . We show that conditions (I), (IIb), and (III) of Theorem 14 are satisfied.

(I)  $\ker(\Gamma_k)$  is generated by the vector  $\left(\frac{k_{32}-2k_{34}}{k_{21}k_{32}-2k_{21}k_{34}+k_{23}k_{34}}, \frac{k_{23}}{k_{21}k_{32}-2k_{21}k_{34}+k_{23}k_{34}}, \frac{1}{k_{45}}\right)^\top$  and hence  $\ker(\Gamma_k) \cap \mathbb{R}_{>0}^4 \neq \emptyset$  iff  $k_{32} - 2k_{34} > 0$ .

(IIb) Since  $L = \mathbb{R}^2$  holds for the monomial difference subspace (and  $L \subseteq S$ ), we get  $L = S$ .

(III) Clearly,  $d = 4 - 1 - 2 = 1$ . Further, since  $\dim(K) = \dim(\text{im } \Gamma_k) = 2$ , we get  $K = L$ .

Using Theorem 14, we find that there exists a unique positive equilibrium in every stoichiometric compatibility class iff  $k_{32} - 2k_{34} > 0$ .

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## Appendix

### A Proof of Theorem 5

*Proof.* In the proof of (iii)  $\implies$  (ii) in Theorem 4, we have shown that  $\tilde{b}_1 \cdot \tilde{b}_\omega < 0$  implies  $|Y_c| \geq 1$  for all  $c$ .

We now show the other direction, i.e.,  $|Y_c| \geq 1$  for all  $c$  implies  $\tilde{b}_1 \cdot \tilde{b}_\omega < 0$ . Let us assume for contradiction that  $\tilde{b}_1 \cdot \tilde{b}_\omega \geq 0$ .

Recall from the proof of (iii)  $\implies$  (ii) in Theorem 4 that the solutions of this system is equivalent to solving  $f(t) = c^*$ , where

$$f(t) = \prod_{i=1}^k (1 + t\tilde{q}_i)^{\tilde{b}_i}.$$

Note that  $\tilde{q}_1 = 1$  and  $\tilde{q}_\omega = -1$ . Consider the following cases:

- (i)  $\tilde{b}_1 = 0$  and  $\tilde{b}_\omega > 0$ : Here  $\lim_{t \rightarrow -1} f(t) = \zeta$ , where  $\zeta > 0$  and  $\lim_{t \rightarrow 1} f(t) = 0$ . This implies that there exists a  $\delta > 0$  such that  $f(t) < \delta$ . This means that if we choose a  $c^*$  (or equivalently a  $c$ ) such that if  $\delta < c^*$ , then  $f(t) = c^*$  has no solution.
- (ii)  $\tilde{b}_1 = 0$  and  $\tilde{b}_\omega < 0$ : Here  $\lim_{t \rightarrow -1} f(t) = \zeta$ , where  $\zeta > 0$  and  $\lim_{t \rightarrow 1} f(t) = \infty$ . Further, note that  $f(t) > 0$  for  $t \in [-1, 1]$ . This implies that there exists a  $\delta > 0$  such that  $f(t) > \delta$ . This means that if we choose a  $c^*$  (or equivalently a  $c$ ) such that if  $\delta > c^*$ , then  $f(t) = c^*$  has no solution.
- (iii)  $\tilde{b}_1 = 0$  and  $\tilde{b}_\omega = 0$ : Here  $\lim_{t \rightarrow -1} f(t) = \zeta_1$ , where  $\zeta_1 > 0$  and  $\lim_{t \rightarrow 1} f(t) = \zeta_2$ , where  $\zeta_2 > 0$ . Further, note that  $f(t) > 0$  for  $t \in [-1, 1]$ . This implies that there exists a  $\delta > 0$  such that  $f(t) < \delta$ . This means that if we choose a  $c^*$  (or equivalently a  $c$ ) such that if  $\delta < c^*$ , then  $f(t) = c^*$  has no solution.

- (iv)  $\tilde{b}_1 > 0$  and  $\tilde{b}_\omega = 0$ : Here  $\lim_{t \rightarrow 1} f(t) = \zeta$ , where  $\zeta > 0$  and  $\lim_{t \rightarrow -1} f(t) = 0$ . This implies that there exists a  $\delta > 0$  such that  $f(t) < \delta$ . This means that if we choose a  $c^*$  (or equivalently a  $c$ ) such that if  $\delta < c^*$ , then  $f(t) = c^*$  has no solution.
- (v)  $\tilde{b}_1 < 0$  and  $\tilde{b}_\omega = 0$ : Here  $\lim_{t \rightarrow 1} f(t) = \zeta$ , where  $\zeta > 0$  and  $\lim_{t \rightarrow -1} f(t) = \infty$ . This implies that there exists a  $\delta > 0$  such that  $f(t) > \delta$ . This means that if we choose a  $c^*$  (or equivalently a  $c$ ) such that if  $\delta > c^*$ , then  $f(t) = c^*$  has no solution.
- (vi)  $\tilde{b}_1 < 0$  and  $\tilde{b}_\omega > 0$ . Note that  $\lim_{t \rightarrow -1} f(t) = 0$  and  $\lim_{t \rightarrow 1} f(t) = 0$ . This means that there exists a  $\delta > 0$  such that  $f(t) < \delta$ . This means that if we choose a  $c^*$  (or equivalently a  $c$ ) such that  $\delta < c^*$ , then  $f(t) = c^*$  has no solution.
- (vii)  $\tilde{b}_1 < 0$  and  $\tilde{b}_\omega < 0$ . Note that  $\lim_{t \rightarrow -1} f(t) = 0$  and  $\lim_{t \rightarrow 1} f(t) = 0$ . This means that there exists a  $\delta > 0$  such that  $f(t) > \delta$ . This means that if we choose a  $c^*$  (or equivalently a  $c$ ) such that  $\delta > c^*$ , then  $f(t) = c^*$  has no solution.

□

## B Reaction networks

### B.1 Index notation

We explicitly state the incidence and source matrices as well as the Laplacian matrix in index notation.

- (i) The incidence matrix  $I_E \in \mathbb{R}_{>}^{V \times E}$  is given by

$$(I_E)_{i,j \rightarrow j'} = \begin{cases} -1, & \text{if } i = j, \\ 1, & \text{if } i = j', \\ 0, & \text{otherwise.} \end{cases}$$

- (ii) The source matrix  $I_{E,s} \in \mathbb{R}_{>}^{V_s \times E}$  is given by

$$(I_{E,s})_{i,j \rightarrow j'} = \begin{cases} 1, & \text{if } i = j, \\ 0, & \text{otherwise.} \end{cases}$$

- (iii) The rectangular Laplacian matrix  $R_k \in \mathbb{R}^{V \times V_s}$  is given by

$$(R_k)_{i,j} = \begin{cases} k_{j \rightarrow i}, & \text{if } (j \rightarrow i) \in E, \\ -\sum_{(i \rightarrow i') \in E} k_{i \rightarrow i'}, & \text{if } i = j, \\ 0, & \text{otherwise.} \end{cases}$$

It can be decomposed as  $R_k = I_E \text{diag}(k)(I_{E,s})^\top$ .

## B.2 Auxiliary graph

We recall the definition of an auxiliary graph from [22].

**Definition 20.** Let  $G = (V, E)$  be a reaction network. We define the auxiliary graph as follows:  $G_{\mathcal{E}} = (V, \mathcal{E})$  with the same set of vertices but edges  $\mathcal{E}$  such that  $\mathcal{E} \subseteq V \times V$  with  $|\mathcal{E}| = |V| - 1$ . The incidence matrix corresponding to  $G_{\mathcal{E}}$  is given as follows:

$$I_{\mathcal{E}}(i, j \rightarrow j') = \begin{cases} -1, & \text{if } i = j, \\ 1, & \text{if } i = j', \\ 0, & \text{otherwise,} \end{cases}$$

## B.3 Proof of the “second salt theorem”

We prove the second salt theorem for rectangular (rather than square) Laplacian matrices.

*Proof of Lemma 19.* Let  $T' = \{1, \dots, t'\} \subseteq T$ . The equations  $R_k \hat{q} = 0$  and  $R_k \mathbf{1}_{V_s} = \beta$  imply

$$\begin{aligned} \sum_{\substack{(i \rightarrow i') \in \\ V \setminus T' \rightarrow T'}} k_{i \rightarrow i'} \hat{q}_i - \sum_{\substack{(i' \rightarrow i) \in \\ T' \rightarrow V \setminus T'}} k_{i' \rightarrow i} \hat{q}_{i'} &= 0, \\ \sum_{\substack{(i \rightarrow i') \in \\ V \setminus T' \rightarrow T'}} k_{i \rightarrow i'} - \sum_{\substack{(i' \rightarrow i) \in \\ T' \rightarrow V \setminus T'}} k_{i' \rightarrow i} &= \sum_{i \in T'} \beta_i. \end{aligned}$$

If  $T' \subset T$ , then the first equation and the order on  $\hat{q}$  imply

$$\hat{q}_{t'+1} \sum_{\substack{(i \rightarrow i') \in \\ V \setminus T' \rightarrow T'}} k_{i \rightarrow i'} \geq \sum_{\substack{(i \rightarrow i') \in \\ V \setminus T' \rightarrow T'}} k_{i \rightarrow i'} \hat{q}_i = \sum_{\substack{(i' \rightarrow i) \in \\ T' \rightarrow V \setminus T'}} k_{i' \rightarrow i} \hat{q}_{i'} \geq \hat{q}_{t'} \sum_{\substack{(i' \rightarrow i) \in \\ T' \rightarrow V \setminus T'}} k_{i' \rightarrow i},$$

and the second equation and  $\hat{q}_{t'} \geq \hat{q}_{t'+1}$  further imply

$$\sum_{i \in T'} \beta_i = \sum_{\substack{(i \rightarrow i') \in \\ V \setminus T' \rightarrow T'}} k_{i \rightarrow i'} - \sum_{\substack{(i' \rightarrow i) \in \\ T' \rightarrow V \setminus T'}} k_{i' \rightarrow i} \geq \left( \frac{q_{t'}}{q_{t'+1}} - 1 \right) \sum_{\substack{(i' \rightarrow i) \in \\ T' \rightarrow V \setminus T'}} k_{i' \rightarrow i} \geq 0.$$

In particular,  $\sum_{i \in T'} \beta_i > 0$  if  $\hat{q}_{t'} > \hat{q}_{t'+1}$ .

If  $T' = T$ , then  $(T \rightarrow V \setminus T) = \emptyset$ , since  $T$  is a terminal strong component, and

$$\sum_{i \in T} \beta_i = \sum_{\substack{(i \rightarrow i') \in \\ V \setminus T \rightarrow T}} k_{i \rightarrow i'} \geq 0.$$

The sum is zero if and only if  $(V \setminus T \rightarrow T) = \emptyset$ , that is,  $T = V$ .  $\square$