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Original Research Article

Autocatalytic recombination systems: A reaction network perspective

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ABSTRACT

Autocatalytic systems called hypercycles are very often incorporated in "origin of life" models. We investigate the dynamics of certain related models called *bimolecular autocatalytic systems*. In particular, we consider the dynamics corresponding to the *relative populations* in these networks, and show that it can be analyzed using well-chosen autonomous polynomial dynamical systems. Moreover, we use results from *reaction network theory* to prove persistence and permanence of several families of bimolecular autocatalytic systems called *autocatalytic recombination systems*.

1. Introduction

Biological networks display a wide range of sophisticated dynamics, due to complex feedback loops and catalytic interactions [1–6]. A particular instance of such sophistication is manifested in autocatalytic reaction systems called *hypercycles*, which have appeared in the "origin of life" models. Introduced by Manfred Eigen [7] and extended in collaboration with Peter Schuster [8,9], hypercycles consist of cyclic connections of molecules that mutually catalyze their own production. Hypercycles are particular instances of the replicator equation [10,11], and have been proposed as a possible solution to Eigen's paradox [7], a famous problem in evolutionary biology.

The classical three dimensional hypercycle is given by the reaction network

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

The dynamical equations corresponding to this hypercycle are given by

$$\begin{aligned} \dot{x_1} &= x_1 x_3 \\ \dot{x_2} &= x_1 x_2 \\ \dot{x_3} &= x_2 x_3. \end{aligned} \tag{1}$$

As is evident from Eq. (1), the dynamical rate equations corresponding to each species consist of a combination of positive (non-constant) monomials. Consequently, the species populations can become unbounded in finite time [12], so it is reasonable to analyze the *relative populations* of species in such networks [11]. Taking cue from the classical hypercycle, we study more general models called *bimolecular autocatalytic systems*, where every reaction is of the form $X_i + X_j \to X_i + X_j + X_k$. A priori, the dynamics of *relative* populations of these systems might *not* be given by autonomous polynomial differential equations. Nevertheless, we show that the relative populations of species in these networks are, after time re-scaling, solutions of autonomous polynomial dynamical systems.

Autocatalytic networks like the hypercycle received widespread attention from several researchers in the 1970's. In particular, Hofbauer, Schuster, Sigmund, and Wolff [13–17] analyzed a dynamical property called *cooperation*, which roughly implies that no species can go extinct. This is related to the property of *persistence* in the theory of reaction networks [18]. A system is persistent if given an initial condition $\boldsymbol{x}(0) \in \mathbb{R}^n_{>0}$, we have $\liminf_{t\to\infty} x_i(t) > 0$ for all species concentrations x_i in the network. *Permanence* is a related notion; a system is permanent if there exist positive lower and upper bounds for all solutions in $\mathbb{R}^n_{>0}$. We show that results from the theory of reaction networks [18–21] can be used to prove permanence (and implicitly persistence) in several kinds of *autocatalytic recombination systems*.

The paper is organized as follows. In Section 2, we recall some definitions and notations from the theory of reaction networks. More specifically, we define *weakly reversible*, *endotactic*, and *strongly endotactic* reaction networks. Further, we define the notions of *persistence* and *permanence* and relate them to the *Global Attractor Conjecture* [22]. In Section 3, we analyze the dynamics of certain bimolecular autocatalytic systems. In Theorem 3.1, we show that the relative populations in bimolecular autocatalytic systems can be obtained as time re-scaled solutions of polynomial mass-action systems. In Theorem 3.5, we explicitly characterize the reaction networks that generate the dynamics of relative populations in such networks. Finally, in Section 4, we

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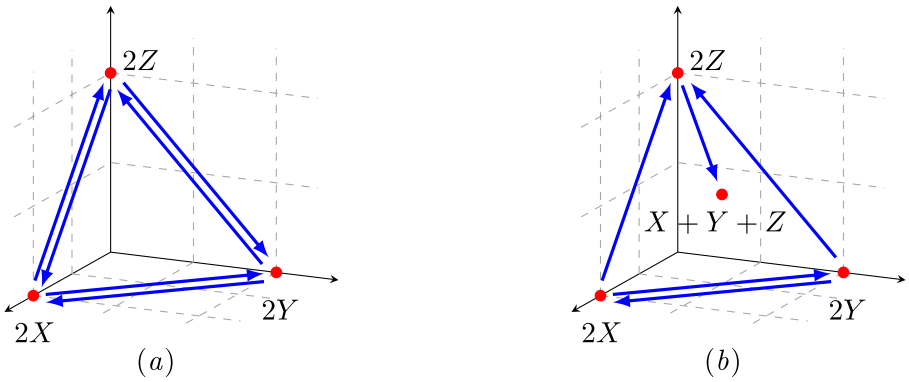


Fig. 1. (a) A reversible reaction network in $\mathbb{R}^3$ with a single linkage class, and a two-dimensional stoichiometric subspace. (b) A strongly endotactic, *not* weakly reversible, reaction network in $\mathbb{R}^3$.

analyze families of certain bimolecular autocatalytic systems called *autocatalytic recombination systems* (which are special cases of bimolecular autocatalytic systems described above). We show that the dynamical systems generated by relative populations of autocatalytic recombination systems is permanent using results from reaction network theory. In Section 5, we summarize our results and discuss possible avenues for future work.

2. Reaction networks

Here, we recall some basic terminology from the theory of reaction networks [23–27]. A *reaction network* can be represented as a directed graph $\mathcal{G} = (V, E)$, where $\emptyset \neq V \subset \mathbb{R}^n$ and $E \neq \emptyset$ are the sets of vertices and edges respectively. Such graphs have also been called *Euclidean embedded graphs* (abbreviated as E-graphs) [28–30]. In what follows, we refer to the edges in $\mathcal{G}$ as reactions. More precisely, if $(\boldsymbol{s}, \boldsymbol{s}') \in E$, then we write $\boldsymbol{s} \to \boldsymbol{s}' \in E$, where $\boldsymbol{s}$ is the *source* vertex and $\boldsymbol{s}'$ is the *target* vertex. Fig. 1 shows a few examples of E-graphs. A reaction network $\mathcal{G}' = (V', E')$ is a *subnetwork* of $\mathcal{G} = (V, E)$ if: (i) $V' \subseteq V$ and (ii) $E' \subseteq E$ with the condition that $(\boldsymbol{s}, \boldsymbol{s}') \in E'$ implies $\boldsymbol{s}, \boldsymbol{s}' \in V'$.

The *stoichiometric subspace* S of a network is the vector space $S = \text{span}\{\boldsymbol{s}' - \boldsymbol{s} \mid \boldsymbol{s} \to \boldsymbol{s}' \in E\}$. For example, the stoichiometric subspace corresponding to the network in Fig. 1(a) is given by $\text{span}\left\{\begin{bmatrix}-2\\2\\0\end{bmatrix}, \begin{bmatrix}0\\-2\\2\end{bmatrix}\right\}$.

For $\boldsymbol{x}_0 \in \mathbb{R}^n_{>0}$, the compatibility class of $\boldsymbol{x}_0$ is the affine subspace $(\boldsymbol{x}_0 + S)$, and the *positive compatibility class of* $\boldsymbol{x}_0$ is the polyhedron $(\boldsymbol{x}_0 + S) \cap \mathbb{R}^n_{>0}$.

Let $\mathcal{G} = (V, E)$ be a reaction network and let V_S denote the set of source vertices. Then

(i) $\mathcal{G}$ is *reversible* if $\boldsymbol{s} \to \boldsymbol{s}' \in E$ implies $\boldsymbol{s}' \to \boldsymbol{s} \in E$. Fig. 1(a) is an example of a reversible reaction network;
(ii) $\mathcal{G}$ is *weakly reversible* if each reaction is part of a directed cycle;
(iii) $\mathcal{G}$ is *endotactic* [18] if for every $\boldsymbol{w} \in \mathbb{R}^n$ and $\boldsymbol{s} \to \boldsymbol{s}' \in E$ with $\boldsymbol{w} \cdot (\boldsymbol{s}' - \boldsymbol{s}) < 0$, there exists $\tilde{\boldsymbol{s}} \to \tilde{\boldsymbol{s}}' \in E$ such that $\boldsymbol{w} \cdot (\tilde{\boldsymbol{s}}' - \tilde{\boldsymbol{s}}) > 0$ and $\boldsymbol{w} \cdot \tilde{\boldsymbol{s}} < \boldsymbol{w} \cdot \boldsymbol{s}$;
(iv) $\mathcal{G}$ is *strongly endotactic* [21] if for every $\boldsymbol{w} \in \mathbb{R}^n$ and $\boldsymbol{s} \to \boldsymbol{s}' \in E$ with $\boldsymbol{w} \cdot (\boldsymbol{s}' - \boldsymbol{s}) < 0$, there exists $\tilde{\boldsymbol{s}} \to \tilde{\boldsymbol{s}}' \in E$ such that $\boldsymbol{w} \cdot (\tilde{\boldsymbol{s}}' - \tilde{\boldsymbol{s}}) > 0$, $\boldsymbol{w} \cdot \tilde{\boldsymbol{s}} < \boldsymbol{w} \cdot \boldsymbol{s}$, and $\boldsymbol{w} \cdot \tilde{\boldsymbol{s}} \leq \boldsymbol{w} \cdot \hat{\boldsymbol{s}}$ for all $\hat{\boldsymbol{s}} \in V_S$. Fig. 1(a) and (b) are examples of strongly endotactic reaction networks;
(v) a set $L \subseteq V$ is a *linkage class* [25] if L is a connected component of $\mathcal{G}$. The reaction networks in Fig. 1(a) and (b) consist of a single linkage class.

Every strongly endotactic reaction network is endotactic. Every weakly reversible network is endotactic [18]. Further, a weakly reversible reaction network with a single linkage class is strongly endotactic [21]. We describe below in Proposition 2.1 a geometric way of checking strong endotacticity, called the *parallel sweep test* for strongly endotactic networks [18,21].

Proposition 2.1. *Consider a reaction network $\mathcal{G}$ and its stoichiometric subspace S. For every vector $\boldsymbol{w} \notin S^\perp$, let H be the hyperplane perpendicular to $\boldsymbol{w}$ that contains a source vertex $\boldsymbol{s}_1$ such that for every other source vertex $\boldsymbol{s}_2$, we have $(\boldsymbol{s}_2 - \boldsymbol{s}_1) \cdot \boldsymbol{w} \geq 0$. If for every reaction $\boldsymbol{s} \to \boldsymbol{s}'$ with $\boldsymbol{s} \in H$, we have $(\boldsymbol{s}' - \boldsymbol{s}) \cdot \boldsymbol{w} \geq 0$, and there exists a reaction $\boldsymbol{s}_0 \to \boldsymbol{s}_0'$ with $\boldsymbol{s}_0 \in H$ such that $(\boldsymbol{s}_0' - \boldsymbol{s}_0) \cdot \boldsymbol{w} > 0$ for all $\boldsymbol{w}$, then the reaction network is said to have **passed** the parallel sweep test, and is strongly endotactic. Else, it is not strongly endotactic.*

One can verify that Fig. 1(a) and (b) satisfy the parallel sweep test for strongly endotactic reaction networks given in Proposition 2.1.

The next proposition provides simple characterization of strong endotacticity for a special class of networks that will be of particular interest to us.

Proposition 2.2. *Let $\mathcal{G}$ be a reaction network such that all the vertices of $\mathcal{G}$ are contained in the convex hull of its source vertices. Then $\mathcal{G}$ is strongly endotactic if and only if for every proper face of the convex hull of the source vertices, there exists a reaction of $\mathcal{G}$ with source vertex on this face and target vertex that does not belong to this face.*

Proof. Let S denote the stoichiometric subspace of $\mathcal{G}$. Let $\boldsymbol{w} \in \mathbb{R}^n$ be such that $\boldsymbol{w} \notin S^\perp$. Let H be the hyperplane perpendicular to $\boldsymbol{w}$ that contains a source vertex $\boldsymbol{s}_1$ such that for every other source vertex $\boldsymbol{s}_2$, we have $(\boldsymbol{s}_2 - \boldsymbol{s}_1) \cdot \boldsymbol{w} \geq 0$. Therefore, the intersection of H with the convex hull of source vertices of $\mathcal{G}$ is a proper face of the convex hull. Let us call this face f. Note that any proper face of the convex hull arises this way.

($\Rightarrow$) First assume that $\mathcal{G}$ is strongly endotactic, so it passes the parallel sweep test given in Proposition 2.1. In particular, for every reaction $\boldsymbol{s} \to \boldsymbol{s}'$ whose source vertex lies on f, we have $(\boldsymbol{s}' - \boldsymbol{s}) \cdot \boldsymbol{w} \geq 0$, and there exists a reaction $\boldsymbol{s}_0 \to \boldsymbol{s}_0'$ with vertex $\boldsymbol{s}_0$ that lies on f such that $(\boldsymbol{s}_0' - \boldsymbol{s}_0) \cdot \boldsymbol{w} > 0$. Since the vertices of $\mathcal{G}$ are contained in the convex hull of its source vertices, the reaction $\boldsymbol{s}_0 \to \boldsymbol{s}_0'$ lies in the convex hull; in particular, the source vertex $\boldsymbol{s}_0$ lies on f and the target vertex does not belong to f.

($\Leftarrow$) Let us assume that there exists a reaction $\boldsymbol{s}_0 \to \boldsymbol{s}_0'$ lying in the convex hull such that the source vertex lies on f and the target vertex does not belong to f. In particular, this implies that $(\boldsymbol{s}_0' - \boldsymbol{s}_0) \cdot \boldsymbol{w} > 0$. We will show that $\mathcal{G}$ is strongly endotactic by showing that $\mathcal{G}$ passes the parallel sweep test given in Proposition 2.1. Since all the vertices of $\mathcal{G}$ are contained in the convex hull of its source vertices, for every reaction $\boldsymbol{s} \to \boldsymbol{s}'$ whose source vertex lies on f, we have $(\boldsymbol{s}' - \boldsymbol{s}) \cdot \boldsymbol{w} \geq 0$. This combined with the fact that $(\boldsymbol{s}_0' - \boldsymbol{s}_0) \cdot \boldsymbol{w} > 0$ shows that $\mathcal{G}$ passes the parallel sweep test and is hence strongly endotactic. □

Remark 2.3. Note that Proposition 2.2 also follows from [21, Remark 3.13].

In particular, we obtain the following.

Corollary 2.4. *Let $\mathcal{G}$ be a reaction network such that all the vertices of $\mathcal{G}$ are contained in the convex hull of its source vertices. If $\mathcal{G}$ is not strongly endotactic, then there exists a proper face of the convex hull of the source vertices of $\mathcal{G}$ such that every reaction with source on this face has target on this face.*

Proof. This follows from Proposition 2.2. □

If we assume that the vertices of $\mathcal{G}$ have non-negative integer components, and that dynamics are given by *mass-action kinetics* [18,22,30], then $\mathcal{G}$ generates a dynamical system on $\mathbb{R}^n_{\geq 0}$ which can be expressed as

$$\frac{d\boldsymbol{x}}{dt} = \sum_{s\to s'\in E} k_{s\to s'}\boldsymbol{x}^{\boldsymbol{s}}(\boldsymbol{s}'-\boldsymbol{s}), \tag{2}$$

where $\boldsymbol{x}^{\boldsymbol{s}} = x_1{}^{s_1}x_2{}^{s_2}\cdots x_n{}^{s_n}$ and $k_{s\to s'} > 0$ is the *rate constant* corresponding to the reaction $\boldsymbol{s}\to\boldsymbol{s}'$. We will denote the dynamical system generated by mass-action kinetics as $\mathcal{G}_{\boldsymbol{k}} = (V, E, \boldsymbol{k})$, where $\boldsymbol{k} = (k_{s\to s'})_{s\to s'\in E}$.

We will say that a dynamical system is *polynomial* if it is of the form

$$\frac{d\boldsymbol{x}}{dt} = \sum_{i=1}^{r} \boldsymbol{x}^{\boldsymbol{s}_i}\boldsymbol{w}_i, \tag{3}$$

where $\boldsymbol{x}\in\mathbb{R}^n_{>0}$, $\boldsymbol{s}_i\in\mathbb{Z}_{\geq 0}$, and $\boldsymbol{w}_i\in\mathbb{R}^n$.

Remark 2.5. A polynomial dynamical system consisting of equations $\frac{dx_i}{dt} = f_i(\boldsymbol{x})$, where $i = 1,2,\ldots,n$ and $\boldsymbol{x} = (x_1,x_2,\ldots,x_n)^T$, is given by mass-action kinetics if and only if x_i divides every monomial with negative coefficient in $f_i(\boldsymbol{x})$ for all $i\in\{1,2,\ldots,n\}$ [31,32].

Definition 2.6 (*Dynamical Equivalence*)**.** Two mass-action systems $\mathcal{G}_{\boldsymbol{k}} = (V,E,\boldsymbol{k})$ and $\tilde{\mathcal{G}}_{\tilde{\boldsymbol{k}}} = (\tilde{V},\tilde{E},\tilde{\boldsymbol{k}})$ are *dynamically equivalent* if they generate the same dynamical system (2), i.e.,

$$\sum_{s\to s'\in E} k_{s\to s'}\boldsymbol{x}^{\boldsymbol{s}}(\boldsymbol{s}'-\boldsymbol{s}) = \sum_{\tilde{s}\to\tilde{s}'\in\tilde{E}} \tilde{k}_{\tilde{s}\to\tilde{s}'}\boldsymbol{x}^{\tilde{\boldsymbol{s}}}(\tilde{\boldsymbol{s}}'-\tilde{\boldsymbol{s}}). \tag{4}$$

Equivalently, for every $\boldsymbol{s}\in V\cup\tilde{V}$ we have

$$\sum_{s\to s'\in E} k_{s\to s'}(\boldsymbol{s}'-\boldsymbol{s}) = \sum_{s\to\tilde{s}'\in\tilde{E}} \tilde{k}_{s\to\tilde{s}'}(\tilde{\boldsymbol{s}}'-\boldsymbol{s}). \tag{5}$$

Note that in Eq. (4), we are summing over all edges, while in Eq. (5), the sum is over all edges with source vertex $\boldsymbol{s}$, where $\boldsymbol{s}$ lies in the union of the vertices of the two E-graphs [33].

For example, mass-action systems generated by the reaction network in Fig. 1(b) can be made dynamically equivalent to the mass-action systems generated by the reaction network in Fig. 1(a). For more details and examples for the construction of dynamically equivalent systems see [33].

A dynamical system is called *autonomous* if it can be written in the form $\frac{d\boldsymbol{x}(t)}{dt} = \boldsymbol{f}(\boldsymbol{x}(t))$. If the rate coefficients depend on time instead of being constants as in Eq. (2), the dynamics is governed by the non-autonomous system

$$\frac{d\boldsymbol{x}}{dt} = \sum_{s\to s'\in E} k_{s\to s'}(t)\boldsymbol{x}^{\boldsymbol{s}}(\boldsymbol{s}'-\boldsymbol{s}), \tag{6}$$

where $k_{s\to s'}(t)$ are assumed to be locally Lipschitz functions. If there exists an $\epsilon > 0$ such that $\epsilon \leq k_{s\to s'}(t) \leq \frac{1}{\epsilon}$ for every $k_{s\to s'}(t)$ in (6), then the dynamical system is called a *variable-k mass-action system*. Note that every autonomous mass-action system is a variable-k mass-action system. We now define some important dynamical properties.

Definition 2.7 (*Persistence*)**.** A dynamical system given by (6) is said to be *persistent* if $\mathbb{R}^n_{>0}$ is forward invariant and for any initial condition $(\boldsymbol{x}_0,t_0)\in\mathbb{R}^n_{>0}\times\mathbb{R}$, the solution $\boldsymbol{x}(t)$ of (6) satisfies $\liminf_{t\to T_{(\boldsymbol{x}_0,t_0)}} x_i(t) > 0$ for all $i = 1,2,\ldots,n$, where $T_{(\boldsymbol{x}_0,t_0)}\in(t_0,\infty]$ is the maximal time for which $\boldsymbol{x}(t)$ is defined.

Definition 2.8 (*Permanence*)**.** A dynamical system given by (6) is said to be *permanent* if for every positive compatibility class C, there exists a compact set $K\subset C$ such that for every solution $\boldsymbol{x}(t)$ of (6) with initial condition $(\boldsymbol{x}_0,t_0)\in C\times\mathbb{R}$, we have $\boldsymbol{x}(t)\in K$ for all t sufficiently large.

A permanent dynamical system is persistent. These two dynamical properties are related to important open problems in reaction network theory. The *Persistence Conjecture* states that weakly reversible mass-action dynamical systems are persistent. This conjecture has been generalized in [18] to the *Extended Permanence Conjecture*, which states that variable-k endotactic mass-action dynamical systems are permanent. These conjectures are intimately related to the more familiar *Global Attractor Conjecture* [22], which says that for *complex balanced dynamical systems*, each positive compatibility class contains a globally attracting steady state.

We will need the following lemma about strongly endotactic networks.

Theorem 2.9. *Dynamical systems generated by strongly endotactic networks under mass-action kinetics are permanent.*

Proof. Follows from [21, Theorem 1.1]. □

3. Autocatalytic systems

One of the goals of this paper is to analyze dynamical properties like persistence and permanence in the context of *autocatalytic networks* [2,34,35] using the framework of reaction network theory. Autocatalytic networks have been studied in the context of origin of life [3,36,37]. An important family of autocatalytic networks called *hypercycles* consists of a cyclic connection of molecules capable of self-replicating themselves by undergoing mutual catalysis. The classical n-dimensional hypercycle refers to the following network: $X_i + X_{i+1}\to X_i + 2X_{i+1}$ for $1\leq i\leq n$, where $X_{n+1} = X_1$ (in the cyclic sense). The dynamics of hypercycles has been a topic of interest since the 1980's when properties like permanence and the existence of a globally attracting fixed point were established for special cases [16,38–40].

The concentration of some or all species in autocatalytic systems can become unbounded in finite time [12]. As a consequence, it makes sense to analyze the dynamics of *relative* populations of species in such networks. There is no reason why the relative population of species of an autonomous dynamical system should correspond to a solution of an autonomous dynamical system. However, under certain assumptions on the original system, we show in Theorem 3.1 that a solution of the system of relative populations is a solution of an autonomous polynomial dynamical system up to time re-scaling. Further, in Theorem 3.5 we show how to build a reaction network whose dynamics corresponds to the relative population of bimolecular autocatalytic network.

Theorem 3.1. *Consider an autonomous dynamical system $\mathcal{A}$ given by $\frac{d\boldsymbol{x}}{dt} = \boldsymbol{f}(\boldsymbol{x})$ with $\boldsymbol{f}(\boldsymbol{x}) = (f_1(\boldsymbol{x}),f_2(\boldsymbol{x}),\ldots,f_n(\boldsymbol{x}))^T$, where each $f_i(\boldsymbol{x})$ is a homogeneous polynomial with real coefficients of degree d. Let $x_T(t) = \sum_{i=1}^n x_i(t)$ denote the total concentration. Then $\tilde{\mathcal{A}}$ can be chosen to be an autonomous polynomial dynamical system such that for any solution $\boldsymbol{x}(t)$ of $\mathcal{A}$, the function*

$$\tilde{\boldsymbol{x}}(t) = \frac{\boldsymbol{x}(t)}{x_T(t)}$$

defined for all time t such that $0 < x_T(t) < \infty$, is, up to time-rescaling, a solution of $\tilde{\mathcal{A}}$. Moreover, if $\mathcal{A}$ is a mass-action system, then $\tilde{\mathcal{A}}$ can also be chosen to be a mass-action system.

Proof. The proof proceeds by construction of $\tilde{\mathcal{A}}$. Let $\tilde{\boldsymbol{x}} = \frac{1}{x_T}\cdot\boldsymbol{x}$, then

$$\frac{d\tilde{\boldsymbol{x}}}{dt} = x_T^{-2}\left(\frac{d\boldsymbol{x}}{dt}x_T - \boldsymbol{x}\sum_{i=1}^n\frac{dx_i}{dt}\right) = x_T^{-2}\left(\boldsymbol{f}(\boldsymbol{x})x_T - \boldsymbol{x}\sum_{i=1}^n f_i(\boldsymbol{x})\right). \tag{7}$$

Since $f_i(\boldsymbol{x})$ is a homogeneous polynomial of degree d and $\boldsymbol{x} = x_T\tilde{\boldsymbol{x}}$, we have $\boldsymbol{f}(\boldsymbol{x}) = x_T^d\boldsymbol{f}(\tilde{\boldsymbol{x}})$. Plugging this into Eq. (7) gives

$$\frac{d\tilde{\boldsymbol{x}}}{dt} = \left(\boldsymbol{f}(\tilde{\boldsymbol{x}}) - \tilde{\boldsymbol{x}}\sum_{i=1}^{n} f_i(\tilde{\boldsymbol{x}})\right)x_T^{d-1}, \tag{8}$$

which is a time-rescaled version of

$$\frac{d\tilde{\boldsymbol{x}}}{dt} = \boldsymbol{f}(\tilde{\boldsymbol{x}}) - \tilde{\boldsymbol{x}}\sum_{i=1}^{n} f_i(\tilde{\boldsymbol{x}}). \tag{9}$$

By *time-rescaled version*, we mean that the vector field defined by Eq. (8) is obtained by multiplying the vector field of (9) by a positive scalar field. Given a solution $\boldsymbol{x}(t)$ of a dynamical system, its *trajectory curve* is the set $\{\boldsymbol{x}(t)\,|\,t \text{ is in the maximal interval of existence of } \boldsymbol{x}(t)\}$. Then Eqs. (8) and (9) have the same sets of trajectory curves within the positive orthant [41], and therefore $\tilde{\boldsymbol{x}}$ is (after time-rescaling) a solution of $\tilde{\mathcal{A}}$ given by $\frac{d\tilde{\boldsymbol{x}}}{dt} = \tilde{\boldsymbol{f}}(\tilde{\boldsymbol{x}})$, where $\tilde{\boldsymbol{f}}(\tilde{\boldsymbol{x}}) = \boldsymbol{f}(\tilde{\boldsymbol{x}}) - \tilde{\boldsymbol{x}}\sum_{i=1}^{n} f_i(\tilde{\boldsymbol{x}})$.

If the system $\mathcal{A}$ was mass-action, then given the form of Eq. (9) and Remark 2.5, it is straightforward to check that $\tilde{\mathcal{A}}$ is also mass-action. □

We now show that a result similar to Theorem 3.1 holds for non-autonomous dynamical system.

Corollary 3.2. *Consider a variable-k dynamical system $\mathcal{A}$ given by $\frac{d\boldsymbol{x}}{dt} = \boldsymbol{f}(\boldsymbol{x})$ with $\boldsymbol{f}(\boldsymbol{x},t) = (f_1(\boldsymbol{x},t), f_2(\boldsymbol{x},t), \dots, f_n(\boldsymbol{x},t))^T$ where each $f_i(\boldsymbol{x},t)$ is a homogeneous polynomial (in $\boldsymbol{x}$) of degree d, with time-dependent coefficients, i.e.*

$$f_i(\boldsymbol{x},t) = \sum_j k_j(t)\boldsymbol{x}^{\boldsymbol{s}_j}\boldsymbol{w}_j,$$

where $\epsilon \le k_j(t) \le \frac{1}{\epsilon}$, $\mathbf{1}\cdot\boldsymbol{s}_j = d$, and $\boldsymbol{w}_j \in \mathbb{R}$. Let $x_T(t) = \sum_{i=1}^{n} x_i(t)$ denote the total concentration. Then $\tilde{\mathcal{A}}$ can be chosen to be a variable-k dynamical system such that for any solution $\boldsymbol{x}(t)$ of $\mathcal{A}$, the function

$$\tilde{\boldsymbol{x}}(t) = \frac{\boldsymbol{x}(t)}{x_T(t)}$$

defined for all time t such that $0 < x_T(t) < \infty$, is, up to time-rescaling, a solution of $\tilde{\mathcal{A}}$.

Proof. The proof proceeds in identical fashion to the proof of Theorem 3.1.

In this case, Eqs. (8) and (9) get transformed to

$$\frac{d\tilde{\boldsymbol{x}}}{dt} = \left(\boldsymbol{f}(\tilde{\boldsymbol{x}},t) - \tilde{\boldsymbol{x}}\sum_{i=1}^{n} f_i(\tilde{\boldsymbol{x}},t)\right)x_T^{d-1}, \tag{10}$$

and

$$\frac{d\tilde{\boldsymbol{x}}}{dt} = \boldsymbol{f}(\tilde{\boldsymbol{x}},t) - \tilde{\boldsymbol{x}}\sum_{i=1}^{n} f_i(\tilde{\boldsymbol{x}},t) \tag{11}$$

respectively. Construct an augmented dynamical system to Eq. (10) given by

$$\begin{aligned}\frac{d\tilde{\boldsymbol{x}}}{dt} &= \left(\boldsymbol{f}(\tilde{\boldsymbol{x}},t) - \tilde{\boldsymbol{x}}\sum_{i=1}^{n} f_i(\tilde{\boldsymbol{x}},t)\right)x_T^{d-1}(t)\\ \frac{d\tilde{y}}{dt} &= 1.\end{aligned} \tag{12}$$

If we assume that the initial condition satisfies $\tilde{y}(t_0) = t_0$, then Eq. (12) can also be expressed as the autonomous dynamical system

$$\begin{aligned}\frac{d\tilde{\boldsymbol{x}}}{dt} &= \left(\boldsymbol{f}(\tilde{\boldsymbol{x}},\tilde{y}) - \tilde{\boldsymbol{x}}\sum_{i=1}^{n} f_i(\tilde{\boldsymbol{x}},\tilde{y})\right)x_T^{d-1}(\tilde{y})\\ \frac{d\tilde{y}}{dt} &= 1.\end{aligned} \tag{13}$$

For initial condition $(\tilde{\boldsymbol{x}}(t_0), \tilde{y}(t_0)) := (\tilde{\boldsymbol{x}}_0, \tilde{y}_0 = t_0) \in \mathbb{R}^n_{>0} \times \mathbb{R}$, let $(\tilde{\boldsymbol{x}}_0(t), \tilde{y}_0(t))$ be the unique solution to (13). Let Γ denote the trajectory curve corresponding to this solution. Consider the system

$$\begin{aligned}\frac{d\tilde{\boldsymbol{x}}^*}{dt} &= \boldsymbol{f}(\tilde{\boldsymbol{x}}^*,\tilde{y}^*) - \tilde{\boldsymbol{x}}^*\sum_{i=1}^{n} f_i(\tilde{\boldsymbol{x}}^*,\tilde{y}^*)\\ \frac{d\tilde{y}^*}{dt} &= \frac{1}{x_T^{d-1}(\tilde{y}^*)}.\end{aligned} \tag{14}$$

Note that the solution of system (14) with the same initial conditions $(\tilde{\boldsymbol{x}}_0, \tilde{y}_0 = t_0)$ also lies on Γ since (14) is a rescaling of (13) by a factor x_T^{d-1} [41]. If we now define $\tilde{k}(t) = k(\tilde{y}^*(t))$, then the solution of the dynamical system given by Eq. (14) restricted to the components of $\tilde{\boldsymbol{x}}^*$, with initial condition $(\tilde{\boldsymbol{x}}_0, \tilde{y}_0 = t_0)$, is the same as the solution of Eq. (11) where we *replace* $\boldsymbol{f}(\boldsymbol{x},t)$ by

$$\tilde{\boldsymbol{f}}(\boldsymbol{x},t) = \sum_j \tilde{k}_j(t)\boldsymbol{x}^{\boldsymbol{s}_j}\boldsymbol{w}_j. \tag{15}$$

The replaced system is our desired $\tilde{\mathcal{A}}$ and is given by the following:

$$\frac{d\tilde{\boldsymbol{x}}}{dt} = \tilde{\boldsymbol{f}}(\tilde{\boldsymbol{x}},t) - \tilde{\boldsymbol{x}}\sum_{i=1}^{n} \tilde{f}_i(\tilde{\boldsymbol{x}},t) \tag{16}$$

Given the form of (15), it follows that $\tilde{\mathcal{A}}$ is also a variable-k dynamical system. □

Corollary 3.3. *Consider a dynamical system $\mathcal{A}$ given by $\frac{d\boldsymbol{x}}{dt} = \boldsymbol{f}(\boldsymbol{x})$ with $\boldsymbol{f}(\boldsymbol{x}) = (f_1(\boldsymbol{x}), f_2(\boldsymbol{x}), \dots, f_n(\boldsymbol{x}))^T$ where each $f_i(\boldsymbol{x})$ is a homogeneous polynomial with real coefficients of degree d. Let $x_T(t) = \sum_{i=1}^{n} x_i(t)$ denote the total concentration. Then the dynamical system corresponding to $\tilde{\boldsymbol{x}}(t) = \frac{\boldsymbol{x}(t)}{x_T(t)}$ is given by*

$$\frac{d\tilde{\boldsymbol{x}}}{dt} = \boldsymbol{f}(\tilde{\boldsymbol{x}})\left(\sum_{i=1}^{n}\tilde{x}_i\right) - \tilde{\boldsymbol{x}}\sum_{i=1}^{n} f_i(\tilde{\boldsymbol{x}}), \tag{17}$$

so that the right-hand side consists of homogeneous polynomials.

Proof. This follows from Eq. (9) in Theorem 3.1 since $\sum_{i=1}^{n}\tilde{x}_i = 1$. □

In what follows in the paper, a lot of results assume that the dynamics is governed by mass-action kinetics. Note that mass-action systems can also be variable-k systems.

Definition 3.4. A reaction network $\mathcal{G}$ is said to be a *bimolecular autocatalytic system* if every reaction in $\mathcal{G}$ is of the form $X_i + X_j \to X_i + X_j + X_l$ for some $i, j, l \in \{1, 2, \dots, n\}$.

The dynamics (after time-rescaling) generated by the relative population variables of a bimolecular autocatalytic system is generated by another reaction network under mass-action kinetics. The next theorem gives a precise constructive procedure for obtaining the relative population reaction network given the original bimolecular autocatalytic system.

Theorem 3.5. *Consider a bimolecular autocatalytic system $\mathcal{M}$ with concentration variables $x_1, x_2, \dots, x_n$ corresponding to species $X_1, X_2, \dots, X_n$. For $1 \le i \le n$, let $\tilde{x}_i(t) = x_i(t)/x_T(t)$ denote the relative population variables and $x_T(t)$ the total concentration. Then $\tilde{x}_1(t), \tilde{x}_2(t), \dots, \tilde{x}_n(t)$ is (after time-rescaling) a solution of the dynamical system generated by a reaction network consisting of the following reactions:*

For every reaction $X_i + X_j \xrightarrow{k_{ijl}(t)} X_i + X_j + X_l$ in the bimolecular autocatalytic system $\mathcal{M}$, where $i, j, l \in \{1, 2, \dots, n\}$, we have the following set of reactions in the relative population network: $\{X_p + X_i + X_j \xrightarrow{k_{ijl}(t)} X_i + X_j + X_l$ such that $p \ne l.\}$

Proof. We will consider a single reaction in the bimolecular autocatalytic system $\mathcal{M}$. By combining the right-hand sides of the other reactions, we will get our desired result.

Consider the reaction $X_i + X_j \xrightarrow{k_{ijl}(t)} X_i + X_j + X_l$ for some $i, j, l \in \{1, 2, \dots, n\}$. We have the following differential equations corresponding

to the species X_i, X_j, X_l, and also for every species X_m that does not appear in the above reaction (i.e., for all $m \neq i, j, l$):

$$\begin{aligned}\frac{dx_i}{dt} &= k_{ijl}(t)x_i x_j \delta_{li}\\ \frac{dx_j}{dt} &= k_{ijl}(t)x_i x_j \delta_{jl}\\ \frac{dx_l}{dt} &= k_{ijl}(t)x_i x_j\\ \frac{dx_m}{dt} &= 0.\end{aligned} \tag{18}$$

(Here δ_{ij} is the Kronecker delta, i.e., $\delta_{ij} = 1$ if $i = j$ and 0 if $i \neq j$.) The dynamical system in (18) can be understood in the following way: If $l \neq i$ and $l \neq j$, then since the species X_i and X_j are not produced, there is no contribution to their rate equations. If either $l = i$ or $l = j$, then we get a contribution of $k_{ijl}(t)x_i x_j$ to the rate equation corresponding to X_i or X_j. For every species X_m that does not appear in the above reaction, there is no net change in X_m. Therefore $\frac{dx_m}{dt} = 0$. Note that the rate constants in (18) are exactly the same as in the original bimolecular autocatalytic reaction $X_i + X_j \xrightarrow{k_{ijl}(t)} X_i + X_j + X_l$.

Some of the equations in (18) may be redundant, e.g., when $i = l$ or $j = l$. According to Corollary 3.3 and using Eq. (18), the dynamical system (up to time-rescaling) for the relative populations variables is

$$\begin{aligned}\frac{d\tilde{x}_i}{dt} &= k_{ijl}(t)\tilde{x}_i\tilde{x}_j\delta_{li}\left(\sum_{r=1}^{n}\tilde{x}_r\right) - k_{ijl}(t)\tilde{x}_i^2\tilde{x}_j\\ \frac{d\tilde{x}_j}{dt} &= k_{ijl}(t)\tilde{x}_i\tilde{x}_j\delta_{jl}\left(\sum_{r=1}^{n}\tilde{x}_r\right) - k_{ijl}(t)\tilde{x}_i\tilde{x}_j^2\\ \frac{d\tilde{x}_l}{dt} &= k_{ijl}(t)\tilde{x}_i\tilde{x}_j\left(\sum_{r=1}^{n}\tilde{x}_r\right) - k(t)\tilde{x}_i\tilde{x}_j\tilde{x}_l\\ \frac{d\tilde{x}_m}{dt} &= -k_{ijl}(t)\tilde{x}_i\tilde{x}_j\tilde{x}_m.\end{aligned} \tag{19}$$

We now show that dynamical system (19) can be generated by the set of reactions

$$\{X_p + X_i + X_j \xrightarrow{k_{ijl}(t)} X_i + X_j + X_l \mid p \neq l\}. \tag{20}$$

There are four cases to consider:

1. $i = j = l$: The set of reactions of the form (20) contribute $k_{ijl}(t)\tilde{x}_i^2\left(\sum_{\substack{1\le r\le n\\ r\neq i}}\tilde{x}_r\right)$ to $\frac{d\tilde{x}_i}{dt}$ and $-k_{ijl}(t)\tilde{x}_i\tilde{x}_j\tilde{x}_m$ to $\frac{d\tilde{x}_m}{dt}$.
2. $i = l$, $j \neq l$: The set of reactions of the form (20) contribute $k_{ijl}(t)\tilde{x}_i\tilde{x}_j\left(\sum_{\substack{1\le r\le n\\ r\neq i}}\tilde{x}_r\right)$ to $\frac{d\tilde{x}_i}{dt}$, $-k_{ijl}(t)\tilde{x}_i\tilde{x}_j^2$ to $\frac{d\tilde{x}_j}{dt}$, and $-k_{ijl}\tilde{x}_i\tilde{x}_j\tilde{x}_m$ to $\frac{d\tilde{x}_m}{dt}$.
3. $i \neq l$, $j = l$: Similar to the case above, the set of reactions of the form (20) contribute $-k_{ijl}(t)\tilde{x}_i^2\tilde{x}_j$ to $\frac{d\tilde{x}_i}{dt}$, $k_{ijl}(t)\tilde{x}_i\tilde{x}_j\left(\sum_{\substack{1\le r\le n\\ r\neq j}}\tilde{x}_r\right)$ to $\frac{d\tilde{x}_j}{dt}$, and $-k_{ijl}(t)\tilde{x}_i\tilde{x}_j\tilde{x}_m$ to $\frac{d\tilde{x}_m}{dt}$.
4. $l \neq i$, $j \neq l$: The set of reactions of the form (20) contribute $-k_{ijl}(t)\tilde{x}_i^2\tilde{x}_j$ to $\frac{d\tilde{x}_i}{dt}$, $-k_{ijl}(t)\tilde{x}_i\tilde{x}_j^2$ to $\frac{d\tilde{x}_j}{dt}$, and $-k_{ijl}(t)\tilde{x}_i\tilde{x}_j\tilde{x}_m$ to $\frac{d\tilde{x}_m}{dt}$ and $k_{ijl}(t)\tilde{x}_i\tilde{x}_j\left(\sum_{\substack{1\le r\le n\\ r\neq l}}\tilde{x}_r\right)$ to $\frac{d\tilde{x}_l}{dt}$.

Therefore, the mass-action system generated by (20) coincides with the sum of (19) for all $m \neq i, j, l$. □

We now illustrate how Theorem 3.5 can be applied in the example below.

Example 3.6. Consider the bimolecular autocatalytic reaction network $\mathcal{G} = \{X_1+X_2 \xrightarrow{k_1(t)} X_1+X_2+X_3, 2X_1 \xrightarrow{k_2(t)} 2X_1+X_2\}$. By Theorem 3.5, the network corresponding to the relative concentrations of $\mathcal{G}$ is obtained by adding all possible species to the reactant side of each reaction in $\mathcal{G}$ (except when it results in a trivial reaction that has the same reactant and product). In this case, the network corresponding to relative concentrations $\tilde{\mathcal{G}}$ consists of the following reactions:

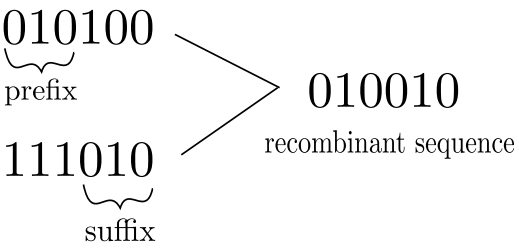


Fig. 2. Recombinant sequence produced from the prefix of one sequence and the suffix of another.

(i) $2X_1 + X_2 \xrightarrow{k_1(t)} X_1 + X_2 + X_3$ (obtained by adding X_1 to the reactants of $X_1 + X_2 \xrightarrow{k_1(t)} X_1 + X_2 + X_3$).
(ii) $X_1 + 2X_2 \xrightarrow{k_1(t)} X_1 + X_2 + X_3$ (obtained by adding X_2 to the reactants of $X_1 + X_2 \xrightarrow{k_1(t)} X_1 + X_2 + X_3$).
(iii) $3X_1 \xrightarrow{k_2(t)} 2X_1 + X_2$ (obtained by adding X_1 to the reactants of $2X_1 \xrightarrow{k_2(t)} 2X_1 + X_2$).
(iv) $2X_1 + X_3 \xrightarrow{k_2(t)} 2X_1 + X_2$ (obtained by adding X_3 to the reactants of $2X_1 \xrightarrow{k_2(t)} 2X_1 + X_2$).

4. Permanence and global stability of autocatalytic recombination networks

Theorems 3.1 and 3.5 are applicable to general bimolecular autocatalytic systems , i.e., systems involving reactions of the form $X_i + X_j \to X_i + X_j + X_l$. In what follows, we consider networks arising from *genetic recombination* that allows us to conclude permanence of the relative population models.

Genetic recombination is a phenomenon widely believed to be responsible for variation among species [1,42]. It involves the exchange of genetic material between molecules of DNA, so the new molecule inherits certain properties of its parents. Most familiar examples of recombination take place during prophase I of meiosis. For a single crossover recombination, two DNA sequences of equal length exchange genetic information to produce a third sequence of the same length that has the *prefix* of one of the sequences and the *suffix* of the other, as illustrated in Fig. 2.

For our purpose, we model genetic recombination as bimolecular autocatalytic systems, as introduced in Definition 3.4.

In particular, in this section we consider networks whose reactions are of the form

$X_i + X_j \to X_i + X_j + X_k$, where X_k represents the gene sequence that combines the information of the parent molecules X_i and X_j.

We shall show that the dynamical systems generated by relative populations of some of these reaction networks are permanent. The dynamical systems that we analyze bear striking resemblance to the fertility equations in [11]. One can also view them as cyclic versions of the *catalytic network equation* in [43].

The rest of this paper focuses on two families of networks. The first, *autocatalytic recombination networks with repeated reactant species* (see Definition 4.1 and Section 4.1), is akin to *homologous* genetic recombination [44,45], which involves the exchange of genetic material in the form of nucleotide sequences between two similar DNA strands. Homologous recombination plays an important role in repairing DNA strands that may be damaged due to chemicals and radiation. In addition, homologous recombination is used in *gene targeting* [46–48], whereby certain genetic traits are introduced in a target organism.

The second, autocatalytic recombination networks with *no* repeated species (see Definition 4.10 and Section 4.2), is closer in spirit to *non-homologous* genetic recombination [49], which involves the exchange of genetic material in the form of nucleotide sequences between two

dissimilar DNA strands. Nonhomologous genetic recombination is used for repairing breaks in DNA strands.

The rest of this section is organized as follow. We analyze autocatalytic recombination networks with repeated reactant species in Section 4.1; in particular, we show that when involving three species or more, the dynamics for relative population is always permanent. We extend the permanence result to bimolecular networks that contain reactions of the specific form $2X_i \to 2X_i + X_j$ (j not necessarily different from i) which result in producing X_j. Moreover, every species in the network is produced by at least one reaction of the above form. Next in Section 4.2, we analyze autocatalytic recombination networks with *no* repeated species. We prove the dynamics for relative population is permanent in dimension 4–6. Whether permanence holds in higher dimension remains an open question. We wrap up this work with Theorem 4.17, where we give a sufficient condition for permanence of the relative population model for networks that contain reactions of the form $X_i + X_j \to X_i + X_j + X_k$.

Many of the theorems we prove use the geometry of a *regular simplex*. Recall that a regular n-simplex is a regular n-polytope formed using the convex hull of $n+1$ vertices in general position [50]. From here on, we shall refer to a regular n-simplex simply as a n-simplex. In addition, we will use the term *extremal point* instead of the more standard term *vertex* for polytopes.

4.1. Autocatalytic recombination networks with repeated reactant species: homologous recombination

In this subsection, we prove that for some models of *homologous* genetic recombination, the relative population dynamics is permanent (see Theorem 4.5). More precisely, we model this process using autocatalytic recombination networks with repeated reactant species, defined below. Moreover, in Theorem 4.8 we extend our result to bimolecular networks that contain subnetworks satisfying some assumptions inspired by this framework for homologous recombination.

Definition 4.1. The *autocatalytic recombination network of dimension n with repeated reactant species* is a reaction network $\mathcal{G}^{\text{rep}}_{\text{recomb}(n)}$ with species $X_1, X_2, \dots, X_n$ consisting of the reactions $2X_i \to 3X_i$ and $2X_i \to 2X_i + X_{i+1}$ for all $i = 1, 2, \dots, n$, where $X_{n+1} = X_1$(in the cyclic sense).

Remark 4.2. Note that the autocatalytic recombination networks with repeated species described in Definition 4.1 are special cases of bimolecular autocatalytic systems defined in Definition 3.4.

We will show that variable-k mass-action systems generated by the relative population networks corresponding to the autocatalytic recombination network with repeated reactant species in n dimensions $\mathcal{G}^{\text{rep}}_{\text{recomb}(n)}$ are permanent.

Before we state and prove the fully general case, it is instructive to look at smaller dimensions in some detail, in order to understand some of the geometric ideas that form the basis of our approach. For example, for $n = 3$, we have:

Proposition 4.3. *Consider the autocatalytic recombination network $\mathcal{G}^{\text{rep}}_{\text{recomb}(3)}$ of dimension three as described in Table 1. Let $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$ be the network corresponding to relative populations as constructed in Theorem 3.5 (the network $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$ is shown in Fig. 3(a)). Then any variable-k mass-action system generated by $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$ is permanent.*

Proof. We will show that $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$ is strongly endotactic. It will then follow from Theorem 2.9 that any variable-k dynamical system generated by it is permanent. The convex hull formed by the source vertices of $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$ is a triangle as shown in Fig. 3.(b). In particular, the triangle contains all the vertices of $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$. By Proposition 2.2, to show that $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$ is strongly endotactic, it suffices to show that for every proper face of the triangle, there exists a reaction with source on this face and target that does not belong to this face. One can check that this is the case from Fig. 3.(a). Therefore, $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$ is strongly endotactic □

Table 1
On the left (right) are listed all the reactions that appear in $\mathcal{G}^{\text{rep}}_{\text{recomb}(3)}$ ($\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$). The algorithm for generating $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$ produces a specific set of reactions from each reaction in $\mathcal{G}^{\text{rep}}_{\text{recomb}(3)}$. The table pairs this subnetwork with the corresponding generating reaction in $\mathcal{G}^{\text{rep}}_{\text{recomb}(3)}$.

Set of reactions in $\mathcal{G}^{\text{rep}}_{\text{recomb}(3)}$	Set of reactions in $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$
$2X_1 \xrightarrow{k_1} 3X_1$	$2X_1 + X_2 \xrightarrow{k_1} 3X_1$
	$2X_1 + X_3 \xrightarrow{k_1} 3X_1$
$2X_1 \xrightarrow{k_2} 2X_1 + X_2$	$3X_1 \xrightarrow{k_2} 2X_1 + X_2$
	$2X_1 + X_3 \xrightarrow{k_2} 2X_1 + X_2$
$2X_2 \xrightarrow{k_3} 3X_2$	$2X_2 + X_3 \xrightarrow{k_3} 3X_2$
	$2X_2 + X_1 \xrightarrow{k_3} 3X_2$
$2X_2 \xrightarrow{k_4} 2X_2 + X_3$	$3X_2 \xrightarrow{k_4} 2X_2 + X_3$
	$2X_2 + X_1 \xrightarrow{k_4} 2X_2 + X_3$
$2X_3 \xrightarrow{k_5} 3X_3$	$2X_3 + X_1 \xrightarrow{k_5} 3X_3$
	$2X_3 + X_2 \xrightarrow{k_5} 3X_3$
$2X_3 \xrightarrow{k_6} 2X_3 + X_1$	$3X_3 \xrightarrow{k_6} 2X_3 + X_1$
	$2X_3 + X_2 \xrightarrow{k_6} 2X_3 + X_1$

Similarly, for $n = 4$, we have:

Proposition 4.4. *Consider the autocatalytic recombination network $\mathcal{G}^{\text{rep}}_{\text{recomb}(4)}$ of dimension four as described in Table 2. Let $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$ be the network corresponding to relative populations as constructed in Theorem 3.5 (the network $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$ is shown in Fig. 4). Then any variable-k mass-action system generated by $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$ is permanent.*

Proof. We will show that $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$ is strongly endotactic. It will then follow from Theorem 2.9 that any variable-k dynamical system generated by it is permanent. The convex hull formed by the source vertices of $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$ is the tetrahedron shown in Fig. 4. In particular, the tetrahedron contains all the vertices of $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$. By Proposition 2.2, to show that $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$ is strongly endotactic, it suffices to show that for every proper face of the tetrahedron, there exists a reaction with source on this face and target that does not belong to this face. One can check that this is the case from Fig. 4. Therefore, $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$ is strongly endotactic. □

Moving to the general case, we define the network $\mathcal{G}^{\text{rep}}_{\text{recomb}(n)}$ consisting of the following reactions

$$\begin{aligned}
&2X_1 \to 3X_1\\
&2X_1 \to 2X_1 + X_2\\
&\quad\vdots\\
&2X_{n-1} \to 3X_{n-1}\\
&2X_{n-1} \to 2X_{n-1} + X_n\\
&2X_n \to 3X_n\\
&2X_n \to 2X_n + X_1.
\end{aligned}$$

In the following theorem, we prove that any variable-k mass-action system generated by $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$ is permanent.

Theorem 4.5. *Let $n \geq 3$. Consider the autocatalytic recombination network of dimension n with repeated reactant species given by $\mathcal{G}^{\text{rep}}_{\text{recomb}(n)}$. Let $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$ be constructed as in Theorem 3.5. Then any variable-k mass-action system generated by $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$ is permanent.*

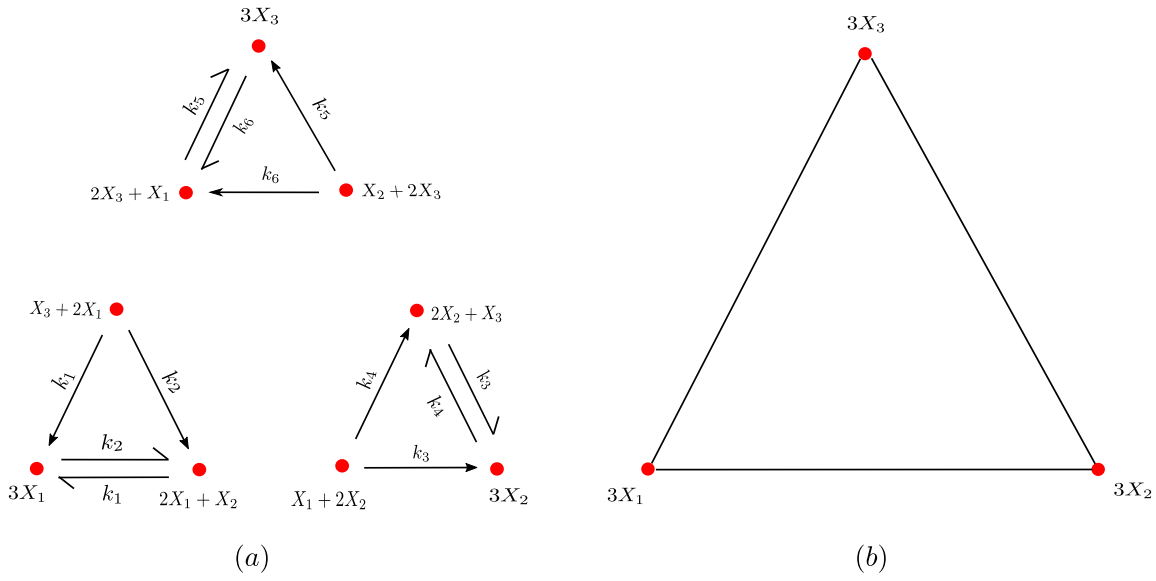


Fig. 3. (a) Reaction network $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(3)}$ that generates the dynamics of relative populations of the recombination network of dimension three with repeated reactant species given by $\mathcal{G}^{\text{rep}}_{\text{recomb}(3)}$ in Table 1. (b) Convex hull of all vertices of the network in Fig. 3(a).

Table 2
On the left (right) are listed all the reactions that appear in $\mathcal{G}^{\text{rep}}_{\text{recomb}(4)}(\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)})$. The algorithm for generating $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$ produces a specific set of reactions from each reaction in $\mathcal{G}^{\text{rep}}_{\text{recomb}(4)}$. The table pairs this subnetwork with the corresponding generating reaction in $\mathcal{G}^{\text{rep}}_{\text{recomb}(4)}$.

Set of reactions in $\mathcal{G}^{\text{rep}}_{\text{recomb}(4)}$	Set of reactions in $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$
$2X_1 \xrightarrow{k_1} 3X_1$	$2X_1 + X_2 \xrightarrow{k_1} 3X_1$
	$2X_1 + X_3 \xrightarrow{k_1} 3X_1$
	$2X_1 + X_4 \xrightarrow{k_1} 3X_1$
$2X_1 \xrightarrow{k_2} 2X_1 + X_2$	$3X_1 \xrightarrow{k_2} 2X_1 + X_2$
	$2X_1 + X_3 \xrightarrow{k_2} 2X_1 + X_2$
	$2X_1 + X_4 \xrightarrow{k_2} 2X_1 + X_2$
$2X_2 \xrightarrow{k_3} 3X_2$	$2X_2 + X_3 \xrightarrow{k_3} 3X_2$
	$2X_2 + X_1 \xrightarrow{k_3} 3X_2$
	$2X_2 + X_4 \xrightarrow{k_3} 3X_2$
$2X_2 \xrightarrow{k_4} 2X_2 + X_3$	$3X_2 \xrightarrow{k_4} 2X_2 + X_3$
	$2X_2 + X_1 \xrightarrow{k_4} 2X_2 + X_3$
	$2X_2 + X_4 \xrightarrow{k_4} 2X_2 + X_3$
$2X_3 \xrightarrow{k_5} 3X_3$	$2X_3 + X_1 \xrightarrow{k_5} 3X_3$
	$2X_3 + X_2 \xrightarrow{k_5} 3X_3$
	$2X_3 + X_4 \xrightarrow{k_5} 3X_3$
$2X_3 \xrightarrow{k_6} 2X_3 + X_4$	$3X_3 \xrightarrow{k_6} 2X_3 + X_4$
	$2X_3 + X_2 \xrightarrow{k_6} 2X_3 + X_4$
	$2X_3 + X_4 \xrightarrow{k_6} 2X_3 + X_4$
$2X_4 \xrightarrow{k_7} 3X_4$	$2X_4 + X_1 \xrightarrow{k_7} 3X_4$
	$2X_4 + X_2 \xrightarrow{k_7} 3X_4$
	$2X_4 + X_3 \xrightarrow{k_7} 3X_4$
$2X_4 \xrightarrow{k_8} 2X_4 + X_1$	$3X_4 \xrightarrow{k_8} 2X_4 + X_1$
	$2X_4 + X_2 \xrightarrow{k_8} 2X_4 + X_1$
	$2X_4 + X_3 \xrightarrow{k_8} 2X_4 + X_1$

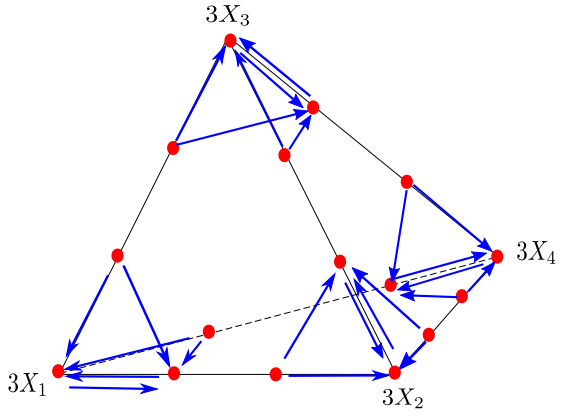


Fig. 4. Reaction network $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(4)}$ of Table 2.

Proof. We claim that $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$ is strongly endotactic; it then follows from Theorem 2.9 that any variable-k mass-action system generated by it is permanent. Consider the convex hull formed by the source vertices in $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$. Note that using Theorem 3.5 we get the following: for every reaction $2X_i \to 2X_i + X_{i+1}$ in $\mathcal{G}^{\text{rep}}_{\text{recomb}(n)}$, we have $3X_i \to 2X_i + X_{i+1}$ as one of the reactions in $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$. As a consequence, each of the vertices $3X_1, 3X_2, \ldots, 3X_n$ is an extremal point of the convex hull of source vertices. Therefore this convex hull is an $(n-1)$-simplex. For contradiction, assume that $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$ is not strongly endotactic. Then by Corollary 2.4, there exists a proper face of this simplex such that every reaction with source on this face has target on this face. Let $F = (3X_{i_1}, 3X_{i_2}, \ldots, 3X_{i_k}) \subset (3X_1, 3X_2, \ldots, 3X_n)$ be this face. Note that $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$ contains reactions of the form $3X_j \to 2X_j + X_{j+1}$ for every $3X_j \in F$. Since $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$ was assumed to be not strongly endotactic, we have $2X_j + X_{j+1} \in F$. Extending the line segment joining $3X_j$ and $2X_j + X_{j+1}$, we also have $3X_{j+1} \in F$. Continuing this way, we conclude $F = (3X_1, 3X_2, \ldots, 3X_n)$, contradicting the fact that F is a proper face of this simplex. Therefore, $\tilde{\mathcal{G}}^{\text{rep}}_{\text{recomb}(n)}$ is strongly endotactic. □

Theorem 4.5 can be generalized to a larger family of reaction networks that have certain properties associated with an object called the *production graph*. The upcoming proposition illustrates this point.

Definition 4.6. Given a reaction network $\mathcal{G} = (V, E)$, the *production graph* $\mathcal{P}(\mathcal{G})$ is the graph whose vertices are given by the species in $\mathcal{G}$, such that there is a directed edge from species X_i to species X_j in $\mathcal{P}(\mathcal{G})$ if there exists an edge $\boldsymbol{y} \to \boldsymbol{y}' \in E$ with $\text{supp}(\boldsymbol{y}) = X_i$ and $X_j \in \text{supp}(\boldsymbol{y}')$.

Proposition 4.7. *Consider a bimolecular autocatalytic system $\mathcal{G} = (V, E)$ consisting of the reactions $2X_i \to 2X_i + X_j$ for each $i = 1, 2, \dots, n$ and $j \neq i$ such that $\mathcal{P}(\mathcal{G})$ is strongly connected. Let $\tilde{\mathcal{G}}$ denote the reaction network corresponding to the relative populations of $\mathcal{G}$. Then any variable-k mass-action system generated by $\tilde{\mathcal{G}}$ is permanent.*

Proof. We claim that $\tilde{\mathcal{G}}$ is strongly endotactic; it then follows from Theorem 2.9 that any variable-k mass-action system generated by it is permanent. Since $P(\mathcal{G})$ is strongly connected, there exists a reaction $2X_i \to 2X_i + X_j$ for each $i = 1, 2, \dots, n$. By Theorem 3.5 there exist reactions in $\tilde{\mathcal{G}}$ which are of the form $3X_j \to 2X_j + X_l$ such that $l \neq j$ for every species X_j. Therefore the convex hull of the source vertices of $\tilde{\mathcal{G}}$ is a simplex with extremal points $(3X_1, 3X_2, \dots, 3X_n)$. For contradiction, assume that $\tilde{\mathcal{G}}$ is not strongly endotactic. Then by Corollary 2.4, there exists a proper face of this simplex such that for every reaction with source on this face has target on this face. Let $F = (3X_{i_1}, 3X_{i_2}, \dots, 3X_{i_k}) \subset (3X_1, 3X_2, \dots, 3X_n)$ be this face. Since $\mathcal{P}(\mathcal{G})$ is strongly connected, one can argue as in the proof of Theorem 4.5 to show that $F = (3X_1, 3X_2, \dots, 3X_n)$, contradicting the fact that F is a proper face of the simplex. Therefore, the network $\tilde{\mathcal{G}}$ is strongly endotactic. □

Under some constraints (to be specified in Theorem 4.8 below), subnetworks of the relative population network $\tilde{\mathcal{G}}$ in Proposition 4.7 can be shown to be strongly endotactic. Consequently the dynamical system generated by them is permanent.

Theorem 4.8. *Consider reaction networks $\mathcal{G}_1$, $\mathcal{G}_2$ such that the following hold:*

1. *$\mathcal{G}_1$ is strongly endotactic.*
2. *$\mathcal{G}_1$ is a subnetwork of $\mathcal{G}_2$.*
3. *The vertices of $\mathcal{G}_2$ lie in the convex hull of the source vertices of $\mathcal{G}_1$.*

Then any variable-k mass-action system generated by $\mathcal{G}_2$ is permanent.

Proof. We claim that $\mathcal{G}_2$ is strongly endotactic; it then follows from Theorem 2.9 that any variable-k mass-action system generated by it is permanent. Since $\mathcal{G}_1 \subseteq \mathcal{G}_2$ and the vertices of $\mathcal{G}_2$ lie in the convex hull of the source vertices of $\mathcal{G}_1$, the convex hull of the source vertices of $\mathcal{G}_1$ is the same as the convex hull of the source vertices of $\mathcal{G}_2$. Note that the stoichiometric subspaces of $\mathcal{G}_1$ and $\mathcal{G}_2$ coincide; call it S. Let $\boldsymbol{w} \in \mathbb{R}^n$ be such that $\boldsymbol{w} \notin S^{\perp}$. Let H be the hyperplane perpendicular to $\boldsymbol{w}$ that contains a source vertex $\boldsymbol{s}_1$ such that for every other source vertex $\boldsymbol{s}_2$, we have $(\boldsymbol{s}_2 - \boldsymbol{s}_1) \cdot \boldsymbol{w} \geq 0$. Therefore, the intersection of H with the convex hull of source vertices of either network is a proper face of the convex hull. Since $\mathcal{G}_1$ is strongly endotactic, by Proposition 2.1, there exists a reaction in $\mathcal{G}_1$ with source on this face such that it points inside this convex hull. Since $\mathcal{G}_1 \subseteq \mathcal{G}_2$, this reaction is also contained in $\mathcal{G}_2$. This implies that $\mathcal{G}_2$ is strongly endotactic. □

Corollary 4.9. *Suppose $\mathcal{G}_1$ is a bimolecular autocatalytic network consisting of the reactions $2X_i \to 2X_i + X_j$ for some $i = 1, 2, \dots, n$ and $j \neq i$ such that $P(\mathcal{G}_1)$ is strongly connected. Suppose $\mathcal{G}_2$ is another bimolecular autocatalytic network such that $\mathcal{G}_1 \subseteq \mathcal{G}_2$. Let $\tilde{\mathcal{G}}_1$ and $\tilde{\mathcal{G}}_2$ be the networks corresponding to the relative populations of $\mathcal{G}_1$ and $\mathcal{G}_2$ respectively. Then any variable-k mass-action system generated by $\tilde{\mathcal{G}}_2$ is permanent.*

Proof. Since $P(\mathcal{G}_1)$ strongly connected and $\mathcal{G}_1$ is a bimolecular autocatalytic network with rectants $2X_1, 2X_2, \dots, 2X_n$, the convex hull of source vertices of $\tilde{\mathcal{G}}_1$ has corners $3X_1, 3X_2, \dots, 3X_n$ (as outlined in the proof of Proposition 4.7). The fact that $\mathcal{G}_2$ is a bimolecular autocatalytic network implies that the vertices of $\mathcal{G}_2$ are contained in convex hull formed by $(3X_1, 3X_2, \dots, 3X_n)$, i.e., the convex hull formed by the sources of $\mathcal{G}_1$. Note that since $\mathcal{G}_1 \subseteq \mathcal{G}_2$, we have $\tilde{\mathcal{G}}_1 \subseteq \tilde{\mathcal{G}}_2$. In addition, $\tilde{\mathcal{G}}_1$ is strongly endotactic by Proposition 4.7. The result now follows from Theorem 4.8. □

Table 3
On the left (right) are listed all the reactions that appear in $\mathcal{G}_{\text{recomb(3)}}$($\tilde{\mathcal{G}}_{\text{recomb(3)}}$). The algorithm for generating $\tilde{\mathcal{G}}_{\text{recomb(3)}}$ produces a specific set of reactions from each reaction in $\mathcal{G}_{\text{recomb(3)}}$. The table pairs this subnetwork with the corresponding generating reaction in $\mathcal{G}_{\text{recomb(3)}}$.

Set of reactions in $\mathcal{G}_{\text{recomb(3)}}$	Set of reactions in $\tilde{\mathcal{G}}_{\text{recomb(3)}}$
$X_1 + X_2 \xrightarrow{k_1} X_1 + 2X_2$	$2X_1 + X_2 \xrightarrow{k_1} X_1 + 2X_2$
	$X_1 + X_2 + X_3 \xrightarrow{k_1} X_1 + 2X_2$
$X_2 + X_3 \xrightarrow{k_2} X_2 + 2X_3$	$2X_2 + X_3 \xrightarrow{k_2} X_2 + 2X_3$
	$X_1 + X_2 + X_3 \xrightarrow{k_2} X_2 + 2X_3$
$X_3 + X_1 \xrightarrow{k_3} X_3 + 2X_1$	$2X_3 + X_1 \xrightarrow{k_3} X_3 + 2X_1$
	$X_1 + X_2 + X_3 \xrightarrow{k_3} X_3 + 2X_1$
$X_1 + X_2 \xrightarrow{k_4} X_1 + X_2 + X_3$	$X_1 + 2X_2 \xrightarrow{k_4} X_1 + X_2 + X_3$
	$2X_1 + X_2 \xrightarrow{k_4} X_1 + X_2 + X_3$
$X_2 + X_3 \xrightarrow{k_5} X_1 + X_2 + X_3$	$X_2 + 2X_3 \xrightarrow{k_5} X_1 + X_2 + X_3$
	$2X_2 + X_3 \xrightarrow{k_5} X_1 + X_2 + X_3$
$X_1 + X_3 \xrightarrow{k_6} X_1 + X_2 + X_3$	$X_1 + 2X_3 \xrightarrow{k_6} X_1 + X_3 + X_3$
	$2X_1 + X_3 \xrightarrow{k_6} X_1 + X_2 + X_3$

4.2. Autocatalytic recombination networks with no repeated reactants: non-homologous recombination

We now consider autocatalytic recombinant networks involving reactants that do *not* have repeated species. This is similar in spirit to *non-homologous* genetic recombination, which involves the exchange of genetic material in the form of nucleotide sequences between two dissimilar DNA strands. Below, we give the precise definition of such networks, and study whether the relative population dynamics is permanent.

We are able to prove permanence of the relative population dynamics for dimensions $n = 4, 5, 6$. Finally, in Theorem 4.17 we extend our result to bimolecular networks that can generate all species using reactions of the form $X_i + X_j \to X_i + X_j + X_k$.

Definition 4.10. Consider a reaction network $\mathcal{G}$ with species $X_1, X_2, \dots, X_n$. Then $\mathcal{G}$ is said to be the *autocatalytic recombination network of dimension n* (and denoted $\mathcal{G}_{\text{recomb}(n)}$) if it consists of the reactions $X_i + X_{i+1} \to X_i + 2X_{i+1}$ and $X_i + X_{i+1} \to X_i + X_{i+1} + X_{i+2}$ for $i = 1, 2, \dots, n$, where $X_{n+1} = X_1$ and $X_{n+2} = X_2$(in the cyclic sense).

Consider the network $\mathcal{G}_{\text{recomb(3)}}$ (given in Table 3). Most notably, species only interact with *other* species. By Theorem 3.5, the dynamics of the relative populations of $\mathcal{G}_{\text{recomb(3)}}$ can be generated by the network $\tilde{\mathcal{G}}_{\text{recomb(3)}}$ shown in Table 3 and Fig. 5(a).

Proposition 4.11. *Any variable-k mass-action system generated by $\tilde{\mathcal{G}}_{\text{recomb(3)}}$ is permanent.*

Proof. The dynamics for the relative population model generated by $\tilde{\mathcal{G}}_{\text{recomb(3)}}$ (see Fig. 5(a)) can also be obtained from the dynamical system generated by the network in Fig. 5(b) (which is weakly reversible and possesses a single linkage class) if we choose the rate constants as shown in Fig. 5. It follows from [51] that any variable-k mass-action system generated by $\tilde{\mathcal{G}}_{\text{recomb(3)}}$ is permanent. □

We now shift our attention to the analysis of autocatalytic recombination networks of dimension four, five and six. First, consider the autocatalytic recombination network $\mathcal{G}_{\text{recomb(4)}}$ of dimension four in Table 4. The network that generates dynamics corresponding to relative populations is given by $\tilde{\mathcal{G}}_{\text{recomb(4)}}$, shown also in Table 4. In Fig. 6(a), we illustrate a subset of reactions in the reaction network $\mathcal{G}_{\text{recomb(4)}}$, namely those reactions with sources $X_1 + X_2$ and $X_2 + X_3$.

In what follows, we show that the reaction networks corresponding to the relative populations of autocatalytic recombinant networks of

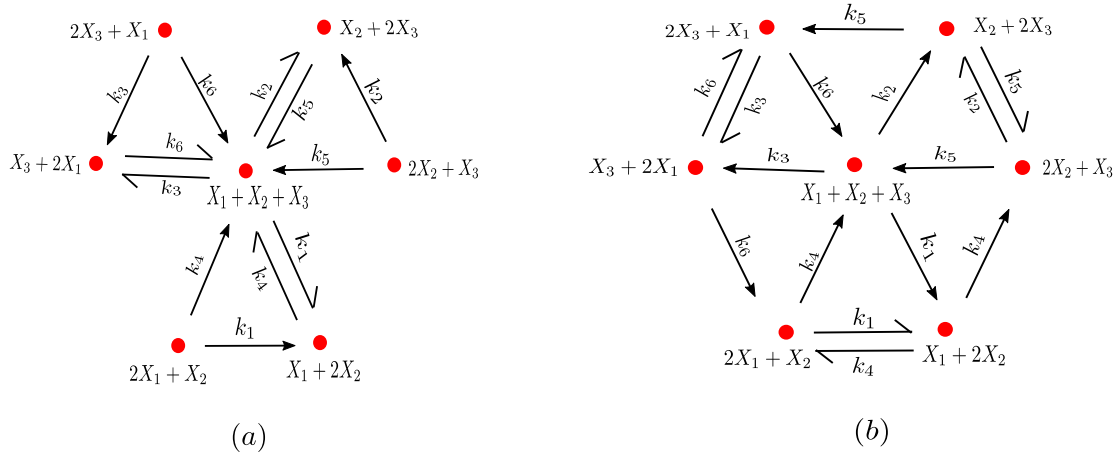


Fig. 5. (a) Reaction network $\tilde{\mathcal{G}}_{\text{recomb(3)}}$ that generates the dynamics of relative populations of the recombination network of dimension three given by $\mathcal{G}_{\text{recomb(3)}}$. (b) Weakly reversible reaction network with single linkage class that generates the same dynamics as that given by the network in Fig. 5(a), if we choose rate constants as shown.

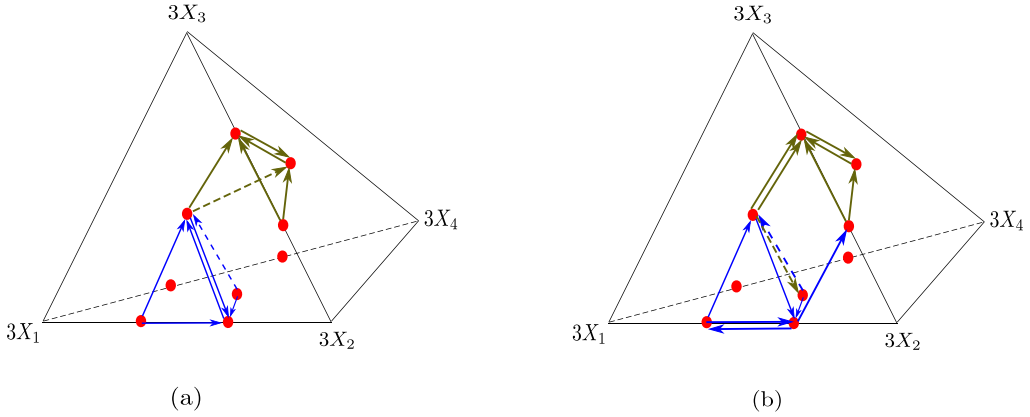
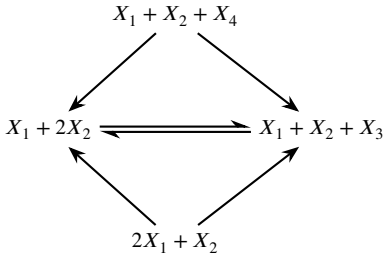


Fig. 6. (a) A network illustrating a subset of reactions in $\tilde{\mathcal{G}}_{\text{recomb(4)}}$. (b) A reaction network that can generate mass-action systems that are dynamically equivalent to the systems generated by the network in (a). The reaction $X_1 + 2X_2 \to X_1 + X_2 + X_3$ (marked with blue in (a)) is split as $X_1 + 2X_2 \to 2X_1 + X_2$ and $X_1 + 2X_2 \to X_3 + 2X_2$ (marked with blue in (b)). The reaction $X_1 + X_2 + X_3 \to X_2 + X_3 + X_4$ (marked with green in (a)) is split as $X_1 + X_2 + X_3 \to X_2 + 2X_3$ and $X_1 + X_2 + X_3 \to X_1 + X_2 + X_4$ (marked with green in (b)).

dimension four, five, and six, i.e., $\tilde{\mathcal{G}}_{\text{recomb(4)}}$, $\tilde{\mathcal{G}}_{\text{recomb(5)}}$ and $\tilde{\mathcal{G}}_{\text{recomb(6)}}$, give rise to mass-action systems that are *dynamically equivalent* to systems generated by weakly reversible reaction networks with a single linkage class. As a consequence, any variable-k mass-action system generated by these networks is permanent [51].

Proposition 4.12. *The mass-action systems generated by the reaction network $\tilde{\mathcal{G}}_{\text{recomb(4)}}$ are dynamically equivalent to systems generated by a weakly reversible reaction network with a single linkage class.*

Proof. For the reactions $X_1 + X_2 \to X_1 + 2X_2$ and $X_1 + X_2 \to X_1 + X_2 + X_3$ in $\mathcal{G}_{\text{recomb(4)}}$, Theorem 3.5 gives us the following subnetwork in $\tilde{\mathcal{G}}_{\text{recomb(4)}}$:



whose geometric embedding is shown in Fig. 6(a). In order for the mass-action systems generated by this subnetwork to be dynamically equivalent to systems generated by a weakly reversible reaction network, it therefore suffices to find appropriate reactions (i.e., satisfying dynamical equivalence, or Eq. (4)) with targets $X_1 + X_2 + X_4$ and $2X_1 + X_2$. We can accomplish this using the following (by keeping the same rate constants as in the original reaction):

(i) *Reaction with target* $2X_1 + X_2$: We split the reaction $X_1 + 2X_2 \to X_1 + X_2 + X_3$ into

$$X_1 + 2X_2 \to 2X_1 + X_2 \text{ and}$$
$$X_1 + 2X_2 \to 2X_2 + X_3,$$

as shown in Fig. 6(b), since $(0,-1,1,0)^T = (1,-1,0,0)^T + (-1,0,1,0)^T$.

(ii) *Reaction with target* $X_1+X_2+X_4$: This can done with the following sequence of reactions

$$X_1 + X_2 + X_4 \to X_1 + X_2 + X_3$$
$$X_1 + X_2 + X_3 \to X_2 + X_3 + X_4$$
$$X_2 + X_3 + X_4 \to X_3 + X_4 + X_1$$
$$X_3 + X_4 + X_1 \to X_1 + X_2 + X_4,$$

which are known to exist in $\tilde{\mathcal{G}}_{\text{recomb(4)}}$ from Table 4.

Repeating this procedure for the remainder of the network, we obtain a weakly reversible reaction network. In addition, the sequence of reactions described in (ii) ensures that this network consists of a single linkage class. Therefore, the mass-action systems generated by

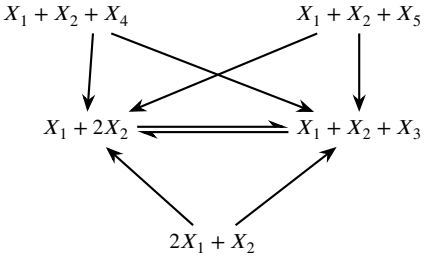
Table 4
On the left (right) are listed all the reactions that appear in $\mathcal{G}_{\text{recomb(4)}}(\tilde{\mathcal{G}}_{\text{recomb(4)}})$. The algorithm for generating $\tilde{\mathcal{G}}_{\text{recomb(4)}}$ produces a specific set of reactions from each reaction in $\mathcal{G}_{\text{recomb(4)}}$. The table pairs this subnetwork with the corresponding generating reaction in $\mathcal{G}_{\text{recomb(4)}}$.

Set of reactions in $\mathcal{G}_{\text{recomb(4)}}$	Set of reactions in $\tilde{\mathcal{G}}_{\text{recomb(4)}}$
$X_1 + X_2 \xrightarrow{k_1} X_1 + 2X_2$	$2X_1 + X_2 \xrightarrow{k_1} X_1 + 2X_2$
	$X_1 + X_2 + X_3 \xrightarrow{k_1} X_1 + 2X_2$
	$X_1 + X_2 + X_4 \xrightarrow{k_1} X_1 + 2X_2$
$X_2 + X_3 \xrightarrow{k_2} X_2 + 2X_3$	$2X_2 + X_3 \xrightarrow{k_2} X_2 + 2X_3$
	$X_1 + X_2 + X_3 \xrightarrow{k_2} X_2 + 2X_3$
	$X_2 + X_3 + X_4 \xrightarrow{k_2} X_2 + 2X_3$
$X_3 + X_4 \xrightarrow{k_3} X_3 + 2X_4$	$2X_3 + X_4 \xrightarrow{k_3} X_3 + 2X_4$
	$X_1 + X_3 + X_4 \xrightarrow{k_3} X_3 + 2X_4$
	$X_2 + X_3 + X_4 \xrightarrow{k_3} X_3 + 2X_4$
$X_4 + X_1 \xrightarrow{k_4} X_4 + 2X_1$	$2X_4 + X_1 \xrightarrow{k_4} X_4 + 2X_1$
	$X_1 + X_2 + X_4 \xrightarrow{k_4} X_4 + 2X_1$
	$X_1 + X_3 + X_4 \xrightarrow{k_4} X_4 + 2X_1$
$X_1 + X_2 \xrightarrow{k_5} X_1 + X_2 + X_3$	$X_1 + 2X_2 \xrightarrow{k_5} X_1 + X_2 + X_3$
	$2X_1 + X_2 \xrightarrow{k_5} X_1 + X_2 + X_3$
	$X_1 + X_2 + X_4 \xrightarrow{k_5} X_1 + X_2 + X_3$
$X_2 + X_3 \xrightarrow{k_6} X_2 + X_3 + X_4$	$X_2 + 2X_3 \xrightarrow{k_6} X_2 + X_3 + X_4$
	$2X_2 + X_3 \xrightarrow{k_6} X_2 + X_3 + X_4$
	$X_1 + X_2 + X_3 \xrightarrow{k_6} X_2 + X_3 + X_4$
$X_3 + X_4 \xrightarrow{k_7} X_3 + X_4 + X_1$	$X_3 + 2X_4 \xrightarrow{k_7} X_3 + X_4 + X_1$
	$2X_3 + X_4 \xrightarrow{k_7} X_3 + X_4 + X_1$
	$X_2 + X_3 + X_4 \xrightarrow{k_7} X_3 + X_4 + X_1$
$X_4 + X_1 \xrightarrow{k_8} X_4 + X_1 + X_2$	$X_4 + 2X_1 \xrightarrow{k_8} X_4 + X_1 + X_2$
	$2X_4 + X_1 \xrightarrow{k_8} X_4 + X_1 + X_2$
	$X_1 + X_3 + X_4 \xrightarrow{k_8} X_4 + X_1 + X_2$

the reaction network $\tilde{\mathcal{G}}_{\text{recomb(4)}}$ are dynamically equivalent to systems generated by a weakly reversible reaction network with a single linkage class. □

Proposition 4.13. *The mass-action systems generated by the reaction network $\tilde{\mathcal{G}}_{\text{recomb(5)}}$ are dynamically equivalent to systems generated by a weakly reversible reaction network with a single linkage class.*

Proof. For the reactions $X_1 + X_2 \to X_1 + 2X_2$ and $X_1 + X_2 \to X_1+X_2+X_3$ in $\mathcal{G}_{\text{recomb(5)}}$, Theorem 3.5 gives us the following subnetwork in $\tilde{\mathcal{G}}_{\text{recomb(5)}}$:



To make the mass-action systems generated by this subnetwork dynamically equivalent to weakly reversible systems, it therefore suffices to find appropriate reactions (as in Eq. (4)) with targets $X_1 + X_2 + X_4, 2X_1 + X_2$, and $X_1 + X_2 + X_5$. We can accomplish this using the following (by keeping the same rate constants as in the original reaction):

(i) *Reaction with target* $2X_1 + X_2$: We split the reaction $X_1 + 2X_2 \to X_1 + X_2 + X_3$ into

$X_1 + 2X_2 \to 2X_1 + X_2$ and

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

since $(0,-1,1,0,0)^T = (1,-1,0,0,0)^T + (-1,0,1,0,0)^T$.

(ii) *Reaction with target* $X_1 + X_2 + X_4$: We split the reaction $X_1 + X_2 + X_3 \to X_2 + X_3 + X_4$ into

$X_1 + X_2 + X_3 \to X_2 + 2X_3$ and

$X_1 + X_2 + X_3 \to X_1 + X_2 + X_4$,

since $(-1,0,0,1,0)^T = (-1,0,1,0,0)^T + (0,0,-1,1,0)^T$.

(iii) *Reaction with target* $X_1+X_2+X_5$: This can done with the following sequence of reactions

$X_1 + X_2 + X_5 \to X_1 + X_2 + X_3$

$X_1 + X_2 + X_3 \to X_2 + X_3 + X_4$

$X_2 + X_3 + X_4 \to X_3 + X_4 + X_5$

$X_3 + X_4 + X_5 \to X_4 + X_5 + X_1$

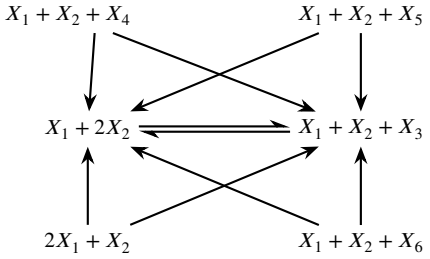
$X_4 + X_5 + X_1 \to X_1 + X_2 + X_5$,

which are known to exist in $\tilde{\mathcal{G}}_{\text{recomb(5)}}$.

Repeating this procedure for the remainder of the network, we obtain a weakly reversible reaction network. In addition, the sequence of reactions described in (iii) ensures that this network consists of a single linkage class. Therefore, the mass-action systems generated by the reaction network $\tilde{\mathcal{G}}_{\text{recomb(5)}}$ can be made dynamically equivalent to systems generated by a weakly reversible reaction network with a single linkage class. □

Proposition 4.14. *The mass-action systems generated by the reaction network $\tilde{\mathcal{G}}_{\text{recomb(6)}}$ are dynamically equivalent to systems generated by a weakly reversible reaction network with a single linkage class.*

Proof. For the reactions $X_1 + X_2 \to X_1 + 2X_2$ and $X_1 + X_2 \to X_1+X_2+X_3$ in $\mathcal{G}_{\text{recomb(6)}}$, Theorem 3.5 gives us the following subnetwork in $\tilde{\mathcal{G}}_{\text{recomb(6)}}$:



To make the mass-action systems generated by this subnetwork dynamically equivalent to weakly reversible single linkage class, it therefore suffices to find appropriate reactions (as in Eq. (4)) with targets $X_1 + X_2 + X_4, 2X_1 + X_2, X_1 + X_2 + X_5$ and $X_1 + X_2 + X_6$. We can accomplish this using the following (by keeping the same rate constants as in the original reaction):

(i) *Reaction with target* $2X_1 + X_2$: We split the reaction $X_1 + 2X_2 \to X_1 + X_2 + X_3$ into

$X_1 + 2X_2 \to 2X_1 + X_2$ and

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

since $(0,-1,1,0,0,0)^T = (1,-1,0,0,0,0)^T + (-1,0,1,0,0,0)^T$.

(ii) *Reaction with target* $X_1 + X_2 + X_4$: We split the reaction $X_1 + X_2 + X_3 \to X_2 + X_3 + X_4$ into

$X_1 + X_2 + X_3 \to X_2 + 2X_3$ and

$X_1 + X_2 + X_3 \to X_1 + X_2 + X_4$,

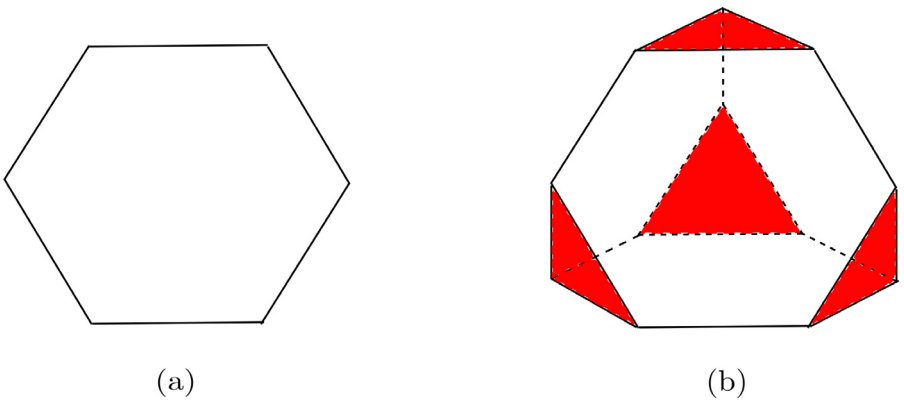


Fig. 7. (a) Truncated 2-simplex, which is a hexagon. The facets of the hexagon are truncated line segments. (b) Truncated 3-simplex. The facets of the truncated 3-simplex are hexagons and triangles (marked in red).

since $(-1,0,0,1,0,0)^T = (-1,0,1,0,0,0)^T + (0,0,-1,1,0,0)^T$.

(iii) *Reaction with target* $X_1+X_2+X_5$: We split the reaction $X_5+X_6+X_1 \to X_6+X_1+X_2$ into

$$X_5+X_6+X_1 \to X_1+X_2+X_5 \text{ and}$$
$$X_5+X_6+X_1 \to X_1+2X_6,$$

since $(0,1,-1,0,0,0)^T = (0,1,0,-1,0,-1)^T + (0,0,-1,1,0,1)^T$.

(iv) *Reaction with target* $X_1+X_2+X_6$: This can done with the following sequence of reactions:

$$\begin{aligned}
X_1+X_2+X_6 &\to X_1+X_2+X_3\\
X_1+X_2+X_3 &\to X_2+X_3+X_4\\
X_2+X_3+X_4 &\to X_3+X_4+X_5\\
X_3+X_4+X_5 &\to X_4+X_5+X_6\\
X_4+X_5+X_6 &\to X_5+X_6+X_1\\
X_5+X_6+X_1 &\to X_1+X_2+X_6,
\end{aligned}$$

which are known to exist in $\tilde{\mathcal{G}}_{\text{recomb(6)}}$.

Repeating this procedure for the remainder of the network, we obtain a weakly reversible reaction network. In addition, the sequence of reactions described in (iv) ensures that this network consists of a single linkage class. Therefore, the mass-action systems generated by the reaction network $\tilde{\mathcal{G}}_{\text{recomb(6)}}$ can be made dynamically equivalent to systems generated by a weakly reversible reaction network with a single linkage class. □

Corollary 4.15. *Any variable-k mass-action system generated by* $\tilde{\mathcal{G}}_{\text{recomb(4)}}$, $\tilde{\mathcal{G}}_{\text{recomb(5)}}$, *or* $\tilde{\mathcal{G}}_{\text{recomb(6)}}$ *is permanent.*

Proof. We have shown above that all mass-action systems generated by $\tilde{\mathcal{G}}_{\text{recomb(4)}}$, $\tilde{\mathcal{G}}_{\text{recomb(5)}}$, and $\tilde{\mathcal{G}}_{\text{recomb(6)}}$ are dynamically equivalent to systems generated by weakly reversible networks with single linkage class. It follows from [51] that any variable-k mass-action system generated by them is permanent. □

We now show in Theorem 4.17 that there is another family of recombinant networks which can be shown to be strongly endotactic, the proof of which is based on truncated n-simplexes. A truncated n-simplex is constructed by truncating (cutting off) each vertex at one-third of the length of the edge of the regular n-simplex. Fig. 7 shows examples of truncated simplices for $n = 2$ and $n = 3$. Note that the facet of a truncated n-simplex is either a face of an $(n-1)$-simplex or a face of a truncated $(n-1)$-simplex.

Lemma 4.16. *For* $n \geq 3$, *any proper face of the truncated n-simplex is either a face of an* $(n-1)$*-simplex facet, or an entire truncated r-simplex for some* $r \leq n-1$, *but not both.*

Proof. By definition, a proper face of a truncated n-simplex is either a face of an $(n-1)$-simplex facet or a face of a truncated $(n-1)$-simplex. It therefore suffices to show that (for a truncated n-simplex) we have: *a face of a truncated* $(n-1)$*-simplex that is not a face of an* $(n-1)$*-simplex facet is an entire truncated r-simplex for some* $r \leq n-1$. We show this by induction.

Base case ($n = 3$): Referring to Fig. 7(b), we see any face of a truncated 3-simplex that is not a face of the 2-simplex facet (i.e., red triangle where the cut happened and shaded in Fig. 7(b)) is either an entire hexagon (which is a truncated 2-simplex) or a certain side of the hexagon that is not a side of the red triangle where the cut occurs (which is a truncated 1-simplex).

Let us assume that the property mentioned above is true for all natural numbers less than n. The induction hypothesis gives us that a face of a truncated $(n-2)$-simplex that is not a face of an $(n-2)$-simplex facet is an entire truncated r-simplex for some $r \leq n-2$. By definition, a proper face of a truncated $(n-1)$-simplex is either a face of a $(n-2)$-simplex facet or a face of a truncated $(n-2)$-simplex. Now note that a face of a truncated $(n-1)$-simplex that is not a face of an $(n-1)$-simplex facet cannot be a face of an $(n-2)$-simplex. This implies that it is a face of a truncated $(n-2)$-simplex that is not a face of an $(n-2)$-simplex. By the induction hypothesis, we get that this face is an entire truncated r-simplex for some $r \leq n-1$. □

Theorem 4.17. *Consider a bimolecular autocatalytic system* $\mathcal{G}_n = (V, E)$ *with n species* $X_1, X_2, \ldots, X_n$, *consisting of reactions of the form* $X_i + X_j \to X_i + X_j + X_k$ *such that* $i \neq j$. *Suppose for any* $i \neq j$ *the following is true: there exists a reaction* $X_i + X_j \to X_i + X_j + X_k$ *where* $k \notin \{i,j\}$, *and there exists a reaction using some of* X_i, X_j, X_k *as reactants that generates a fourth species* X_ℓ *(with* $\ell \notin \{i,j,k\}$*), and then the same for a fifth species* X_m *(with* $m \notin \{i,j,k,\ell\}$*), and so on, until we get all n species. Let us denote by* $\tilde{\mathcal{G}}_n$ *the reaction network corresponding to the relative populations of* $\mathcal{G}_n$. *Then any variable-k mass-action system generated by* $\tilde{\mathcal{G}}_n$ *is permanent.*

Proof. We prove that $\tilde{\mathcal{G}}_n$ is strongly endotactic; it then follows from Theorem 2.9 that any variable-k mass-action system generated by it is permanent. From the hypothesis of the theorem, we have that for all $i \neq j$ there exists a reaction in $\mathcal{G}_n$ that is of the form $X_i + X_j \to X_i + X_j + X_k$, with $k \neq \{i,j\}$. By Theorem 3.5, $\tilde{\mathcal{G}}_n$ has complexes of the form $2X_i + X_j$ and $X_i + 2X_j$ as sources, for all $i \neq j$, and these are the vertices of the truncated $(n-1)$-simplex. Therefore, the convex hull of the source vertices of $\tilde{\mathcal{G}}_n$ is a truncated $(n-1)$-simplex. Since all the vertices of $\tilde{\mathcal{G}}_n$ are contained in the convex hull of its source vertices, by Proposition 2.2, $\tilde{\mathcal{G}}_n$ is strongly endotactic if and only if for every face of the convex hull of the source vertices, there is a reaction with source on this face that points away from this face. Consider a face f of the truncated $(n-1)$-simplex. By Lemma 4.16, we know that f is either a face of a $(n-2)$-simplex or f is an entire truncated r-simplex generated

by some species $X_{i_1}, \ldots, X_{i_r}$ for some $r \leq n-2$. We have the following cases:

1. If f is a face of a $(n-2)$-simplex: Take a point of the form $2X_i+X_j$ on f and consider the following reaction in $\mathcal{G}_n$: $X_i+X_j \to X_i+X_j+X_k$ where $k \notin \{i,j\}$. By Theorem 3.5, the network $\tilde{\mathcal{G}}_n$ contains a reaction $2X_i+X_j \to X_i+X_j+X_k$. Note that $X_i+X_j+X_k$ does not belong to the $(n-2)$-simplex. Therefore, $X_i+X_j+X_k$ does not belong to f.
2. If f is an entire truncated r-simplex generated by some species $X_{i_1}, \ldots, X_{i_r}$: We now use the property that, for any distinct indices $i, j \in \{1,2,\ldots,n\}$, there exists a reaction $X_i+X_j \to X_i+X_j+X_k$ in $\mathcal{G}_n$ with $k \notin \{i,j\}$, and there exists a way to use X_i, X_j, X_k to make a fourth species, then a fifth species, $\ldots$, until we get all the n species. Therefore, there exists a way to use some of the species $X_{i_1}, \ldots, X_{i_r}$ to obtain a species X_{i_s} that is not on the face f, which gives us our desired reaction.

Therefore, $\tilde{\mathcal{G}}_n$ is strongly endotactic. □

5. Discussion and future work

Autocatalytic networks are ubiquitous in nature [2,34,37,52]. The populations of species in autocatalytic networks may become unbounded in finite time [12], so it becomes important to analyze the *relative* sizes of these populations. In general, relative populations are *not* solutions of autonomous dynamical systems, even if the original populations are solutions of such systems. On the other hand, using time-rescaling and certain assumptions on the original reaction network, we show that the relative populations do become solutions of autonomous polynomial dynamical systems (Theorem 3.1). Moreover, in Theorem 3.5, we give explicit reaction networks that generate the dynamics corresponding to the relative populations of bimolecular autocatalytic systems.

In Section 4, we have studied special examples of bimolecular autocatalytic systems called *autocatalytic recombination networks*. In Section 4.1 we have shown that autocatalytic recombination networks with repeated species (denoted by $\mathcal{G}^{\text{rep}}_{\text{recomb}(n)}$, and corresponding to homologous recombination) are permanent for all n. In Section 4.2, we have shown that autocatalytic recombination networks with no repeated species (denoted by $\tilde{\mathcal{G}}_{\text{recomb}(n)}$, and corresponding to nonhomologous recombination) are permanent for $n \leq 6$.

In particular, the mass-action systems generated by the network $\tilde{\mathcal{G}}_{\text{recomb}(n)}$ can be made dynamically equivalent to systems generated by a *weakly reversible* reaction network with single linkage class for $n \leq 6$. The method we used to show this dynamical equivalence does not work for $n \geq 7$; nevertheless it is possible that these networks also give rise to permanent systems.

Generalizing these results to higher dimensions may involve some challenging polyhedral geometry/combinatorics problems, and is an interesting question for future work.

Another direction for future investigation would be to find conditions under which the results of "gene targeting" via homologous recombination (as described in Section 4) can be guaranteed to persist in large populations of cells, and across multiple generations.

Autocatalytic networks are also related to the notion of *critical siphons*, as remarked in [53]. A *siphon* is a set of species which, if absent initially, remains absent forever. A *critical siphon* is a siphon that does not contain the support of a conserved quantity. This approach is of specific relevance in the DNA programming community [54–56] where critical siphons can be viewed as building blocks for constructing complicated biological circuits. In addition, the presence/absence of critical siphons has important repercussions on the dynamics of the underlying reaction network. It is known that critical siphons give rise to *autocatalytic sets* in a precise sense [53]. Further, mass-action systems without critical siphons are persistent [57]. In other words, the presence of critical siphons may cause extinction. In future work, one can try to study critical siphons in more depth using some of the methods described here, for the purpose of finding special classes of critical siphons that do not lead to extinction.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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