Graphically balanced equilibria and stationary measures of reaction networks

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Abstract

The graph-related symmetries of a reaction network give rise to certain special equilibria (such as complex balanced equilibria) in deterministic models of dynamics of the reaction network. Correspondingly, in the stochastic setting, when modeled as a continuous-time Markov chain, these symmetries give rise to certain special stationary measures. Previous work by Anderson, Craciun and Kurtz identified stationary distributions of a complex balanced network; later Cappelletti and Wiuf developed the notion of complex balancing for stochastic systems. We define and establish the relations between reaction balanced measure, complex balanced measure, reaction vector balanced measure, and cycle balanced measure and prove that with mild additional hypotheses, the former two are stationary distributions. Furthermore, in spirit of earlier work by Joshi, we give sufficient conditions under which detailed balance of the stationary distribution of Markov chain models implies the existence of positive detailed balance equilibria for the related deterministic reaction network model. Finally, we provide a complete map of the implications between balancing properties of deterministic and corresponding stochastic reaction systems, such as complex balance, reaction balance, reaction vector balance and cycle balance.

1 Introduction

Reaction networks are widely used mathematical models in biochemistry [3, 10]. In these models, a finite collection of chemical species interact according to a finite set of possible chemical transformations. An example of a reaction network is given by

$$\begin{align*}
A + B &\xrightleftharpoons^{\kappa_1}_{\kappa_2} 2C \\
&\xrightleftharpoons^{\kappa_3}_{\kappa_4} A \rightleftharpoons B
\end{align*}$$

In this case, \(A\), \(B\) and \(C\) denote some distinct chemical species. Here, a molecule of \(A\) and a molecule of \(B\) can be turned into two molecules of \(C\), and two molecules of \(C\) can be turned back into one molecule of \(A\) and one molecule of \(B\). Additionally, a molecule of \(A\) can be turned reversibly into a molecule of \(B\). The numbers \(\kappa_i\) denote the mass action reaction rate constants – a larger value of a rate constant is associated with a higher propensity of the corresponding reaction. A more formal introduction is provided in Section 2.

In the setting of biochemistry, different modeling regimes are considered. Specifically, if the counts of the molecules in the system of interest are low, then the evolution of these counts is modeled through a continuous time Markov chain. If more molecules are present, then the dynamical variables describe the concentrations of the different chemical species rather than their counts, and their time evolution is described by a system of stochastic differential equations [16]. Finally, if the number of molecules is so large that the random fluctuations in their counts can be safely ignored, then the time evolution of the species concentrations is modeled via a system of ordinary differential equations (ODEs).

There is a rich history of relating the graphical properties of reaction networks with their dynamical features, especially for the ODE model [11, 12, 8, 5, 9]. A theory that connects a graph to dynamics is naturally appealing, since graphical properties are simple to check, while the consequences for the dynamics are far-reaching. In this context, an important class of reaction network models is that of

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complex balanced systems, whose positive equilibria satisfy a graphical balance condition (see Section 3). It is known that if a positive complex balanced equilibrium exists, then all equilibria of the system are complex balanced and locally asymptotically stable. A special case of a complex balanced equilibrium is that of a detailed balanced equilibrium, which is of particular importance in thermodynamics. A generalization of complex balanced equilibria has recently been studied in [6].

As an example, by simply looking at the graphical properties, we know that, when deterministically modeled, the chemical reaction network (1.1) has positive detailed balanced equilibria for any choice of positive rate constants $\kappa_1, \kappa_2, \kappa_3$ and $\kappa_4$. We also know that the dynamics of the solution of the corresponding ODE can neither be chaotic nor have oscillations, and will eventually converge to a locally stable positive equilibrium.

Another topic of interest concerns the connection between dynamical properties of a continuous time Markov chain model and its corresponding ODE model. This study dates back to [15], where the ODE model is proven to be the weak limit of the continuous time Markov chain model, when the counts of the molecules is increased and properly rescaled. The interest in this topic is motivated by the desire to infer properties of the continuous time Markov chain model from the theory that has been developed for the deterministic model over the years. More recently, advances have been made in connecting complex balanced equilibria of the ODE models with the stationary distribution of the corresponding Markov chain model. Specifically, in [2] it is shown that if an ODE model equipped with mass action kinetics has a positive complex balanced equilibrium, then the Markov chain model has a product form Poisson stationary distribution (Theorem 5.1). In [1] it is further proven that such models are non-explosive. In [13] it is proven that if an ODE model with mass action kinetics has a positive detailed balanced equilibrium, then the stationary distributions of the corresponding Markov chain model are detailed balanced, in the classical probabilistic sense [19]. Finally, in [7] it is shown that if an ODE model with mass action kinetics is complex balanced, then the stochastic counterpart has a so called complex balanced stationary distribution, and the converse holds as well. More properties of complex balanced stationary distributions are then studied in [7], and a stochastic formulation of the Deficiency Zero Theorem is given.

In this paper, we extend the work of [7], by studying graphically balanced measures, and not only balanced distributions. In particular, we define and establish the relations between reaction balanced measure, complex balanced measure and reaction vector balanced measure (see Definition 4.1) and prove that with mild additional hypotheses, the former two are stationary distributions (see Theorem 4.8) while the same does not hold in general for the latter (see Remark 4.5). Further, in the spirit of [2, 13, 7], we relate properties of the stationary measures of the Markov chain model with similar features of the equilibria of the corresponding ODE model. We prove that a complete symmetry between the results concerning graphical balancing equilibria and the results dealing with graphical balancing measures is
lacking: specifically, in the stochastic sense two forms of graphical balance, namely reaction vector balance and complex balance, imply reaction balance (Theorem 4.9). The same does not hold for the ODE model, as it is shown in Remark 5.3.

In the spirit of [13], we give sufficient conditions capable of “lifting” detailed balance of the Markov chain model to detailed balance of the ODE model. Specifically, in Corollary 5.7 we prove that if the Markov chain model has a detailed balanced stationary distribution which is complex balanced, then the associated ODE model admits a positive detailed balanced equilibrium (hence all equilibria are detailed balanced and locally asymptotically stable).

Finally, Figure 1 presents a complete map of all connections shown in this paper between different kinds of balanced systems (see Definitions 3.2 and 4.2), both in the deterministic and stochastic settings.

The paper is organized as follows: in Section 2 the necessary definitions of reaction network theory are given. In Section 3 equilibria of the ODE models with graphical balancing properties are discussed, and known results are presented. In Section 4 invariant measures for the continuous time Markov chain are dealt with: graphical balance in this framework is discussed, and new properties are stated together with some known results. Sections 3 and 4 have a similar structure. In particular, in both sections we first deal with graphical balance under arbitrary kinetics, then specialize to results for mass action kinetics. In Section 5, connections between equilibria of the ODE model and stationary distributions of the corresponding Markov chain model are proven, under the assumption of mass action kinetics.

2 Background

2.1 Notation

Let $\mathbb{R}$, $\mathbb{R}_{\geq 0}$ and $\mathbb{R}_{>0}$ represent the reals, the nonnegative reals and the positive reals, respectively. Let $\mathbb{Z}$, $\mathbb{Z}_{\geq 0}$ and $\mathbb{Z}_{>0}$ represent the integers, the nonnegative integers and the positive integers, respectively. For $v \in \mathbb{R}^n$, $\|v\|_1 = |v_1 + \ldots + v_n|$. For $v, w \in \mathbb{R}^n$, $v \leq w$ ($v < w$) means that $v_i \leq w_i$ ($v_i < w_i$) for all $i \in \{1, \ldots, n\}$. For $v, w \in \mathbb{R}^n$, we define

$$
\mathbb{1}_{\{v \leq w\}} = \begin{cases} 1 & , v \leq w \\ 0 & , otherwise. 
\end{cases}
$$

If $v > 0$ then $v$ is said to be positive. If $x \in \mathbb{R}_{\geq 0}^n$ and $v \in \mathbb{Z}_{\geq 0}^n$, we define

$$
x^v = \prod_{i=1}^n x_i^{v_i}, \quad \text{and} \quad v! = \prod_{i=1}^n v_i!,
$$

with the conventions that $0! = 1$ and $0^0 = 1$.

2.2 Reaction networks

A reaction network is a triple $\mathcal{G} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$, where $\mathcal{S} = \{X_1, X_2, \ldots, X_n\}$ is a set of $n$ species, $\mathcal{C}$ is a set of $m$ complexes, and $\mathcal{R} \subseteq \mathcal{C} \times \mathcal{C}$ is a set of $r$ reactions, such that $(y, y') \notin \mathcal{R}$ for any $y \in \mathcal{C}$. The complexes are linear combinations of species over $\mathbb{Z}_{\geq 0}$, identified with vectors in $\mathbb{Z}_{\geq 0}^n$ (which can be therefore embedded in $\mathbb{R}^n$). A reaction $(y, y') \in \mathcal{R}$ is denoted by $y \rightarrow y'$, and the vector $y' - y$ is the corresponding reaction vector. We refer to $y$ as the reactant complex of the reaction $y \rightarrow y'$ and to $y'$ as the product complex. We require that every species has a nonzero coordinate in at least one complex and that every complex is either a reactant complex or a product complex of at least one reaction. With this convention, there are no “redundant” species or complexes and $\mathcal{G}$ is uniquely determined by $\mathcal{R}$. In [14], there are $n = 3$ species $(A, B, C)$, $m = 2$ complexes $(A + B, 2B)$, and $r = 2$ reactions.

Suppose that $\mathcal{G} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ is a reaction network and $\mathcal{R}' \subseteq \mathcal{R}$. Then $\mathcal{F} = (\mathcal{S}|_{\mathcal{R}'}, \mathcal{C}|_{\mathcal{R}'}, \mathcal{R}')$ is said to be a subnetwork of $\mathcal{G}$. Since a reaction network is determined by its set of reactions, we will equivalently say that $\mathcal{R}'$ determines a subnetwork of $\mathcal{R}$ (or of $\mathcal{G}$) without any loss of clarity.

A reaction network $\mathcal{G} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ can be viewed as a graph with node set $\mathcal{C}$ and edge set $\mathcal{R}$ in a natural manner. We will frequently use the viewpoint of a reaction network as a graph in the rest of the paper.
A reaction network $\mathcal{G}$ is weakly reversible if every reaction $y \to y' \in \mathcal{R}$ is contained in a closed directed path. Moreover, $\mathcal{G}$ is reversible if for any reaction $y \to y' \in \mathcal{R}$, $y' \to y$ is in $\mathcal{R}$. It is clear that each reversible reaction network is also weakly reversible, since every reaction $y \to y'$ is contained in the cycle $y \to y' \to y$. As an example, the network in (1.1) is reversible, and therefore weakly reversible.

The stoichiometric subspace of $\mathcal{G}$ is the linear subspace of $\mathbb{R}^n$ generated by the reaction vectors, namely

$$S = \text{span}(y' - y | y \to y' \in \mathcal{R}).$$

For $v \in \mathbb{R}^n$, the sets $(v + S) \cap \mathbb{R}^n_{\geq 0}$ are called the stoichiometric compatibility classes of $\mathcal{G}$.

2.3 Reaction systems

We will consider dynamics of a reaction network with $n$ species both on $\mathbb{R}^n_{\geq 0}$ and $\mathbb{Z}^n_{\geq 0}$. $\mathbb{R}^n_{\geq 0}$ is the usual underlying state space for deterministic models involving ordinary differential equations, while the state space is $\mathbb{Z}^n_{\geq 0}$ for stochastic models involving continuous-time Markov chains. We do not consider stochastic differential equations (ordinary differential equations with a noise term) in this paper, but in passing we mention that this is an instance where a stochastic model has the underlying state space $\mathbb{R}^n_{\geq 0}$ (see for example [10], and [17] [4] for more recent developments on the subject).

**Definition 2.1.** Let $\mathcal{G}$ be a reaction network. Suppose that to each reaction $y \to y' \in \mathcal{R}$ there is associated a nonnegative-valued rate function $\lambda_{y \to y'}$, whose domain is the state space ($\lambda_{y \to y'} : \mathbb{R}^n_{\geq 0} \to \mathbb{R}_{\geq 0}$ or $\lambda_{y \to y'} : \mathbb{Z}^n_{\geq 0} \to \mathbb{R}_{\geq 0}$). By kinetics on $\mathcal{G}$, we mean the correspondence between reactions and rate functions.

$$\Lambda : (y \to y') \mapsto \lambda_{y \to y'}$$

The pair $(\mathcal{G}, \Lambda)$ will be referred to as a reaction system.

The range of $\lambda_{y \to y'}$ besides being nonnegative real-valued has some reasonable restrictions, which prevent the trajectory from exiting the nonnegative orthant. However, we will not be explicit about these restrictions because they are not necessary for the results in this article.

It is natural to think of the kinetic system $(\mathcal{G}, \Lambda)$ as a labelled graph, where $\mathcal{G}$ is the underlying graph and the rate function $\lambda_{y \to y'}$ labels each edge $y \to y' \in \mathcal{R}$.

2.3.1 Deterministic/continuous dynamics

Let $(\mathcal{G}, \Lambda)$ be a deterministic reaction system. In the deterministic case, the evolution of the species concentrations $z(t) \in \mathbb{R}^n_{\geq 0}$ is determined by the following system of ODEs

$$\frac{dz}{dt} = \sum_{y \to y' \in \mathcal{R}} (y' - y) \lambda_{y \to y'}(z)$$

The evolution of the deterministic reaction system is confined to its (stoichiometric) compatibility class,

$$z(t) \in (z(0) + S) \cap \mathbb{R}^n_{\geq 0} =: \mathcal{P}_z(0),$$

where $\mathcal{P}_z$ denotes the compatibility class containing $z \in \mathbb{R}^n$. Every $z \in \mathbb{R}^n$ is contained in some compatibility class, thus the compatibility classes partition $\mathbb{R}^n$. We say that a compatibility class $\mathcal{P}_z$ is positive if $\mathcal{P}_z \cap \mathbb{R}^n_{>0}$ is nonempty. $c \in \mathbb{R}^n$ is said to be an equilibrium of the deterministic reaction system $(\mathcal{G}, \Lambda)$ if

$$\sum_{y \to y' \in \mathcal{R}} (y' - y) \lambda_{y \to y'}(c) = 0.$$ 

If $c \in \mathbb{R}^n_{>0}$ ($c \in \mathbb{R}^n_{\geq 0}$), we say that $c$ is positive (nonnegative) and denote it by $c > 0$ ($c \geq 0$).
2.3.2 Stochastic/discrete dynamics

Let \((G, \Lambda)\) be a stochastic reaction system. In the discrete setting, the underlying state space is \(\mathbb{Z}_+^n\). A vector \(x = (x_1, \ldots, x_n) \in \mathbb{Z}_+^n\) represents the population \(x_i\) of each species \(i = 1, \ldots, n\). We say that a reaction \(y \to y' \in R\) is active at \(x\) if \(\lambda_{y \to y'}(x) > 0\). When a reaction \(y \to y'\) that is active at \(x\) occurs, the population changes from \(x\) to \(x + y' - y\).

We say that \(x' \in \mathbb{Z}_+^n\) is accessible from \(x \in \mathbb{Z}_+^n\), if either \(x' = x\) or there is a sequence of states \(x = u_0, u_1, \ldots, u_n = x'\) such that for each consecutive pair of states \((u_i, u_{i+1})\) (\(0 \leq i \leq n - 1\)), there is an active reaction \(y \to y' \in R\) at \(u_i\) with \(y' - y = u_{i+1} - u_i\). A non-empty set \(\Gamma \subseteq \mathbb{Z}_+^n\) is an irreducible component of \((G, \Lambda)\) if for all \(x \in \Gamma\) and all \(u \in \mathbb{Z}_+^n\), \(u\) is accessible from \(x\) if and only if \(u \in \Gamma\). An irreducible component \(\Gamma\) is positive if for all reactions \(y \to y' \in R\) there exists a state \(x \in \Gamma\) such that \(y \to y'\) is active at \(x\).

**Definition 2.2.** Let \((G, \Lambda)\) be a stochastic reaction system and let \(\pi\) be a measure on \(\mathbb{Z}_+^n\). \(\pi\) is said to be a stationary measure of \((G, \Lambda)\) if the following holds for all \(x \in \mathbb{Z}_+^n\):

\[
\pi(x) = \sum_{y \to y' \in R} \lambda_{y \to y'}(x) = \sum_{y \to y' \in R} \pi(x + y' - y) \lambda_{y' \to y}(x + y' - y),
\]

**Definition 2.3.** 1. \(\pi\) is said to be a \(\sigma\)-finite measure if \(\pi(x) < \infty\) for all \(x \in \mathbb{Z}_+^n\). \(\pi\) is said to be a finite measure if \(\pi(\mathbb{Z}_+^n) < \infty\). \(\pi\) is said to be a distribution if \(\pi(\mathbb{Z}_+^n) = 1\).

2. We define support of a measure \(\pi\) on \(\mathbb{Z}_+^n\), denoted by \(\text{supp}(\pi)\), to be the smallest set \(T\) such that \(\pi(\mathbb{Z}_+^n \setminus T) = 0\).

3. If \(\Omega \subseteq \mathbb{Z}_+^n\) is such that \(\text{supp}(\pi) \cap \Omega \neq \emptyset\), we say that \(\pi\) is non-null on \(\Omega\).

4. If \(\Omega \subseteq \mathbb{Z}_+^n\) is such that \(\text{supp}(\pi)\) is nonempty and is contained in \(\Omega\), then we say that \(\pi\) exists within \(\Omega\).

We note here that if \(\pi\) is a non-null stationary measure of \((G, \Lambda)\), then \(\pi\) must exist within the union of all irreducible components of \((G, \Lambda)\).

2.3.3 Mass action kinetics

An important choice of kinetics, both deterministic and stochastic, is mass action kinetics. The deterministic ODE mass action model has been shown to arise as a certain large population limit of the stochastic mass action model [15]. For the purposes of this article, we will assume the two mass action models as given without explicitly realizing one model as a limit of the other. We define the two models below.

**Definition 2.4.** Consider a reaction network \(G = (S, C, R)\).

1. By deterministic mass action kinetics, we mean the correspondence \(K_D : (y \to y') \mapsto \lambda_{y \to y'}\) where

\[\lambda_{y \to y'}(z) = \kappa_{y \to y'} z^h\text{ for some }\kappa_{y \to y'} > 0\text{ and for all } z \in \mathbb{R}_+^n\]

The pair \((G, K_D)\) is called a deterministic mass action system.

2. By stochastic mass action kinetics, we mean the correspondence \(K_S : (y \to y') \mapsto \lambda_{y \to y'}\) where

\[\lambda_{y \to y'}(x) = \kappa_{y \to y'} \frac{x!}{(x-y)!} \mathbb{I}_{\{x \geq y\}}\text{ for some }\kappa_{y \to y'} > 0\text{ and for all } x \in \mathbb{Z}_+^n\]

The pair \((G, K_S)\) is called a stochastic mass action system.

In both cases, the constants \(\kappa_{y \to y'}\) are referred to as rate constants.

We will often need to refer to a deterministic mass action system \((G, K_D)\) and its corresponding stochastic mass action system \((G, K_S)\) within the same context. The correspondence is via the reaction network \(G\), which is the same, and by making the same choice of rate constants.
Remark 2.1. An equivalent formulation of the stochastic mass action rates is the following:

\[
\lambda_{y \rightarrow y'}(x) = \kappa_{y \rightarrow y'} \frac{x!}{(x-y)!} \prod_{x \geq y} = \kappa_{y \rightarrow y'} \prod_{i=1}^{n} x_i(x_i-1) \cdots (x_i-y_i+1)
\]

for all \( x \in \mathbb{Z}_{\geq 0}^n \). Note that no indicator function appears on the right-hand side of the equation. The rates of stochastic mass action kinetics are multivariate polynomial functions, restricted to nonnegative integer arguments. Moreover, the polynomials \( \prod_{i=1}^{n} x_i(x_i-1) \cdots (x_i-y_i+1) \) for different \( y \) have different leading terms (by ordering the terms first according to their degree, then according to lexicographic order), and therefore are linearly independent on \( \mathbb{R} \).

3 Graph-related equilibria in deterministic reaction systems

In the deterministic setting, graph-related symmetries of a reaction network result in certain special states, which we now define.

Definition 3.1. Consider a deterministic reaction system \((\mathcal{G}, \Lambda)\), and let \( c \in \mathbb{R}_{\geq 0}^n \). Then

(a) \( c \) is said to be a reaction balanced state of \((\mathcal{G}, \Lambda)\) (or detailed balanced state of \((\mathcal{G}, \Lambda)\)) if for every pair of complexes \( y, y' \in \mathcal{C} \),

\[
\lambda_{y \rightarrow y'}(c) = \lambda_{y' \rightarrow y}(c)
\]

(b) \( c \) is said to be a complex balanced state of \((\mathcal{G}, \Lambda)\) if for every complex \( y \in \mathcal{C} \),

\[
\sum_{y' \in \mathcal{C}} \lambda_{y \rightarrow y'}(c) = \sum_{y' \in \mathcal{C}} \lambda_{y' \rightarrow y}(c)
\]

(c) \( c \) is said to be a reaction vector balanced state of \((\mathcal{G}, \Lambda)\) if for all \( \xi \in \mathbb{R}^n \),

\[
\sum_{y \rightarrow y' \in \mathcal{R} : y' - y = \xi} \lambda_{y \rightarrow y'}(c) = \sum_{y \rightarrow y' \in \mathcal{R} : y' - y = \xi} \lambda_{y' \rightarrow y}(c)
\]

(d) \( c \) is said to be a cycle balanced state of \((\mathcal{G}, \Lambda)\) if for every sequence of distinct complexes \((y_1, \ldots, y_j) \subseteq \mathcal{C} \) where \( j \geq 3 \),

\[
\prod_{i=1}^{j} \lambda_{y_i \rightarrow y_{i+1}}(c) = \prod_{i=1}^{j} \lambda_{y_{i+1} \rightarrow y_i}(c)
\]

where by definition \( y_{j+1} := y_1 \).

In all four parts, we assume that \( \lambda_{y \rightarrow y'} = 0 \) if \( y \rightarrow y' \notin \mathcal{R} \).

Part (a) of Definition 3.1 appears as ‘detailed balanced state’ in the chemical reaction network theory literature. For the purposes of this paper, we refer to the concept as ‘reaction balanced state’ instead, in order to avoid any potential confusion with the concept of detailed balance of Markov chain theory literature.

Example 3.1. Consider the following deterministic reaction system \((\mathcal{G}, \Lambda)\).

\[
\begin{align*}
A + B & \\
\lambda_1^+ & \lambda_1^- \\
\lambda_2^- & \lambda_2^+ \\
2A & \lambda_3^- \\
\lambda_3^+ & 2B
\end{align*}
\]

For purposes of this example, \( \lambda_i \) that is written on top of an arrow denotes the rate function (and not the mass action rate constant) of the corresponding reaction.
(a) $c$ is a reaction balanced state of $(G, \Lambda)$ if the following hold:

(i) $\lambda_1(c) = \lambda_1(c)$,
(ii) $\lambda_2(c) = \lambda_2(c)$,
(iii) $\lambda_3(c) = \lambda_3(c)$.

(b) $c$ is a complex balanced state of $(G, \Lambda)$ if the following hold:

(i) $\lambda_2(c) + \lambda_1(c) = \lambda_2(c) + \lambda_1(c)$,
(ii) $\lambda_3(c) + \lambda_2(c) = \lambda_3(c) + \lambda_2(c)$,
(iii) $\lambda_1(c) + \lambda_3(c) = \lambda_1(c) + \lambda_3(c)$.

(c) $c$ is a reaction vector balanced state of $(G, \Lambda)$ if the following hold:

(i) $\lambda_1(c) + \lambda_2(c) = \lambda_1(c) + \lambda_2(c)$,
(ii) $\lambda_3(c) = \lambda_3(c)$.

(d) $c$ is a cycle balanced state of $(G, \Lambda)$ if the following hold:

$\lambda_1(c) \lambda_2(c) \lambda_3(c) = \lambda_1(c) \lambda_2(c) \lambda_3(c)$.

We now define what it means for a deterministic reaction system to be graphically balanced.

**Definition 3.2.** Let $(G, \Lambda)$ be a deterministic reaction system. Suppose that $(G, \Lambda)$ possesses at least one positive equilibrium and every positive equilibrium of $(G, \Lambda)$ is complex balanced (or reaction balanced, or reaction vector balanced or cycle balanced, resp.). Then we say that $(G, \Lambda)$ is a complex balanced (or reaction balanced, or reaction vector balanced or cycle balanced, resp.) reaction system.

### 3.1 Results for arbitrary kinetics

**Theorem 3.1** (Balanced states are equilibria). Let $(G, \Lambda)$ be a deterministic reaction system and let $c \in \mathbb{R}^n_{\geq 0}$. Suppose that any one of the following conditions holds:

(i) $c$ is a reaction balanced state of $(G, \Lambda)$.

(ii) $c$ is a complex balanced state of $(G, \Lambda)$.

(iii) $c$ is a reaction vector balanced state of $(G, \Lambda)$.

Then $c$ is an equilibrium of $(G, \Lambda)$.

**Proof.** By summing (3.1) over $y' \in C$, we see that a reaction balanced state is a complex balanced state. To see that a complex balanced state is an equilibrium, multiply both sides of (3.2) by $y$ and then sum over $y \in \mathcal{C}$. If $c$ is a reaction vector balanced state, and $\xi$ is a reaction vector, then $-\xi$ must also be a reaction vector, i.e. the sets $\{\xi : \xi = y' - y \text{ for some } y \to y' \in \mathcal{C}\}$ and $\{ -\xi : \xi = y' - y \text{ for some } y \to y' \in \mathcal{C}\}$ are identical. Multiply both sides of (3.3) by $\xi$ and then sum over $\xi$ on the left and $-\xi$ on the right to get the result.

**Remark 3.1.** A cycle balanced state is not necessarily an equilibrium. In fact, for a deterministic mass action system, either every state is cycle balanced or no positive state is cycle balanced. For instance, consider the mass action system in (3.5), which has reaction rates $\lambda_1(z) = k_1 z_A^2$, $\lambda_2(z) = k_2 z_B^2$, $\lambda_3(z) = k_3 z_A z_B$, $\lambda_1(z) = k_1 z_A$, $\lambda_2(z) = k_2 z_B$, and $\lambda_3(z) = k_3 z_A^2$. Then every $c \in \mathbb{R}^n_{\geq 0}$ is cycle balanced if $k_1 k_2 k_3 = \frac{k_1 k_2 k_3}{k_1 k_2 k_3}$. On the other hand, no $c \in \mathbb{R}^n_{\geq 0}$ is cycle balanced if $k_1 k_2 k_3 \neq k_1 k_2 k_3$.

**Theorem 3.2** (Necessary conditions for existence of a balanced state). Let $(G, \Lambda)$ be a deterministic reaction system and let $c \in \mathbb{R}^n_{\geq 0}$.

(i) If $c$ is a reaction balanced state of $(G, \Lambda)$, then $G$ is reversible.

(ii) If $c$ is a complex balanced state of $(G, \Lambda)$, then $G$ is weakly reversible.
(iii) If $c$ is a reaction vector balanced state of $(\mathcal{G}, \Lambda)$, then for every $y \rightarrow y' \in \mathcal{R}$, there exists $\tilde{y} \rightarrow \tilde{y}' \in \mathcal{R}$ with $y + \tilde{y} = y' + \tilde{y}'$.

(iv) Let $c$ be a cycle balanced state of $(\mathcal{G}, \Lambda)$. If for a sequence of distinct complexes $(y_1, \ldots, y_j)$ where $j \geq 3$, $\prod_{i=1}^{j} \lambda_{y_i \rightarrow y_{i+1}}(c) > 0$ with $y_{j+1} = y_1$, then $y_i \rightarrow y_{i+1}$ is a reversible reaction for all $i \in \{1, \ldots, j\}$.

Proof. The proof of parts (i), (iii) and (iv) follows immediately from Definition 3.1 by noticing that for the balancing conditions to hold, if one side of the equations is nonzero, then so must be the other side. The statement of part (ii) is a restated version of Theorem 2B of [12], where the result was first proven.

Theorem 3.3 (Relations between different balanced states). Let $(\mathcal{G}, \Lambda)$ be a deterministic reaction system. Let $c \in \mathbb{R}^{n}_{\geq 0}$.

(i) If $c$ is reaction balanced then it is reaction vector balanced, complex balanced and cycle balanced.

(ii) If $c$ is complex balanced and cycle balanced, then $c$ is reaction balanced.

Proof. Let $c$ be a reaction balanced state of $(\mathcal{G}, \Lambda)$. Then it follows, by summing $[3.1]$ over $y' \in \mathcal{C}$ that $c$ is a complex balanced state. Furthermore, by summing $[3.1]$ over $y \rightarrow y' \in \mathcal{R} : y' - y = \xi$ it follows that $c$ is a reaction vector balanced state. For every sequence $(y_1, \ldots, y_j)$, reaction balance of $c$ implies that $\lambda_{y_i \rightarrow y_{i+1}}(c) = \lambda_{y_{i+1} \rightarrow y_i}(c)$. Cycle balance of $c$ then follows from taking the product over $i \in \{1, \ldots, j\}$ on both sides of the identity. For part (ii), if $\lambda_{y \rightarrow y'}(c) = 0$ for all $y \rightarrow y' \in \mathcal{R}$ then clearly $c$ is reaction balanced. Otherwise, consider the subnetwork $\tilde{\mathcal{G}}$ which is defined by the reactions $y \rightarrow y'$ with $\lambda_{y \rightarrow y'}(c) > 0$. Moreover, let $\tilde{c} \in \mathbb{R}^n_{> 0}$ be such that $\tilde{c}_i = c_i$ if $c_i > 0$, and $\tilde{c}_i = 1$ otherwise. Following an idea in the proof of [9] Theorem 5.1], we equip $\tilde{\mathcal{G}}$ with mass action kinetics $K_D$, with rate constants $\kappa_{y \rightarrow y'} = \lambda_{y \rightarrow y'}(c)\tilde{c}^{-y}$. It follows that $c$ is reaction balanced, complex balanced or cycle balanced for $(\mathcal{G}, \Lambda)$ if and only if $\tilde{c}$ is reaction balanced, complex balanced or cycle balanced for $(\tilde{\mathcal{G}}, K_D)$, respectively. Hence, the proof is concluded by [9] Theorem 1.1. □

Remark 3.2. In general, no one individual condition of the three: complex balance, reaction vector balance, and cycle balance implies any of the remaining two. We check the remaining pairwise conditions below.

1. (Complex balance & Reaction vector balance $\not\Rightarrow$ Cycle balance) Consider the mass action system $(\mathcal{G}, K_D)$ shown below:

\[
\begin{align*}
3A & \xrightarrow{2} 2A + B \\
2 & \xrightarrow{1} 1 & 1 & \xrightarrow{1} 2 \\
A + 2B & \xleftarrow{2} 3B
\end{align*}
\]

The state $(1, 1)$ is complex balanced and reaction vector balanced. However, $(1, 1)$ is neither reaction balanced nor cycle balanced. In fact, all positive equilibria are of the form $(s, s)$ for some $s > 0$ and each of these equilibria is both complex balanced and reaction vector balanced. This shows that $(\mathcal{G}, K_D)$ is complex balanced as well as reaction vector balanced (see Definition 3.2), but $(\mathcal{G}, K_D)$ is neither cycle balanced nor reaction balanced.
2. (Reaction vector balance & Cycle balance $\iff$ Complex balance) Consider the reaction system in (3.5), endowed with mass action kinetics with the following rate constants:

\[
\begin{align*}
2A & \xrightarrow{1} 1 & A + B & \xrightarrow{2} 2B \\
2A & \xrightarrow{1} 1 & 2B & \xrightarrow{2} 1 \\
2A & \xrightarrow{2} 1 & 2B & \xrightarrow{1} 2
\end{align*}
\]

Then, $(1,1)$ is a positive equilibrium of the mass action system $(G, K_D)$ that is both reaction vector balanced and cycle balanced, but is not complex balanced. Moreover, all equilibria are of the form $(s,s)$ for some $s \geq 0$, and they are all reaction vector balanced and cycle balanced. It follows that $(G, K_D)$ is reaction vector balanced and cycle balanced (see Definition 3.2) but it is not complex balanced.

3.2 Results for mass action kinetics

The following result on complex balancing is a classical result for mass action systems [12, 11], and the analogous result for reaction balancing is easily obtainable from known results.

**Theorem 3.4 (Existence and uniqueness of positive equilibria).** Let $(G, K_D)$ be a deterministic mass action system. If $(G, K_D)$ possesses a positive complex balanced (reaction balanced, resp.) state, then there exists a unique positive equilibrium within every positive compatibility class of $(G, K_D)$, and every positive equilibrium of $(G, K_D)$ is complex balanced (reaction balanced, resp.).

**Proof.** The result on complex balance is known [12, 11]. Let $c$ be a positive reaction balanced state of $(G, K_D)$. By Theorem 3.3, $c$ is cycle balanced and complex balanced. By Remark 3.1, every state in $\mathbb{R}_{\geq 0}^n$ is cycle balanced. By the result on complex balance, there is a unique positive equilibrium within every positive compatibility class of $(G, K_D)$ and every one of these positive equilibria is complex balanced. Since these equilibria are both complex balanced and cycle balanced, by part (ii) of Theorem 3.3 these equilibria are reaction balanced.

Note that uniqueness of positive equilibria within positive compatibility classes is not guaranteed for complex balanced systems with arbitrary kinetics (see, for instance, [18]).

**Remark 3.3.** Since the positive compatibility classes of $(G, K_D)$ partition $\mathbb{R}_{\geq 0}^n$, Theorem 3.4 implies that if a mass action system $(G, K_D)$ possesses a positive complex balanced (resp. reaction balanced) state, then every positive equilibrium of $(G, K_D)$ is complex balanced (resp. reaction balanced). Therefore, a mass action system $(G, K_D)$ which possesses a positive complex balanced (resp. reaction balanced) state is complex balanced (resp. reaction balanced). Moreover, due to Remark 3.1, a mass action system $(G, K_D)$ possessing a positive cycle balanced equilibrium is cycle balanced.

**Remark 3.4.** While a reaction vector balanced state is an equilibrium, there is no statement about uniqueness corresponding to Theorem 3.4. To see this consider the following mass action system $(G, K_D)$.

\[
\begin{align*}
6 & \xrightarrow{0} 11 & 2A & \xrightarrow{6} 3A \\
6 & \xrightarrow{11} 1 & 1
\end{align*}
\]

$(G, K_D)$ has three distinct positive reaction vector balanced equilibria $z = 1$, $z = 2$, and $z = 3$. Furthermore, even when a positive reaction vector balanced state exists, there may be positive compatibility classes which do not contain any positive equilibria. To see this, consider the following mass action system.

\[
B \xrightarrow{1} A \quad A + B \xrightarrow{1} 2B
\]

(3.8)

There exists a positive equilibrium $(1, l-1)$ within every compatibility class with $z_A + z_B = l > 1$, and each of these equilibria is reaction vector balanced. However, there is no positive equilibrium in the positive compatibility classes with $z_A + z_B = l \leq 1$. 

|
4 Graph-related stationarity in stochastic reaction systems

In the stochastic setting, graph-related symmetries of a reaction network result in certain special measures, which we now define.

**Definition 4.1.** Consider a stochastic reaction system $\langle G, \Lambda \rangle$, and let $\pi$ be a measure with support in $\mathbb{Z}_{\geq 0}^n$. Then

(a) $\pi$ is said to be a reaction balanced measure if for every pair of complexes $y, y' \in C$ and every $x \in \mathbb{Z}_{\geq 0}^n$

$$\pi(x)\lambda_{y \rightarrow y'}(x) = \pi(x + y' - y)\lambda_{y' \rightarrow y}(x + y' - y).$$

(b) $\pi$ is said to be a complex balanced measure if for every complex $y \in C$ and every $x \in \mathbb{Z}_{\geq 0}^n$

$$\pi(x) \sum_{y' \in C} \lambda_{y \rightarrow y'}(x) = \sum_{y' \in C} \pi(x + y' - y)\lambda_{y' \rightarrow y}(x + y' - y).$$

(c) $\pi$ is said to be a reaction vector balanced measure if for every $x \in \mathbb{Z}_{\geq 0}^n$ and every $\xi \in C$

$$\pi(x) \sum_{y \in \mathbb{R}: y' \rightarrow y = \xi} \lambda_{y \rightarrow y'}(x) = \pi(x + \xi) \sum_{y \in \mathbb{R}: y \rightarrow y' = \xi} \lambda_{y' \rightarrow y}(x + \xi).$$

(d) $\pi$ is said to be a cycle balanced measure if for every $x \in \mathbb{Z}_{\geq 0}^n$ and every sequence of distinct complexes $(y_1, \ldots, y_j) \subseteq C$ where $j \geq 3$,

$$\prod_{i=1}^{j} \pi(x + y_i)\lambda_{y_i \rightarrow y_{i+1}}(x + y_i) = \prod_{i=1}^{j} \pi(x + y_{i+1})\lambda_{y_{i+1} \rightarrow y_i}(x + y_{i+1}).$$

In all parts, we assume that $\lambda_{y \rightarrow y'} = 0$ if $y \rightarrow y' \notin \mathbb{R}$ and $\pi(x) = 0$ if $x \notin \mathbb{Z}_{\geq 0}^n$.

The definition of a complex balanced distribution is owed to [2], here we extend the definition by considering more general measures. Note that the terms involving $\pi$ in (4.3) can be cancelled if they are positive, hence the property of cycle balance is more related to $\text{supp}(\pi)$ rather than $\pi$ itself. We summarize the different types of balanced equilibria and balanced measures in Table 1.

| Reaction balance | Deterministic setting | Stochastic setting | Holds $\forall$
|------------------|----------------------|--------------------|----------------|
| $\lambda_{y \rightarrow y'}(c) = \lambda_{y' \rightarrow y}(c)$ | $\pi(x)\lambda_{y \rightarrow y'}(x) = \pi(x + y' - y)\lambda_{y' \rightarrow y}(x + y' - y)$ | $x, y, y'$ |
| Reaction vector balance | $\sum_{y \in \mathbb{R}: y' \rightarrow y} \lambda_{y \rightarrow y'}(c) = \sum_{y \in \mathbb{R}: y \rightarrow y'} \lambda_{y' \rightarrow y}(c)$ | $\pi(x) \sum_{y \in \mathbb{R}: y' \rightarrow y} \lambda_{y \rightarrow y'}(x) = \pi(x + \xi) \sum_{y \in \mathbb{R}: y \rightarrow y'} \lambda_{y' \rightarrow y}(x + \xi)$ | $x, \xi$
| Complex balance | $\prod_{y \in \mathbb{R}} \lambda_{y \rightarrow y'}(c) = \prod_{y \in \mathbb{R}} \lambda_{y' \rightarrow y}(c)$ | $\prod_{y \in \mathbb{R}} \pi(x) \lambda_{y \rightarrow y'}(x) = \prod_{y \in \mathbb{R}} \pi(x + y' - y)\lambda_{y' \rightarrow y}(x + y' - y)$ | $x, y$
| Cycle balance | $\prod_{y \in \mathbb{R}} \lambda_{y \rightarrow y'}(x) = \prod_{y \in \mathbb{R}} \lambda_{y' \rightarrow y}(x)$ | $\prod_{y \in \mathbb{R}} \pi(x)\lambda_{y \rightarrow y'}(x) = \prod_{y \in \mathbb{R}} \pi(x + y' - y)\lambda_{y' \rightarrow y}(x + y' - y)$ | $x, (y_1, \ldots, y_j)$ with $y_i$ distinct and $j \geq 3$
| Stationary measure | $\pi(x) \sum_{y \in \mathbb{R}: y' \rightarrow y} \lambda_{y \rightarrow y'}(x) = \sum_{y \in \mathbb{R}: y \rightarrow y'} \pi(x + y' - y)\lambda_{y' \rightarrow y}(x + y' - y)$ | $x$ |
| Equilibrium | $\sum_{y \in \mathbb{R}: y' \rightarrow y} \pi(x + y' - y)\lambda_{y \rightarrow y'}(x)$ |

Table 1: Summary of definitions of various balanced equilibria in deterministic setting and various balanced measures in corresponding stochastic setting.

Note that part (a) of Definition 4.1 is the natural stochastic analog of part (a) of Definition 3.1 which is usually called detailed balance in reaction network theory. However, we could not refer to part (a) of Definition 4.1 as to detailed balance, since "detailed balance measure" is a reserved name in general Markov chain theory. In the case of reaction networks, the usual detailed balance of Markov chain theory coincides with reaction vector balance defined in part (c) of Definition 4.1.

We now define what it means for a stochastic reaction system to be graphically balanced.

---

*Detailed Balance of Chemical Reaction Network Theory
†Detailed Balance of Markov Chain Theory*
Definition 4.2. Let $(G, \Lambda)$ be a stochastic reaction system. Suppose that $(G, \Lambda)$ possesses at least one stationary distribution within a positive irreducible component and every stationary distribution of $(G, \Lambda)$ is complex balanced (or reaction balanced, or reaction vector balanced, or cycle balanced, resp.). Then we say that $(G, \Lambda)$ is a complex balanced (or reaction balanced, or reaction vector balanced, or cycle balanced, resp.) reaction system.

4.1 Results for arbitrary kinetics

Theorem 4.1 (Balanced measures are stationary). Let $(G, \Lambda)$ be a stochastic reaction system. Suppose that $\pi$ is a measure that satisfies at least one of the following:

(i) $\pi$ is reaction balanced measure of $(G, \Lambda)$.

(ii) $\pi$ is complex balanced measure of $(G, \Lambda)$.

(iii) $\pi$ is reaction vector balanced measure of $(G, \Lambda)$.

Then $\pi$ is a stationary measure of $(G, \Lambda)$.

Proof. To see that a reaction balanced measure is stationary, sum (4.1) over $y \rightarrow y'$ in $\mathcal{R}$. We get that a complex balanced measure is stationary by summing (4.2) over $y \in \mathcal{C}$. To see that a reaction vector balanced measure is stationary, sum (4.3) over all reaction vectors $\xi$.

There is no result corresponding to the following in the deterministic setting. We say that a reaction system $(G, \Lambda)$ is non-explosive if for every initial distribution, the resulting stochastic process is not explosive (in the sense of [19]).

Proposition 4.2. Let $(G, \Lambda)$ be a stochastic reaction system. If there exists a cycle balanced stationary distribution $\pi$ with $\text{supp}(\pi) = \mathbb{Z}_{\geq 0}^n$, then $(G, \Lambda)$ is cycle balanced. Moreover, if $(G, \Lambda)$ is non-explosive and if there exists a complex balanced (or reaction balanced, or reaction vector balanced, resp.) distribution $\pi$ with $\text{supp}(\pi) = \mathbb{Z}_{\geq 0}^n$, then $(G, \Lambda)$ is complex balanced (or reaction balanced, or reaction vector balanced, resp.).

Proof. If $\pi$ is cycle balanced and $\text{supp}(\pi) = \mathbb{Z}_{\geq 0}^n$, we can cancel $\pi$ on the two sides of (4.4) and we have that for every $x \in \mathbb{Z}_{\geq 0}^n$ and for every sequence of distinct complexes $(y_1, \ldots, y_j) \subseteq \mathcal{C}$ of $G$ where $j \geq 3$

$$j \prod_{i=1}^{j} \lambda_{y_i \rightarrow y_{i+1}}(x + y_i) = \prod_{i=1}^{j} \lambda_{y_{i+1} \rightarrow y_i}(x + y_{i+1}),$$

where as usual $y_{j+1} := y_1$ and $\lambda_{y \rightarrow y'} = 0$ if $y \rightarrow y' \notin \mathcal{R}$. Necessarily, every $\sigma$-finite measure (whether or not it is a stationary distribution) must be cycle balanced. Finally, if $(G, \Lambda)$ is non-explosive, then within every irreducible component the only stationary distribution is proportional to $\pi$ [19]. The conclusion follows by noting that equations (4.4), (4.5) and (4.6) still hold after multiplication by a constant.

Remark 4.1. The above proposition may also be stated by only assuming that $\text{supp}(\pi)$ is the union of irreducible components, and at least one positive irreducible component exists. It is worth noting here that complex balanced (and therefore reaction balanced) stochastic mass action systems are necessarily non-explosive [19].

The following result is analogous to Theorem 3.3 for graphically balanced states. The proof of part (ii) is by analogy with a similar proof in the deterministic setting, first obtained in [14].

Theorem 4.3 (Relations between different balanced measures). Let $(G, \Lambda)$ be a stochastic reaction system.

(i) A reaction balanced measure of $(G, \Lambda)$ is reaction vector balanced, complex balanced and cycle balanced.

(ii) If $\pi$ is a complex balanced and cycle balanced measure of $(G, \Lambda)$, then $\pi$ is reaction balanced.
Proof. Suppose that \( \pi \) is a reaction balanced measure of \((\mathcal{G}, \Lambda)\). Then, summing (4.1) over \( y' \in \mathcal{C} \) gives (4.2), and summing (4.1) over the reaction vectors gives (4.3). For every sequence \((y_1, \ldots, y_j)\), reaction balance of \( \pi \) implies that \( \pi(x + y_i)\lambda_{y_i \to y_i+1}(x + y_i) = \pi(x + y_{i+1})\lambda_{y_{i+1} \to y_i}(x + y_{i+1}) \). Cycle balance then follows from taking the product over \( i \in \{1, \ldots, j\} \) on both sides of the identity. To prove part (ii), suppose that \( \pi \) is a complex balanced but not reaction balanced measure of \((\mathcal{G}, \Lambda)\). We will show that \( \pi \) is not cycle balanced. We use the convention that if \( y \to y' \notin \mathcal{R} \), then \( \lambda_y \to y'(x) = 0 \) for all \( x \in \mathbb{Z}^n_{\geq 0} \).

Define the flux at \( x \in \mathbb{Z}^n_{\geq 0} \) from the complex \( y' \in \mathcal{C} \) to the complex \( y \in \mathcal{C} \) to be

\[
\rho_{y,y'}(x) := \pi(x + y - y')\lambda_{y' \to y}(x + y - y') - \pi(x)\lambda_{y \to y'}(x).
\]

Since \( \pi \) is not reaction balanced, there exists an \( x \in \mathbb{Z}^n_{\geq 0} \) and a pair of complexes \( y_1, y_2 \in \mathcal{C} \) such that \( \rho_{y_1,y_2}(x) \neq 0 \). Clearly, \( \rho_{y_1,y_2}(x) > 0 \) if and only if \( \rho_{y_2,y_1}(x + y_2 - y_1) < 0 \). So we assume without loss of generality that there exists an \( x \in \mathbb{Z}^n_{\geq 0} \) and a pair of complexes \( y_1, y_2 \in \mathcal{C} \) such that \( \rho_{y_1,y_2}(x) > 0 \). Since \( \pi \) is complex balanced (but not reaction balanced), there exists a complex \( y_3 \neq y_1, y_2 \in \mathcal{C} \) such that \( \rho_{y_2,y_3}(x + y_2 - y_1) > 0 \). Continuing this argument, there exists a sequence of complexes \((y_1, y_2, y_3, \ldots)\) such that \( \rho_{y_{i-1}, y_i}(x + y_{i-1} - y_i) > 0 \) for all \( i \geq 1 \). However, since there are only finitely many complexes in a reaction network, eventually we get a nontrivial cycle, i.e. a state \( x \in \mathbb{Z}^n_{\geq 0} \) and a sequence of distinct complexes \( \{z_1, z_2, \ldots, z_{i-1}\} \subseteq \mathcal{C} \) such that \( \rho_{z_i, z_{i+1}}(x + z_i - z_{i+1}) > 0 \) where \( i \in \{1, \ldots, j\} \) and \( z_{j+1} = z_1 \).

This implies that for \( i \in \{1, \ldots, j\} \), \( \pi(x + z_{i+1} - z_i)\lambda_{z_{i+1} \to z_i}(x + z_{i+1} - z_i) > \pi(x + z_i - z_{i+1})\lambda_{z_i \to z_{i+1}}(x + z_i - z_{i+1}) \). Taking product over \( i \in \{1, \ldots, j\} \), we get that \( \prod_{i=1}^j \pi(x + z_{i+1} - z_i)\lambda_{z_{i+1} \to z_i}(x + z_{i+1} - z_i) > \prod_{i=1}^j \pi(x + z_i - z_{i+1})\lambda_{z_i \to z_{i+1}}(x + z_i - z_{i+1}) \), which implies that \( \pi \) is not cycle balanced, thus completing the proof of the claim.

Remark 4.2. As in the deterministic setting (see Remark 7.2), reaction vector balance and cycle balance does not imply complex balance for a stochastic reaction system. To see this, consider the mass action system \((\mathcal{G}, \mathcal{K}_S)\) depicted below:

\[
\begin{align*}
1/2 & \rightarrow A \quad , \quad 2A \rightarrow 3A \quad , \\
0 & \rightarrow 1 \quad , \quad 1 \rightarrow 3
\end{align*}
\]

Cycle balance is trivially satisfied, since there are no cycles involving three or more non-repeating complexes. The resulting stochastic process is a birth and death process on \( \mathbb{Z}_{\geq 0} \) with a unique stationary distribution, which is reaction vector balanced [10]. Hence, \((\mathcal{G}, \mathcal{K}_S)\) is cycle balanced and reaction vector balanced. We only need to check that for \((\mathcal{G}, \mathcal{K}_S)\), the stationary distribution is not reaction balanced. In fact, the only measure balancing the first pair of reversible reactions is \( \pi(n) = (1/2)^n / n! \), which does not balance the second pair of reversible reactions. This shows that \((\mathcal{G}, \mathcal{K}_S)\) is not reaction balanced.

Surprisingly enough, and in contrast to deterministic mass action systems, in the setting of stochastic mass action systems, complex balance and reaction vector balance imply reaction balance (see Theorem 4.4).

Due to [7] Corollary 19 [stated here as Theorem 5.3], the following holds:

**Proposition 4.4.** Let \((\mathcal{G}, \Lambda)\) be a stochastic reaction system, and let \( \pi \) be a complex balanced distribution within a positive irreducible component of \((\mathcal{G}, \Lambda)\). Then \( \mathcal{G} \) is weakly reversible.

The following results extend Proposition 4.4 by only requiring measures in the hypotheses instead of distributions, and also extends to reaction balance and reaction vector balance as well.

**Theorem 4.5** (Necessary conditions for existence of a balanced measure). Let \((\mathcal{G}, \Lambda)\) be a stochastic reaction system and let \( \pi \) be a measure within a positive irreducible component of \((\mathcal{G}, \Lambda)\).

(i) If \( \pi \) is a reaction balanced measure of \((\mathcal{G}, \Lambda)\), then \( \mathcal{G} \) is reversible.

(ii) If \( \pi \) is a complex balanced measure of \((\mathcal{G}, \Lambda)\), then \( \mathcal{G} \) is weakly reversible.

(iii) If \( \pi \) is a reaction vector balanced measure of \((\mathcal{G}, \Lambda)\), then for every \( y \to y' \in \mathcal{R} \), there exists \( \tilde{y} \to \tilde{y}' \in \mathcal{R} \) with \( y + \tilde{y} = y' + \tilde{y}' \).

**Proof.** Let \( \Gamma' \) be a positive irreducible component of \((\mathcal{G}, \Lambda)\), and let \( \pi \) be a measure within \( \Gamma \). If \( \pi \) is either reaction balanced, complex balanced or reaction vector balanced, then by Theorem 4.4 \( \pi \) is a stationary measure. It follows from the standard theory of Markov chains that \( \pi \) is positive on every
state of $\Gamma$. By positivity of $\Gamma$, every reaction is active on at least one $x \in \Gamma$. Consider $y \rightarrow y' \in \mathcal{R}$, and let $x \in \Gamma$ be such that $\lambda_{y \rightarrow y'}(x) > 0$. If $\pi$ is reaction balanced, then from \eqref{eq:reaction-balanced}, it follows that $\lambda_{y \rightarrow y'}(x + y' - y) > 0$, so that $y' \rightarrow y \in \mathcal{R}$. If $\pi$ is reaction vector balanced, then from \eqref{eq:reaction-balanced}, it follows that there is a $\tilde{y} \rightarrow \tilde{y}' \in \mathcal{R}$ such that $\tilde{y} - \tilde{y}' = y' - y$. Finally, if $\pi$ be complex balanced, we consider the continuous time Markov chain with state space $\mathcal{C}$ and transition rate from complex $y'$ to $y''$ to be $\varrho(y', y'') := \lambda_{y' \rightarrow y''}(x - y + y')$, where as usual the expression is 0 if $y' \rightarrow y'' \notin \mathcal{R}$ or $x - y + y' \notin \mathcal{Z}_{>0}$. Since $\pi$ is complex balanced, $\nu(y'') := \pi(x - y + y'')$ is a stationary distribution for the contructed Markov chain. Since $\nu(y) = \pi(x) > 0$, $y$ must be recurrent, which implies that $y \rightarrow y'$ is necessarily contained in a directed cycle $y \rightarrow y' \rightarrow \cdots \rightarrow y$, which concludes the proof.

4.2 Results for mass action kinetics

The main result in this section is the stochastic analog of the classical Horn, Jackson and Feinberg theory for deterministic mass action reaction systems. We start with a consequence of \cite[Corollary 19]{7}. The original result \cite[Corollary 19]{7} is restated in Section 5 of this paper as Theorem 5.3.

**Theorem 4.6.** Let $(\mathcal{G}, K_S)$ be a stochastic mass action system. If $(\mathcal{G}, K_S)$ possesses a complex balanced distribution within some positive irreducible component of $(\mathcal{G}, K_S)$, then there exists a unique stationary distribution within every irreducible component of $(\mathcal{G}, K_S)$, and every stationary distribution of $(\mathcal{G}, K_S)$ is complex balanced.

In the following result, we extend Theorem 4.6 by only requiring the hypothesis of a complex balanced measure instead of a complex balanced distribution. Moreover, we also consider reaction balanced measures, in analogy with the deterministic statement in Theorem 3.4.

**Theorem 4.7 (Existence and uniqueness of stationary distribution).** Let $(\mathcal{G}, K_S)$ be a stochastic mass action system. If $(\mathcal{G}, K_S)$ possesses a $\sigma$-finite complex balanced (reaction balanced, resp.) measure within some positive irreducible component of $(\mathcal{G}, K_S)$, then there exists a unique stationary distribution within every irreducible component of $(\mathcal{G}, K_S)$, and every stationary distribution of $(\mathcal{G}, K_S)$ is complex balanced (reaction balanced, resp.).

Theorem 4.7 will be proved after stating and proving Proposition 4.8.

**Remark 4.3.** Theorem 4.7 implies that a stochastic mass action system which possesses a $\sigma$-finite, complex balanced (reaction balanced, resp.) measure within some irreducible component is a complex balanced (reaction balanced, resp.) reaction system.

**Remark 4.4.** In general, a statement analogous to Theorem 4.7 does not hold when reaction balance or complex balance is replaced by reaction vector balance.

1. Consider the mass action system

\[
0 \xrightarrow{1} A \quad A + B \xrightarrow{1/2} 2A + B
\]

The positive irreducible components are given by $x_D = l$ where $l \in \mathcal{Z}_{>0}$. Within every component, the associated process is a birth and death process with a unique stationary measure (up to multiplication by constants). Moreover, the process is positive recurrent only for $l = 1$. It follows that a reaction vector balanced stationary distribution within a component exists, but no stationary distribution exists for $l \geq 2$.

2. Even in cases where a stationary distribution exists within every irreducible component, the stationary distribution may be reaction vector balanced in some irreducible components and not in
The irreducible components correspond to $x_B = l$ with $l \in \mathbb{Z}_{\geq 0}$ is a nonnegative integer. It can be checked that a stationary distribution exists within every irreducible component. The reactions corresponding to the edges in red have reaction vector $\pm (1,0)$ while the reactions corresponding to the edges in black have reaction vector $\pm (2,0)$. We denote by $q_i(i,j)$ the transition rate from the state $(i,l)$ to $(j,l)$. We have

\[
q_i(i+1, i) = i + 1, \quad q_i(i+2, i) = (i+1)(i+2), \\
q_i(i-1, i) = 2i - 1, \quad q_i(i-2, i) = i(i-1)[4i^2 + 2i(6-10l) + 24l - 21]
\]

and $q_i(i,j) = 0$ otherwise. If a reaction vector balanced measure $\pi$ exists within an irreducible component, then it must be a stationary measure for the subnetwork determined by the red reactions. The only possibility is that

\[
\pi(i,l) = M_l \prod_{j=0}^{i-1} \frac{1}{2j+1},
\]

where $M_l$ is a normalization constant depending on the irreducible component $x_B = l$. It can be checked that $\pi$ is a stationary measure only for $l = 1$. It follows that the stationary distribution within $x_B = 1$ is reaction vector balanced, and the stationary distributions within other irreducible components are not.

**Proposition 4.8** (Existence of stationary distribution). Let $(\mathcal{G}, K_S)$ be a stochastic mass action system and let $\pi$ be a $\sigma$-finite complex balanced measure within an irreducible component of $(\mathcal{G}, K_S)$. Then $\pi$ is a finite measure (and so is a stationary distribution, up to a normalization constant).

**Proof.** Let $\mu$ be a $\sigma$-finite complex balanced measure within the irreducible component $\Gamma$ of the mass action system $(\mathcal{G}, K_S)$. By Theorem 4.1, $\mu$ is a stationary measure, and therefore from standard theory of continuous time Markov chains, $\mu$ is positive on all states of $\Gamma$.

Now, consider the largest subnetwork $\tilde{\mathcal{G}} = (\tilde{S}, \tilde{C}, \tilde{R})$ of $\mathcal{G}$ for which $\Gamma$ is a positive irreducible component. In other words, $\tilde{\mathcal{G}}$ consists only of reactions of $\mathcal{G}$ which are active on some state $x \in \Gamma$. Clearly, the dynamics of the system $(\mathcal{G}, K_S)$ and $(\tilde{\mathcal{G}}, K_S)$ coincide on $\Gamma$. Since $\mu$ is a complex balanced measure of $(\tilde{\mathcal{G}}, K_S)$, by Theorems 4.3, the network $\tilde{\mathcal{G}}$ is weakly reversible.

Now introduce a set of fictitious species $\{S_y\}_{y \in \tilde{C}}$, one fictitious species for one complex of $\tilde{\mathcal{G}}$, and consider the mass action system, denoted by $(\tilde{\mathcal{G}}, K_S)$ and described by the set of reactions

\[
\tilde{\mathcal{R}} := \{y + S_y \rightarrow y' + S_{y'} : y \rightarrow y' \in \tilde{\mathcal{R}}\},
\]

The resulting reaction network $\tilde{\mathcal{G}}$ is clearly weakly reversible since the reactions $\tilde{\mathcal{R}}$ are in one-to-one correspondence with the reactions $\mathcal{R}$. By using this correspondence, we equip $\tilde{\mathcal{G}}$ with mass action kinetics, with the same rate constants as $(\tilde{\mathcal{G}}, K_S)$. Furthermore, $\tilde{\mathcal{G}} = (\tilde{S}, \tilde{C}, \tilde{R})$ has deficiency zero. (See the proof of Theorem 18. In the same paper, a definition of deficiency is given, together with a discussion on its meaning.) Since the reaction network $\tilde{\mathcal{G}}$ has deficiency zero and is weakly reversible, from Theorem 13, it follows that the network $(\tilde{\mathcal{G}}, K_{D})$ is complex balanced for every choice of positive reaction rate constants.

Let $n$ be the number of species of $\mathcal{G}$ and $\bar{m}$ be the number of complexes of $\tilde{\mathcal{G}}$ (equivalently of $\tilde{\mathcal{G}}$) and let $(x, \tilde{x}) \in \mathbb{Z}_{\geq 0}^n \times \mathbb{Z}_{\geq 0}^{\bar{m}}$ denote a state of $(\tilde{\mathcal{G}}, K_S)$, where the entries of $x$ and $\tilde{x}$ refer to the original
and fictitious species, respectively. Let \( e_y \) denote the vector of \( \mathbb{Z}^n \) whose entry relative to the complex \( y \) is 1, and whose other entries are zero. Consider the set \( \hat{\Gamma} = \Gamma \times \{ e_y \}_{y \in \mathcal{C}} \). Since \( \Gamma \) is an irreducible component of \( (\hat{\mathcal{G}}, K_S) \), it follows that \( \hat{\Gamma} \) is a closed set for the reaction network \( (\hat{\mathcal{G}}, K_S) \), in the sense that no state outside \( \hat{\Gamma} \) is accessible from within \( \hat{\Gamma} \). Furthermore, from the state \((x, e_y)\) only the states \((x - y + y', e_{y'})\) are accessible, provided that \( x \geq y \) and that there is a path from \( y \) to \( y' \) in the reaction graph of \( \hat{\mathcal{G}} \), which is equivalent to the existence of a path from \( y + S_y \) to \( y' + S_{y'} \) in the reaction graph of \( \hat{\mathcal{G}} \).

Since finitely many states are accessible from any given state, every irreducible component of \( (\hat{\mathcal{G}}, K_S) \) has finitely many states. Finally, since \( \hat{\mathcal{G}} \) is weakly reversible, \((x, e_y)\) is accessible from \((x', e_{y'})\) if and only if \((x, e_y)\) is accessible from \((x', e_{y'})\). Thus, we have shown that \( \hat{\Gamma} \) is a union of irreducible components of \( (\hat{\mathcal{G}}, K_S) \), each of which has finitely many states.

Now define a measure \( \hat{\mu} \) on \( \hat{\Gamma} \) by

\[
\hat{\mu}(x, e_y) = \mu(x) \quad \text{for all } (x, e_y) \in \hat{\Gamma}.
\]

Clearly, \( \hat{\mu} \) is positive on every state of \( \hat{\Gamma} \). We now show that \( \hat{\mu} \) is a non-null stationary measure. Noting that \( \lambda_{y' \rightarrow y'}(x, e_y) \) is nonzero and equal to the rate \( \lambda_{y \rightarrow y'}(x) \) of \((\hat{\mathcal{G}}, K_S)\) if and only if \( y' = y \), for every \((x, e_y)\) in \( \hat{\Gamma} \) we have

\[
\sum_{y'' \in \mathcal{C}} \sum_{y' \in \mathcal{C}} \hat{\mu}(x, e_y) \lambda_{y' \rightarrow y''}(x, e_y) = \sum_{y'' \in \mathcal{C}} \mu(x) \lambda_{y \rightarrow y''}(x)
= \sum_{y'' \in \mathcal{C}} \mu(x + y'') \lambda_{y' \rightarrow y}(x + y'' - y)
= \sum_{y'' \in \mathcal{C}} \sum_{y' \in \mathcal{C}} \hat{\mu}(x + y'', e_{y''}) \lambda_{y'' \rightarrow y'}(x + y'' - y', e_{y''})
\]

where in the second equality, we used that \( \mu \) is a complex balanced measure on \( \Gamma \). This shows that \( \hat{\mu} \) is stationary.

Let \( L \) be an irreducible component within \( \Gamma \). Since \( \hat{\mu} \) is a non-null, \( \sigma \)-finite stationary measure on \( L \) which has only a finite number of states, it follows that \( \hat{\mu} \) is finite on \( L \), and therefore \( \hat{\mu} \) is a constant multiple of the stationary distribution on \( L \). As noted earlier in the proof, every deterministic mass action system defined on the network \( \hat{\mathcal{G}} \) is complex balanced. Let \( c \) be a positive complex balanced equilibrium of the mass action system \( (\hat{\mathcal{G}}, K_D) \). Hence, by [2] Theorem 4.1 (stated here as Theorem 5.1) we have that within every irreducible component \( L \subset \hat{\Gamma} \)

\[
\hat{\mu}(x, e_y) = M_L \frac{c^x}{x!} \quad \text{for all } (x, e_y) \in L,
\]

for some \( M_L > 0 \).

We now show that \( M_L \) does not depend on the irreducible component \( L \). First, it follows from \( \hat{\mu}(x, e_y) = \mu(x) \) that \( M_L = \mu(x)x!/c^x =: f(x) \). To show that \( M_L = M_{L'} \) for two different irreducible components \( L, L' \subset \hat{\Gamma} \), it suffices to show that \( f(x) = f(x') \) for \( x \) and \( x' \) such that \((x, e_y) \in L \) and \((x', e_{y'}) \in L' \), for some \( y, y' \in \mathcal{C} \). Since \( x, x' \in \Gamma \), \( x' \) is accessible from \( x \), i.e. there is a finite sequence of reactions that takes \( x \) to \( x' \). Therefore, to argue by induction, it is sufficient to show that \( f(x) = f(x') \) assuming that \( x' = x - y + y'' \) and \( \lambda_{y \rightarrow y''}(x) > 0 \). Under the last assumption \((x, e_y)\) and \((x', e_{y''})\) are in the same irreducible component \( L \), so necessarily \( f(x) = M_L = f(x') \). Thus, we have that for every \( x \in \Gamma \), \( \mu(x) = M c^x/x! \) and therefore,

\[
\sum_{x \in \Gamma} \mu(x) = M \sum_{x \in \Gamma} \frac{c^x}{x!} \leq M \sum_{x \in \mathbb{Z}^n_{\geq 0}} \frac{c^x}{x!} = M \prod_{i=1}^n e^{c_i} < \infty.
\]

Thus \( \mu \) is finite, which concludes the proof.

\[ \square \]

**Remark 4.5.** Since a reaction balanced measure is complex balanced, a similar result as Proposition 4.8 can be stated for a reaction balanced measure. Unlike the case of reaction balance and complex balance, a \( \sigma \)-finite reaction vector balanced measure within an irreducible component is not necessarily finite, as shown in Remark 4.4(1).
We are now ready to prove Theorem 4.7.

Proof of Theorem 4.7. Suppose that \( \mu \) is a \( \sigma \)-finite complex balanced measure within \( \Gamma \), a positive irreducible component of \( (G, K_S) \). By Proposition 4.8 \( \mu(\Gamma) < \infty \), and therefore \( \mu \) is a stationary distribution, up to a positive multiplicative constant. The claim is then proved by Theorem 4.6.

Suppose now that \( \mu \) is a \( \sigma \)-finite reaction balanced measure within \( \Gamma \), a positive irreducible component of \( (G, K_S) \). Since a reaction balanced measure is complex balanced, we have already shown that there exists a unique stationary distribution within every irreducible component \( \Gamma' \) of \( (G, K_S) \), and by Corollary 19 (stated here as Theorem 5.3) they are of the form \( \pi_{\Gamma'}(x) = M_{\xi, x}' c^x / x! \), where \( c > 0 \) and \( M_{\xi, x}' > 0 \). In particular, \( \pi_{\Gamma} = \mu \) is a reaction balanced measure, hence by plugging \( \pi_{\Gamma}(x) = M_{\xi, x}' c^x / x! \) and the mass action reaction rates in \( 4.1 \) and by simplifying, we obtain

\[
\left( k_{y \to y'} - k_{y' \to y} e^{y' - y} \right) \mathbb{1}_{\langle x \geq y \rangle} = 0
\]

for all \( x \in \Gamma \) and every \( y \to y' \in \mathcal{R} \). Since \( \Gamma \) is a positive irreducible component, every reaction \( y \to y' \in \mathcal{R} \) is active at some state \( x \), i.e. for every \( y \to y' \in \mathcal{R} \) there is a state \( x \in \Gamma \) such that \( x \geq y \). Therefore, \( k_{y \to y'} = k_{y' \to y} e^{y' - y} \) for every \( y \to y' \in \mathcal{R} \). It follows that for every irreducible component \( \Gamma' \), for all \( x \in \Gamma' \) and all \( y \to y' \in \mathcal{R} \), we have \( \pi_{\Gamma'}(x) \lambda_y - \pi_{\Gamma'}(x + y' - y) \lambda_{y' \to y'}(x + y' - y) \), which concludes the proof.

The following results explore sufficient conditions for reaction balance, given in terms of complex balance and reaction vector balance.

**Theorem 4.9.** Suppose that \( \pi \) is a \( \sigma \)-finite complex balanced measure of a stochastic mass action system \( (G, K_S) \). Assume that \( \text{supp}(\pi) \) includes a subset \( A \) such that no nonzero polynomial of degree at most \( \max_{y, y' \in \mathcal{R}} \|y\|_1 \) vanishes on \( A \). Furthermore, suppose that (4.8) holds for \( \xi \in \mathbb{R}^n \) and \( x \in A \). Then, \( (G, K_S) \) is reaction balanced.

The proof of Theorem 4.9 makes use of results developed in Section 5. Hence, it is deferred to Subsection 5.3. The following result is an immediate corollary.

**Corollary 4.10.** Suppose that \( \pi \) is a \( \sigma \)-finite complex balanced measure of a stochastic mass action system \( (G, K_S) \). Assume that \( \pi \) is also reaction vector balanced and such that no nonzero polynomial of degree at most \( \max_{y, y' \in \mathcal{R}} \|y\|_1 \) vanishes on \( \text{supp}(\pi) \). Then, \( (G, K_S) \) is reaction balanced and cycle balanced.

We give here an example that shows that the somewhat technical conditions in the statement of Theorem 4.9 and of Corollary 4.10 are necessary.

**Example 4.1.** Consider the stochastic mass action system \( (G, K_S) \) depicted below:

\[
\begin{array}{c}
A & \xrightarrow{1} & B \\
2 & \xrightarrow{1} & 2
\end{array}
\]

\[
\pi(x) = (x_A x_B l)^{-1} \text{ for } x \in \mathbb{Z}_{\geq 0}^3 \text{ is a complex balanced measure with } \text{supp}(\pi) = \mathbb{Z}_{\geq 0}^3, \text{ thus } (G, K_S) \text{ is complex balanced by Proposition 4.3 and Remark 4.7. The irreducible components of the stochastic mass action system } (G, K_S) \text{ are given by } x_C = 1 \text{ with } l \in \mathbb{Z}_{\geq 0}. \text{ It can be checked that the stationary distribution } \pi_1 \text{ within the irreducible component with } l = 1 \text{ is reaction vector balanced, but no stationary distribution of } (G, K_S) \text{ is reaction balanced. This does not contradict Theorem 4.9 because the nonzero polynomial } x_C - 1 \text{ (of degree } 0 < 2 = \max_{y, y' \in \mathcal{R}} \|y\|_1) \text{ vanishes on } \text{supp}(\pi_1).\]

The following result is somewhat surprising, as it breaks down the symmetry between the results for graphical balance in the deterministic sense (Section 5) and the results for graphical balance in the stochastic sense. Indeed, the corresponding statement for the deterministic case is not true in general (see Remark 4.2 (1)).
Corollary 4.11 (Complex balance & reaction vector balance → Reaction balance). Suppose that $(G, K_S)$ is a complex balanced stochastic mass action system. If $(G, K_S)$ is reaction vector balanced, then $G$ is reversible and $(G, K_S)$ is reaction balanced.

Proof. By Proposition 4.3 (due to [7]), $G$ is weakly reversible. Hence, due to [20], $Z_{\geq 0}^n$ is a union of irreducible components. Therefore, there exists a complex balanced distribution $\pi$ with $\text{supp}(\pi) = Z_{\geq 0}^n$, which is necessarily reaction vector balanced by assumption. The conclusion follows from Corollary 4.10.

5 Bridging deterministic and stochastic mass action systems

The main focus of this section is to relate graphical balance of a deterministic mass action system with graphical balance of the corresponding stochastic mass action system, and vice versa. We begin by stating some known results.

5.1 Existing results

Connection between equilibria of particular deterministic mass action systems and the stationary distributions of the stochastic counterparts have been shown in [2, 13, 7].

The first result in this sense is [2, Theorem 4.1], which states the following:

Theorem 5.1. Let $(G, K_D)$ be a deterministic mass action system with a positive complex balanced equilibrium $c \in \mathbb{R}_{\geq 0}^n$. Then, the corresponding stochastic mass action system $(G, K_S)$ has a product-form Poisson-like stationary distribution within every irreducible component $\Gamma$ given by the expression

$$\pi_\Gamma(x) = M_\Gamma^c \frac{c^x}{x!} \text{ for } x \in \Gamma,$$

where $M_\Gamma^c$ is a normalizing constant.

The study is then carried on in [13, 7], where further relations between stochastic and deterministic models are unveiled. We start with presenting one of the main results of [13, Theorems 5.9 and 5.10]:

Theorem 5.2. If the deterministic mass action system $(G, K_D)$ is reaction balanced (i.e. detailed balanced as a reaction network), then the corresponding stochastic mass action system $(G, K_S)$ is reaction vector balanced (i.e. detailed balanced as a Markov chain). Moreover, the converse holds if the function $y \rightarrow y' \iff y' - y$ is a one-to-one correspondence between the reactions in $R$ and their reaction vectors.

In [7], a study on complex balanced distribution is conducted, and a stochastic counterpart for the deterministic model deficiency zero theory is developed. In particular, [7, Corollary 19] states the following:

Theorem 5.3. If a stochastic reaction system $(G, K_S)$ admits a complex balanced distribution within a positive irreducible component then $G$ is weakly reversible. Moreover, a stochastic mass action system $(G, K_S)$ admits a complex balanced distribution within a positive irreducible component if and only if the corresponding deterministic mass action system $(G, K_D)$ admits a positive complex balanced state. If this is the case, then on every irreducible component $\Gamma$ there exists a unique stationary distribution $\pi_\Gamma$. Such $\pi_\Gamma$ is a complex balanced distribution and it has the form (5.1), where $c$ is a positive complex balanced equilibrium of $(G, K_D)$.

Moreover, the following is implied by [7, Theorem 23 and discussion in Section 5.1]

Theorem 5.4. Let $A \subseteq Z_{\geq 0}^n$ be any set such that no nonzero polynomial of degree at most $\max_{y, y' \in R} \|y\|$, vanishes on $A$. Let $	ilde{A} := A \cup \{x \in Z_{\geq 0}^n : x \geq y \text{ for some } y \rightarrow y' \in R \text{ and such that } x - y + y' \in A\}$. Suppose that $\pi$ is a stationary distribution of a stochastic mass action system $(G, K_S)$ such that $\pi(x) = M(x)c^x/x!$ for $x \in \tilde{A}$, where $M(x) = M(x')$ for any $x, x'$ within the same irreducible component. Then $(G, K_D)$ is complex balanced and $c$ is a complex balanced equilibrium of $(G, K_D)$.

Corollary 5.5. Suppose that $\pi = c^x/x!$ for $x \in Z_{\geq 0}^n$ is a stationary measure of a stochastic mass action system $(G, K_S)$. Then $(G, K_D)$ is complex balanced and $c$ is a complex balanced equilibrium of $(G, K_D)$.
5.2 Expanding the bridge

In this section, we establish further connections between a deterministic mass action system \((\mathcal{G}, K_D)\) and the corresponding stochastic mass action system \((\mathcal{G}, K_S)\).

**Theorem 5.6.** Suppose that \((\mathcal{G}, K_D)\) is a deterministic mass action system and \((\mathcal{G}, K_S)\) is the corresponding stochastic mass action system.

1. \((\mathcal{G}, K_D)\) is reaction balanced if and only if \((\mathcal{G}, K_S)\) is reaction balanced.
2. \((\mathcal{G}, K_D)\) is complex balanced if and only if \((\mathcal{G}, K_S)\) is complex balanced.
3. \((\mathcal{G}, K_D)\) is cycle balanced if and only if \((\mathcal{G}, K_S)\) is cycle balanced.

**Proof.** Suppose that \((\mathcal{G}, K_D)\) is reaction balanced. Let \(c \in \mathbb{R}^C\) be a positive reaction balanced equilibrium of \((\mathcal{G}, K_D)\). In other words, for every \(y \rightarrow y' \in \mathcal{R}\), the following holds:

\[
\kappa_{y \rightarrow y'} c^y = \kappa_{y' \rightarrow y} c^{y'}
\]

Then \(c\) is a complex balanced equilibrium of \((\mathcal{G}, K_D)\) and by Theorem 5.1, \(\pi(x) = c^x/x!\) for all \(x \in \mathbb{Z}_+^C\) defines a complex balanced measure of \((\mathcal{G}, K_S)\). It is straightforward to verify by a direct calculation that \(\pi\) is a reaction balanced stationary measure of \((\mathcal{G}, K_S)\). On the other hand, if \((\mathcal{G}, K_S)\) is reaction balanced, by Theorems 5.1 and 5.3 there is a \(c > 0\) such that \(\pi(x) = c^x/x!\) for all \(x \in \mathbb{Z}_+^C\) defines a reaction balanced stationary measure. But this implies that \(c\) is a reaction balanced equilibrium of \((\mathcal{G}, K_D)\) which proves that \((\mathcal{G}, K_D)\) is reaction balanced (by Theorem 5.3).

2. This follows from Theorem 5.3.

3. In the case of mass action kinetics, both the deterministic cycle balance condition (3.4) for a positive vector \(c\) and the stochastic cycle balance condition (4.3) for a distribution \(\pi\) on a positive irreducible component reduce to the same condition on reaction rate constants. Both \((\mathcal{G}, K_D)\) and \((\mathcal{G}, K_S)\) are cycle balanced if and only if for every sequence of distinct complexes \((y_1, \ldots, y_j) \subseteq \mathcal{C}\) with \(j \geq 3\), the reaction rate constants satisfy

\[
\prod_{i=1}^{j} \kappa_{y_i \rightarrow y_{i+1}} = \prod_{i=1}^{j} \kappa_{y_{i+1} \rightarrow y_i}
\]

where by assumption \(\kappa_{y \rightarrow y'} = 0\) if \(y \rightarrow y' \notin \mathcal{R}\), and \(y_{j+1} := y_1\). To see this in the stochastic setting, note that by positivity of irreducible component \(\Gamma\), for \(y_i \rightarrow y_0 \in \mathcal{R}\) there exists \(x \in \Gamma\) with \(x \geq y_i\) and for all \(1 \leq i \leq j\), if \(x \geq y_i\), then \(x - y_i + y_{i+1} \geq y_{i+1}\). It follows that \((\mathcal{G}, K_D)\) is cycle balanced if and only if \((\mathcal{G}, K_S)\) is cycle balanced.

**Remark 5.1.** Theorem 5.6 implies that we can talk about complex balanced, reaction balanced and cycle balanced mass action systems regardless whether we are considering the stochastic or deterministic modeling regime.

**Remark 5.2.** In general, the corresponding statement in Theorem 5.6 for reaction vector balance is not true in either direction. We give examples to illustrate this point.

1. **(Deterministic reaction vector balance \(\Rightarrow\) Stochastic reaction vector balance.)** Denote the deterministic mass action system in (3.9) by \((\mathcal{G}, K_D)\). We saw earlier that \((\mathcal{G}, K_D)\) is reaction vector balanced and complex balanced but not reaction balanced. By Theorem 5.6, it follows that the corresponding stochastic mass action \((\mathcal{G}, K_S)\) is complex balanced. Now suppose that \((\mathcal{G}, K_S)\) is reaction vector balanced, so that by Corollary 4.11, \((\mathcal{G}, K_S)\) is reaction balanced. This implies that, by Theorem 5.6, \((\mathcal{G}, K_D)\) is reaction balanced, which is a contradiction. Therefore, \((\mathcal{G}, K_S)\) cannot be (stochastically) reaction vector balanced.

Another example is given by the deterministic mass action system (3.8), which is reaction vector balanced. However, the corresponding stochastic mass action system has no positive irreducible components and therefore no stationary distributions within a positive irreducible component. Hence, it cannot be reaction vector balanced.
2. (Stochastic reaction vector balance $\nRightarrow$ Deterministic reaction vector balance.) Consider the stochastic mass action system $(G, K_S)$ depicted below:

![Diagram](image)

Similarly to Remark 4.4 (2), the reactions corresponding to the edges in red have reaction vector $\pm 1$ while the reactions corresponding to the edges in black have reaction vector $\pm 2$. The only irreducible component is $Z_{\geq 0}$, and the only stationary distribution is

$$\pi(x) = M \prod_{j=0}^{x-1} \frac{1}{2j + 1} \text{ for } x \in Z_{\geq 0},$$

where $M$ is a normalizing constant. It can be checked that $\pi$ is reaction vector balanced, which implies that $(G, K_S)$ is reaction vector balanced. The reaction vector balanced equilibria of the corresponding deterministic mass action system $(G, K_D)$ are solutions of

$$0 = 1 - 2a^2,$$
$$0 = 4 + 2a + 2a^2 - 24a^3 - 8a^4.$$

The only positive solution of the first equation is $a = 1/\sqrt{2}$, which is not a solution of the second equation. Thus $(G, K_D)$ does not have any reaction vector balanced equilibria.

As an immediate consequence of Corollary 4.11 and Theorem 5.6, the following can be stated, in the spirit of Theorem 5.2 (due to [13]):

**Corollary 5.7.** If the stochastic mass action system $(G, K_S)$ is reaction vector balanced (i.e. detailed balanced as a Markov chain) and complex balanced, then the corresponding deterministic mass action system $(G, K_D)$ is reaction balanced (i.e. detailed balanced as a reaction system).

Note that the converse does not hold: deterministic complex balance and reaction vector balance does not imply stochastic reaction vector balance (hence reaction balance), as highlighted in Remark 5.2(1).

Our results complete the framework of [2, 13, 7]. Indeed, given a stochastic mass action system $(G, K_S)$, we say that a set $A \subseteq \mathbb{Z}_{\geq 0}^n$ has property $P$ if no nonzero polynomial of degree at most $\max_{y \rightarrow y'} \|g\|_1$ vanishes on $A$. Then, we have the following scheme of implications:

- $(G, K_S)$ is reaction vector balanced
- Existence of a reaction vector balanced measure $\pi$ with $\text{supp}(\pi) = \mathbb{Z}_{\geq 0}^n$
- Existence of a reaction vector balanced measure within one positive irreducible component
- $\pi(x) = c^x/x!$ for $x \in \mathbb{Z}_{\geq 0}^n$, $\pi$ is reaction vector balanced, and $\text{supp}(\pi)$ has property $P$

- $(G, K_S)$ is reaction balanced
- Existence of a reaction balanced measure $\pi$ with $\text{supp}(\pi) = \mathbb{Z}_{\geq 0}^n$
- Existence of a reaction balanced measure within one positive irreducible component
- $\pi(x) = c^x/x!$ for $x \in \mathbb{Z}_{\geq 0}^n$, $\pi$ is a stationary measure, and $\text{supp}(\pi)$ has property $P$

- $(G, K_S)$ is complex balanced
- Existence of a complex balanced measure $\pi$ with $\text{supp}(\pi) = \mathbb{Z}_{\geq 0}^n$
- Existence of a complex balanced measure within one positive irreducible component
- $\pi(x) = c^x/x!$ for $x \in \mathbb{Z}_{\geq 0}^n$, $\pi$ is a stationary measure, and $\text{supp}(\pi)$ has property $P$
Further implications connecting the deterministic and stochastic models are summarized in Figure 1.

5.3 Proof of Theorem 4.9

Since $\pi$ is a $\sigma$-finite complex balanced measure of $(\mathcal{G}, K_S)$, by Proposition 4.8, $\pi(\mathbb{Z}_{\geq 0}^n) < \infty$. Fix $y \to y' \in \mathcal{R}$. Since $(\mathcal{G}, K_S)$ is a mass action system, $\lambda_{y \to y'}(x) = \kappa_{y \to y'} \prod_{i=1}^{n} x_i(x_i - 1) \cdots (x_i - y_i + 1)$ for some $\kappa_{y \to y'} > 0$ (see Remark 2.1). By assumption, $\lambda_{y \to y'}$ cannot vanish on supp($\pi$), so there exists an irreducible component in supp($\pi$) such that $y \to y'$ is active at some state of $\Gamma$. Since $\pi$ is complex balanced, by [7, Theorem 18] the set of reactions that are active at some state of $\Gamma$ describe a weakly reversible subnetwork by some $\kappa$. For all $x \in \mathcal{R}$, it follows that $\mathcal{G}$ is weakly reversible. Therefore, the subnetworks $\mathcal{G}_F$ are necessarily a union of connected components of $\mathcal{G}$; if $x \geq y$, then $x - y + y' \geq y'$, so if $y \to y'$ is active at some state of $\Gamma$, the same holds for $y' \to y''$, and so on. In conclusion, since (3.2) only concerns reactions in the same connected component, $(\mathcal{G}_F, K_D)$ is complex balanced. By Theorem 5.1 for all $x \in \text{supp}(\pi)$, $\pi(x) = M_F c^x/x!$, where $M_F$ is a positive constant depending on the irreducible component containing $x$, and $c \in \mathbb{Z}_{\geq 0}^n$. By assumption, (1.3) holds for all $x \in A$ and all reaction vectors $\xi$. Substituting the expressions for $\pi$ and $\lambda$ into the reaction vector balance condition (1.3) and simplifying yields

$$\sum_{y \to y': y' = y + \xi} (\kappa_{y \to y'} - c^y \kappa_{y' \to y''}) \prod_{i=1}^{n} x_i(x_i - 1) \cdots (x_i - y_i + 1) = 0$$

for all $x \in A$ and all reaction vectors $\xi$. It follows that the polynomial on the left-hand side is null. By linear independence of the polynomials $\prod_{i=1}^{n} x_i(x_i - 1) \cdots (x_i - y_i + 1)$ in the sense of Remark 2.1, the expressions $\kappa_{y \to y'} - c^y \kappa_{y' \to y''}$ must be equal to zero for all $y \to y' \in \mathcal{R}$. This implies that $c$ is a reaction balanced state and therefore by Theorem 5.1 $\pi$ is a reaction balanced measure. \hfill \Box

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