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The structure of the toric locus of a reaction network

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Abstract

We consider *toric dynamical systems*, which are also called *complex-balanced mass-action systems*. These are remarkably stable polynomial dynamical systems that arise from the analysis of mathematical models of reaction networks when, under the assumption of mass-action kinetics, they can give rise to *complex-balanced equilibria*. Given a reaction network, we study the *set of parameter values* for which the network gives rise to toric dynamical systems, also called *the toric locus* of the network. The toric locus is an algebraic variety, and we are especially interested in its topological properties. We show that complex-balanced equilibria *depend continuously* on the parameter values in the toric locus, and, using this result, we prove that the toric locus has a remarkable *product structure*: it is homeomorphic to the product of the set of complex-balanced flux vectors and the affine invariant polyhedron of the network. In particular, it follows that the toric locus is a *contractible manifold*. Finally, we show that the toric locus is invariant with respect to bijective affine transformations of the generating reaction network.

Keywords: toric dynamical systems, complex-balanced mass-action systems, reaction networks, equilibria, toric locus

Mathematics Subject Classification:
80A30, 92C42, 37N25, 92C45, 14P25, 14M25

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1. Introduction

Nonlinear dynamical systems are among the most common mathematical models used in the study of population dynamics, epidemiology, biochemistry, just to name a few [43]. However, the analysis of long-term dynamical behavior of nonlinear dynamical systems is a very difficult problem. Finding explicit, quantitative answers to the question of how a system evolves in continuous time is usually impossible. Inspired by the work of Poincaré [37], mathematicians started tackling the qualitative aspects of these systems. However, this task is also a difficult one. For instance, consider the second part of Hilbert's 16th problem, concerning polynomial dynamical systems in the real plane. After more than a century, the problem of finding an upper bound for the number of limit cycles remains open even in the quadratic case; for technical details and historical aspects of Hilbert's 16th problem, we refer the reader to [28], [33, chapter 11]. Another example meant to show that nonlinear dynamical systems are challenging is the Lorenz system: a quadratic polynomial dynamical system, in the three-dimensional Euclidean space, which exhibits chaotic dynamics [32].

1.1. Context

We focus on polynomial dynamical systems generated by *reaction networks*, which are represented by directed graphs in Euclidean space. One of the goals of reaction network theory is to determine information about the qualitative long-term dynamics from the algebro-combinatorial structure of the network. In order to model the evolution in time of the concentrations of interacting species, we use autonomous systems of ordinary differential equations, dictated by the network structure. Under the assumption of mass-action kinetics [19, section 2.1.2], this leads to fruitful interactions between the study of reaction networks and applied algebraic geometry (see [17]), because these systems have polynomial right-hand side. The law of mass-action is very commonly used in mathematical modeling, for instance in population dynamics, ecology, biochemistry, and chemical engineering [5, 19, 43].

In particular, we are interested in *complex-balanced* mass-action systems (see [19, chapter 15]). Introduced by Horn and Jackson in [27], these represent a large class of polynomial dynamical systems that are known to have a stable dynamical behavior that is very desirable in applications. For instance, Horn and Jackson proved that complex-balanced dynamical systems possess exactly one positive equilibrium up to conservation laws (i.e. one within each invariant polyhedron) and that this equilibrium is locally asymptotically stable (see [27], [43, theorem 2.3]). One of the most important lines of research in the field of reaction network theory is *the Global Attractor Conjecture*, which says that this equilibrium is actually *globally* asymptotically stable. This has been already proven in several cases, under various additional hypotheses. For a description of the state of the art, we refer the reader to [43]. A proof in full generality of the Global Attractor Conjecture has been proposed in [12].

Besides their stable dynamical behavior, another advantage of complex-balanced dynamical systems is the fact that tools from commutative algebra, computational, applied, real algebraic geometry turn out to be useful in deducing qualitative dynamical properties, which are often encoded or hidden in the geometric structure of the associated reaction networks. For instance, in [13] complex-balanced dynamical systems have also been called *toric dynamical systems* by Craciun, Dickenstein, Shiu and Sturmfels, to emphasize their strong combinatorial aspects and the remarkable algebraic properties of their toric locus. To be more precise, consider the full parameter space of a reaction network. The subset of parameters that gives rise to complex-balanced dynamical systems is called the *toric locus*; in particular, up to a change of coordinates, this set is a variety given by a binomial ideal, intersected with the positive orthant (see [13]). Toric varieties appear in numerous applications [35] and are very well studied and understood by algebraic geometers, who use them often in their quest for examples and counterexamples, due to their combinatorial representation and their computational assets. For a presentation of toric varieties from the point of view of Nonlinear Algebra, the reader may refer to [35, chapter 8]; according to [35, p 126], 'the world is toric'.

Increasing interest in the toric locus of a network has been shown recently. For instance, methods to expand the toric locus from a set of Lebesgue measure zero to a positive measure set using the *disguised toric locus* are proposed in the form of a systematic algorithm in [36], where the authors leverage some properties of the notion of *dynamical equivalence* from [15]. See also [24], where the authors show that the disguised toric locus is invariant under invertible affine transformations of the network.

1.2. Main contributions

The results of this paper concern the topological structure of the toric locus. One of our main contributions is to show that the complex-balanced equilibria *depend continuously on the parameter values*, i.e. *reaction rate constants* (theorem 3.5). We then use this result to prove that the toric locus of any reaction network is *connected* (theorem 3.17). Next, in theorem 4.7 we show that the toric locus is *homeomorphic to the product* of the set of complex-balanced flux vectors (definition 4.2) and the affine invariant polyhedron (definition 2.8).

Being homeomorphic to the product of two path-connected spaces, it also follows that the toric locus is path-connected. Hence, given any two points in the toric locus of a toric dynamical system, there will exist a continuous path between them. This might be advantageous in computations, for instance when using numerical methods for constructing the set of equilibria along a path in parameter space. Recall that the main strategy used by homotopy continuation methods is tracking the solutions of systems of polynomial equations which are easier to solve than the given system, or which are already known (for instance BERTINI [4], Julia HomotopyContinuation [3, 8, 9, 18, 39, 42]). Such tracking can take advantage of the path connectivity of the toric locus.

Furthermore, we recover a result from [13, theorem 9], which says that the codimension of the toric locus in the parameter space is equal to the deficiency of the network (see definition 4.12). We also show that the toric locus is invariant under bijective affine transformations of a network (theorem 4.17). This result has recently been extended in [24], where the authors show that the *disguised* toric locus is also invariant under bijective affine transformations of a network.

1.3. Structure of the paper

In section 2, we introduce standard terminology and notations concerning dynamical systems generated by reaction networks, mostly focusing on mass-action complex-balanced dynamical systems, also called toric. In section 3, we prove that complex-balanced equilibria depend continuously on the parameter values in $\mathcal{K}(G)$. Leveraging this result, in section 3.1 we show that the toric locus is connected. In section 4, we first prove that the toric locus is homeomorphic to a product space. Using this property, in section 4.3 we show proposition 4.13 which gives a precise formula for the dimension of the toric locus of the network. In section 4.4, we prove theorem 4.17 showing that any bijective affine transformation of the network preserves the toric locus.

2. Preliminary notions

In this section, mostly following [43], we present standard terminology concerning a special class of nonlinear dynamical systems that are generated by (bio-chemical) reaction networks, under the assumption of mass-action kinetics. For an introduction to the general theory of nonlinear dynamical systems, the reader could refer for instance to the textbooks [30, 40].

First, we give some classical definitions and notations relevant to the study of mass-action dynamical systems and to (bio-chemical) reaction networks. Next, we present a special class of these systems: *complex-balanced* dynamical systems, which are also called *toric* dynamical systems. More details can be found in the textbooks [19] and [10], the latter one with a view toward Nonlinear Algebra. See also [11, 13, 15, 36].

Notation 2.1. (a) We let $\mathbb{R}^n_{\geqslant 0}$ and $\mathbb{R}^n_{>0}$ denote the sets of vectors with non-negative and positive entries respectively. Similarly, $\mathbb{Z}^n_{\geqslant 0}$ is the set of vectors with non-negative integer components. We denote the cardinality of a set A as $|A|$, and the disjoint union of sets A and B is denoted by $A \sqcup B$.

(b) Let us consider two vectors $\boldsymbol{x}, \boldsymbol{y} \in \mathbb{R}^n$ with $\boldsymbol{x} = (x_1, \ldots, x_n)^\intercal$ and $\boldsymbol{y} = (y_1, \ldots, y_n)^\intercal$. The following are the vector operations that will be used in this paper:

$$\boldsymbol{x} \circ \boldsymbol{y} := (x_1 y_1, \ldots, x_n y_n)^\intercal,$$

$$\exp(\boldsymbol{x}) := (\exp(x_1), \ldots, \exp(x_n))^\intercal.$$

For $\boldsymbol{x} \in \mathbb{R}^n_{>0}$ we also define

$$\ln(\boldsymbol{x}) := (\ln(x_1), \ldots, \ln(x_n))^\intercal,$$

$$\boldsymbol{x}^{\boldsymbol{y}} := x_1^{y_1} x_2^{y_2} \ldots x_n^{y_n}.$$

(c) We also apply vector operations on a subset of $\mathbb{R}^n$, where they are applied to all elements of the subset. For example, given a vector $\boldsymbol{x} \in \mathbb{R}^n$ and a set $A \subseteq \mathbb{R}^n$,

$$\boldsymbol{x} \circ A := \{\boldsymbol{x} \circ \boldsymbol{y} : \boldsymbol{y} \in A\}.$$

2.1. Dynamics of reaction networks with mass-action kinetics

We work with deterministic, autonomous, and continuous dynamical systems, generated by reaction networks. The goal is to model the variation in time of the concentrations of the species involved, under the assumption of mass-action kinetics. Mostly following the terminology and notations from [43], let us give precise definitions of these classical notions.

The classical definition of a reaction network involves *species, complexes, and reactions*, as illustrated in figure 1 (and explained in detail below). In a recent work [12], it was observed that the equivalent definition of reaction network as a *directed graph embedded in Euclidean space* leads to very convenient notations, see figure 2; this is why we employ this definition here.

Definition 2.2. (a) We denote by n the **number of species** involved in the reaction network, and denote by $X_1, \ldots, X_n$ the **species** of the network.

(b) Denote by x_i the **concentration** of the species X_i, for $i = 1, \ldots, n$. We consider x_i as functions of time t: $x_i = x_i(t)$. At any time $t \geqslant 0$, this gives us a vector $\boldsymbol{x} = (x_1, \ldots, x_n)^\intercal \in \mathbb{R}^n$, also called a **state** of the system.

(c) A formal linear combination of species $\{X_i\}_{i=1}^n$, with non-negative real coefficients is called a **complex**. A **reaction** is a directed edge between two distinct complexes.

Definition 2.3. A **reaction network**, also called a **Euclidean embedded graph** (or **E-graph**), is a directed graph $G = (V, E)$ such that the set $V \subset \mathbb{R}^n$ is a finite set of **vertices** and the set

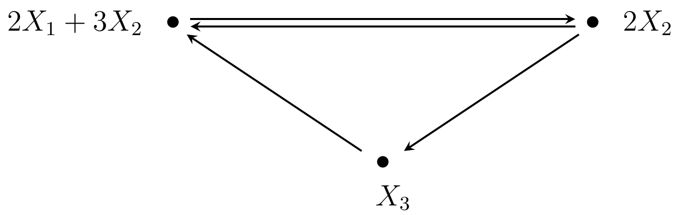


Figure 1. A reaction network with three species, three complexes, and four reactions.

$E \subseteq V \times V$ represents the finite set of **edges**. We assume that there are neither self-loops nor isolated vertices.

(a) We denote the **number of vertices** by m, and let $V = \{\boldsymbol{y}_1, \ldots, \boldsymbol{y}_m\}$, where each vertex $\boldsymbol{y}_i \in V$ corresponds to a complex. The entries of the vertex are the coefficients of the species in the corresponding formal linear combination.
(b) A directed edge connecting two vertices $\boldsymbol{y}_i \in V$ to $\boldsymbol{y}_j \in V$ is denoted by $\boldsymbol{y}_i \to \boldsymbol{y}_j \in E$ and represents a reaction in the network. We call the difference vector $\boldsymbol{y}_j - \boldsymbol{y}_i \in \mathbb{R}^n$, the **reaction vector**. Here $\boldsymbol{y}_i$ and $\boldsymbol{y}_j$ denote the **source vertex** and **target vertex** respectively.

As we mentioned above, reaction networks can either be represented as sets of reactions (see figure 1), or, equivalently, by using E-graphs, where the vertices correspond to the complexes (see figure 2). This is illustrated in the example below.

Example 2.4. Let us consider the reaction network from figure 1. There are three interacting species: X_1, X_2, X_3, and three complexes:

$$2X_1 + 3X_2,\ 2X_2,\ X_3,$$

and four reactions (directed edges between complexes):

$$2X_1 + 3X_2 \to 2X_2,\ 2X_2 \to 2X_1 + 3X_2,\ 2X_2 \to X_3,\ X_3 \to 2X_1 + 3X_2.$$

The real coefficients from each formal linear combination of species appearing in the complexes from the reaction network in figure 1 give rise to vectors in the three-dimensional Euclidean space:

$$\boldsymbol{y}_1 = \begin{pmatrix} 2 \\ 3 \\ 0 \end{pmatrix},\ \boldsymbol{y}_2 = \begin{pmatrix} 0 \\ 2 \\ 0 \end{pmatrix},\ \boldsymbol{y}_3 = \begin{pmatrix} 0 \\ 0 \\ 1 \end{pmatrix}.$$

This gives rise to an E-graph (see figure 2), whose edges represent vectors $\boldsymbol{y}_i - \boldsymbol{y}_j \in \mathbb{R}^3$.

Definition 2.5. Let $G = (V, E)$ be an E-graph.

(a) The set of vertices V is partitioned according to the connected components of G, and we identify each connected component by the subset of vertices that belong to that connected component. We denote the **number of connected components** by ℓ, and let $V = V_1 \sqcup V_2 \cdots \sqcup V_\ell$, where each V_i represents a connected component of G.
(b) A connected component is called **strongly connected** if every edge is part of an oriented cycle. Furthermore, a strongly connected component $L \subseteq V$ is **terminal strongly connected**, if for every vertex $\boldsymbol{y} \in L$ and $\boldsymbol{y} \to \boldsymbol{y}' \in E$, we have $\boldsymbol{y}' \in L$.

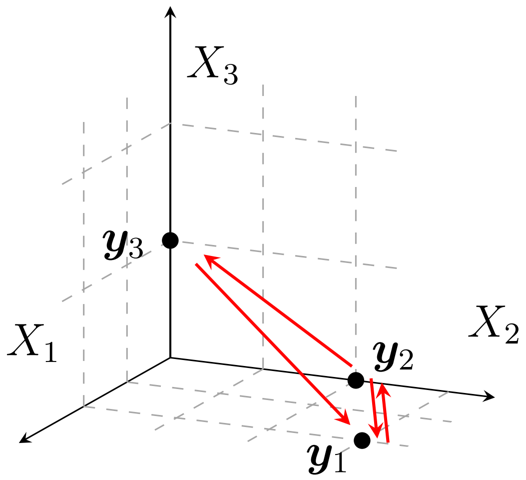


Figure 2. The E-graph of the network from figure 1.

(c) The graph $G = (V, E)$ is **weakly reversible**, if every connected component is strongly connected.

We work under the assumption of *mass-action kinetics*, which says that the rate with which a reaction takes place is directly proportional to the product of the concentrations of the reactant species (see [43] and references therein). Under this assumption, the dynamics can be modeled using the ODE system (1) below. Starting with the work of Gatermann (see [13, 21]), the polynomial structure of the right-hand side of (1) has given rise to fruitful interactions between the field of reaction networks and the methods of computational algebra.

Definition 2.6. Given an E-graph $G = (V, E)$, each edge $\boldsymbol{y}_i \to \boldsymbol{y}_j$ is decorated with a positive constant $k_{\boldsymbol{y}_i \to \boldsymbol{y}_j}$ or k_{ij}, called a **reaction rate constant**. Further, we denote by $\boldsymbol{k} := (k_{ij}) \in \mathbb{R}^E_{>0}$ the **vector of reaction rate constants**. The **associated mass-action system** generated by $(G, \boldsymbol{k})$ on $\mathbb{R}^n_{>0}$ is given by

$$\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i} \left(\boldsymbol{y}_j - \boldsymbol{y}_i\right). \tag{1}$$

For example, consider the E-graph from figure 2 (see example 2.4). Under mass-action kinetics, the associated dynamical system is

$$\begin{aligned}
\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} &= k_{12}x_1^2x_2^3\left(\boldsymbol{y}_2 - \boldsymbol{y}_1\right) + k_{21}x_2^2\left(\boldsymbol{y}_1 - \boldsymbol{y}_2\right) + k_{23}x_2^2\left(\boldsymbol{y}_3 - \boldsymbol{y}_2\right) + k_{31}x_3\left(\boldsymbol{y}_1 - \boldsymbol{y}_3\right) \\
&= k_{12}x_1^2x_2^3\begin{pmatrix}-2\\-1\\0\end{pmatrix} + k_{21}x_2^2\begin{pmatrix}2\\1\\0\end{pmatrix} + k_{23}x_2^2\begin{pmatrix}0\\-2\\1\end{pmatrix} + k_{31}x_3\begin{pmatrix}2\\3\\-1\end{pmatrix} \\
&= \begin{pmatrix}-2k_{12}x_1^2x_2^3 + 2k_{21}x_2^2 + 2k_{31}x_3\\ -k_{12}x_1^2x_2^3 + (k_{21} - 2k_{23})x_2^2 + 3k_{31}x_3\\ k_{23}x_2^2 - k_{31}x_3\end{pmatrix}.
\end{aligned} \tag{2}$$

Before the end of this subsection, we define *affine invariant polyhedra*; they will play an important role in the proof of our main results, starting with section 3.

Remark 2.7 ([43]). Note that we set the domain of (1) to be $\mathbb{R}^n_{>0}$. In general, systems of ODEs do not allow $\mathbb{R}^n_{>0}$ to be forward-invariant. But under the assumption that $V \subset \mathbb{Z}^n_{\geqslant 0}$, the positive orthant $\mathbb{R}^n_{>0}$ is forward-invariant under system (1). See also [24, remark 2.3, p 3]: we could also allow $V \subset \mathbb{R}^n_{\geqslant 0}$ or $V \subset \mathbb{R}^n$.

Definition 2.8. Let $G = (V, E)$ be an E-graph. We denote the **stoichiometric subspace** of G by $\mathcal{S}$, which is

$$\mathcal{S} = \text{span}\left\{\boldsymbol{y}_j - \boldsymbol{y}_i : \boldsymbol{y}_i \to \boldsymbol{y}_j \in E\right\}. \tag{3}$$

By remark 2.7 and the fact that the right-hand side of (1) is in $\mathcal{S}$, any solution to (1) with initial condition $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$ and $V \subset \mathbb{Z}^n_{\geqslant 0}$, is confined to $(\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$. The set $(\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$ is called the **affine invariant polyhedron** of $\boldsymbol{x}_0$. For the sake of simplicity, we use the following notation:

$$\mathcal{S}_{\boldsymbol{x}_0} := (\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}.$$

2.2. Complex-balanced dynamical systems and their properties

The importance of complex-balanced dynamical systems is mostly due to their strong stability properties. For more details, we advise the reader to consult [27], [43, theorem 2.3]. Using a strictly convex Lyapunov function, Horn and Jackson proved in [27] that if a mass-action system has a complex-balanced equilibrium, then all its positive equilibria are also complex-balanced, and that there is a unique and locally asymptotically stable equilibrium within each affine invariant polyhedron.

Definition 2.9. Consider the associated mass-action system generated by $(G, \boldsymbol{k})$:

$$\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i} \left(\boldsymbol{y}_j - \boldsymbol{y}_i\right).$$

A state $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$ is called a **positive equilibrium** of the system if

$$\sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} (\boldsymbol{x}^*)^{\boldsymbol{y}_i} \left(\boldsymbol{y}_j - \boldsymbol{y}_i\right) = \boldsymbol{0}. \tag{4}$$

A positive equilibrium $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$ is called a **complex-balanced equilibrium** if for each vertex $\boldsymbol{y}_0 \in V$,

$$\sum_{\boldsymbol{y}_0 \to \boldsymbol{y}' \in E} k_{\boldsymbol{y}_0 \to \boldsymbol{y}'} (\boldsymbol{x}^*)^{\boldsymbol{y}_0} = \sum_{\boldsymbol{y} \to \boldsymbol{y}_0 \in E} k_{\boldsymbol{y} \to \boldsymbol{y}_0} (\boldsymbol{x}^*)^{\boldsymbol{y}}. \tag{5}$$

We say the pair $(G, \boldsymbol{k})$ **satisfies the complex-balanced conditions** if it has a complex-balanced equilibrium; and in this case the mass-action system generated by $(G, \boldsymbol{k})$ is called **a complex-balanced system** or **toric dynamical system**.

The following classical theorem illustrates some of the most important dynamical properties of complex-balanced systems.

Theorem 2.10 ([43, theorem 2.3]). *Consider a complex-balanced system $(G, \boldsymbol{k})$ such that $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$ is a complex-balanced equilibrium of the system. Denote the associated stoichiometric subspace by $\mathcal{S}$. Then the following hold:*

(a) *All positive equilibria are complex-balanced. There is exactly one equilibrium within each affine invariant polyhedron $\mathcal{S}_{\boldsymbol{x}_0} := (\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$.*

(b) *Every complex-balanced equilibrium* $\boldsymbol{x}$ *satisfies the following relation:* $\ln \boldsymbol{x} - \ln \boldsymbol{x}^* \in \mathcal{S}^{\perp}$.
(c) *Every complex-balanced equilibrium is locally asymptotically stable within its affine invariant polyhedron.*

Additionally, the mass-action system (1) admits a matrix decomposition, which helps us in studying complex-balanced equilibria. Recall that the number of species is denoted by n, and the number of vertices is denoted by m. Following [13], we set the $n \times m$ matrix Y, whose columns correspond to vertices:

$$Y := (\boldsymbol{y}_1, \boldsymbol{y}_2, \ldots, \boldsymbol{y}_m) = (y_{ji}) \in \mathbb{R}^{n \times m},$$

Next, we build the following vector of monomials:

$$\Psi(\boldsymbol{x}) := \begin{pmatrix} \boldsymbol{x}^{\boldsymbol{y}_1} \\ \vdots \\ \boldsymbol{x}^{\boldsymbol{y}_m} \end{pmatrix} \in \mathbb{R}^m.$$

Since each directed edge $\boldsymbol{y}_i \to \boldsymbol{y}_j \in E$ has a reaction rate constant $k_{ij} \in \mathbb{R}_{>0}$, we construct the $m \times m$ **Kirchoff matrix** $A_{\boldsymbol{k}}$, which is the transpose of the negative of the graph Laplacian of $(V, E, \boldsymbol{k})$:

$$[A_{\boldsymbol{k}}]_{ji} := \begin{cases} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j}, & \text{if } \ i \neq j \text{ and } \boldsymbol{y}_i \to \boldsymbol{y}_j \in E \\ -\sum\limits_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j}, & \text{if } \ i = j, \\ 0, & \text{otherwise.} \end{cases} \tag{6}$$

Then the mass-action dynamical system (1) generated by $(G, \boldsymbol{k})$ can be written in the following vectorial representation:

$$\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = Y \cdot A_{\boldsymbol{k}} \cdot \Psi(\boldsymbol{x}). \tag{7}$$

Remark 2.11. Note that the notation we use in (7) is different from the one in [13, p 2], by transposing.

Under direct computation, the ith component of $A_{\boldsymbol{k}} \cdot \Psi(\boldsymbol{x})$ is

$$[A_{\boldsymbol{k}} \cdot \Psi(\boldsymbol{x})]_i = \sum_{\boldsymbol{y}_j \to \boldsymbol{y}_i \in E} k_{\boldsymbol{y}_j \to \boldsymbol{y}_i} \boldsymbol{x}^{\boldsymbol{y}_j} - \sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i}.$$

Therefore, the equality (5) is equivalent to

$$A_{\boldsymbol{k}} \cdot \Psi(\boldsymbol{x}^*) = \boldsymbol{0} \tag{8}$$

where $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$ is a complex-balanced equilibrium for the mass-action system $(G, \boldsymbol{k})$.

The following lemma 2.12 is a key result that we will use in the proof of proposition 3.9, where we give a characterization of the complex-balanced equilibria.

Lemma 2.12 ([20, p 94]). *Consider a mass-action system* $(G, \boldsymbol{k})$ *with terminal strongly connected components* $T_1, T_2, \ldots, T_t$ *and vertices* $\{\boldsymbol{y}_1, \boldsymbol{y}_2, \ldots, \boldsymbol{y}_m\}$. *Then* ker$(A_{\boldsymbol{k}})$ *(see equation (6) for the definition of* $A_{\boldsymbol{k}}$*) has a basis* $\{\boldsymbol{e}_1, \ldots, \boldsymbol{e}_t\}$, *such that*

$$\boldsymbol{e}_p = \begin{cases} [\boldsymbol{e}_p]_i > 0, & \text{if } \boldsymbol{y}_i \in T_p, \\ [\boldsymbol{e}_p]_i = 0, & \text{otherwise,} \end{cases}$$

where $1 \leqslant i \leqslant m$ *and* $1 \leqslant p \leqslant t$.

For the proof of lemma 2.12, we refer the reader to [20, p 94] or [23, theorem 4.2].

Example 2.13. Revisiting example 2.4, we have

$$Y = (\boldsymbol{y}_1, \boldsymbol{y}_2, \boldsymbol{y}_3) = \begin{pmatrix} 2 & 0 & 0 \\ 3 & 2 & 0 \\ 0 & 0 & 1 \end{pmatrix},$$

and

$$A_{\boldsymbol{k}} = \begin{pmatrix} -k_{12} & k_{21} & k_{31} \\ k_{12} & -k_{21} - k_{23} & 0 \\ 0 & k_{23} & -k_{31} \end{pmatrix}, \quad \Psi(\boldsymbol{x}) = \begin{pmatrix} \boldsymbol{x}^{\boldsymbol{y}_1} \\ \boldsymbol{x}^{\boldsymbol{y}_2} \\ \boldsymbol{x}^{\boldsymbol{y}_3} \end{pmatrix} = \begin{pmatrix} x_1^2 x_2^3 \\ x_2^2 \\ x_3 \end{pmatrix}.$$

Following equation (7), we derive

$$\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = Y \cdot A_{\boldsymbol{k}} \cdot \Psi(\boldsymbol{x}) = \begin{pmatrix} -2k_{12}x_1^2x_2^3 + 2k_{21}x_2^2 + 2k_{31}x_3 \\ -k_{12}x_1^2x_2^3 + (k_{21} - 2k_{23})x_2^2 + 3k_{31}x_3 \\ k_{23}x_2^2 - k_{31}x_3 \end{pmatrix},$$

which gives the same ODE system as (2).

2.3. *The toric locus* $\mathcal{K}(G)$

Here we introduce the notion of *toric locus*, which is a key concept in this paper. See also [36, definition 2.2].

Definition 2.14. Consider an E-graph $G = (V, E)$. Let $\mathcal{K}(G) \subseteq \mathbb{R}^E_{>0}$ denote the set of parameters $\boldsymbol{k} \in \mathbb{R}^E_{>0}$, for which the dynamical system generated by $(G, \boldsymbol{k})$ is toric (i.e. complex-balanced). We refer to $\mathcal{K}(G)$ as the **toric locus** of the E-graph G.

The following theorem shows us that only weakly reversible E-graphs can give rise to complex-balanced mass-action systems.

Theorem 2.15 ([26]). *Every E-graph that generates a complex-balanced mass-action system is weakly reversible. Moreover, every E-graph that is weakly reversible permits complex-balanced mass-action systems.*

As a consequence, given an E-graph $G = (V, E)$, we conclude that

- If $G = (V, E)$ is weakly reversible, then $\mathcal{K}(G) \neq \emptyset$.
- If $G = (V, E)$ is not weakly reversible, then $\mathcal{K}(G) = \emptyset$.

Since we are not interested in the case when $\mathcal{K}(G)$ is empty, we always assume the E-graph $G = (V, E)$ is weakly reversible when working with $\mathcal{K}(G)$ in this paper.

Next, we want to study $\mathcal{K}(G)$. In practical applications, it is difficult to compute precise values for the parameters $k_{ij} \in \mathbb{R}_{>0}$, so we usually choose a symbolic approach and consider them as unspecified parameters, as in [13].

Example 2.16. Revisit example 2.4, suppose $\boldsymbol{x} = (x_1, x_2, x_3)$ is a complex-balanced equilibrium. The conditions (5) satisfied by complex-balanced equilibrium $\boldsymbol{x}$ are as follows:

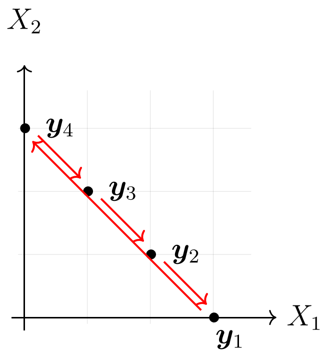


Figure 3. Cycle on four vertices.

$$
\begin{aligned}
k_{21}x_2^2 + k_{31}x_3 &= k_{12}x_1^2x_2^3, \\
k_{12}x_1^2x_2^3 &= k_{21}x_2^2 + k_{23}x_2^2, \\
k_{23}x_2^2 &= k_{31}x_3.
\end{aligned}
$$

Surprisingly, the toric locus $\mathcal{K}(G)$ in example 2.4 is the whole positive orthant $\mathbb{R}^4_{>0}$. This follows from a classical result, known as the *Deficiency Zero Theorem*. We will revisit this example and show the details in section 4.3.

For small E-graphs one can successfully use Computer Algebra software such as Macaulay2 [22], in order to apply Elimination theory [35, chapter 4] or Real quantifier elimination [2, chapter 12.3] for computing the toric locus $\mathcal{K}(G)$.

In general, the toric locus can have quite a complicated algebraic description and it is not easy to study. This is reflected by example 2.17 below, which shows that even for very simple E-graphs the toric locus can be nontrivial.

Example 2.17. Consider the mass-action system $(G,\boldsymbol{k})$ in figure 3, with four vertices:

$$
\boldsymbol{y}_1 = \begin{pmatrix} 3 \\ 0 \end{pmatrix}, \ \boldsymbol{y}_2 = \begin{pmatrix} 2 \\ 1 \end{pmatrix}, \ \boldsymbol{y}_3 = \begin{pmatrix} 1 \\ 2 \end{pmatrix}, \ \boldsymbol{y}_4 = \begin{pmatrix} 0 \\ 3 \end{pmatrix}.
$$

Suppose $\boldsymbol{x} = (x_1, x_2)$ is a complex-balanced equilibrium, then the complex-balanced conditions follow:

$$
k_{14}x_1^3 = k_{21}x_1^2x_2 = k_{32}x_1x_2^2 = k_{43}x_2^3.
$$

By eliminating x_1, x_2 above (either by hand, e.g. $k_{14}/k_{21} = k_{32}/k_{43}$, or via computer algebra software), the toric locus $\mathcal{K}(G) \subset \mathbb{R}^4_{>0}$ is the following algebraic variety given by equations (9) and (10), intersected with the positive orthant

$$
(k_{43}k_{32}k_{21})(k_{21}k_{14}k_{43}) = (k_{14}k_{43}k_{32})^2, \tag{9}
$$

and

$$
(k_{14}k_{43}k_{32})(k_{32}k_{21}k_{14}) = (k_{21}k_{14}k_{43})^2. \tag{10}
$$

In general, after a polynomial change of variables the toric locus becomes the intersection of a toric variety with the positive orthant (this can be done for any weakly reversible network using the *matrix-tree theorem*, see [13]). More precisely, in this case, equations (9) and (10) become

$$K_1 K_3 - K_2^2 = 0, \tag{11}$$

and

$$K_2 K_4 - K_3^2 = 0, \tag{12}$$

where we set $K_1 := k_{43}k_{32}k_{21},\ K_2 := k_{14}k_{43}k_{32},\ K_3 := k_{21}k_{14}k_{43},\ K_4 := k_{32}k_{21}k_{14}$.

From the algebraic point of view, binomial equations are desirable in computations and toric varieties are a cornerstone of algebraic geometry, since they provide many tractable examples due to their combinatorial structure, which is well understood [35, chapter 8].

3. Complex-balanced equilibria depend continuously on the parameter values in the toric locus $\mathcal{K}(G)$

In this section, we show the first main result of this paper: complex-balanced equilibria depend continuously on the parameters $\boldsymbol{k}$ in the toric locus $\mathcal{K}(G)$. Now we introduce a map from $\mathcal{K}(G)$ to $\mathcal{S}_{\boldsymbol{x}_0}$, which is crucial in the later proofs.

Definition 3.1. Let $G = (V, E)$ be a weakly reversible E-graph with the stoichiometric subspace $\mathcal{S}$. Given a state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, we define the following map:

$$Q_{\boldsymbol{x}_0} : \mathcal{K}(G) \to (\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}, \tag{13}$$

such that for any $\boldsymbol{k} \in \mathcal{K}(G)$, $Q_{\boldsymbol{x}_0}(\boldsymbol{k})$ is the complex-balanced equilibrium in the invariant polyhedron $\mathcal{S}_{\boldsymbol{x}_0}$, under the mass-action system $(G, \boldsymbol{k})$.

The map $Q_{\boldsymbol{x}_0}$ is well-defined for any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$ and $\boldsymbol{k} \in \mathcal{K}(G)$. This follows from theorem 2.10, where every complex-balanced system admits a unique equilibrium within each invariant polyhedron. Now we show some basic properties of the map $Q_{\boldsymbol{x}_0}$.

Lemma 3.2. *For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the map $Q_{\boldsymbol{x}_0}$ from definition 3.1 is surjective.*

Proof. To prove the surjectivity of $Q_{\boldsymbol{x}_0}$, we show that for any point $\hat{\boldsymbol{x}} \in (\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$, there exists $\hat{\boldsymbol{k}} \in \mathcal{K}(G)$ such that $Q_{\boldsymbol{x}_0}(\hat{\boldsymbol{k}}) = \hat{\boldsymbol{x}}$.

From definition 2.14, given some parameters $\boldsymbol{k} \in \mathcal{K}(G)$, there exists $\boldsymbol{x} \in \mathbb{R}^n_{>0}$ such that $Q_{\boldsymbol{x}_0}(\boldsymbol{k}) = \boldsymbol{x}$ and the pair $(\boldsymbol{k}, \boldsymbol{x})$ satisfies the complex-balanced conditions (5), namely: for each vertex $\boldsymbol{y}_i \in V$,

$$\sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i} = \sum_{\boldsymbol{y}_j \to \boldsymbol{y}_i \in E} k_{\boldsymbol{y}_j \to \boldsymbol{y}_i} \boldsymbol{x}^{\boldsymbol{y}_j}. \tag{14}$$

Now we define the set of parameters $\hat{\boldsymbol{k}} = (\hat{k}_{\boldsymbol{y}_i \to \boldsymbol{y}_j})$ as

$$\hat{k}_{\boldsymbol{y}_i \to \boldsymbol{y}_j} := \frac{k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i}}{\hat{\boldsymbol{x}}^{\boldsymbol{y}_i}}. \tag{15}$$

From (14) and (15), we derive that for each vertex $\boldsymbol{y}_i \in V$,

$$\sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \hat{k}_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \hat{\boldsymbol{x}}^{\boldsymbol{y}_i} = \sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i} = \sum_{\boldsymbol{y}_j \to \boldsymbol{y}_i \in E} k_{\boldsymbol{y}_j \to \boldsymbol{y}_i} \boldsymbol{x}^{\boldsymbol{y}_j} = \sum_{\boldsymbol{y}_j \to \boldsymbol{y}_i \in E} \hat{k}_{\boldsymbol{y}_j \to \boldsymbol{y}_i} \hat{\boldsymbol{x}}^{\boldsymbol{y}_j}. \tag{16}$$

It is clear that $\hat{\boldsymbol{k}} \in \mathbb{R}^{E}_{>0}$. Thus, from (16) we get $\hat{\boldsymbol{k}} \in \mathcal{K}(G)$ and the pair $(\hat{\boldsymbol{k}}, \hat{\boldsymbol{x}})$ satisfies the complex-balanced conditions (5). Hence, we conclude $Q_{\boldsymbol{x}_0}(\hat{\boldsymbol{k}}) = \hat{\boldsymbol{x}}$.

□

Lemma 3.3. *For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, consider the map $Q_{\boldsymbol{x}_0}$ from definition 3.1. Given any state $\boldsymbol{x} \in (\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$, the preimage $Q^{-1}_{\boldsymbol{x}_0}(\boldsymbol{x})$ is convex and thus connected.*

Proof. Suppose any $\boldsymbol{x} \in (\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$. From lemma 3.2, we have $Q^{-1}_{\boldsymbol{x}_0}(\boldsymbol{x}) \neq \emptyset$. Follow definition 3.1, for any $\boldsymbol{k} \in Q^{-1}_{\boldsymbol{x}_0}(\boldsymbol{x}) \subset \mathcal{K}(G)$, the pair $(\boldsymbol{k}, \boldsymbol{x})$ satisfies the complex-balanced conditions, such that for each vertex $\boldsymbol{y}_i \in V$,

$$\sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i} = \sum_{\boldsymbol{y}_j \to \boldsymbol{y}_i \in E} k_{\boldsymbol{y}_j \to \boldsymbol{y}_i} \boldsymbol{x}^{\boldsymbol{y}_j}. \tag{17}$$

Now we claim that the fiber $Q^{-1}_{\boldsymbol{x}_0}(\boldsymbol{x})$ is a convex set. Suppose both $\boldsymbol{k}^*, \boldsymbol{k}^{**} \in \mathcal{K}(G)$ satisfy (17). We will show that any convex combination of $\boldsymbol{k}^*$ and $\boldsymbol{k}^{**}$ also satisfies (17). Let us consider the following set:

$$L(\boldsymbol{k}^*, \boldsymbol{k}^{**}) := \{a\boldsymbol{k}^* + (1-a)\boldsymbol{k}^{**} : 0 \leqslant a \leqslant 1\}. \tag{18}$$

Under direct computation, we obtain for each vertex $\boldsymbol{y}_i \in V$ and any $0 \leqslant a \leqslant 1$,

$$\sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \left(a k^*_{\boldsymbol{y}_i \to \boldsymbol{y}_j} + (1-a) k^{**}_{\boldsymbol{y}_i \to \boldsymbol{y}_j}\right) \boldsymbol{x}^{\boldsymbol{y}_i} = \sum_{\boldsymbol{y}_j \to \boldsymbol{y}_i \in E} \left(a k^*_{\boldsymbol{y}_j \to \boldsymbol{y}_i} + (1-a) k^{**}_{\boldsymbol{y}_j \to \boldsymbol{y}_i}\right) \boldsymbol{x}^{\boldsymbol{y}_j}. \tag{19}$$

Hence, we prove that $L(\boldsymbol{k}^*, \boldsymbol{k}^{**}) \subseteq Q^{-1}_{\boldsymbol{x}_0}(\boldsymbol{x})$. This shows the preimage $Q^{-1}_{\boldsymbol{x}_0}(\boldsymbol{x})$ is a convex set, and we conclude $Q^{-1}_{\boldsymbol{x}_0}(\boldsymbol{x})$ is connected. □

Lemma 3.4. *For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the map $Q_{\boldsymbol{x}_0}$ from definition 3.1 is open.*

Proof. Pick a point $\hat{\boldsymbol{k}} \in \mathcal{K}(G)$ and assume that $Q_{\boldsymbol{x}_0}(\hat{\boldsymbol{k}}) = \hat{\boldsymbol{x}}$. It suffices for us to prove that for any $0 < \epsilon \ll 1$, there exists $\delta > 0$ such that for all $\boldsymbol{x}$ satisfying $\|\boldsymbol{x} - \hat{\boldsymbol{x}}\| \leqslant \delta$, there is a point $\boldsymbol{k} \in \mathcal{K}(G)$, such that $\boldsymbol{x} = Q_{\boldsymbol{x}_0}(\boldsymbol{k})$ and $\|\boldsymbol{k} - \hat{\boldsymbol{k}}\| \leqslant \epsilon$.

For any $\boldsymbol{x} \in \mathcal{S}_{\boldsymbol{x}_0}$, we define the set of parameters $\boldsymbol{k} = (k_{\boldsymbol{y}_i \to \boldsymbol{y}_j})$ as

$$k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} := \frac{\hat{k}_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \hat{\boldsymbol{x}}^{\boldsymbol{y}_i}}{\boldsymbol{x}^{\boldsymbol{y}_i}}. \tag{20}$$

Using lemma 3.2, we get $\boldsymbol{k} \in \mathcal{K}(G)$ and $Q_{\boldsymbol{x}_0}(\boldsymbol{k}) = \boldsymbol{x}$. For each reaction $\boldsymbol{y}_i \to \boldsymbol{y}_j \in E$ and $0 < \epsilon \ll 1$, the continuity of the function $\boldsymbol{x}^{\boldsymbol{y}_i}$ in (20) guarantees the existence of $\delta_{\boldsymbol{y}_i \to \boldsymbol{y}_j}$ such that for any $\boldsymbol{x}$ satisfying $\|\boldsymbol{x} - \hat{\boldsymbol{x}}\| \leqslant \delta_{\boldsymbol{y}_i \to \boldsymbol{y}_j}$ we have

$$|k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} - \hat{k}_{\boldsymbol{y}_i \to \boldsymbol{y}_j}| \leqslant \epsilon / |E|.$$

Then we do the same on all reactions in E and set $\delta = \min_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \{\delta_{\boldsymbol{y}_i \to \boldsymbol{y}_j}\}$. Now suppose any state $\boldsymbol{x}$ satisfying $\|\boldsymbol{x} - \hat{\boldsymbol{x}}\| \leqslant \delta$, we derive that

$$\|\boldsymbol{k} - \hat{\boldsymbol{k}}\| \leqslant \sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} |k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} - \hat{k}_{\boldsymbol{y}_i \to \boldsymbol{y}_j}| \leqslant \epsilon.$$

□

Now we state the main result of this section, theorem 3.5. We will use this result in the following sections, for proof of the connectedness of the toric locus.

Theorem 3.5. *For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the map $Q_{\boldsymbol{x}_0}$ from definition 3.1 is continuous. In other words, the complex-balanced equilibrium within the invariant polyhedron $S_{\boldsymbol{x}_0}$ depends continuously on the parameter values in $\mathcal{K}(G)$.*

Theorem 3.5 represents a crucial step in the proof of theorem 4.7 (more precisely, in lemma 4.11), where we will show the product structure of the toric locus. Before proving theorem 3.5, we need to address some necessary notations and lemmas.

Definition 3.6. Let $G = (V, E)$ be a strongly connected E-graph.

(a) We call $\mathcal{T}$ a **spanning tree** of G, if it is a connected, acyclic subgraph of G that contains all vertices in V.
(b) For a spanning tree $\mathcal{T}$ of G, the vertex $\boldsymbol{y} \in V$ is called a **sink** of $\mathcal{T}$, if $\boldsymbol{y}$ is the target vertex for all reactions in $\mathcal{T}$ involving $\boldsymbol{y}$.
(c) For a spanning tree $\mathcal{T}$ of G and a vertex $\boldsymbol{y}_i \in V$, then we call $\mathcal{T}$ a **spanning $\boldsymbol{y}_i$-tree** (or ***i*-tree**) if $\boldsymbol{y}_i$ is the only sink of $\mathcal{T}$.

Notation 3.7. Let $G = (V, E)$ be a strongly connected E-graph.

(a) Consider a spanning tree $\mathcal{T}$ of G, we denote by $\boldsymbol{k}^{\mathcal{T}}$ the product of all the reaction rate constants associated with reactions in the spanning tree $\mathcal{T}$.
(b) Consider every spanning $\boldsymbol{y}_i$-tree of G, let K_i denote the sum of all products associated with spanning $\boldsymbol{y}_i$-trees, such that
$$K_i := \sum_{\mathcal{T} \text{ an } i\text{-tree}} \boldsymbol{k}^{\mathcal{T}}.$$

Proposition 3.8 ([13, proposition 3]). *Consider a mass-action system $(G, \boldsymbol{k})$ with the strongly connected E-graph $G = (V, E)$. Let $A_{\boldsymbol{k}}$ be its corresponding Kirchoff matrix $A_{\boldsymbol{k}}$ (see equation (6) for the definition of $A_{\boldsymbol{k}}$), and $\mathcal{M}_i$ be the matrix obtained by removing the ith row and the ith column of $A_{\boldsymbol{k}}$, then*

$$\det(\mathcal{M}_i) = (-1)^{m-1} K_i, \tag{21}$$

where $K_i = \sum\limits_{\mathcal{T} \text{ an } i\text{-tree}} \boldsymbol{k}^{\mathcal{T}}$ defined in notation 3.7.

The following proposition 3.9 gives a characterization of the complex-balanced equilibria. The similar conclusion can be obtained from [13]. For the completeness of the paper, we sketch the proof here.

Proposition 3.9. *Consider a weakly reversible mass-action system $(G, \boldsymbol{k})$ with ℓ connected components. For any two vertices $\boldsymbol{y}_i$ and $\boldsymbol{y}_j$, we construct the following equation:*

$$K_i \boldsymbol{x}^{\boldsymbol{y}_j} - K_j \boldsymbol{x}^{\boldsymbol{y}_i} = 0, \tag{22}$$

where $K_i = \sum_{\mathcal{T} \text{ an } i\text{-tree}} \boldsymbol{k}^{\mathcal{T}}$ is defined in notation 3.7. Then $\boldsymbol{x}$ is a complex-balanced equilibrium for the reaction rate vector $\boldsymbol{k}$ if and only if equations (22) are satisfied for every pair of vertices $\boldsymbol{y}_i$ and $\boldsymbol{y}_j$ in the same connected component in G.

Proof. From (6), we get $[A_{\boldsymbol{k}}]_{ji} \neq 0$, if $\boldsymbol{y}_i \to \boldsymbol{y}_j \in E$ or $i = j$. After we relabel the vertices according to the connected components of G, the Kirchoff matrix $A_{\boldsymbol{k}}$ will be a block diagonal matrix, where each diagonal block corresponds to a connected component of G.

Following equation (8), $\boldsymbol{x}$ is a complex-balanced equilibrium if and only if $A_{\boldsymbol{k}} \cdot \Psi(\boldsymbol{x}) = \boldsymbol{0}$ under the reaction rate vector $\boldsymbol{k}$. Since we consider $A_{\boldsymbol{k}}$ as a block diagonal matrix, it suffices to prove the proposition when the system has a single connected component (i.e. $\ell = 1$).

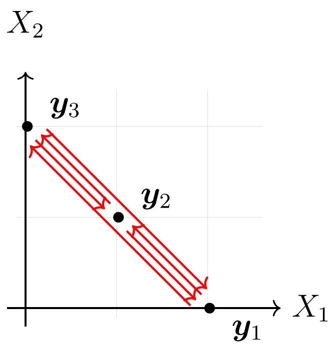


Figure 4. Complete bidirected graph with three vertices, considered in example 3.10.

Now suppose $G = (V, E)$ has one connected component, thus it is strongly connected. Applying lemma 2.12 on the system $(G, \boldsymbol{k})$, we deduce that

$$\dim(\ker(A_{\boldsymbol{k}})) = 1, \text{ and } \det(A_{\boldsymbol{k}}) = 0. \tag{23}$$

Let $M_{i,j}$ denote the (i,j) minor of the matrix $A_{\boldsymbol{k}}$. Since the column sums of $A_{\boldsymbol{k}}$ are zero, $M_{i,j}$ is independent of the choice of rows, that is,

$$M_{1,j} = \cdots = M_{m,j}, \text{ for every } j = 1, \ldots, m.$$

Using proposition 3.8 and expanding the determinant of $A_{\boldsymbol{k}}$ in terms of its minors, we derive that

$$A_{\boldsymbol{k}} \cdot \boldsymbol{K} = \boldsymbol{0}, \tag{24}$$

where $\boldsymbol{K} = (K_1, K_2, \ldots, K_m)^\intercal$.

Now we obtain both $\boldsymbol{K}$ and $\Psi(\boldsymbol{x})$ belongs to the null-space of $A_{\boldsymbol{k}}$. One can check that they are both positive vectors. From $\dim(\ker(A_{\boldsymbol{k}})) = 1$ in equation (23), we deduce that the two vectors $\boldsymbol{K}$ and $\Psi(\boldsymbol{x})$ are proportional. Hence, it is clear that $A_{\boldsymbol{k}} \cdot \Psi(\boldsymbol{x}) = \boldsymbol{0}$ if and only if equations (22) are satisfied for every pair of vertices of G. Again using equation (8), we conclude this proposition. □

Example 3.10 (see also [25, equation (3.12)]). Consider a strongly connected mass-action system $(G, \boldsymbol{k})$ in figure 4, with three vertices:

$$\boldsymbol{y}_1 = \begin{pmatrix} 2 \\ 0 \end{pmatrix}, \ \boldsymbol{y}_2 = \begin{pmatrix} 1 \\ 1 \end{pmatrix}, \ \boldsymbol{y}_3 = \begin{pmatrix} 0 \\ 2 \end{pmatrix}.$$

For the vertex $\boldsymbol{y}_1$, we list all spanning $\boldsymbol{y}_1$-trees of G in figure 5 below:

From notation 3.7, we obtain that

$$K_1 = k_{21}k_{31} + k_{32}k_{21} + k_{23}k_{31}.$$

Analogously, we can derive K_2, K_3 corresponding to the vertices $\boldsymbol{y}_2, \boldsymbol{y}_3$ in G,

$$K_2 = k_{12}k_{32} + k_{13}k_{32} + k_{31}k_{12}$$
$$K_3 = k_{13}k_{23} + k_{21}k_{13} + k_{12}k_{23}.$$

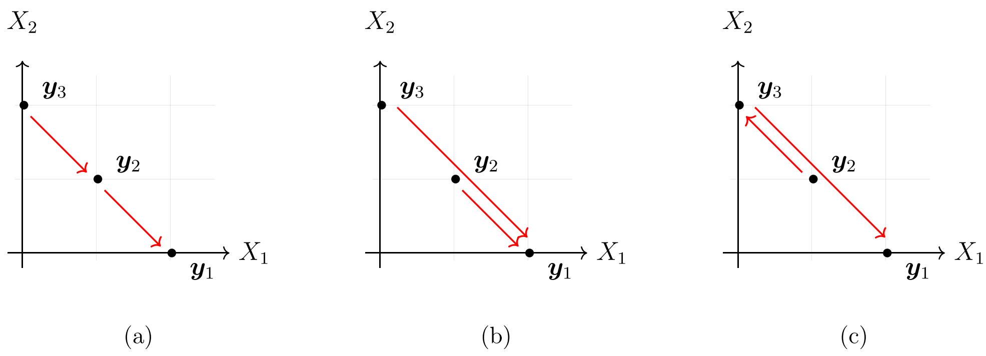


Figure 5. Spanning $\boldsymbol{y}_1$-trees of G.

Suppose $\boldsymbol{x} = (x_1, x_2)$ is a complex-balanced equilibrium. Using proposition 3.9, we get that $\boldsymbol{k} \in \mathcal{K}(G)$, if and only if

$$\frac{K_1}{\boldsymbol{x}^{\boldsymbol{y}_1}} = \frac{K_2}{\boldsymbol{x}^{\boldsymbol{y}_2}} = \frac{K_3}{\boldsymbol{x}^{\boldsymbol{y}_3}}. \tag{25}$$

This is equivalent to

$$\frac{K_1}{x_1^2} = \frac{K_2}{x_1 x_2} = \frac{K_3}{x_2^2}. \tag{26}$$

By eliminating x_1, x_2 in equation (26), the toric locus $\mathcal{K}(G) \subset \mathbb{R}^6_{>0}$ is defined by the following binomial:

$$K_1 K_3 - K_2^2 = 0. \tag{27}$$

Therefore, we recover the result from [25, equation (3.12)] (see also [13, example 1], [10, p 195]): the toric locus can be written as

$$\begin{aligned} \mathcal{K}(G) = \big\{ \boldsymbol{k} \in \mathbb{R}^6_{>0} : \ & (k_{21}k_{31} + k_{32}k_{21} + k_{23}k_{31})(k_{13}k_{23} + k_{21}k_{13} + k_{12}k_{23}) \\ & - (k_{12}k_{32} + k_{13}k_{32} + k_{31}k_{12})^2 = 0 \big\}. \end{aligned} \tag{28}$$

Definition 3.11 ([38]). Consider two manifolds A and B in the Euclidean space $\mathbb{R}^n$. We say that A and B **intersect transversally**, if at any intersection point $x \in A \cap B$, $T_x(A) + T_x(B) = \mathbb{R}^n$, that is, their tangent spaces span $\mathbb{R}^n$.

Before we proceed to the proof of theorem 3.5 we also need the following lemma:

Lemma 3.12 ([16, lemma 5.4]). *Let $\boldsymbol{x}_1, \boldsymbol{x}_2 \in \mathbb{R}^n_{>0}$ be positive vectors. Consider a vector subspace S in $\mathbb{R}^n$, and two manifolds $\boldsymbol{x}_1 + S$ and $\boldsymbol{x}_2 \circ \exp(S^{\perp})$ of $\mathbb{R}^n$. Then the two manifolds intersect transversally, i.e.*

$$T_{\mathbf{p}}(\boldsymbol{x}_1 + S) + T_{\mathbf{p}}\left(\boldsymbol{x}_2 \circ \exp\left(S^{\perp}\right)\right) = \mathbb{R}^n,$$

for any point $\mathbf{p} \in (\boldsymbol{x}_1 + S) \cap (\boldsymbol{x}_2 \circ \exp(S^{\perp}))$.

Finally, we are prepared to prove theorem 3.5. Let us roughly explain the main ideas of the proof. We will show that the set of complex-balanced equilibria depends continuously on $\boldsymbol{K}$ (see Notation 3.7). There are two main steps. First, we prove the theorem in the case where the graph G has only one connected component; second, we generalize the result for any number of connected components. In the case of one connected component, we proceed as follows. For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the corresponding complex-balanced equilibrium is the unique intersection between the set of complex-balanced equilibria and the affine invariant polyhedron $(\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$. We find a vector $\boldsymbol{X}^* \in \mathcal{S}$, such that $\exp(\boldsymbol{X}^*)$ is a complex-balanced equilibrium of the system $(G, \boldsymbol{k})$. By lemma 3.12 we have that $(\boldsymbol{x}_0 + \mathcal{S})$ and $\exp(\boldsymbol{X}^* + \mathcal{S}^{\perp})$ intersect transversally, thus the unique intersection point varies continuously as a function of $\boldsymbol{X}^*$. Since $\boldsymbol{X}^*$ depends continuously on $\boldsymbol{K}$, we conclude the proof for the case of one connected component, and then extend to the general case.

Proof of theorem 3.5. Here, for the sake of simplicity, we temporarily make the following abuse of notation:

$$\boldsymbol{X} = (X_1, \cdots, X_n)^{\intercal} := \ln \boldsymbol{x} = (\ln x_1, \ldots, \ln x_n)^{\intercal}. \tag{29}$$

Recall notation 3.7, for each vertex $\boldsymbol{y}_i \in V$, we have

$$K_i = \sum_{\mathcal{T} \text{ an } i\text{-tree}} \boldsymbol{k}^{\mathcal{T}},$$

where $\boldsymbol{k}^{\mathcal{T}}$ is the product of reaction rates k_{ij} associated with reactions in the spanning $\boldsymbol{y}_i$-tree $\mathcal{T}$ of G. It is standard to derive that the vector $\boldsymbol{K} = (K_i) \in \mathbb{R}^m_{>0}$ depends smoothly on the reaction rate vector $\boldsymbol{k} = (k_{ij}) \in \mathbb{R}^E_{>0}$. Hence, it suffices for us to show that the set of complex-balanced equilibria depends continuously on $\boldsymbol{K}$.

By proposition 3.9, a state $\boldsymbol{x}$ is a complex-balanced equilibrium if and only if for any two vertices $\boldsymbol{y}_i, \boldsymbol{y}_j$ in the same connected component of G,

$$K_i \boldsymbol{x}^{\boldsymbol{y}_j} = K_j \boldsymbol{x}^{\boldsymbol{y}_i}. \tag{30}$$

Taking the log of both sides in equation (30), we derive

$$\ln(K_i) + \boldsymbol{y}_j{}^{\intercal} \cdot \ln(\boldsymbol{x}) = \ln(K_j) + \boldsymbol{y}_i{}^{\intercal} \cdot \ln(\boldsymbol{x}). \tag{31}$$

Thus, we can rewrite (31) as

$$\ln(K_i / K_j) = \left(\boldsymbol{y}_i{}^{\intercal} - \boldsymbol{y}_j{}^{\intercal}\right) \cdot \boldsymbol{X}, \tag{32}$$

where $\boldsymbol{y}_i$ and $\boldsymbol{y}_j$ are two vertices belonging to the same connected component of G.

We show the rest of the proof in two steps. First, we prove the theorem under the assumption that the graph G has only one connected component. Next, we explain how to generalize the result into an arbitrary number of connected components.

Now suppose the graph G has a single connected component (i.e. $\ell = 1$), then all vertices $\{\boldsymbol{y}_1, \ldots, \boldsymbol{y}_m\}$ are in the same connected component. It is clear that equation (32) are equivalent to the following system of linear equations in $\boldsymbol{X}$:

$$\begin{bmatrix} \ln(K_1/K_2) \\ \ln(K_2/K_3) \\ \vdots \\ \ln(K_{m-1}/K_m) \end{bmatrix} = \begin{bmatrix} \boldsymbol{y}_1^{\intercal} - \boldsymbol{y}_2^{\intercal} \\ \boldsymbol{y}_2^{\intercal} - \boldsymbol{y}_3^{\intercal} \\ \vdots \\ \boldsymbol{y}_{m-1}^{\intercal} - \boldsymbol{y}_m^{\intercal} \end{bmatrix} \begin{bmatrix} X_1 \\ X_2 \\ \vdots \\ X_n \end{bmatrix}. \tag{33}$$

After we set

$$\Delta \boldsymbol{y} := \begin{bmatrix} \boldsymbol{y}_1^{\intercal} - \boldsymbol{y}_2^{\intercal} \\ \boldsymbol{y}_2^{\intercal} - \boldsymbol{y}_3^{\intercal} \\ \vdots \\ \boldsymbol{y}_{m-1}^{\intercal} - \boldsymbol{y}_m^{\intercal} \end{bmatrix}, \text{ and } \Delta \boldsymbol{K} := \begin{bmatrix} K_1/K_2 \\ K_2/K_3 \\ \vdots \\ K_{m-1}/K_m \end{bmatrix},$$

the system (33) can be expressed as

$$\ln(\Delta \boldsymbol{K}) = (\Delta \boldsymbol{y})\boldsymbol{X}. \tag{34}$$

Since G is strongly connected, its stoichiometric subspace is

$$\mathcal{S} = \operatorname{span}\left\{\boldsymbol{y}_1^\intercal - \boldsymbol{y}_2^\intercal, \boldsymbol{y}_2^\intercal - \boldsymbol{y}_3^\intercal, \ldots, \boldsymbol{y}_{m-1}^\intercal - \boldsymbol{y}_m^\intercal\right\}.$$

Let s be the dimension of $\mathcal{S}$, then we deduce that $s \leqslant \min\{m-1, n\}$, and the matrix $\Delta \boldsymbol{y}$ has exactly s linearly independent rows. W.l.o.g. we assume the first s rows in $\Delta \boldsymbol{y}$ are linearly independent. Thus, we obtain

$$\mathcal{S} = \operatorname{span}\left\{\boldsymbol{y}_1^\intercal - \boldsymbol{y}_2^\intercal, \boldsymbol{y}_2^\intercal - \boldsymbol{y}_3^\intercal, \ldots, \boldsymbol{y}_s^\intercal - \boldsymbol{y}_{s+1}^\intercal\right\}. \tag{35}$$

Furthermore, we consider the system of equations as follows:

$$\ln(\Delta_s \boldsymbol{K}) = (\Delta_s \boldsymbol{y})\boldsymbol{X}, \tag{36}$$

where

$$\Delta_s \boldsymbol{y} := \begin{bmatrix} \boldsymbol{y}_1^\intercal - \boldsymbol{y}_2^\intercal \\ \boldsymbol{y}_2^\intercal - \boldsymbol{y}_3^\intercal \\ \vdots \\ \boldsymbol{y}_s^\intercal - \boldsymbol{y}_{s+1}^\intercal \end{bmatrix}, \text{ and } \Delta_s \boldsymbol{K} := \begin{bmatrix} K_1/K_2 \\ K_2/K_3 \\ \vdots \\ K_s/K_{s+1} \end{bmatrix}.$$

Since $\boldsymbol{k} \in \mathcal{K}(G)$, by theorem 2.10, the complex-balanced system $(G, \boldsymbol{k})$ must admit one complex-balanced equilibrium $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$, i.e. $\ln \boldsymbol{x}^*$ is a solution to (34). From theorem 2.10, any complex-balanced equilibrium $\boldsymbol{x}$ satisfies $\ln \boldsymbol{x} - \ln \boldsymbol{x}^* \in \mathcal{S}^\perp$, where $\mathcal{S}^\perp$ denotes the orthogonal complement of $\mathcal{S}$. Thus the solutions to (34) can be written as $\boldsymbol{X} = \ln \boldsymbol{x}^* + \mathcal{S}^\perp$, and this shows the dimension of the set of solutions to (34) is $n - s$.

Moreover, the solutions of (34) must solve (36). Since the rows in the matrix $\Delta_s \boldsymbol{y}$ are linearly independent, the set of solutions to (36) is also of dimension $n - s$. Therefore, we conclude that system (34) is equivalent to system (36) in solving $\boldsymbol{X}$.

Next, we construct a special solution $\boldsymbol{X}^*$ to system (36) with $\boldsymbol{X}^* \in \mathcal{S}$. Recall that $s \leqslant \min\{m-1, n\}$. Based on the dimension of the stoichiometric subspace s, we consider two cases: $s = n$ and $s < n$.

Case 1: $s = n$. Then the stoichiometric subspace $\mathcal{S} = \mathbb{R}^n$, and $\Delta_s \boldsymbol{y} \in \mathbb{R}_{n \times n}$ is a square full rank matrix, i.e. $\Delta_s \boldsymbol{y}$ is invertible. Thus, we derive a solution of (36) as

$$\boldsymbol{X}^* = (\Delta_s \boldsymbol{y})^{-1} \ln(\Delta_s \boldsymbol{K}). \tag{37}$$

It is clear that $\boldsymbol{X}^* \in \mathcal{S} = \mathbb{R}^n$, and $\exp(\boldsymbol{X}^*)$ satisfies equation (30) by construction. This ensures that $\exp(\boldsymbol{X}^*)$ is a complex-balanced equilibrium.

Case 2: $s < n$. Recall that $\mathcal{S}^\perp$ denotes the orthogonal complement of $\mathcal{S}$. Since the stoichiometric subspace $\mathcal{S} \subset \mathbb{R}^n$, we obtain that $\mathcal{S}^\perp \neq \emptyset$ and

$$0 < \dim\left(\mathcal{S}^\perp\right) = n - \dim(\mathcal{S}) = n - s. \tag{38}$$

Then we consider a basis of $\mathcal{S}^\perp$, denoted by B, such that

$$B = \{\boldsymbol{v}_1, \boldsymbol{v}_2, \ldots, \boldsymbol{v}_{n-s}\} \subset \mathbb{R}^n.$$

Furthermore, we build another matrix and vector below

$$\tilde{\Delta}\boldsymbol{y} := \begin{bmatrix} \Delta_s \boldsymbol{y} \\ \boldsymbol{v}_1^\intercal \\ \vdots \\ \boldsymbol{v}_{n-s}^\intercal \end{bmatrix}, \text{ and } \tilde{\Delta}\boldsymbol{K} := \begin{bmatrix} \Delta_s \boldsymbol{K} \\ 0 \\ \vdots \\ 0 \end{bmatrix}, \tag{39}$$

and consider the following system:

$$\ln\left(\tilde{\Delta}\boldsymbol{K}\right) = \left(\tilde{\Delta}\boldsymbol{y}\right)\boldsymbol{X}. \tag{40}$$

The solutions of (40) must solve (36). From (35) and $\{\boldsymbol{v}_1, \ldots, \boldsymbol{v}_{n-s}\}$ forming a basis of $\mathcal{S}^\perp$, we deduce that $\tilde{\Delta}\boldsymbol{y} \in \mathbb{R}_{n\times n}$ is an invertible matrix. Hence, we obtain a solution of (40) as

$$\boldsymbol{X}^* = \left(\tilde{\Delta}\boldsymbol{y}\right)^{-1} \ln\left(\tilde{\Delta}\boldsymbol{K}\right). \tag{41}$$

Moreover, for $i = 1, \cdots, n-s$, we have

$$\boldsymbol{v}_i^\intercal \cdot \boldsymbol{X}^* = 0,$$

and this shows that $\boldsymbol{X}^* \in \mathcal{S}$. By construction, $\exp(\boldsymbol{X}^*)$ must solve equation (30), thus it is a complex-balanced equilibrium.

In conclusion, we have found a vector $\boldsymbol{X}^* \in \mathcal{S}$, such that $\exp(\boldsymbol{X}^*)$ is a complex-balanced equilibrium of the system $(G, \boldsymbol{k})$ in both cases. Further, using the fact that both $(\Delta_s \boldsymbol{y})^{-1}$ and $(\tilde{\Delta}\boldsymbol{y})^{-1}$ are fixed real matrices, we deduce $\boldsymbol{X}^*$ depends smoothly on the vector $\boldsymbol{K}$. From theorem 2.10(b), given a complex-balanced system $(G, \boldsymbol{k})$ and one complex-balanced equilibrium $\exp(\boldsymbol{X}^*)$ constructed above, the set of all complex-balanced equilibria of the system can be written as $\exp(\boldsymbol{X}^* + \mathcal{S}^\perp)$.

More specifically, for any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the corresponding complex-balanced equilibrium is the unique intersection between the set of complex-balanced equilibria $\exp(\boldsymbol{X}^* + \mathcal{S}^\perp)$ and the affine invariant polyhedron $(\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$. Using lemma 3.12, we get that the two manifolds $(\boldsymbol{x}_0 + \mathcal{S})$ and $\exp(\boldsymbol{X}^* + \mathcal{S}^\perp)$ intersect transversally. Hence, given a state $\boldsymbol{x}_0$, the (unique) intersection point varies continuously as a function of $\boldsymbol{X}^*$. Together with the fact that $\boldsymbol{X}^*$ depends continuously on $\boldsymbol{K}$, which additionally varies continuously on $\boldsymbol{k}$, we conclude that the map $Q_{\boldsymbol{x}_0}$ is continuous on $\boldsymbol{k} \in \mathcal{K}(G)$ when the graph G has only one connected component.

Finally, we consider the case when the graph G has multiple connected components, $V_1, \ldots, V_\ell$ with $\ell > 1$. Following the proof in proposition 3.9, we can relabel the vertices according to the connected components of G, i.e. for $1 \leqslant p \leqslant \ell$,

$$V_p = \left\{\boldsymbol{y}_{m_{p-1}+1}, \ldots, \boldsymbol{y}_{m_p}\right\},$$

such that the Kirchoff matrix $A_{\boldsymbol{k}}$ will be a block diagonal matrix, where each diagonal block corresponds to a connected component of G.

Recall from equation (32), a state $\boldsymbol{x}$ is a complex-balanced equilibrium, if and only if for any two vertices $\boldsymbol{y}_i, \boldsymbol{y}_j$ in the same connected component of G,

$$\ln(K_i/K_j) = \left(\boldsymbol{y}_i{}^\intercal - \boldsymbol{y}_j{}^\intercal\right) \cdot \boldsymbol{X},$$

which is equivalent to the following system of linear equations in $\boldsymbol{X}$:

$$\underbrace{\begin{bmatrix} \ln\left(K_1/K_2\right) \\ \vdots \\ \ln\left(K_{m_1-1}/K_{m_1}\right) \\ \hdashline \ln\left(K_{m_1+1}/K_{m_1+2}\right) \\ \vdots \\ \ln\left(K_{m_2-1}/K_{m_2}\right) \\ \hdashline \vdots \\ \ln\left(K_{m_\ell-1}/K_{m_\ell}\right) \end{bmatrix}}_{\ln(\Delta \boldsymbol{K})} = \underbrace{\begin{bmatrix} \boldsymbol{y}_1^{\intercal} - \boldsymbol{y}_2^{\intercal} \\ \vdots \\ \boldsymbol{y}_{m_1-1}^{\intercal} - \boldsymbol{y}_{m_1}^{\intercal} \\ \hdashline \boldsymbol{y}_{m_1+1}^{\intercal} - \boldsymbol{y}_{m_1+2}^{\intercal} \\ \vdots \\ \boldsymbol{y}_{m_2-1}^{\intercal} - \boldsymbol{y}_{m_2}^{\intercal} \\ \hdashline \vdots \\ \boldsymbol{y}_{m_\ell-1}^{\intercal} - \boldsymbol{y}_{m_\ell}^{\intercal} \end{bmatrix}}_{\Delta \boldsymbol{y}} \begin{bmatrix} X_1 \\ X_2 \\ \vdots \\ X_n \end{bmatrix}, \tag{42}$$

and we can express it as

$$\ln\left(\Delta \boldsymbol{K}\right) = \left(\Delta \boldsymbol{y}\right) \boldsymbol{X}. \tag{43}$$

Since G has ℓ connected components, its stoichiometric subspace is

$$\mathcal{S} = \text{span}\left\{\boldsymbol{y}_1^{\intercal} - \boldsymbol{y}_2^{\intercal}, \ldots, \boldsymbol{y}_{m_1-1}^{\intercal} - \boldsymbol{y}_{m_1}^{\intercal}, \boldsymbol{y}_{m_1+1}^{\intercal} - \boldsymbol{y}_{m_1+2}^{\intercal}, \ldots, \boldsymbol{y}_{m_\ell-1}^{\intercal} - \boldsymbol{y}_{m_\ell}^{\intercal}\right\}.$$

Let s be the dimension of $\mathcal{S}$. Then we deduce that $s \leqslant \min\{m-\ell, n\}$, and the matrix $\Delta \boldsymbol{y}$ has exactly s linearly independent rows.

Analogously, we pick s linear independent rows in $\Delta \boldsymbol{y}$, and they also span stoichiometric subspace $\mathcal{S}$. Moreover, these rows in $\Delta \boldsymbol{y}$ formulate a full row rank matrix $\Delta_s \boldsymbol{y}$, while the corresponding rows in $\ln(\Delta \boldsymbol{K})$ give us the vector $\ln(\Delta_s \boldsymbol{K})$. And it is easy to check that system (43) is equivalent to the following system in $\boldsymbol{X}$:

$$\ln\left(\Delta_s \boldsymbol{K}\right) = \left(\Delta_s \boldsymbol{y}\right) \boldsymbol{X}. \tag{44}$$

Next, we construct a special solution $\boldsymbol{X}^*$ to system (44) with $\boldsymbol{X}^* \in \mathcal{S}$. Similarly, we consider s the dimension of the stoichiometric subspace in two cases: $s = n$ and $s < n$.

If $s = n$, then $\Delta_s \boldsymbol{y}$ is an invertible matrix. Thus, we derive a solution of (44) as

$$\boldsymbol{X}^* = \left(\Delta_s \boldsymbol{y}\right)^{-1} \ln\left(\Delta_s \boldsymbol{K}\right).$$

It is easy to see that $\boldsymbol{X}^* \in \mathcal{S} = \mathbb{R}^n$, and $\exp(\boldsymbol{X}^*)$ is a complex-balanced equilibrium.

If $s < n$, we obtain $\dim(\mathcal{S}^{\perp}) = n - s > 0$, and consider a basis $B = \{\boldsymbol{v}_1, \ldots, \boldsymbol{v}_{n-s}\}$ of $\mathcal{S}^{\perp}$. Similar as in equations (39)–(41), we first add $\boldsymbol{v}_1^{\intercal}, \ldots, \boldsymbol{v}_{n-s}^{\intercal}$ on the bottom of the matrix $\Delta_s \boldsymbol{y}$, and adapt $n - s$ zeros to the vector $\ln(\Delta_s \boldsymbol{K})$. Then, we obtain the desired solution $\boldsymbol{X}^* \in \mathcal{S}$ of (44), with $\exp(\boldsymbol{X}^*)$ is a complex-balanced equilibrium.

Together with both cases, we deduce $\boldsymbol{X}^*$ depends smoothly on the vector $\boldsymbol{K}$. We omit the rest of the proof since it directly follows from the single connected component case. □

The following is a direct consequence of results within the proof of the theorem 3.5, since we gave explicit formulae that are given by smooth functions at each step in the construction of $\boldsymbol{x}^*$.

Corollary 3.13. *Let $G = (V, E)$ be a weakly reversible E-graph with the stoichiometric subspace $\mathcal{S}$. For any $\boldsymbol{k} \in \mathcal{K}(G)$, there exists a unique complex-balanced equilibrium $\boldsymbol{x}^*$, such that $\ln(\boldsymbol{x}^*) \in \mathcal{S}$ and $\boldsymbol{x}^*$ depends smoothly on the parameter values $\boldsymbol{k} \in \mathcal{K}(G)$.*

Definition 3.14 ([31]). A surjective, continuous, and open map is called a **quotient map**.

Corollary 3.15. *For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the map $Q_{\boldsymbol{x}_0}$ from definition 3.1 is a quotient map.*

Proof. From lemmas 3.2 and 3.4, we proved the map $Q_{\boldsymbol{x}_0}$ is surjective and open. Together with theorem 3.5, we conclude the map $Q_{\boldsymbol{x}_0}$ is a quotient map. □

3.1. The toric locus $\mathcal{K}(G)$ is connected

The main result of this section is theorem 3.17, where we show the connectedness of the toric locus $\mathcal{K}(G)$. We first recall a fundamental result in general topology as follows:

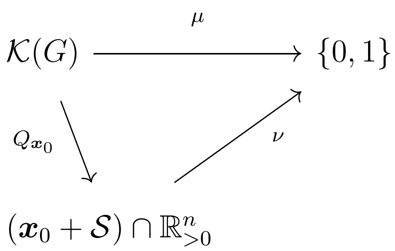
Lemma 3.16 ([41, theorem 9.4]). *Consider three topological spaces A, B, C and a surjective map $f : A \to B$. Let B be endowed with the quotient topology induced by f. Given an arbitrary map $g : B \to C$, then g is continuous if and only if the map $g \circ f : A \to C$ is continuous.*

Theorem 3.17. *Let $G = (V, E)$ be a weakly reversible E-graph. Then the toric locus $\mathcal{K}(G)$ is connected.*

Proof. We will argue by contradiction. Suppose the set $\mathcal{K}(G)$ is not connected. For a given state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, there exists *surjective continuous* map μ, such that

$$\mu : \mathcal{K}(G) \to \{0, 1\},$$

where μ is constant on every connected subset of $\mathcal{K}(G)$. Next we consider the following commutative diagram:



The map $\nu : (\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0} \to \{0, 1\}$ in the diagram satisfies

$$\mu = \nu \circ Q_{\boldsymbol{x}_0}.$$

By lemma 3.3, for any state $\boldsymbol{x} \in (\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$, the preimage $Q^{-1}_{\boldsymbol{x}_0}(\boldsymbol{x})$ is convex and thus connected. Combined with the surjectivity of $Q_{\boldsymbol{x}_0}$ from lemma 3.2, this ensures that the map ν is well-defined. Therefore such a function ν makes the above diagram commute.

By corollary 3.15, the map $Q_{\boldsymbol{x}_0}$ is a quotient map. Hence, by lemma 3.16 we derive that ν is continuous if and only if μ is continuous. Since μ is continuous, we conclude that ν is a continuous map. We also derive that ν is surjective from μ being a surjective map.

Note that the invariant polyhedron $(\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}$ is connected, while the set $\{0, 1\}$ is clearly disconnected. This leads to a contradiction since every continuous function maps a connected set to a connected set. Thus the initial supposition is false, and we conclude that $\mathcal{K}(G)$ is connected. □

4. The toric locus $\mathcal{K}(G)$ is a product space

In this section, we first show that the toric locus $\mathcal{K}(G)$ is a product space when the E-graph $G = (V, E)$ is weakly reversible (see theorem 4.7). Next, we apply this result to deficiency theory and bijective affine transformations in sections 4.3 and 4.4.

4.1. The set of complex-balanced flux vectors $\mathcal{B}(G)$

Definition 4.1. Given an E-graph $G = (V, E)$, we let $\boldsymbol{\beta} = (\beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j})_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \in \mathbb{R}^E_{>0}$ denote a **flux vector**, where the component $\beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j} > 0$ is called the **flux** of the reaction $\boldsymbol{y}_i \to \boldsymbol{y}_j$. Moreover, the pair $(G, \boldsymbol{\beta})$ is called a **flux system**.

Definition 4.2. Consider an E-graph $G = (V, E)$. A flux vector $\boldsymbol{\beta} \in \mathbb{R}^E_{>0}$ is called a **steady flux vector** on G if

$$\sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \left(\boldsymbol{y}_j - \boldsymbol{y}_i\right) = \mathbf{0}. \tag{45}$$

A steady flux vector $\boldsymbol{\beta}$ is called a **complex-balanced flux vector** if for each vertex $\boldsymbol{y}_0 \in V$,

$$\sum_{\boldsymbol{y} \to \boldsymbol{y}_0 \in E} \beta_{\boldsymbol{y} \to \boldsymbol{y}_0} = \sum_{\boldsymbol{y}_0 \to \boldsymbol{y}' \in E} \beta_{\boldsymbol{y}_0 \to \boldsymbol{y}'}, \tag{46}$$

and in this case we say that the pair $(G, \boldsymbol{\beta})$ is a **complex-balanced flux system**.

Definition 4.3. Given an E-graph $G = (V, E)$, we define the **set of complex-balanced flux vectors** on G as follows:

$$\mathcal{B}(G) := \left\{\boldsymbol{\beta} \in \mathbb{R}^E_{>0} \mid \boldsymbol{\beta} \text{ is a complex-balanced flux vector on } G\right\}. \tag{47}$$

Analogous to complex-balanced mass-action systems, complex-balanced flux systems also have connections with E-graphs.

Lemma 4.4. *Every E-graph that permits a complex-balanced flux system is weakly reversible. Moreover, every E-graph that is weakly reversible permits complex-balanced flux systems.*

Proof. First, suppose the E-graph $G = (V, E)$ allows a complex-balanced flux system $\boldsymbol{\beta} = (\beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j})_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \in \mathbb{R}^E_{>0}$. We define a mass-action system $(G, \boldsymbol{k})$ with reaction rate constants

$$k_{\boldsymbol{y} \to \boldsymbol{y}'} = \beta_{\boldsymbol{y} \to \boldsymbol{y}'}, \text{ for every } \boldsymbol{y} \to \boldsymbol{y}' \in E.$$

Then, it is clear that $\boldsymbol{x}^* = (1, \ldots, 1)^T$ is a complex-balanced equilibrium. Applying theorem 2.15, we deduce that $G = (V, E)$ is weakly reversible.

Next, assume that the E-graph $G = (V, E)$ is weakly reversible. From theorem 2.15, there exists a complex-balanced mass-action system $(G, \boldsymbol{k})$ with a equilibrium $\boldsymbol{x}^*$. We define a flux system $(G, \boldsymbol{\beta})$ with fluxes

$$\beta_{\boldsymbol{y} \to \boldsymbol{y}'} := k_{\boldsymbol{y} \to \boldsymbol{y}'} (\boldsymbol{x}^*)^{\boldsymbol{y}}, \text{ for every } \boldsymbol{y} \to \boldsymbol{y}' \in E.$$

Inputting $\boldsymbol{\beta}$ into (46), we derive that $(G, \boldsymbol{\beta})$ is a complex-balanced flux system. □

Subsequently, given an E-graph $G = (V, E)$, we conclude that

- If $G = (V, E)$ is weakly reversible, then $\mathcal{B}(G) \neq \emptyset$.
- If $G = (V, E)$ is not weakly reversible, then $\mathcal{B}(G) = \emptyset$.

Since we are not interested in the case when $\mathcal{B}(G)$ is empty, thus we always assume that the E-graph $G = (V, E)$ is weakly reversible when working on $\mathcal{B}(G)$.

Lemma 4.5. *Let $G = (V, E)$ be a weakly reversible E-graph. Then the set of complex-balanced flux vectors $\mathcal{B}(G)$ is a convex cone in $\mathbb{R}^E_{>0}$, and thus is path-connected.*

Proof. Suppose two flux vectors $\boldsymbol{\beta}^*, \boldsymbol{\beta}^{**} \in \mathcal{B}(G)$, then we get

$$\sum_{\boldsymbol{y} \to \boldsymbol{y}_0 \in E} \beta^*_{\boldsymbol{y} \to \boldsymbol{y}_0} = \sum_{\boldsymbol{y}' \to \boldsymbol{y} \in E} \beta^*_{\boldsymbol{y}' \to \boldsymbol{y}}, \text{ and } \sum_{\boldsymbol{y} \to \boldsymbol{y}_0 \in E} \beta^{**}_{\boldsymbol{y} \to \boldsymbol{y}_0} = \sum_{\boldsymbol{y}' \to \boldsymbol{y} \in E} \beta^{**}_{\boldsymbol{y}' \to \boldsymbol{y}}. \tag{48}$$

Now we consider the following set:

$$L(\boldsymbol{\beta}^*, \boldsymbol{\beta}^{**}) := \{a\boldsymbol{\beta}^* + (1-a)\boldsymbol{\beta}^{**} : 0 \leqslant a \leqslant 1\}. \tag{49}$$

Under direct computation, we obtain for any number $0 \leqslant a \leqslant 1$,

$$\sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \left(a\beta^*_{\boldsymbol{y}_i \to \boldsymbol{y}_j} + (1-a)\beta^{**}_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \right) = \sum_{\boldsymbol{y}_j \to \boldsymbol{y}_i} \left(a\beta^*_{\boldsymbol{y}_j \to \boldsymbol{y}_i} + (1-a)\beta^{**}_{\boldsymbol{y}_j \to \boldsymbol{y}_i} \right). \tag{50}$$

Therefore, $L(\boldsymbol{\beta}^*, \boldsymbol{\beta}^{**}) \subset \mathcal{B}(G)$ and we prove this Lemma. □

4.2. The toric locus $\mathcal{K}(G)$ is a product space

The goal of this section is to establish the *product structure* of the toric locus via an explicitly constructed homeomorphism.

Let us recall the well-known definition of a homeomorphism (see for instance [31]):

Definition 4.6. A function $f : X \to Y$ between two topological spaces is a **homeomorphism**, if it has the following properties: f is bijective, continuous and the inverse function f^{-1} is continuous. If such a function f exists, we say that X and Y are homeomorphic, and write this as $X \simeq Y$.

Now we present the main result in this paper.

Theorem 4.7. *Let $G = (V, E)$ be a weakly reversible E-graph. For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the toric locus $\mathcal{K}(G) \subseteq \mathbb{R}^E_{>0}$ is homeomorphic to the product space $\mathcal{S}_{\boldsymbol{x}_0} \times \mathcal{B}(G)$, that is,*

$$\mathcal{K}(G) \simeq \mathcal{S}_{\boldsymbol{x}_0} \times \mathcal{B}(G), \tag{51}$$

where $\mathcal{S}_{\boldsymbol{x}_0}$ is the invariant polyhedron, and $\mathcal{B}(G)$ is the set of complex-balanced flux vectors. In particular, the toric locus is a contractible manifold.

To prove theorem 4.7, we start by constructing a function φ between the product space $\mathcal{S}_{\boldsymbol{x}_0} \times \mathcal{B}(G)$ and the toric locus $\mathcal{K}(G)$. Then we show that φ is a homeomorphism.

Definition 4.8. Let $G = (V, E)$ be a weakly reversible E-graph. Given a state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, we define the following map:

$$\varphi : \mathcal{S}_{\boldsymbol{x}_0} \times \mathcal{B}(G) \to \mathcal{K}(G), \tag{52}$$

such that for any $\boldsymbol{x} \in \mathcal{S}_{\boldsymbol{x}_0}$ and $\boldsymbol{\beta} = (\beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j})_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \in \mathcal{B}(G)$,

$$\varphi(\boldsymbol{x}, \boldsymbol{\beta}) := \left(\varphi_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \right)_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E}, \text{ with } \varphi_{\boldsymbol{y}_i \to \boldsymbol{y}_j} := \frac{\beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j}}{\boldsymbol{x}^{\boldsymbol{y}_i}}. \tag{53}$$

Lemma 4.9. *For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the map φ is well-defined and continuous.*

Proof. For any $\boldsymbol{\beta} \in \mathcal{B}(G) \subseteq \mathbb{R}^E_{>0}$ and $\boldsymbol{x} \in \mathcal{S}_{\boldsymbol{x}_0} \subseteq \mathbb{R}^n_{>0}$, we get

$$\varphi(\boldsymbol{x}, \boldsymbol{\beta}) = \left(\frac{\beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j}}{\boldsymbol{x}^{\boldsymbol{y}_i}} \right)_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \in \mathbb{R}^E_{>0}. \tag{54}$$

Since $\boldsymbol{\beta}$ is a complex-balanced flux vector, then for each vertex $\boldsymbol{y}_i \in V$,

$$\sum_{\boldsymbol{y}_i \to \boldsymbol{y} \in E} \varphi_{\boldsymbol{y}_i \to \boldsymbol{y}} \boldsymbol{x}^{\boldsymbol{y}_i} = \sum_{\boldsymbol{y}' \to \boldsymbol{y}_i \in E} \varphi_{\boldsymbol{y}' \to \boldsymbol{y}_i} \boldsymbol{x}^{\boldsymbol{y}'}.$$

Hence, $\varphi(\boldsymbol{x}, \boldsymbol{\beta})$ is a vector of reaction rate constants for which $\boldsymbol{x} \in \mathcal{S}_{\boldsymbol{x}_0}$ is a complex-balanced equilibrium of G. Therefore, we conclude that $\varphi(\boldsymbol{x}, \boldsymbol{\beta}) \in \mathcal{K}(G)$, and φ is well-defined. Further, from (54) we can directly get that φ is a continuous map. □

Lemma 4.10. *For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the map φ is bijective.*

Proof. First, we show that φ is surjective. By theorem 2.10, for any reaction rate vector $\boldsymbol{k} \in \mathcal{K}(G)$, there exists a (unique) complex-balanced equilibrium $\boldsymbol{x} \in \mathcal{S}_{\boldsymbol{x}_0}$. Then we define a flux vector $\boldsymbol{\beta} = (\beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j})_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E}$ as follows:

$$\beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j} := k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i}.$$

Using lemma 4.4, we derive that $\boldsymbol{\beta} \in \mathcal{B}(G)$, and $\varphi(\boldsymbol{x}, \boldsymbol{\beta}) = \boldsymbol{k}$.

Next, we show φ is injective. Assume that $(\hat{\boldsymbol{x}}, \hat{\boldsymbol{\beta}}), (\tilde{\boldsymbol{x}}, \tilde{\boldsymbol{\beta}}) \in \mathcal{S}_{\boldsymbol{x}_0} \times \mathcal{B}(G)$, such that

$$\varphi\left(\hat{\boldsymbol{x}}, \hat{\boldsymbol{\beta}}\right) = \varphi\left(\tilde{\boldsymbol{x}}, \tilde{\boldsymbol{\beta}}\right).$$

Following (53), we derive two reaction rate vectors $\hat{\varphi}$ and $\tilde{\varphi}$ as follows:

$$\varphi\left(\hat{\boldsymbol{x}}, \hat{\boldsymbol{\beta}}\right) := \left(\frac{\hat{\beta}_{\boldsymbol{y}_i \to \boldsymbol{y}_j}}{\hat{\boldsymbol{x}}^{\boldsymbol{y}_i}} \right)_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E}, \text{ and } \varphi\left(\tilde{\boldsymbol{x}}, \tilde{\boldsymbol{\beta}}\right) := \left(\frac{\tilde{\beta}_{\boldsymbol{y}_i \to \boldsymbol{y}_j}}{\tilde{\boldsymbol{x}}^{\boldsymbol{y}_i}} \right)_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \tag{55}$$

From $\varphi(\hat{\boldsymbol{x}}, \hat{\boldsymbol{\beta}}) = \varphi(\tilde{\boldsymbol{x}}, \tilde{\boldsymbol{\beta}})$ and lemma 4.9, the uniqueness on the complex-balanced equilibrium within each affine invariant polyhedron, we obtain $\hat{\boldsymbol{x}} = \tilde{\boldsymbol{x}}$. Then from equation (55), it is clear that $\hat{\boldsymbol{\beta}} = \tilde{\boldsymbol{\beta}}$, and we conclude the injectivity. □

Lemma 4.11. *For any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the map φ^{-1} is well-defined and continuous.*

Proof. Since we have proved that the map φ is bijective in lemma 4.10, it is standard that φ^{-1} is well-defined.

Now we show that φ^{-1} is continuous. From lemma 4.9, given any $(\boldsymbol{x}, \boldsymbol{\beta}) \in \mathcal{S}_{\boldsymbol{x}_0} \times \mathcal{B}(G)$, $\varphi(\boldsymbol{x}, \boldsymbol{\beta})$ forms a complex-balanced rate vector with $\boldsymbol{x}$ being the complex-balanced equilibrium. Since φ is bijective and the complex-balanced equilibrium is unique in $\mathcal{S}_{\boldsymbol{x}_0}$, for any complex-balanced rate vector $\boldsymbol{k} = (k_{\boldsymbol{y}_i \to \boldsymbol{y}_j})_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \in \mathcal{K}(G)$, we have

$$\varphi^{-1}(\boldsymbol{k}) = (\boldsymbol{x}, \boldsymbol{\beta}), \tag{56}$$

such that

$$\boldsymbol{x} = Q_{\boldsymbol{x}_0}(\boldsymbol{k}) \text{ and } \beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j} := k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i}, \text{ with } \boldsymbol{\beta} = \left(\beta_{\boldsymbol{y}_i \to \boldsymbol{y}_j}\right)_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E}. \tag{57}$$

Applying theorem 3.5, we get the map $Q_{\boldsymbol{x}_0}$ is continuous, which says that $\boldsymbol{x}$ depends continuously on $\boldsymbol{k}$. Moreover, every component in $\boldsymbol{\beta}$ can be written as a polynomial of $\boldsymbol{k}$ and $\boldsymbol{x}$. This reveals that $\boldsymbol{\beta}$ also depends continuously on $\boldsymbol{k}$.

After showing that both components in the product space $\mathcal{S}_{\boldsymbol{x}_0} \times \mathcal{B}(G)$ vary continuously in $\boldsymbol{k}$, we conclude the continuity of the map φ^{-1}.

□

Finally, we are able to prove theorem 4.7.

Proof of theorem 4.7. From definition 4.6, it suffices to show that the map φ is a homeomorphism. Applying lemma 4.10, we derive φ as a bijective function. From lemmas 4.9 and 4.11, we show that both φ and φ^{-1} are continuous functions. Therefore, we conclude φ is a homeomorphism, and prove this theorem. Now, to conclude the contractibility of the toric locus, recall that a cartesian product of two convex sets is convex ([6, p 38]) and the fact that convex sets in Euclidean spaces are contractible (see for instance [34]). □

4.3. Connection to deficiency theory

The notion of deficiency of a reaction network or E-graph was introduced by Feinberg and Horn [20, 26]. It is an invariant of the network and plays a key role in the study of complex-balanced equilibria of a network [19, 27].

Definition 4.12 ([19, 43]). Consider an E-graph $G = (V, E)$ with ℓ connected components and m vertices. Let s be the dimension of the stoichiometric subspace $\mathcal{S}$. The **deficiency** of an E-graph G is the non-negative integer

$$\delta := m - \ell - s. \tag{58}$$

Under mass-action kinetics, networks with low deficiency have special dynamical properties. For example, the Deficiency Zero Theorem shows that weakly reversible deficiency zero networks are complex-balanced for any choices of rate constants [20, 26]. In [13], it was shown that given a weakly reversible E-graph G, the set $\mathcal{K}(G)$ is an algebraic variety of codimension δ in $\mathbb{R}^E_{>0}$. In the following, we will recover this result by using the product structure of the toric locus $\mathcal{K}(G)$ from theorem 3.17.

Proposition 4.13. *Consider an E-graph $G = (V, E)$ with ℓ connected components and m vertices. Let s be the dimension of the stoichiometric subspace $\mathcal{S}$, then*

$$\dim(\mathcal{K}(G)) = |E| - m + s + \ell.$$

Proof. Recall that the dimension of a product of topological spaces is a topological invariant and it is given by the sum of the dimensions of the factors [31]. In addition, the dimension of a variety at any regular point is the dimension of its tangent vector space at that point, thus it is the same dimension when seen as a manifold as well as when seen as a variety [29].

From definition 2.8, $\mathcal{S}_{\boldsymbol{x}_0}$ is the intersection of an affine linear subspace with the positive orthant. Moreover, lemma 4.5 shows that $\mathcal{B}(G)$ is an open and convex cone in $\mathbb{R}^E_{>0}$. As both $\mathcal{S}_{\boldsymbol{x}_0}$ and $\mathcal{B}(G)$ are path-connected smooth manifolds, and $\mathcal{K}(G)$ is the product space $\mathcal{S}_{\boldsymbol{x}_0} \times \mathcal{B}(G)$, it follows that $\mathcal{K}(G)$ has the same dimension everywhere. Now using theorem 4.7, we have for any state $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$,

$$\dim(\mathcal{K}(G)) = \dim((\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}) + \dim(\mathcal{B}(G)), \tag{59}$$

and it is clear that $\dim\big((\boldsymbol{x}_0 + \mathcal{S}) \cap \mathbb{R}^n_{>0}\big) = \dim(\mathcal{S}) = s$.

Recall that $\mathcal{B}(G) \subseteq \mathbb{R}^E_{>0}$ represents the set of complex-balanced flux vectors that satisfy (46). Following Kirchhoff junction rules, for each connected component of G with m_i vertices, there are $m_i - 1$ independent conditions among the linear conditions defining $\mathcal{B}(G)$

in (46). Further, we can check that linear conditions are independent when working on different connected components of G. Hence, we get

$$\dim(\mathcal{B}(G)) = |E| - \sum_{i=1}^{l}(m_i - 1) = |E| - m + l.$$

Together with (59), we conclude the proposition. □

The following corollary is a direct consequence of proposition 4.13. It was first proved by a different method in [13].

Corollary 4.14. *Let $G = (V,E)$ be a weakly reversible E-graph. Then the codimension of the toric locus $\mathcal{K}(G) \subseteq \mathbb{R}^E_{>0}$ is δ.*

Proof. From proposition 4.13 and definition 4.12, the codimension on $\mathcal{K}(G)$ follows

$$\mathrm{codim}(\mathcal{K}(G)) = |E| - \dim(\mathcal{K}(G)) = |E| - (|E| - m + s + l) = \delta.$$

□

Example 4.15. Revisit example 2.4, the reaction network G from figure 1 has three vertices $(m = 3)$ and four edges $(|E| = 4)$ in one connected component $(\ell = 1)$. In addition, the dimension of the stoichiometric subspace of the reaction network is two $(s = 2)$. Thus, the deficiency is $\delta = 3 - 1 - 2 = 0$. From proposition 4.13, we obtain that

$$\dim(\mathcal{K}(G)) = |E| - m + s + l = 4 - 3 + 2 + 1 = 4.$$

This shows that the toric locus $\mathcal{K}(G)$ in example 2.4 is the whole positive orthant $\mathbb{R}^4_{>0}$.

4.4. Bijective affine transformations preserve the toric locus

In this subsection we prove that the toric locus is preserved by bijective affine transformations of the network.

Definition 4.16. Consider a network $G = (V,E)$ in $\mathbb{R}^n$. Suppose $T : \mathbb{R}^n \to \mathbb{R}^n$ is a bijective affine transformation. Denote by

$$T(V) := \{T(\boldsymbol{y}) \mid \boldsymbol{y} \in V\}, \text{ and } T(E) := \left\{T(\boldsymbol{y}_i) \to T\left(\boldsymbol{y}_j\right) \mid \boldsymbol{y}_i \to \boldsymbol{y}_j \in E\right\}.$$

Then we call the graph $T(G) := (T(V), T(E))$ the **bijective affine image of G by T**.

Theorem 4.17. *Consider a weakly reversible E-graph G_1. If G_2 is a bijective affine image of the graph G_1, then G_1 and G_2 have the same toric locus, i.e. $\mathcal{K}(G_1) = \mathcal{K}(G_2)$.*

Proof. The result follows from proposition 3.9 that the polynomial equations characterizing the parameter values $\boldsymbol{k} \in \mathcal{K}(G_1)$ are identical to those for $\boldsymbol{k} \in \mathcal{K}(G_2)$. As discussed in [13], these polynomial equations can be reformulated as binomial equations in terms of a variable vector $\boldsymbol{K} = (K_i)_{1 \leqslant i \leqslant m} \in \mathbb{R}^m_{>0}$, where $\boldsymbol{K}$ is obtained from the matrix-tree theorem (see notation 3.7), i.e. by summing over spanning $\boldsymbol{y}_i$-trees in the graph. Special cases of this have been demonstrated in examples 2.17 and 3.10.

Since the graphs G_1 and G_2 are bijective affine images of each other, they share the same spanning $\boldsymbol{y}_i$-trees and therefore the same parameters $\boldsymbol{K}$. Moreover, G_1 and G_2 produce the same binomial equations for the variable vector $\boldsymbol{K}$, because these binomial equations are given by linear relationships between the vertex points of the graph, as explained in [13, theorem 9]. This implies the desired result. □

As a consequence of this theorem, we can conclude that any complete graph with exactly three collinear vertices, where the middle vertex is positioned halfway between the other two vertices, must have its torus locus given by equation (28). Similarly, any two reversible networks that are rectangle-shaped (or even parallelogram-shaped) share the same toric locus. This fact can be useful for analyzing the *disguised toric locus* of an E-graph G, i.e. the set of parameter values $\boldsymbol{k}$ for which the corresponding mass-action system $(G, \boldsymbol{k})$ can be realized as complex-balanced via dynamical equivalence; see [15, 36], and especially [24].

5. Discussion and future work

There has been strong interest in the study of the toric locus of a reaction network, i.e. the set of parameters for the network that give rise to complex-balanced dynamical systems. This interest is due to the very stable dynamical behavior of these systems; for instance, the complex-balanced equilibria are known to have unique positive equilibria that are *locally asymptotically stable* within each invariant polyhedron.

Since important properties of complex-balanced dynamical systems can be analyzed using Nonlinear Algebra tools (see for example [7, chapter 6]), the authors of [13] called these systems *toric dynamical systems* (see also [10, chapter 5]). Indeed, not only the toric locus of a reaction network is a toric variety, but also the steady-state locus (i.e. the fixed points) of toric dynamical systems can be described by binomial equations; see [21]. Another computational advantage of this fact is that one may describe the equilibria of such a system in terms of monomial parametrizations (see [1]). The fruitful combinatorial and computational properties of binomial ideals are well-known and they are desirable in applications, since toric algebraic varieties are well-understood.

In this paper we prove that, given a mass-action system and positive initial data, the positive complex-balanced equilibria vary continuously in function of the parameters that give a complex-balanced system. Next, using this result, we show that the toric locus is connected and we reveal an explicit product structure of the toric locus. Namely, we prove that there exists a homeomorphism between the toric locus and the product of the set of complex-balanced flux vectors and the affine invariant polyhedron. Also, we provide an explicit parametrization of the toric locus of a reaction network, in terms of its invariant polyhedron and its set of complex-balanced fluxes, as shown in (53).

In future work [14], we will use some of the approaches developed here to show that the positive complex-balanced equilibria of a complex-balanced mass-action system actually depend *smoothly* on the reaction rate constants and the initial data. Furthermore, the approach used here in order to construct this homeomorphism will allow us to derive additional regularity properties of the toric variety $\mathcal{K}(G)$.

Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

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