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RESEARCH

Weakly reversible single linkage class realizations of polynomial dynamical systems: an algorithmic perspective

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Abstract

Systems of differential equations with polynomial right-hand sides are very common in applications. In particular, when restricted to the positive orthant, they appear naturally (according to the law of *mass-action kinetics*) in ecology, population dynamics, as models of biochemical interaction networks, and models of the spread of infectious diseases. Their mathematical analysis is very challenging in general; in particular, it is very difficult to answer questions about the long-term dynamics of the variables (species) in the model, such as questions about persistence and extinction. Even if we restrict our attention to mass-action systems, these questions still remain challenging. On the other hand, if a polynomial dynamical system has a *weakly reversible single linkage class* (WR^1) *realization*, then its long-term dynamics is known to be remarkably robust: all the variables are persistent (i.e., no species goes extinct), irrespective of the values of the parameters in the model. Here we describe an algorithm for finding WR^1 realizations of polynomial dynamical systems, whenever such realizations exist.

Keywords Weakly reversible · Single linkage class · Realization

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1 Introduction

By a system of differential equations with polynomial right-hand sides (or simply a *polynomial dynamical system*), we mean a dynamical system of the form

$$\begin{aligned}
\frac{dx_1}{dt} &= p_1(x_1, \ldots, x_n),\\
\frac{dx_2}{dt} &= p_2(x_1, \ldots, x_n),\\
&\vdots\\
\frac{dx_n}{dt} &= p_n(x_1, \ldots, x_n),
\end{aligned} \tag{1}$$

where each $p_i(x_1, \ldots, x_n)$ is a polynomial in the variables $x_1, \ldots, x_n$. In general, such systems are very difficult to analyze due to nonlinearities and feedbacks that may give rise to bifurcations, multiple basins of attraction, oscillations, and even chaotic dynamics. The second part of Hilbert's 16th problem (about the number of limit cycles of polynomial dynamical systems in the plane) is still essentially unsolved, even for *quadratic* polynomials [1]. Even the simplest object associated to (1), its steady state set, can give rise to highly nontrivial questions in real algebraic geometry.

Polynomial dynamical systems show up very often as standard models (based on *mass-action kinetics*) in biology, chemistry, population dynamics, infectious disease models, and many other areas of applications. In such models the variables x_i represent populations, concentrations, or other quantities that *cannot become negative, and the domain of* (1) *is restricted to the positive orthant*. For example, in a biochemical network we may have the reaction $X_1 + X_2 \to X_3$, which consumes X_1 and X_2 and produces X_3; according to mass-action kinetics, this reaction contributes a negative monomial term of the form "$-kx_1x_2$" on the right-hand side of $\frac{dx_1}{dt}$ and $\frac{dx_2}{dt}$, and a positive monomial term "kx_1x_2" on the right-hand side of $\frac{dx_3}{dt}$, where x_1, x_2, x_3 denote the concentrations of the chemical species X_1, X_2, X_3. The parameter k is called *reaction rate constant*. A *reaction network* consists of a set of such reactions, and if we add all these terms for all the reactions in the network (each one with its own reaction rate constant) we obtain standard dynamical system models for the network. In general, one cannot just rely on numerical simulations to deduce the dynamical properties of these models, because the values of the reaction rate constants cannot usually be estimated accurately. Therefore, it becomes very important to relate the *structural properties* of the reaction network with *dynamical properties* that can be generated by it [2–9].

Alternatively, one may start with a system of the form (1) obtained from fitting some experimental data, with little or no information on the generating reaction network. In general, if a polynomial dynamical system is generated by some reaction network, then there are actually infinitely many other networks that also generate it [4]. This *lack of unique identifiability* of an underlying network can actually be leveraged to analyze the dynamics of a system of the form (1): if a network with certain properties can be found to generate it, then we may be able to immediately infer information about its dynamic behavior [2, 7].

Some of the most important questions for polynomial systems (1) are related to the *long-term dynamics* of its solutions, which is usually analyzed in terms of the mathematical properties of *persistence* and *permanence*. The property of *persistence* means that no species can "go extinct", i.e., for any solution $\boldsymbol{x}(t)$ of the system, we have $\liminf_{t\to\infty}\boldsymbol{x}_i(t) > 0$ for all species i. The (stronger) property of *permanence* means that the system has a globally attracting compact set.

A class of networks whose long-term dynamics is best understood is the family of *weakly reversible single linkage class networks* [2]; here we call them simply "WR^1 *networks*", and we will refer to polynomial systems (1) that have WR^1 realizations as " WR^1 *systems*". Specifically, WR^1 systems have been shown to be persistent and permanent in a very robust way, which even allows for the explicit construction of globally attracting invariant sets [6, 10]. Moreover, complex-balanced WR^1 systems have been shown to be *globally stable*, i.e., they have a *globally attracting point* within each linear invariant subspace [11].

The notion of *deficiency* also plays an important role in the analysis of reaction networks. In particular, weakly reversible networks having low deficiency (0 or 1) have many robust dynamical properties like the existence of a globally attracting steady state or the existence of a Lyapunov function and are related to the *Deficiency One Theorem* [9]. We will expand upon this in the later sections of our paper.

Not only are the long-term dynamical properties of WR^1 systems well understood, but also their persistence and permanence properties hold *for any choices of parameter values*, in a sense that will be made clear below. This fact is very important in applications because the exact values of the coefficients in the polynomial right-hand sides of these dynamical systems are often very difficult to estimate accurately.

In this paper, we describe an efficient algorithm for determining whether a given polynomial dynamical system[1] (1) admits a WR^1 realization, and for finding such a realization whenever it exists.

A motivation for finding such an algorithm comes from biological models, such as repressilator networks [12, 13]. One example of dynamics corresponding to such networks is given by

$$\begin{aligned} \frac{dx}{dt} &= 7 - 3x + 5z - 2xz, \\ \frac{dy}{dt} &= 6 + 3x - 4y - 3xy, \\ \frac{dz}{dt} &= 7 + 4y - 3z - 3yz. \end{aligned} \tag{2}$$

Here x denotes the concentration of mRNA, y denotes the concentration of a repressor protein and z denotes the concentration of the product. *A question we answer here is: do there exist any WR^1 realizations that generate these differential equations?* Our

[1] All the results in this paper apply without change to the case where the functions on the right-hand side of (1) are "generalized polynomials", where the exponents of the monomials are allowed to take on any real values, i.e., they are *not* restricted to nonnegative integers.

Algorithm 1 asserts that such realizations do exist; in particular, our algorithm *finds* the maximal WR^1 realization (see Definitions 2.15 and 2.16), which is given by the following reaction network:

$$\begin{aligned}
&\emptyset \underset{2}{\overset{3}{\rightleftharpoons}} X \\
&\emptyset \underset{1}{\overset{3}{\rightleftharpoons}} Y \\
&\emptyset \underset{1}{\overset{2}{\rightleftharpoons}} Z \\
&\emptyset \xrightarrow{1} X + Y \\
&\emptyset \xrightarrow{2} Y + Z \\
&\emptyset \xrightarrow{3} X + Z \\
&X \underset{3}{\overset{2}{\rightleftharpoons}} X + Y \\
&Y \underset{3}{\overset{1}{\rightleftharpoons}} Y + Z \\
&Z \underset{2}{\overset{3}{\rightleftharpoons}} X + Z \\
&X \xrightarrow{1} Y \\
&Y \xrightarrow{3} Z \\
&Z \xrightarrow{2} X
\end{aligned} \tag{3}$$

The dynamical system (2) is a relatively simple example, for which maybe a WR^1 realization could be found “by hand”, by relying on geometric considerations in $\mathbb{R}^3$. In higher dimensions, it is much more difficult to find such realizations by hand, due to a lack of geometric intuition. As a consequence, there is a need for an algorithm that finds WR^1 realizations whenever they exist.

Structure of the paper. In Sect. 2, we introduce some basic terminology of reaction networks. Primarily, we present the notion of *net reaction vectors*, which play a key role in the main algorithm. In Sect. 3, we propose Algorithm 1 to find if there exists a weakly reversible reaction network consisting of a single connected component that generates a given dynamical system. In Sect. 4, we discuss some special cases of weakly reversible realizations with a single linkage class and go through the steps in Algorithm 1 using several examples. Moreover, we illustrate how to implement this algorithm in practice. In Sect. 5, we summarize our findings in this paper and outline directions for future work.

Notation. We denote by $\mathbb{R}^n_{\geq 0}$ and $\mathbb{R}^n_{>0}$ the set of vectors in $\mathbb{R}^n$ with non-negative and positive entries respectively. Given two vectors $\boldsymbol{x} \in \mathbb{R}^n_{>0}$ and $\boldsymbol{y} \in \mathbb{R}^n$, we use the following notation for a monomial with exponents given by $\boldsymbol{y}$:

$$\boldsymbol{x}^{\boldsymbol{y}} = x_1^{y_1} \dots x_n^{y_n},$$

where $\boldsymbol{x} = (x_1, \dots, x_n)^\intercal$ and $\boldsymbol{y} = (y_1, \dots, y_n)^\intercal$.

2 Reaction networks

Definition 2.1 A **reaction network**, also called a **Euclidean embedded graph** (or simply **E-graph**), is a directed graph $G = (V, E)$ in $\mathbb{R}^n$, where $V \subset \mathbb{R}^n$ is a finite set of **vertices**, $E \subseteq V \times V$ represents the set of **edges**, and such that there are neither self-loops nor isolated vertices in G. We denote the number of vertices by m, and let $V = \{\boldsymbol{y}_1, \dots, \boldsymbol{y}_m\}$. A directed edge $(\boldsymbol{y}_i, \boldsymbol{y}_j) \in E$ represents a **reaction** in the network, and is also denoted by $\boldsymbol{y}_i \to \boldsymbol{y}_j$. Moreover, we define the **reaction vector** of the edge $\boldsymbol{y}_i \to \boldsymbol{y}_j$ as $\boldsymbol{y}_j - \boldsymbol{y}_i \in \mathbb{R}^n$. Here $\boldsymbol{y}_i$ and $\boldsymbol{y}_j$ denote the **source vertex** and **target vertex**, respectively.

Definition 2.2 Let $G = (V, E)$ be a Euclidean embedded graph. The **stoichiometric subspace** of G is the vector space spanned by the reaction vectors as follows:

$$S = \text{span}\{\boldsymbol{y}' - \boldsymbol{y} \mid \boldsymbol{y} \to \boldsymbol{y}' \in \text{E}\}.$$

Moreover, for any positive vector $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the affine polyhedron $(\boldsymbol{x}_0 + S) \cap \mathbb{R}^n_{>0}$ is called the **stoichiometric compatibility class** of $\boldsymbol{x}_0$.

Definition 2.3 Let $G = (V, E)$ be a Euclidean embedded graph.

(a) The set of vertices V is partitioned by its **connected components** (also called **linkage classes**), which correspond to the subset of vertices belonging to that connected component.
(b) A connected component $L \subseteq V$ is **strongly connected**, if every edge is part of an oriented cycle. Further, a strongly connected component $L \subseteq V$ is called a **terminal strongly connected component** if for every vertex $\boldsymbol{y} \in L$ and $\boldsymbol{y} \to \boldsymbol{y}' \in E$, we have $\boldsymbol{y}' \in L$.
(c) $G = (V, E)$ is said to be **weakly reversible**, if every connected component is strongly connected, i.e., every edge is part of an oriented cycle.

Remark 2.4 For a weakly reversible reaction network $G = (V, E)$, every vertex $\boldsymbol{y} \in V$ is a source and a target vertex. Furthermore, every linkage class is a strong linkage class, as well as a terminal strong linkage class.

Definition 2.5 Let $G = (V, E)$ be a Euclidean embedded graph, with m vertices and ℓ connected components. Suppose the dimension of the stoichiometric subspace S is $s = \dim(S)$, then the **deficiency** of the network G is the non-negative integer defined as follows:

$$\delta = m - \ell - s.$$

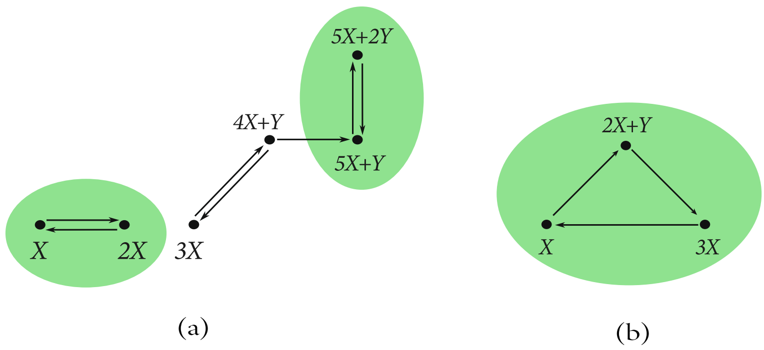


Fig. 1 **a** This reaction network has two linkage classes, and two terminal strongly connected components (shown in the green shaded region). It has a stoichiometric subspace of dimension 2 and the deficiency $\delta = m - \ell - s = 6 - 2 - 2 = 2$. **b** This reaction network is weakly reversible and has one terminal strongly connected component. It has a stoichiometric subspace of dimension 2 and the deficiency $\delta = m - \ell - s = 3 - 1 - 2 = 0$ (color figure online)

Remark 2.6 Note that weakly reversible networks with low deficiencies have many robust dynamical properties like the existence of a globally attracting steady state or the existence of a Lyapunov function or the Deficiency One Theorem [9]. More details will be discussed in Sect. 4.

Figure 1 shows two examples of reaction networks. A reaction network can generate a wide range of dynamical systems. We are interested in mass-action kinetics, which has been extensively studied in [2, 8, 14–17].

Definition 2.7 Let $G = (V, E)$ be a Euclidean embedded graph, we denote the **vector of reaction rate constants** by $\boldsymbol{k} = (k_{\boldsymbol{y}_i \to \boldsymbol{y}_j})_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} \in \mathbb{R}^E_{>0}$, and $k_{\boldsymbol{y}_i \to \boldsymbol{y}_j}$ or k_{ij} is called the **reaction rate constant** on the edge $\boldsymbol{y}_i \to \boldsymbol{y}_j$. The **mass-action system** generated by $(G, \boldsymbol{k})$ is a dynamical system on $\mathbb{R}^n_{>0}$ given by:

$$\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{x}^{\boldsymbol{y}_i} (\boldsymbol{y}_j - \boldsymbol{y}_i). \tag{4}$$

Remark 2.8 As we pointed out in the introduction, in this paper we do *not* restrict the monomial exponents $\boldsymbol{y}_1, \boldsymbol{y}_2, \ldots, \boldsymbol{y}_m$ to be either nonnegative or integer (i.e., they are allowed to be arbitrary vectors $\boldsymbol{y}_j \in \mathbb{R}^n$). Therefore, the notion of "mass-action system" defined above is more general than the *classical* notion of mass-action systems, where $\boldsymbol{y}_j \in \mathbb{Z}^n_{\geq 0}$ for all j (see for example [9]).

In particular, note that *all polynomial (or generalized polynomial) systems of the form* (1) *can be written in the form of* (4), while *not all* dynamical systems with polynomial right-hand side can be realized using *classical* mass-action kinetics. Specifically, a polynomial dynamical system (1) can be generated by *classical* mass-action kinetics if and only if every monomial with negative coefficient in $p_i(\boldsymbol{x})$ is divisible by $\boldsymbol{x}_i$ for all $i \in \{1, 2, \ldots, n\}$ [9, 18].

Remark 2.9 Recall that for classical mass-action systems the positive orthant $\mathbb{R}^n_{>0}$ *is a forward invariant set* [9]. This is of course not true for general polynomial dynamical systems. But, if a polynomial dynamical system (or a generalized polynomial dynamical system) has a WR^1 realization, then this system is *also* guaranteed to have the positive orthant as a forward invariant set, because it is *permanent* [6, 10].

Definition 2.10 Consider the mass-action system generated by $(G, \boldsymbol{k})$ in (4). A point $\boldsymbol{x}^* \in \mathbb{R}^n_{>0}$ is called a **positive steady state** if

$$\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t}\bigg|_{\boldsymbol{x}=\boldsymbol{x}^*} = \sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} (\boldsymbol{x}^*)^{\boldsymbol{y}_i} (\boldsymbol{y}_j - \boldsymbol{y}_i) = \boldsymbol{0}. \tag{5}$$

Definition 2.11 Consider the mass-action system generated by $(G, \boldsymbol{k})$ in (4). Then $(G, \boldsymbol{k})$ is said to be **complex-balanced**, if there exists a positive steady state $\boldsymbol{x}_0$ such that the following holds for every vertex $\boldsymbol{y}_0 \in V$,

$$\sum_{\boldsymbol{y}_0 \to \boldsymbol{y} \in E} k_{\boldsymbol{y}_0 \to \boldsymbol{y}} \boldsymbol{x}_0^{\boldsymbol{y}_0} = \sum_{\boldsymbol{y}' \to \boldsymbol{y}_0 \in E} k_{\boldsymbol{y}' \to \boldsymbol{y}_0} \boldsymbol{x}_0^{\boldsymbol{y}'}. \tag{6}$$

It is well known that every mass-action system admits a matrix decomposition [19]. Hence, we can illustrate the mass-action system (4) in the following vectorial representation:

$$\frac{d\boldsymbol{x}}{dt} = \boldsymbol{Y} \boldsymbol{A}_{\boldsymbol{k}} \boldsymbol{x}^{\boldsymbol{Y}}, \tag{7}$$

where $\boldsymbol{Y}$ is a matrix whose columns are the vertices, defined as

$$\boldsymbol{Y} = (\boldsymbol{y}_1,\ \boldsymbol{y}_2,\ \ldots,\ \boldsymbol{y}_m),$$

and $\boldsymbol{A}_{\boldsymbol{k}}$ is the negative transpose of the graph Laplacian of $(G, \boldsymbol{k})$, defined as

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

and $\boldsymbol{x}^{\boldsymbol{Y}}$ is the vector of monomials given by

$$\boldsymbol{x}^{\boldsymbol{Y}} = (\boldsymbol{x}^{\boldsymbol{y}_1}, \boldsymbol{x}^{\boldsymbol{y}_2}, \ldots, \boldsymbol{x}^{\boldsymbol{y}_m})^\intercal.$$

In general, $\boldsymbol{Y}$ is called the **matrix of vertices**, and $\boldsymbol{A}_{\boldsymbol{k}}$ is called the **Kirchoff** matrix.

Here, we list one of the most important properties of the Kirchoff matrix $\boldsymbol{A}_{\boldsymbol{k}}$.

Theorem 2.12 [20] *Let* $(G, \boldsymbol{k})$ *be a mass-action system, and* $T_1, T_2, \ldots, T_t$ *be the terminal strongly connected components of* G. *Then there exists a basis* $\{\boldsymbol{e}_1, \boldsymbol{e}_2, \ldots, \boldsymbol{e}_t\}$ *for* $\ker(\boldsymbol{A}_{\boldsymbol{k}})$, *such that for* $1 \le p \le t$,

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

Example 2.13 We will revisit the network shown in Fig. 1a to verify Theorem 2.12. First, we set all vertices in the network as follows:

$$X \equiv \boldsymbol{y}_1 = (1, 0)^\intercal, \;\; 2X \equiv \boldsymbol{y}_2 = (2, 0)^\intercal, \;\; 3X \equiv \boldsymbol{y}_3 = (3, 0)^\intercal,$$
$$4X + Y \equiv \;\boldsymbol{y}_4 = (4, 1)^\intercal, \;\; 5X + Y \equiv \boldsymbol{y}_5 = (5, 1)^\intercal, \;\; 5X + 2Y \equiv \boldsymbol{y}_6 = (5, 2)^\intercal.$$

The Kirchoff matrix of the network is given by:

$$\boldsymbol{A_k} = \begin{bmatrix} -k_{12} & k_{21} & 0 & 0 & 0 & 0 \\ k_{12} & -k_{21} & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_{34} & k_{43} & 0 & 0 \\ 0 & 0 & k_{34} & -k_{43} - k_{45} & 0 & 0 \\ 0 & 0 & 0 & k_{45} & -k_{56} & k_{65} \\ 0 & 0 & 0 & 0 & k_{56} & -k_{65} \end{bmatrix}.$$

Using a direct computation, the following vectors form a basis for $\ker(\boldsymbol{A_k})$:

$$\boldsymbol{e}_1 = (k_{21}, k_{12}, 0, 0, 0, 0)^\intercal, \;\; \boldsymbol{e}_2 = (0, 0, 0, 0, k_{65}, k_{56})^\intercal.$$

Thus, the supports of these vectors are

$$\operatorname{supp}(\boldsymbol{e}_1) = \{1, 2\}, \text{ and } \operatorname{supp}(\boldsymbol{e}_2) = \{5, 6\}.$$

The supports of two basis vectors relate to two terminal strongly connected components $\{X, 2X\}$ and $\{5X + Y, 5X + 2Y\}$.

Motivated by the matrix decomposition in (7), we introduce a crucial concept: net reaction vector, and another matrix decomposition in terms of net reaction vectors, which play an important role in finding a realization.

Definition 2.14 Consider a mass-action system $(G, \boldsymbol{k})$, and let $V_S = \{\boldsymbol{y}_1, \boldsymbol{y}_2, \ldots, \boldsymbol{y}_{m_s}\} \subseteq V$ be the set of source vertices of G. For each source vertex $\boldsymbol{y}_i \in V_S$, the **net reaction vector** $\boldsymbol{w}_i$ corresponding to $\boldsymbol{y}_i$ is given by:

$$\boldsymbol{w}_i = \sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} (\boldsymbol{y}_j - \boldsymbol{y}_i), \tag{8}$$

Moreover, we denote the **matrix of net reaction vectors** as follows:

$$\boldsymbol{W} = \left(\boldsymbol{w}_1, \; \boldsymbol{w}_2, \; \ldots, \; \boldsymbol{w}_{m_s}\right). \tag{9}$$

Following Definition 2.14, for each source vertex $\boldsymbol{y}_i \in V_S$, we can rewrite the corresponding net reaction vector $\boldsymbol{w}_i$ as

$$\boldsymbol{w}_i = \sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \boldsymbol{y}_j - \left(\sum_{\boldsymbol{y}_i \to \boldsymbol{y}_j \in E} k_{\boldsymbol{y}_i \to \boldsymbol{y}_j} \right) \boldsymbol{y}_i. \tag{10}$$

Using a direct computation, we can rewrite the matrix decomposition in (7) as

$$\frac{d\boldsymbol{x}}{dt} = \boldsymbol{W}\boldsymbol{x}^{\boldsymbol{Y}_s}, \tag{11}$$

where $\boldsymbol{x}^{\boldsymbol{Y}_s}$ is the vector of monomials given by

$$\boldsymbol{x}^{\boldsymbol{Y}_s} = (\boldsymbol{x}^{\boldsymbol{y}_1}, \boldsymbol{x}^{\boldsymbol{y}_2}, \ldots, \boldsymbol{x}^{\boldsymbol{y}_{m_s}})^\intercal.$$

Further, we let $\boldsymbol{Y}_s = (\boldsymbol{y}_1, \ \boldsymbol{y}_2, \ \ldots, \ \boldsymbol{y}_{m_s})$ denote the **matrix of source vertices**, whose columns are the source vertices.

Definition 2.15 Consider a dynamical system given by Eq. (1). If there exists an E-graph G and a vector of rate constants $\boldsymbol{k}$, such that the mass-action system generated by $(G, \boldsymbol{k})$ is exactly given by Eq. (1), then $(G, \boldsymbol{k})$ is said to be a **mass-action realization** (or simply a **realization**) of Eq. (1).

Definition 2.16 Consider a fixed set of vertices V and all possible E-graphs of the form $G = (V, E)$. A realization $(G, \boldsymbol{k})$ of the dynamical system given by Eq. (1) is said to be a **maximal realization with the set of vertices** V (or simply a **maximal realization**) if it contains a maximal set of reactions among all realizations with the set of vertices V of that dynamical system.

Remark 2.17 Note that for a system given by Eq. (1), any *positive convex combination* of different realizations $(G_i, \boldsymbol{k}_i)$ for some E-graphs $G_i = (V, E_i)$ is *also* a realization with the set of vertices V, and its set of reactions is the union of E_i. Therefore, if a system given by Eq. (1) admits some realizations with the set of vertices V, then a maximal realization with the set of vertices V must exist, and its corresponding *set of edges E is unique*.

The following Lemma concerns the matrix of net reaction vectors when the mass-action system is weakly reversible.

Lemma 2.18 *Consider a weakly reversible mass-action system generated by $(G, \boldsymbol{k})$ with vertices $\{\boldsymbol{y}_i\}_{i=1}^m$ and stoichiometric subspace S. Let $\{\boldsymbol{w}_i\}_{i=1}^m$ be the net reaction vectors of G, and $\boldsymbol{W} = (\boldsymbol{w}_1, \boldsymbol{w}_2, \ldots, \boldsymbol{w}_m)$ be the matrix of net reaction vectors. Then we have*

$$\mathrm{Im}(\boldsymbol{W}) = S. \tag{12}$$

Proof It is clear that $\mathrm{Im}(\boldsymbol{W}) \subseteq S$ from Definition 2.14. Suppose that $\mathrm{Im}(\boldsymbol{W}) \subset S$, then there exists a non-zero vector $\boldsymbol{v}$, such that

$$\boldsymbol{v} \in S, \ \text{and} \ \ \boldsymbol{v} \perp \boldsymbol{W}.$$

Since $\boldsymbol{0} \neq \boldsymbol{v} \in S$, there exists a reaction $\boldsymbol{y}_i \to \boldsymbol{y}_j \in E$ such that $\boldsymbol{v} \cdot (\boldsymbol{y}_j - \boldsymbol{y}_i) \neq 0$. This implies that the set $\{\boldsymbol{v} \cdot \boldsymbol{y}_i\}_{i=1}^m$ has at least two different numbers. Now let $V_{\max}$ be the subset of vertices which maximizes the dot product as follows.

$$V_{\max} = \{\boldsymbol{y}_i \in V : \boldsymbol{v} \cdot \boldsymbol{y}_i = \max_j(\boldsymbol{v} \cdot \boldsymbol{y}_j)\}.$$

Since G is weakly reversible, there exists an edge from a vertex in $V_{\max}$ to a vertex not belonging to it. Without loss of generality, let $\boldsymbol{y}_1 \in V_{\max}$, $\boldsymbol{y}_2 \notin V_{\max}$ and $\boldsymbol{y}_1 \to \boldsymbol{y}_2$ be this edge. Note that for all $i = 1, 2, \ldots, m$, we have $\boldsymbol{v} \cdot (\boldsymbol{y}_i - \boldsymbol{y}_1) \leq 0$. Thus, we obtain

$$\boldsymbol{v} \cdot \boldsymbol{w}_1 = \sum_{\boldsymbol{y}_j \in V} k_{\boldsymbol{y}_1 \to \boldsymbol{y}_j} \boldsymbol{v} \cdot (\boldsymbol{y}_j - \boldsymbol{y}_1) \leq k_{\boldsymbol{y}_1 \to \boldsymbol{y}_2} \boldsymbol{v} \cdot (\boldsymbol{y}_2 - \boldsymbol{y}_1) < 0.$$

This contradicts with $\boldsymbol{v} \perp \boldsymbol{W}$, and the result follows. □

At the end of this section, we introduce some important dynamical properties.

Definition 2.19 Consider a mass-action system generated by $(G, \boldsymbol{k})$. This system is said to be **persistent**, if every solution $\boldsymbol{x}(t)$ with initial condition $\boldsymbol{x}(0) \in \mathbb{R}^n_{>0}$ satisfies

$$\liminf_{t \to \infty} x_i(t) > 0, \ \text{ for } i = 1, 2, \ldots, n.$$

Definition 2.20 Consider a mass-action system generated by $(G, \boldsymbol{k})$. This system is said to be **permanent**, if given any stoichiometric compatibility class A there exists a compact subset $D \subset A$, such that for any solution $\boldsymbol{x}(t)$ with initial condition $\boldsymbol{x}(0) \in A$, there exists a time T such that

$$\boldsymbol{x}(t) \in D, \ \text{ for all } t > T.$$

Definition 2.21 Consider a mass-action system generated by $(G, \boldsymbol{k})$. A point $\tilde{\boldsymbol{x}} \in \mathbb{R}^n_{>0}$ is said to be a **global attractor** within its stoichiometric compatibility class A, if for any solution $\boldsymbol{x}(t)$ with initial condition $\boldsymbol{x}(0) \in A$ we have

$$\lim_{t \to \infty} \boldsymbol{x}(t) = \tilde{\boldsymbol{x}}.$$

It is known that weakly reversible dynamical systems consisting of a single linkage class are permanent; moreover, complex-balanced systems consisting of a single linkage class have a globally attracting point within every stoichiometric compatibility class [6, 10].

3 Main result

The goal of this section is to present the main algorithm of this paper, Algorithm 1, which searches for the existence of a weakly reversible realization consisting of a single linkage class. In particular, this algorithm outputs a maximal realization, whenever it exists.

3.1 Algorithm for a weakly reversible realization with a single linkage class

Here, we sketch the key idea behind Algorithm 1: if for a dynamical system of the form (1) there exists some weakly reversible realization with a single linkage class, denoted $G = (V, E)$, *then its maximal realization with vertex set V is guaranteed to be weakly reversible and has a single linkage class.* Therefore, an algorithm that relies on *maximal* realizations can be used when looking for WR^1 realizations. We present such an algorithm below and then give proof of its correctness (Fig. 2).

Algorithm 1 (Check the existence of a weakly reversible realization with a single linkage class)

Input: A dynamical system of the form $\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum\limits_{i=1}^{m} \boldsymbol{x}^{\boldsymbol{y}_i} \boldsymbol{w}_i$, which is specified by two matrices: $\boldsymbol{Y}_s = (\boldsymbol{y}_1, \ldots, \boldsymbol{y}_m)$, and $\boldsymbol{W} = (\boldsymbol{w}_1, \ldots, \boldsymbol{w}_m)$.

Output: Either return a weakly reversible realization consisting of a single linkage class, or print that such a realization does not exist.

for $i = 1, 2, \ldots, m$ **do**
  Define the matrix $\boldsymbol{B}_i \in \mathbb{R}_{n \times m}$, with k^{th} column $B_{i,k} := (\boldsymbol{y}_k - \boldsymbol{y}_i)$ for $1 \le k \le m$.
  if there exists a vector $\boldsymbol{v}^* = (\boldsymbol{v}_1^*, \ldots, \boldsymbol{v}_m^*) \in \mathbb{R}^m_{\ge 0}$, such that $\boldsymbol{B}_i \boldsymbol{v}^* = \boldsymbol{w}_i$ **then**
    Set $\boldsymbol{v}_i^* = 1$.
  else
    Print: There is no WR^1 realization. **Exit.**
  end if
  Set $S_i = \mathrm{supp}(\boldsymbol{v}^*)$.
  for $j = 1, 2, \ldots, m$ **do**
    if $j \in S_i$ **then**
      Continue
    else
      if there exists a vector $\boldsymbol{v} \in \mathbb{R}^m_{\ge 0}$, such that $\boldsymbol{B}_i \boldsymbol{v} = \boldsymbol{w}_i$ and $\boldsymbol{v}_j > 0$ **then**
        $S_i = S_i \cup \mathrm{supp}(\boldsymbol{v})$.
      end if
    end if
  end for
end for
Define vector $r_i := (r_{i,1}, r_{i,1}, \cdots, r_{i,m})^{\intercal}$, with

$$r_{i,j} = \begin{cases} 1, & \text{for } j \in S_i,\, j \neq i, \\ 0, & \text{for } j \notin S_i, \\ -\sum\limits_{l \neq i} r_{i,l}, & \text{for } j = i. \end{cases} \tag{13}$$

Collect the vectors $\{r_i\}_{i=1}^m$ and construct the Kirchoff matrix $Q = (r_1, r_2, \ldots, r_m) \in \mathbb{R}_{m \times m}$.
if $\dim(\ker(Q)) = 1$ and $\mathrm{supp}(\ker(Q)) = \{1, \ldots, m\}$ **then**
  Print: There exists a weakly reversible realization with a single linkage class.
  Print: The vertices of this realization are given by $V = \{\boldsymbol{y}_1, \ldots, \boldsymbol{y}_m\}$.
  Print: The edges of this realization are given by $E = \{\boldsymbol{y}_i \to \boldsymbol{y}_j : r_{i,j} > 0\}$.
else
  Print: There is no WR^1 realization.
end if

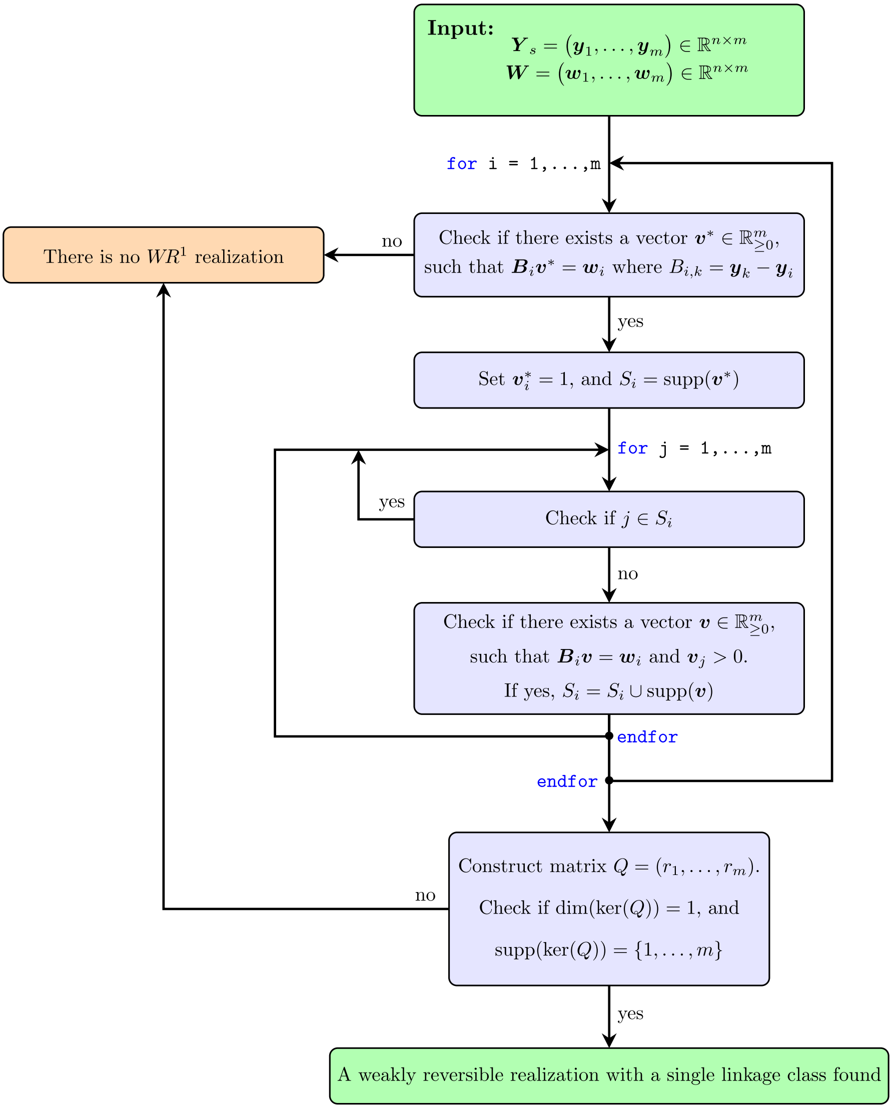


Fig. 2 A flowchart diagram for Algorithm 1. Given a dynamical system of the form $\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum_{i=1}^m \boldsymbol{x}^{\boldsymbol{y}_i}\boldsymbol{w}_i$, this algorithm either finds a WR^1 realization for it, or reports that no such realization exists

We show the correctness of Algorithm 1 via the following two Lemmas.

Lemma 3.1 *Suppose Algorithm 1 reaches line 21 and satisfies the conditions on line 21. Then there exists a weakly reversible realization consisting of a single linkage class that generates the dynamical system* $\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum_{i=1}^{m} \boldsymbol{x}^{\boldsymbol{y}_i}\boldsymbol{w}_i$.

Proof If the algorithm passes the condition on line 3 for all $i = 1, \dots, m$, then all net reaction vectors $\{\boldsymbol{w}_i\}_{i=1}^m$ can be realized by conical combinations of the vectors $B_{i,k} = (\boldsymbol{y}_k - \boldsymbol{y}_i)$, with $1 \le k \le m$.

For $i = 1, \dots, m$, we denote S_i by the union of supports on some vectors $\boldsymbol{v} \in \mathbb{R}^m_{\ge 0}$, such that

$$\boldsymbol{B}_i \boldsymbol{v} = \boldsymbol{w}_i. \tag{14}$$

Suppose there exist a_i distinct vectors $\boldsymbol{v}^1, \dots, \boldsymbol{v}^{a_i} \in \mathbb{R}^m_{\ge 0}$, with $S_i = \bigcup_{q=1}^{a_i} \operatorname{supp}(\boldsymbol{v}^q)$. Then we consider the following vector:

$$\tilde{\boldsymbol{v}} = \frac{1}{a_i} \sum_{q=1}^{a_i} \boldsymbol{v}^q, \tag{15}$$

and it satisfies

$$\boldsymbol{B}_i \tilde{\boldsymbol{v}} = \boldsymbol{w}_i, \text{ and } \tilde{\boldsymbol{v}} \in \mathbb{R}^m_{\ge 0}.$$

Recall that each $\boldsymbol{v}^i$ represents one realization corresponding to the net reaction vector $\boldsymbol{w}_i$. Here we choose the vector $\tilde{\boldsymbol{v}}$ in (15), where we have weighted all vectors $\{\boldsymbol{v}^q\}_{q=1}^{a_i}$ equally in the graph. Hence, it is clear that the reaction $\boldsymbol{y}_i \to \boldsymbol{y}_j$ represented by $j \in S_i$ is included in the realization. Further, we note that scaling the reaction rates neither affects weak reversibility nor the number of linkage classes. Hence, the Kirchoff matrix from line 20 of the algorithm can be constructed.

Using Theorem 2.12, we know that the kernel of the Kirchoff matrix has a basis consisting of non-negative vectors whose supports are the terminal strongly connected components. Recall that since the algorithm satisfies the condition on line 21, we have

$$\dim(\ker(Q)) = 1, \text{ and } \operatorname{supp}(\ker(Q)) = \{1, \dots, m\}. \tag{16}$$

This implies that all vertices corresponding to the Kirchoff matrix Q are in the same terminal strongly connected component. Therefore, this realization is weakly reversible and consists of a single linkage class. □

Lemma 3.2 *Suppose there exists a weakly reversible realization consisting of a single linkage class of* $\frac{d\boldsymbol{x}}{dt} = \sum_{i=1}^m \boldsymbol{x}^{\boldsymbol{y}_i} \boldsymbol{w}_i$. *Then the conditions on line 3 and line 21 in Algorithm 1 are satisfied.*

Proof From the existence of a realization, all net reaction vectors $\{\boldsymbol{w}_i\}_{i=1}^m$ can be realized by conical combinations of the vectors $(\boldsymbol{y}_k - \boldsymbol{y}_i)_{k=1}^m$. Thus, the algorithm must satisfy the condition on line 3, for $i = 1, \dots, m$. Now it suffices for us to show

$$\dim(\ker(Q)) = 1, \text{ and } \operatorname{supp}(\ker(Q)) = \{1, \dots, m\}. \tag{17}$$

Here we claim that the realization produced by Algorithm 1 consists of the maximum number of reactions. To realize the system $\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum_{i=1}^{m} \boldsymbol{x}^{\boldsymbol{y}_i} \boldsymbol{w}_i$, we need to find a vector $\boldsymbol{v}$ for each vertex $\boldsymbol{y}_i$, such that

$$\boldsymbol{B}_i \boldsymbol{v} = \boldsymbol{w}_i, \text{ and } \boldsymbol{v} \in \mathbb{R}^m_{\geq 0}. \tag{18}$$

First, for $i = 1, \ldots, m$, we get a vector $\boldsymbol{v}^* \in \mathbb{R}^m_{\geq 0}$ from line 3, which solves Eq. (18). After setting[2] $\boldsymbol{v}_i^* = 1$, we define the initial support set S_i as follows:

$$S_i = \operatorname{supp}(\boldsymbol{v}^*). \tag{19}$$

Next, we build an inner loop on $j = 1, \ldots, m$. If $j \in S_i$, this implies that we already incorporated the reaction $\boldsymbol{y}_i \to \boldsymbol{y}_j$ in the realization. Otherwise, for each $j \notin S_i$, we further check whether there exists a vector $\boldsymbol{v} \in \mathbb{R}^m_{\geq 0}$, such that

$$\boldsymbol{B}_i \boldsymbol{v} = \boldsymbol{w}_i, \text{ and } \boldsymbol{v}_j > 0. \tag{20}$$

Once we find such vector $\boldsymbol{v}$, we update the set S_i as

$$S_i := S_i \cup \operatorname{supp}(\boldsymbol{v}). \tag{21}$$

This implies that whenever $j \in \operatorname{supp}(\boldsymbol{v})$, we have $j \in S_i$.

After going through the whole inner loop, we obtain the complete version of set S_i. Then we follow the construction in (15), and it is clear that the reaction $\boldsymbol{y}_i \to \boldsymbol{y}_j$ represented by $j \in S_i$ is included in the realization.

Now suppose there is a vector $\hat{\boldsymbol{v}}$, solving Eq. (18) and $\operatorname{supp}(\hat{\boldsymbol{v}}) \nsubseteq S_i$. This implies that there exists $j \in \operatorname{supp}(\hat{\boldsymbol{v}})$ with $j \notin S_i$, which contradicts Eq. (21). Thus, the set S_i contains the *maximal* number of positive entries.

From the claim above and line 20, we deduce that for any realization of the system, all reactions between $\{\boldsymbol{y}_i\}_{i=1}^m$ are included in the realization given by the Kirchoff matrix Q. Note that adding more reactions among the current vertices of a weakly reversible single linkage class network will preserve the properties of weak reversibility and the single linkage class condition. This implies that if there exists a weakly reversible realization consisting of a single linkage class, then the realization generated by Q will also be weakly reversible and consist of a single linkage class. By Theorem 2.12, we conclude (17). □

The following remark is a direct consequence of Lemma 3.2.

Remark 3.3 If Algorithm 1 fails at lines 3 or 21, then $\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum\limits_{i=1}^{m} \boldsymbol{x}^{\boldsymbol{y}_i} \boldsymbol{w}_i$ does not admit a weakly reversible realization with a single linkage class.

[2] Note that the i^{th} column of the matrix B_i (denoted by $B_{i,i}$ in Algorithm 1) is the zero column vector. Therefore, if there exists a vector $\boldsymbol{v}^*$ that satisfies $B_i \boldsymbol{v}^* = w_i$, then $\boldsymbol{v}_i^*$ can be set to any arbitrary real number without influencing the solvability. In particular, we set $v_i^* = 1$ to ensure a unique solution.

4 Special cases and the implementation of Algorithm 1

After showing Algorithm 1, we focus on some special cases and the implementation of the algorithm. We will discuss various properties of weakly reversible realizations consisting of a single linkage class but having different deficiencies, and the corresponding implementation of the algorithm.

The following Lemma allows us to compute the deficiency of the realization obtained from Algorithm 1.

Lemma 4.1 *Suppose that the dynamical system* $\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum\limits_{i=1}^{m} \boldsymbol{x}^{\boldsymbol{y}_i} \boldsymbol{w}_i$ *with* m *vertices, and the matrix of net reaction vectors* $\boldsymbol{W} = (\boldsymbol{w}_1, \ldots, \boldsymbol{w}_m)$ *passes Algorithm 1 and outputs a weakly reversible realization consisting of a single linkage class. Then the deficiency of this realization is* $m - 1 - \mathrm{Im}(\boldsymbol{W})$.

Proof From Lemma 2.18, we have $\mathrm{Im}(W) = S$. Therefore, the deficiency of realization obtained from Algorithm 1 is

$$\delta = m - \ell - s = m - 1 - \mathrm{Im}(\boldsymbol{W}).$$

□

4.1 Weakly reversible deficiency zero realizations consisting of a single linkage class

We first consider the case when a dynamical system admits a weakly reversible deficiency zero realization consisting of a single linkage class.

It is well known that weakly reversible deficiency zero networks are complex-balanced for any choice of positive rate constants [19]. In addition, for complex-balanced dynamical systems consisting of a single linkage class, there exists a globally attracting positive steady state within each stoichiometric compatibility class [11]. This leads to the following Lemma.

Lemma 4.2 *For a weakly reversible deficiency zero reaction network consisting of a single linkage class, every stoichiometric compatibility class admits a globally attracting positive steady state.*

This is our primary motivation for finding weakly reversible deficiency zero realizations consisting of a single linkage class. Now we state the upcoming Lemma that relates these realizations to the existence of a vector in line 3 of Algorithm 1.

Lemma 4.3 *Consider a weakly reversible deficiency zero reaction network* G *consisting of a single linkage class* $L = \{\boldsymbol{y}_1, \ldots, \boldsymbol{y}_m\}$. *Let* $\{\boldsymbol{w}_1, \ldots, \boldsymbol{w}_m\}$ *denote the net reaction vectors corresponding to these vertices. Define the matrix* $\boldsymbol{B}_i \in \mathbb{R}_{n\times m}$, *with* k^{th} *column* $B_{i,k} := (\boldsymbol{y}_k - \boldsymbol{y}_i)$ *for* $1 \leq k \leq m$. *For each vertex* $\boldsymbol{y}_i \in L$, *there exists a unique vector* $\boldsymbol{v} \in \mathbb{R}^m_{\geq 0}$, *such that*

$$\boldsymbol{B}_i \boldsymbol{v} = \boldsymbol{w}_i, \text{ and } \boldsymbol{v}_{\mathrm{i}} = 1. \tag{22}$$

Proof For each vertex $\boldsymbol{y}_i \in L$, we write the stoichiometric subspace as

$$S = \text{span}\{\boldsymbol{y}_k - \boldsymbol{y}_i\}_{k=1}^m.$$

Since G has a single linkage class and deficiency zero, we obtain

$$0 = m - 1 - \dim(S).$$

This shows that

$$\dim(\text{span}\{\boldsymbol{y}_k - \boldsymbol{y}_i\}_{k=1}^m) = \dim(S) = m - 1.$$

From weak reversibility and Lemma 2.18, we deduce that

$$\dim(\ker(\boldsymbol{B}_i)) = m - \dim(\text{Im}(\boldsymbol{B}_i)) = m - \dim(S) = 1.$$

Since $\boldsymbol{B}_{i,i} = \mathbf{0}$, it is easy to see that $\mathbf{e_i} \in \ker(\boldsymbol{B}_i)$ where $\mathbf{e_i}$ represents the unit vector in the i-th coordinate. Then, we have

$$\ker(\boldsymbol{B}_i) \cap \{z \in \mathbb{R}^m : z_i = 0\} = \mathbf{0}. \tag{23}$$

Since the net reaction vectors $\{\boldsymbol{w}_i\}_{i=1}^m$ come from the dynamics generated by network G, all of them can be realized. Applying (23), we conclude that Eq. (22) has a unique solution for each vertex $y_i \in L$. □

Remark 4.4 It is worth mentioning that if the dynamical system $\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum_{i=1}^m \boldsymbol{x}^{\boldsymbol{y}_i} \boldsymbol{w}_i$ admits a weakly reversible realization consisting of a single linkage class L, such that for each vertex $y_i \in L$, the Eq. 3 in Algorithm 1 has a unique solution, such realization still can have a positive deficiency. For example, the network in Example 4.9 has a unique solution to Eq. 3 for each vertex $y_i \in L$, but it has deficiency one.

Example 4.5 Consider the matrices corresponding to the source vertices and net reaction vectors given by

$$\boldsymbol{Y}_s = \begin{pmatrix} 1 & 2 & 2 \\ 0 & 0 & 1 \end{pmatrix}, \text{ and } \boldsymbol{W} = \begin{pmatrix} 1 & 0 & -1 \\ 0 & 1 & -1 \end{pmatrix}. \tag{24}$$

respectively, which are inputs to Algorithm 1. These inputs generate the following system of differential equations

$$\begin{aligned} \dot{x} &= x - x^2 y, \\ \dot{y} &= x^2 - x^2 y. \end{aligned} \tag{25}$$

We have $n = 2$ for two state variables x, y, and $m = 3$ for two distinct monomials.

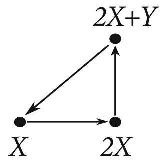


Fig. 3 The deficiency zero network from Example 4.5

Next, applying line 3 in algorithm on $\boldsymbol{Y}_s = (\boldsymbol{y}_1, \boldsymbol{y}_2, \boldsymbol{y}_3)$, we obtain

$$\boldsymbol{B}_1 = \begin{pmatrix} 0 & 1 & 1 \\ 0 & 0 & 1 \end{pmatrix}, \quad \boldsymbol{B}_2 = \begin{pmatrix} -1 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix}, \quad \boldsymbol{B}_3 = \begin{pmatrix} -1 & 0 & 0 \\ -1 & -1 & 0 \end{pmatrix},$$

and

$$\boldsymbol{v}_1^* = (1, 1, 0)^T, \quad \boldsymbol{v}_2^* = (0, 1, 1)^T, \quad \boldsymbol{v}_3^* = (1, 0, 1)^T,$$

where $\boldsymbol{v}_i^* \in \mathbb{R}^3_{\geq 0}$ and $\boldsymbol{B}_i \boldsymbol{v}_i^* = \boldsymbol{w}_i$, for $i = 1, 2, 3$.

Then, we can compute that for $i = 1, 2, 3$,

$$\ker(\boldsymbol{B}_i) \cap \{z \in \mathbb{R}^m : z_i = 0\} = \mathbf{0}, \tag{26}$$

and derive

$$S_1 = \{1, 2\}, \quad S_2 = \{2, 3\}, \quad S_3 = \{1, 3\}.$$

Note that $\dim(\ker(\mathrm{B_i})) = 1$. Together with Eq. (26), we deduce that $\boldsymbol{v}_i^*$ is the unique solution to the equations $\boldsymbol{B}_i \boldsymbol{v} = \boldsymbol{w}_i$ and $\boldsymbol{v}_i = 1$ for $i = 1, 2, 3$. Therefore, we do not need to execute the inner loop given by lines 9-17 in Algorithm 1.

Following line 20, we construct the Kirchoff matrix:

$$Q = \begin{pmatrix} -1 & 0 & 1 \\ 1 & -1 & 0 \\ 0 & 1 & -1 \end{pmatrix}.$$

It is easy to check that $\ker(Q) = \mathrm{span}\{(1, 1, 1)^\top\}$, and we deduce that

$$\dim(\ker(Q)) = 1, \text{ and } \mathrm{supp}(\ker(Q)) = \{1, 2, 3\}.$$

Therefore, we conclude that the system given by (25) admits a weakly reversible realization with a single linkage class, whose E-graph is shown in Fig. 3.

Example 4.6 Consider the matrices of source vertices and net reaction vectors given by

$$\boldsymbol{Y}_s = \begin{pmatrix} 1 & 2 \\ 0 & 0 \end{pmatrix}, \text{ and } \boldsymbol{W} = \begin{pmatrix} -1 & 1 \\ 0 & 0 \end{pmatrix}. \tag{27}$$

respectively, which are inputs to Algorithm 1. These inputs generate the following system of differential equations

$$\begin{aligned} \dot{x} &= -x + x^2, \\ \dot{y} &= 0. \end{aligned} \tag{28}$$

We have $n = 2$ for two state variables x, y, and $m = 2$ for two distinct monomials.

Next, following line 3 in algorithm on $\boldsymbol{Y}_s = (\boldsymbol{y}_1, \boldsymbol{y}_2)$, we obtain

$$\boldsymbol{B}_1 = \begin{pmatrix} 0 & 1 \\ 0 & 0 \end{pmatrix}, \text{ and } \boldsymbol{B}_2 = \begin{pmatrix} -1 & 0 \\ 0 & 0 \end{pmatrix}. \tag{29}$$

However, there does not exist a positive vector $\boldsymbol{v}^*$, which solves $\boldsymbol{B}_1 \boldsymbol{v}^* = \boldsymbol{w}_1$. Therefore, there exists no weakly reversible realization consisting of a single linkage class that generates the dynamical system given by Eq. 28.

4.2 Weakly reversible deficiency one realizations consisting of a single linkage class

In this section, we analyze the case when a dynamical system admits a weakly reversible deficiency one realization consisting of a single linkage class.

If a reaction network satisfies the conditions of the Deficiency One Theorem, then every stoichiometric compatibility class contains a unique positive steady state (if it exists) [9, 21]. On the other hand, for any weakly reversible network, there always exists a positive steady state within every stoichiometric compatibility class [22]. It is easy to check that every weakly reversible deficiency one network with a single linkage class must satisfy all conditions in the Deficiency One Theorem. Therefore, we get the following Lemma.

Lemma 4.7 *For a weakly reversible deficiency one network consisting of a single linkage class, there exists a unique positive steady state within every stoichiometric compatibility class.*

This explains the importance of discovering weakly reversible deficiency one realizations with a single linkage class. Moreover, we introduce the next Lemma showing the existence of a vector in line 3 of Algorithm 1.

Lemma 4.8 *Consider a weakly reversible and deficiency one reaction network G consisting of a single linkage class given by $L = \{\boldsymbol{y}_1, \ldots, \boldsymbol{y}_m\}$. Let $\{\boldsymbol{w}_1, \ldots, \boldsymbol{w}_m\}$ denote the net reaction vectors corresponding to these vertices. Define the matrix $\boldsymbol{B}_i \in \mathbb{R}_{n \times m}$, with k^{th} column $B_{i,k} := (\boldsymbol{y}_k - \boldsymbol{y}_i)$ for $1 \leq k \leq m$. For each vertex $\boldsymbol{y}_i \in L$, the following system*

$$\begin{aligned} \boldsymbol{B}_i \boldsymbol{v} &= \boldsymbol{w}_i, \\ \boldsymbol{v}_i &= 1, \textit{ and } \ \boldsymbol{v} \in \mathbb{R}^m_{\geq 0}. \end{aligned} \tag{30}$$

has at most two linearly independent solutions.

Proof For each vertex $y_i \in L$, we denote the stoichiometric subspace by S, such that

$$S = \text{span}\{\boldsymbol{y}_k - \boldsymbol{y}_i\}_{k=1}^{m}. \tag{31}$$

Since G has a single linkage class and deficiency one, we obtain

$$\delta = 1 = m - 1 - \dim(S). \tag{32}$$

This shows that

$$\dim(\text{span}\{\boldsymbol{y}_k - \boldsymbol{y}_i\}_{k=1}^{m}) = \dim(S) = m - 2. \tag{33}$$

From the Rank-Nullity Theorem, $\dim(\ker(\boldsymbol{B}_i)) + \dim(\text{Im}(\boldsymbol{B}_i)) = m$. Since G is weakly reversible, using Lemma 2.18, we get

$$\dim(\text{Im}(\boldsymbol{B}_i)) = \dim(S), \tag{34}$$

thus we obtain that $\dim(\ker(\boldsymbol{B}_i)) = m - \dim(S) = 2$.

Since $\boldsymbol{B}_{i,i} = \boldsymbol{0}$, we deduce $\ker(\boldsymbol{B}_i)$ has one vector $\boldsymbol{u} \in \mathbb{R}^m$ such that $\boldsymbol{u}_i \neq 0$. Then, we have

$$\dim(\ker(\boldsymbol{B}_i) \cap \{\boldsymbol{z} \in \mathbb{R}^m : \boldsymbol{z}_i = 0\}) = 1. \tag{35}$$

Since the net reaction vectors $\{\boldsymbol{w}_i\}_{i=1}^{m}$ come from the dynamics generated by the network G, all of them can be realized. Together with (35), the conclusion follows. □

Example 4.9 Consider the matrices corresponding to the source vertices and net reaction vectors given by

$$\boldsymbol{Y}_s = \begin{pmatrix} 1 & 2 & 2 & 1 \\ 0 & 0 & 1 & 1 \end{pmatrix}, \text{ and } \boldsymbol{W} = \begin{pmatrix} 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & -1 \end{pmatrix}. \tag{36}$$

respectively, which are inputs to Algorithm 1. These inputs generate the following system of differential equations

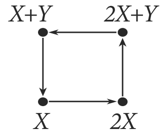
$$\begin{aligned} \dot{x} &= x - x^2 y, \\ \dot{y} &= x^2 - xy. \end{aligned} \tag{37}$$

We have $n = 2$ for two state variables x, y, and $m = 4$ for four distinct monomials.

Next, applying line 3 in algorithm on $\boldsymbol{Y}_s = (\boldsymbol{y}_1, \boldsymbol{y}_2, \boldsymbol{y}_3, \boldsymbol{y}_4)$, we obtain

$$\boldsymbol{B}_1 = \begin{pmatrix} 0 & 1 & 1 & 0 \\ 0 & 0 & 1 & 1 \end{pmatrix}, \quad \boldsymbol{B}_2 = \begin{pmatrix} -1 & 0 & 0 & -1 \\ 0 & 0 & 1 & 1 \end{pmatrix},$$
$$\boldsymbol{B}_3 = \begin{pmatrix} -1 & 0 & 0 & -1 \\ -1 & -1 & 0 & 0 \end{pmatrix}, \quad \boldsymbol{B}_4 = \begin{pmatrix} 0 & 1 & 1 & 0 \\ -1 & -1 & 0 & 0 \end{pmatrix},$$

Fig. 4 The deficiency one network from Example 4.9



and

$$\boldsymbol{v}_1^* = (1, 1, 0, 0)^T, \ \boldsymbol{v}_2^* = (0, 1, 1, 0)^T, \ \boldsymbol{v}_3^* = (0, 0, 1, 1)^T, \ \boldsymbol{v}_4^* = (1, 0, 0, 1)^T,$$

where $\boldsymbol{v}_i^* \in \mathbb{R}^4_{\geq 0}$ with $\boldsymbol{v}_{i,i}^* = 1$ and $\boldsymbol{B}_i \boldsymbol{v}_i^* = \boldsymbol{w}_i$, for $1 \leq i \leq 4$. This implies that this system has exactly one solution and hence illustrates Lemma 4.8.

Then, we get the initial S_i for $1 \leq i \leq 4$,

$$S_1 = \{1, 2\}, \quad S_2 = \{2, 3\}, \quad S_3 = \{3, 4\}, \quad S_4 = \{1, 4\}.$$

After executing the inner loop in lines 9–17, we do not have any update on S_i.

Now we follow line 20, and construct the Kirchoff matrix:

$$Q = \begin{pmatrix} -1 & 0 & 0 & 1 \\ 1 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & -1 \end{pmatrix}.$$

It is easy to check that $\ker(Q) = \text{span}\{(1, 1, 1, 1)^\intercal\}$, which shows

$$\dim(\ker(Q)) = 1, \ \text{and} \ \ \text{supp}(\ker(Q)) = \{1, 2, 3, 4\}.$$

Therefore, we conclude that (37) admits a weakly reversible realization with a single linkage class, whose E-graph is shown in Fig. 4.

Example 4.10 Consider the matrices corresponding to the source vertices and net reaction vectors given by

$$\boldsymbol{Y}_s = \begin{pmatrix} 1 & 2 & 3 \end{pmatrix}, \ \text{and} \ \ \boldsymbol{W} = \begin{pmatrix} 1 & 1 & -1 \end{pmatrix}. \tag{38}$$

respectively, which are inputs to Algorithm 1. These inputs generate the following differential equation

$$\dot{x} = x + x^2 - x^3. \tag{39}$$

We have $n = 1$ for the state variables x, and $m = 3$ for three distinct monomials.

Next, applying line 3 in algorithm on $\boldsymbol{Y}_s = (\boldsymbol{y}_1, \boldsymbol{y}_2, \boldsymbol{y}_3)$, we obtain

$$\boldsymbol{B}_1 = \begin{pmatrix} 0 & 1 & 2 \end{pmatrix}, \quad \boldsymbol{B}_2 = \begin{pmatrix} -1 & 0 & 1 \end{pmatrix}, \quad \boldsymbol{B}_3 = \begin{pmatrix} -2 & -1 & 0 \end{pmatrix},$$

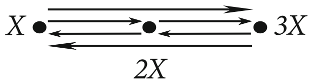


Fig. 5 The deficiency one network from Example 4.10

and

$$\boldsymbol{v}_1^* = (1, 1, 0)^T, \quad \boldsymbol{v}_2^* = (0, 1, 1)^T, \quad \boldsymbol{v}_3^* = (0, 1, 1)^T,$$

where $\boldsymbol{v}_i^* \in \mathbb{R}^3_{\geq 0}$ and $\boldsymbol{B}_i \boldsymbol{v}_i^* = \boldsymbol{w}_i$, for $i = 1, 2, 3$.

Then, we get the initial S_i for $i = 1, 2, 3$,

$$S_1 = \{1, 2\}, \quad S_2 = \{2, 3\}, \quad S_3 = \{2, 3\}.$$

Following the inner loop in lines 9-17, we can compute that

$$\begin{aligned} \boldsymbol{B}_1 \boldsymbol{v}^1 &= \boldsymbol{w}_1, \text{ with } \boldsymbol{v}^1 = (1, 0, 1/2)^\intercal, \\ \boldsymbol{B}_2 \boldsymbol{v}^2 &= \boldsymbol{w}_2, \text{ with } \boldsymbol{v}^2 = (1, 1, 2)^\intercal, \\ \boldsymbol{B}_3 \boldsymbol{v}^3 &= \boldsymbol{w}_3, \text{ with } \boldsymbol{v}^3 = (1/2, 0, 1)^\intercal. \end{aligned}$$

This shows that this system has two linearly independent solutions and hence illustrates Lemma 4.8.

After updating S_i with $\boldsymbol{v}^i$ for $i = 1, 2, 3$, we derive

$$S_1 = S_2 = S_3 = \{1, 2, 3\}.$$

Now we follow line 20, and construct the Kirchoff matrix:

$$Q = \begin{pmatrix} -2 & 1 & 1 \\ 1 & -2 & 1 \\ 1 & 1 & -2 \end{pmatrix}.$$

It is easy to check that $\ker(Q) = \operatorname{span}\{(1, 1, 1)^\intercal\}$, and we deduce that

$$\dim(\ker(Q)) = 1, \text{ and } \operatorname{supp}(\ker(Q)) = \{1, 2, 3\}.$$

Therefore, we conclude (39) admits a weakly reversible realization with a single linkage class, and the E-graph of the maximal realization is shown in Fig. 5.

4.3 Weakly reversible realizations with a single linkage class and arbitrary deficiency

Now we list some properties of weakly reversible realizations of arbitrary positive deficiency consisting of a single linkage class.

Table 1 .

Reactions in G	Reactions in $\tilde{G}$
$X_1 + X_2 \xrightarrow{k_1} 2X_1 + X_2$	$X_1 + 2X_2 \xrightarrow{k_1} 2X_1 + X_2$ $X_1 + X_2 + X_3 \xrightarrow{k_1} 2X_1 + X_2$
$X_2 + X_3 \xrightarrow{k_2} 2X_2 + X_3$	$X_2 + 2X_3 \xrightarrow{k_2} 2X_2 + X_3$ $X_1 + X_2 + X_3 \xrightarrow{k_2} 2X_2 + X_3$
$X_3 + X_1 \xrightarrow{k_3} 2X_3 + X_1$	$2X_1 + X_3 \xrightarrow{k_3} 2X_3 + X_1$ $X_1 + X_2 + X_3 \xrightarrow{k_3} 2X_3 + X_1$
$X_1 + X_2 \xrightarrow{k_4} X_1 + X_2 + X_3$	$X_1 + 2X_2 \xrightarrow{k_4} X_1 + X_2 + X_3$ $2X_1 + X_2 \xrightarrow{k_4} X_1 + X_2 + X_3$
$X_2 + X_3 \xrightarrow{k_5} X_1 + X_2 + X_3$	$X_2 + 2X_3 \xrightarrow{k_5} X_1 + X_2 + X_3$ $2X_2 + X_3 \xrightarrow{k_5} X_1 + X_2 + X_3$
$X_1 + X_3 \xrightarrow{k_6} X_1 + X_2 + X_3$	$X_1 + 2X_3 \xrightarrow{k_6} X_1 + X_3 + X_3$ $2X_1 + X_3 \xrightarrow{k_6} X_1 + X_2 + X_3$

Our motivation comes from autocatalytic networks, which are often associated with the context of the origin of life models [23–26]. Owing to their autocatalytic nature, the concentrations of species in these networks can go unbounded. The crucial component in their analysis is the dynamics corresponding to the relative concentration of species. Given species $X_1, X_2, \ldots, X_n$ with concentrations $x_1, x_2, \ldots, x_n$, the relative concentration corresponding to species X_i is given by $(\sum_{i=1}^{n} x_i)^{-1} x_i$. It can be shown that for certain autocatalytic networks, the dynamics corresponding to the relative concentration of species can be generated by a reaction network [27].

In particular, we present an example of an autocatalytic network such that the network corresponding to the relative concentration of species is weakly reversible and consists of a single linkage class. Table 1 illustrates this fact. The left column of the table describes the reactions in G, which is an autocatalytic network. The right column of the table describes the reactions in $\tilde{G}$, which is the network corresponding to the relative concentration of species in G. The reactions in $\tilde{G}$ are obtained in the following way: for every reaction in G, there exists a corresponding pair of reactions in $\tilde{G}$ that is generated using [27, Theorem 3.5]. In particular, the reactions in $\tilde{G}$ are generated by adding all possible species to the reactants of the corresponding reaction in G.

The network $\tilde{G}$ is depicted in Fig. 6a. Note that the deficiency of $\tilde{G}$ is given by $\delta = 7 - 1 - 3 = 3$. Using some modifications, we can construct a network shown in Fig. 6b which generates the dynamics as Fig. 6a. Figure 6b is a weakly reversible network consisting of a single linkage class. By [10], the dynamics generated by it is permanent. This implies that the dynamics generated by $\tilde{G}$ is also permanent.

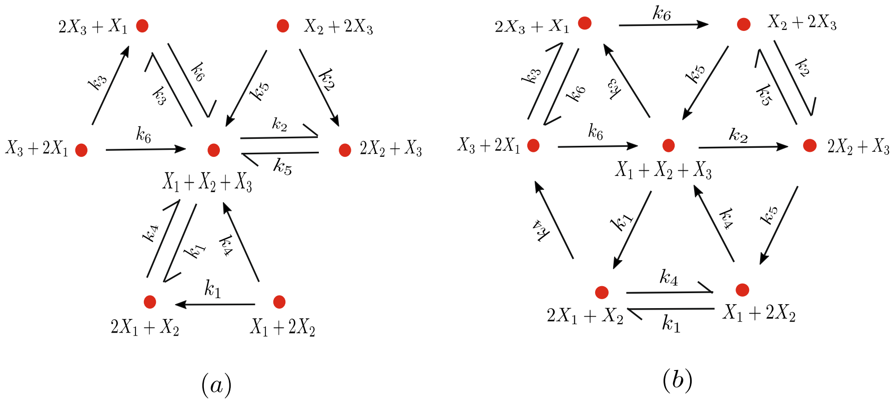


Fig. 6 **a** The network $\tilde{G}$ corresponds to the relative concentrations of species in network G. **b** Splitting certain reactions in (**a**) gives a weakly reversible network consisting of a single linkage class. The dynamics generated by this network is known to be permanent [10]

4.4 Implementation of Algorithm 1

In this section, we discuss the implementation aspects of Algorithm 1. The algorithm is designed to find a weakly reversible realization consisting of a single linkage class for $\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \sum_{i=1}^{m} \boldsymbol{x}^{\boldsymbol{y}_i} \boldsymbol{w}_i$, and it has three key steps:

1. Check for the existence of a vector $\boldsymbol{v}^* \in \mathbb{R}^m_{\geq 0}$, such that for $i = 1, \ldots, m$,
$$\boldsymbol{B}_i \boldsymbol{v}^* = \boldsymbol{w}_i.$$
2. Check for the existence of a vector $\boldsymbol{v} \in \mathbb{R}^m_{\geq 0}$, such that for $i, j = 1, \ldots, m$,
$$\boldsymbol{B}_i \boldsymbol{v} = \boldsymbol{w}_i, \text{ and } \boldsymbol{v}_j > 0.$$
3. Check $\dim(\ker(Q)) = 1$, and $\operatorname{supp}(\ker(Q)) = \{1, \ldots, m\}$.

In step 1, we compute the positive vector solving $\boldsymbol{B}_i \boldsymbol{v}^* = \boldsymbol{w}_i$ and consider the implementation as a sequence of linear programming problems. For $i = 1, \ldots, m$, set the matrix $\boldsymbol{B}_i \in \mathbb{R}_{n \times m}$ as in line 2,

$$\begin{aligned} &\text{Find a vector } \boldsymbol{x}, \\ &\text{subject to} \quad \boldsymbol{B}_i \boldsymbol{x} = \boldsymbol{w}_i, \\ &\qquad\qquad\quad\; \boldsymbol{x} \geq \boldsymbol{0}. \end{aligned} \tag{40}$$

From Lemma 3.2, if there exists some number $1 \leq i \leq m$, such that there is no solution for (40), then the implementation fails. Therefore, no weakly reversible realization with a single linkage class exists.

In step 2, we compute the positive vector solving $\boldsymbol{B}_i \boldsymbol{v} = \boldsymbol{w}_i$ and $\boldsymbol{v}_j > 0$. Recall that $S_i = \operatorname{supp}(\boldsymbol{v}^*)$, where $\boldsymbol{v}^*$ is the vector found in Step 1. For each $j = 1, \ldots, m$, if

$j \notin S_i$, we do the following:

$$\begin{aligned} &\text{Find a vector} && \boldsymbol{x}, \\ &\text{that maximizes} && \boldsymbol{x}_j, \\ &\text{subjected to} && \boldsymbol{B}_i \boldsymbol{x} = \boldsymbol{0}, \\ & && \boldsymbol{x} \geq \boldsymbol{0}, \ \text{and} \ \boldsymbol{x}_j \leq 1. \end{aligned} \tag{41}$$

The solution to (41) is the desired vector if its j-th component is positive. Meanwhile, if the j-th component of the solution is zero, then implementation fails. Furthermore, we restrict $\boldsymbol{x}_j \leq 1$ to avoid the risk that $\boldsymbol{x}_j$ can be arbitrarily large.

Here we explain why adding the restriction on j-th component in (41) does not change the solvability of the problem. From $j \notin S_i$, we have that j is the index such that $\boldsymbol{v}^*_j = 0$ where $\boldsymbol{v}^*$ is the vector found in Step 1. Hence, there must exist a vector $\boldsymbol{x}^* \in \mathbb{R}^m_{\geq 0}$, such that

$$\boldsymbol{B}_i \boldsymbol{x}^* = \boldsymbol{w}_i, \ \text{and} \ \boldsymbol{x}^*_j = 0.$$

Suppose there is a vector $\boldsymbol{x} \in \mathbb{R}^m_{\geq 0}$, which solves

$$\boldsymbol{B}_i \boldsymbol{x} = \boldsymbol{w}_i, \ \text{and} \ \boldsymbol{x}_j > 0. \tag{42}$$

Then we can always find a sufficient small constant ϵ with $\boldsymbol{x}^\epsilon := (1 - \epsilon)\boldsymbol{x}^* + \epsilon \boldsymbol{x}$, such that

$$\boldsymbol{B}_i \boldsymbol{x}^\epsilon = \boldsymbol{w}_i, \ \text{and} \ 0 < \boldsymbol{x}^\epsilon_j = \epsilon \boldsymbol{x}_j \leq 1.$$

This implies that if (42) admits a solution, there must exist another solution for (41).

In step 3, the implementation needs a rank-revealing factorization; we need to find a basis of $\ker(Q)$, and then we can check the number of vectors in this basis and their support. This again can be done by solving a linear programming problem.

5 Discussion

Weakly reversible networks consisting of a single linkage class form an important class of networks, owing to the robust properties of the dynamical systems they generate. In particular, the dynamics produced by these networks (according to mass-action kinetics) is known to be persistent and permanent for all choices of reaction rate parameters [6, 10].

We describe an algorithm that determines if there exists a weakly reversible realization consisting of a single linkage class that generates a given polynomial dynamical system. Our input consists of two matrices: a matrix of source monomials and a matrix containing the corresponding net reaction vectors. The algorithm outputs a maximal weakly reversible realization consisting of a single linkage class (if one exists), which generates the dynamical system formed by the inputs. We also describe approaches for efficient implementations of this algorithm; in particular, we show that all the key steps in our algorithm reduce to solving simple linear programming problems.

Other approaches for finding weakly reversible realizations of polynomial dynamical systems are based primarily on mixed integer programming methods [28–31]. The algorithm we describe here uses a simpler *greedy* approach, which works specifically because we are looking for realizations consisting of a *single* linkage class.

At the same time, our algorithm lays down the foundation for some future work. In particular, extending our algorithm to check the existence of more general realizations (e.g., weakly reversible realizations with *multiple* linkage classes that satisfy other desirable properties) is a potential avenue worthy of exploration. More specifically, the problem of finding weakly reversible realizations that satisfy the conditions of the *Deficiency One Theorem* [9] is a possibility that will be explored in a follow-up paper [32].

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Declarations

Conflicts of interest The authors have no competing interests to declare that are relevant to the content of this article.

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