Dominance and deficiency for Petri nets and chemical reaction networks

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Dominance and Deficiency for Petri Nets and Chemical Reaction Networks

Robert Brijder

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Abstract Inspired by Anderson et al. [J. R. Soc. Interface, 2014] we study the long-term behavior of discrete chemical reaction networks (CRNs). In particular, using techniques from both Petri net theory and CRN theory, we provide a powerful sufficient condition for a structurally-bounded CRN to have the property that none of the non-terminal reactions can fire for any of its recurrent configurations. We compare this result and its proof with a related result of Anderson et al. and show its consequences for the case of CRNs with deficiency one.

1 Introduction

Chemical reaction network (CRN) theory studies the behavior of chemical systems. Traditionally, the primary focus is on continuous CRNs, where mass action kinetics is assumed, see, e.g., [2, 8, 9, 10]. In this setting a state is determined by the concentration of each species and the system evolves through ordinary differential equations. However, in scenarios where the number of molecules is small one needs to resort to discrete CRNs. In a discrete CRN a state (also called configuration) is determined by the counts of each species, and one often associates a probability to each reaction. In this paper we consider only discrete CRNs without probabilities, and so, from now on, by CRN we will always mean a discrete CRN without probabilities.

A CRN essentially consists of a finite set of reactions such as $A + B \to 2B$, which means that during this reaction one molecule of species A and one molecule of species B are consumed and as a result two molecules of species B are produced. We may depict a CRN as a graph, the reaction graph, where the vertices are the left-hand and right-hand sides of reactions and the edges are the reactions, see Figure 1 for an example. We focus in this paper on the long-term behavior of CRNs for which the total number of molecules cannot grow unboundedly. For such CRNs, called structurally-bounded CRNs, each configuration eventually reaches a configuration c such that c is reachable from any configuration c' reachable from

Hasselt University, Belgium. E-mail: robert.brijder@uhasselt.be

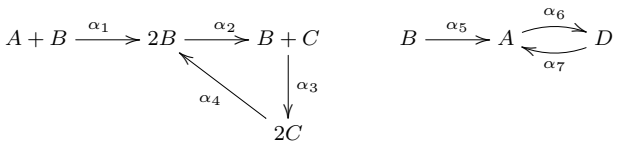

Fig. 1 The reaction graph of a CRN N.

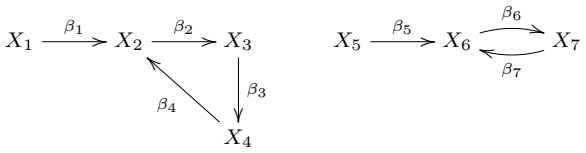

Fig. 2 The reaction graph of the CRN N' obtained from N by introducing a distinct species X_i for each vertex.

c (i.e., we can always go back to c). Such configurations are called recurrent. The CRN N of Figure 1 is structurally-bounded.

Now, let us consider the CRN N' obtained from N by replacing every vertex by one molecule of a distinct species X_i, see Figure 2. We easily observe that for N', the recurrent configurations are exactly those without molecules of species X_1 or X_5. In other words, the reactions β_1 and β_5 cannot fire for any recurrent configuration of N'. Notice that the reaction graph of N' has two strongly connected components without outgoing edges: one having the vertices X_2, X_3, and X_4 and one having the vertices X_6 and X_7. The reactions outside these two strongly connected components are called non-terminal. Thus N' has the property that none of the non-terminal reactions can fire for any of its recurrent configurations. But what about the original CRN N? The dynamics of N are clearly more involved since we can go, for example, from configuration $A + B$ back to $A + B$ by firing reaction α_1 followed by firing reaction α_5.

The main result of this paper, cf. Theorem 3.1, provides a sufficient condition for a structurally-bounded CRN to have the property that none of the non-terminal reactions can fire for any of its recurrent configurations (we recall the notion of non-terminal reaction in Section 3). Those CRNs have relatively simple long-term behavior. The sufficient condition of Theorem 3.1 is structural/syntactical and can be checked for many CRNs in a computationally efficient way. Various non-trivial CRNs from the literature satisfy the sufficient condition of Theorem 3.1 (see, e.g., the CRNs given in [1]), and so it can make non-trivial predictions about the long-term behavior of those CRNs. In particular, the CRN N of Figure 1 satisfies the sufficient condition. Moreover, this result can also be used as a tool for engineering CRNs that perform deterministic computations (independent of the probabilities), such as in the computational model of [5]. Indeed, such CRNs generally require relatively simple long-term behavior which may be partially verified by Theorem 3.1.

Theorem 3.1 is inspired by the main technical result of [1] (which in turn was inspired by the main result of [16]), which provides another sufficient condition for the non-applicability of non-terminal reactions for recurrent configurations. How-

ever, there are a number of differences between the two results. Firstly, Theorem 3.1 is derived in a basic combinatorial setting using notions from Petri net theory such as the notion of T-invariant, without considering stochastics. In contrast, the intricate proof of the main result of [1] is derived in a very different setting that uses non-trivial arguments from both mass action kinetics and stochastics. Secondly, we show examples where the main result of [1] is silent, while Theorem 3.1 makes a prediction. We compare both results in detail in Section 4. While we focus in this paper on recurrent configurations of CRNs, we mention that the related concept of recurrent CRN has been investigated in [14].

Deficiency is a useful and well-studied notion to classify CRNs. With Theorem 3.1 in place we consider in Subsection 3.4 (as is similarly done in [1]) its consequences for the case of CRNs with deficiency one.

While formulated in terms of CRNs, the results in this paper equally apply to Petri nets, which is a very well studied model of parallel computation, see, e.g., [15]. Using the small "dictionary" provided for the reader with a Petri net background (see Subsection 2.2), it is straightforward to reformulate the results in this paper in terms of Petri nets.

A conference version of this paper, containing selected results without proofs, was presented at DNA 21 [4].

2 Standard graph and CRN/Petri net notions

2.1 Preliminaries

Let $\mathbb{N} = \{0, 1, \ldots\}$. Let X and Y be arbitrary sets. The set of vectors indexed by X with entries in Y (i.e., the set of functions $\varphi : X \to Y$) is denoted by Y^X. For $v, w \in \mathbb{N}^X$, we write $v \leq w$ if $v(x) \leq w(x)$ for all $x \in X$. Moreover, we write $v < w$ if $v \leq w$ and $v \neq w$. The *support* of v, denoted by $\mathrm{supp}(v)$, is the set $\{x \in X \mid v(x) > 0\}$. For finite sets X and Y, a $X \times Y$ matrix A is a matrix where the rows and columns are indexed by X and Y, respectively.

We consider digraphs $G = (V, E, F)$ where V and E are finite sets of vertices and edges and $F : E \to V^2$ assigns to each edge $e \in E$ an ordered vertex pair (u, v). We denote V by $V(G)$ and E by $E(G)$. The *incidence matrix* of G is the $V(G) \times E(G)$ matrix A where for $e \in E$ with $F(e) = (v, w)$ we have entries $A(v, e) = -1$, $A(w, e) = 1$, and $A(u, e) = 0$ for all $u \in V \setminus \{v, w\}$ if $v \neq w$, and $A(u, e) = 0$ for all $u \in V$ if $v = w$. The number of connected components of a digraph G is denoted by $c(G)$. It is well known that the rank $r(A)$ of the incidence matrix A of a digraph G is equal to $|V| - c(G)$ (where it does not matter over which field the rank is computed, see, e.g., [13, Proposition 5.1.2]). From now on we let the field $\mathbb{Q}$ of rational numbers be the field in which we compute.

A walk π in G is described by (particular) strings over E. Let $\Phi(\pi)$ denote the *Parikh image* of π, i.e., $\Phi(\pi) \in \mathbb{N}^E$ where $(\Phi(\pi))(e)$ is the number of occurrences of e in π. We write $\mathrm{supp}(\pi) = \mathrm{supp}(\Phi(\pi))$, i.e., $\mathrm{supp}(\pi)$ is the set of elements that occur in π. The vectors v of $\ker(A) \cap \mathbb{N}^E$ describe the cycles of G, i.e., they describe the Parikh images of closed walks in G.

For convenience we identify a digraph G with its $V(G) \times E(G)$ incidence matrix. Hence, we may for example speak of the rank $r(G)$ of G. We say that $e \in E(G)$ is a *bridge* if e is not contained in any closed walk of G. The *induced subgraph* G' of G

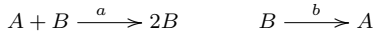

Fig. 3 The reaction graph of the CRN N_1 of Example 2.1.

with respect to $X \subseteq V(G)$ is the digraph $G' = (X, E', F')$ where E' is the preimage of X^2 under F and F' is the restriction of F to E'. A *strongly connected component* (*SCC*, for short) is an induced subgraph G' of G with respect to $X \subseteq V(G)$ such that G' contains no bridge and X is maximal (with respect to inclusion) with this property.

2.2 CRNs and Petri nets

We now recall the notion of a chemical reaction network.

Definition 2.1 A *chemical reaction network* (or *CRN* for short) N is a 3-tuple (S, R, F) where S and R are finite sets and F is a function that assigns to each $r \in R$ an ordered pair $F(r) = (v, w)$ where $v, w \in \mathbb{N}^S$. Vector v is denoted by $\mathrm{in}(r)$ and w by $\mathrm{out}(r)$.

The elements of S are called the *species* of N, the elements of R are called the *reactions* of N, and F is called the *reaction function*. For a reaction r, $\mathrm{in}(r)$ and $\mathrm{out}(r)$ are called the *reactant vector* and *product vector* of r, respectively.

It is common in the literature of CRNs to omit the function F and have R as a set of tuples (v, w). However, this would not allow two different reactions to have the same reactant and product vectors (such situations are common in Petri net theory).

In CRN theory, it is common to write vectors in additive notation, so, e.g., if $S = \{A, B, C\}$, then $A + 2B$ denotes the vector v with $v(A) = 1$, $v(B) = 2$, and $v(C) = 0$.

Example 2.1 Consider the CRN $N_1 = (S, R, F)$ with $S = \{A, B\}$, $R = \{a, b\}$, $F(a) = (A + B, 2B)$ and $F(b) = (B, A)$. This CRN is taken from [16] (see also [1]). This example is the running example of this section.

We now define a natural digraph for a CRN N, called the reaction graph of N. The name is from [11], and the concept is originally defined in [8].

Definition 2.2 Let $N = (S, R, F)$ be a CRN. The *reaction graph* of N, denoted by $\mathcal{R}_N$, is the labeled digraph (V, R, F) with $V = \{\mathrm{in}(r) \mid r \in R\} \cup \{\mathrm{out}(r) \mid r \in R\}$.

Note that in the reaction graph each reactant and product vector becomes a single vertex. The vertices of the reaction graph are called *complexes*. The reaction graph of the CRN N_1 of our running example (Example 2.1) is depicted in Figure 3.

A *configuration* c of N is a vector $c \in \mathbb{N}^S$. Let $r \in R$. We say that r can *fire* on c if $\mathrm{in}(r) \leq c$. In this case we also write $c \to^r c'$ where $c' = c - \mathrm{in}(r) + \mathrm{out}(r)$. Note that c' is a configuration as well. Moreover, we write $c \to c'$ if $c \to^r c'$ for some $r \in R$. For $\tau \in R^*$ (as usual, R^* is Kleene star on R) we write $c \to^\tau c'$ if $c \to^{\tau_1} c_1 \cdots \to^{\tau_n} c'$ where $\tau = \tau_1 \cdots \tau_n$ and $\tau_i \in R$ for all $i \in \{1, \ldots, n\}$. The reflexive and transitive closure of the relation $\to$ is denoted by $\to^*$. If $c \to^* c'$, then

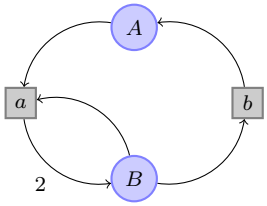

Fig. 4 The Petri net-style depiction of the CRN N_1 of the running example.

we say that c' is *reachable* from c. We say that a configuration c is *recurrent* if for all c' with $c \to^* c'$ we have $c' \to^* c$. Note that if c is recurrent and $c \to^* c'$, then c' is recurrent.

It is didactically useful to view the firing relation as an edge relation. The *configuration graph* CG_N of N is an infinite edge-labeled digraph, where the configurations are the vertices and there is an edge from configuration c to configuration c' labeled by $r \in R$ precisely when $c \to^r c'$. Note that c' is reachable from c if and only if there is a path from c to c' in CG_N. Also note that a configuration c is recurrent if and only if the SCC C of CG_N containing c does not have outgoing edges (i.e., there is no edge of CG_N from a configuration of C to a configuration outside C).

Example 2.2 Consider again the running example. We have, e.g., $2A + B \to^{aabb} 2A + B$. However, $2A + B$ is not recurrent as $2A + B \to^b 3A$ and in configuration $3A$ no reaction can fire. In fact, the recurrent configurations of N_1 are precisely those that do not contain any B. Indeed, assume c is recurrent. Then we can fire b until we obtain a configuration c' that does not contain any B. No reaction can fire for c' and so $c = c'$ since c is recurrent.

The definition of a CRN is equivalent to that of a Petri net [15] (minus its initial marking). In a Petri net, species are called *places* p, reactions are called *transitions*, and configurations are called *markings*. A Petri net is often depicted as a graph with two types of vertices, one type for the places and one for the transitions. The Petri net-style depiction of the CRN N_1 of the running example is given in Figure 4. The round vertices are the places and the rectangular vertices are the transitions. We use in this paper several standard Petri net notions, which are recalled in the next subsection.

2.3 P/T-invariants

The notions of this subsection are all taken from Petri net theory [15]. We first recall the notion of an incidence matrix of a CRN, which is not to be confused with the notion of an incidence matrix of a digraph (as recalled above). In fact, we will compare in the next subsection the incidence matrix of a CRN with the incidence matrix of its reaction graph.

Definition 2.3 For a CRN $N = (S, R, F)$, the *incidence matrix* of N, denoted by $\mathcal{I}_N$, is the $S \times R$ matrix A where for each $r \in R$ the column of A belonging to r is equal to $\mathrm{out}(r) - \mathrm{in}(r)$.

Example 2.3 Consider again the CRN N_1 of the running example. Then

$$\mathcal{I}_{N_1} = \begin{array}{c} \\ A \\ B \end{array} \begin{array}{c} \begin{array}{cc} a & b \end{array} \\ \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix} \end{array}.$$

Note that if $c \to^\tau c'$, then $c' = c + \mathcal{I}_N \Phi(\tau)$, where $\Phi(\tau)$ denotes again the Parikh image of τ.

A $v \in \mathbb{N}^S$ is called a *P-invariant* of N if $v^T \mathcal{I}_N = 0$ (here 0 denotes a zero vector of suitable dimension indexed by R). Similarly, $v \in \mathbb{N}^R$ is called a *T-invariant* of N if $\mathcal{I}_N v = 0$, i.e., $v \in \ker(\mathcal{I}_N)$.[1] A P-invariant or T-invariant are also sometimes called P-semiflow and T-semiflow, respectively, in the literature. Intuitively, a P-invariant assigns a weight to each species in a way that is invariant under applying reactions. Observe that if $c \to^\tau c'$, then $\Phi(\tau)$ is a T-invariant if and only if $c' = c$. A CRN N is called *conservative* if there is a P-invariant v such that $\mathrm{supp}(v) = S$. Also, N is called *consistent* if there is a T-invariant v such that $\mathrm{supp}(v) = R$.

A CRN N is said to be *structurally bounded* when for every configuration c, there is a $k_c \in \mathbb{N}$ such that for each configuration c' with $c \to^* c'$ we have that each entry of c' is at most k_c. Note that a CRN N is structurally bounded if and only if the number of different configurations reachable from any given configuration is finite. In other words, N is structurally bounded if and only if every connected component of CG_N is finite. Consequently, assuming fairness, the recurrent configurations of a structurally-bounded CRN are the possible configurations of the CRN in the long term.

The following result is well known, but for completeness we recall its short proof.

Proposition 2.1 ([12]) *Let N be a CRN. If N is conservative, then N is structurally bounded.*

Proof Let $v \in \mathbb{N}^S$ be a P-invariant with $\mathrm{supp}(v) = S$ and let c be a configuration. Let $c \to^\tau c'$ for some $\tau \in R^*$. We have $c' = c + \mathcal{I}_N \Phi(\tau)$. Thus $v^T c' = v^T c + v^T \mathcal{I}_N \Phi(\tau) = v^T c$ and so for all $s \in S$, $v(s)c'(s) \leq v^T c$ and therefore $c'(s) \leq v^T c / v(s)$. □

Example 2.4 The CRN N_1 of the running example is both conservative and consistent. Indeed, any $v \in \mathbb{N}^S$ with $v(A) = v(B) \geq 1$ is a P-invariant of N_1 with $\mathrm{supp}(v) = S$ and any $w \in \mathbb{N}^R$ with $w(a) = w(b) \geq 1$ is T-invariant of N_1 with $\mathrm{supp}(w) = R$.

2.4 Deficiency

The notions that we recall in this subsection are originally from chemical reaction theory (and are less studied within Petri net theory).

Let $N = (S, R, F)$ be a CRN and let $V = \{\mathrm{in}(r) \mid r \in R\} \cup \{\mathrm{out}(r) \mid r \in R\}$. We denote by $\mathcal{Y}_N$ the $S \times V$ matrix with for all $s \in S$ and $v \in V$, entry $\mathcal{Y}_N(s, v)$ is equal to $v(s)$.

[1] The P and T in P/T-invariant are short for Place and Transition (from Petri net theory). We choose to use these well-known names instead of calling them "S-invariant" and "R-invariant" for Species and Reaction, respectively.

$$A + B \xrightarrow{a} 2B \qquad A \xrightarrow{b} B$$

Fig. 5 The reaction graph of a CRN N_2 discussed in Example 2.5.

The next lemma relates the incidence matrix $\mathcal{I}_N$ of a CRN N with the incidence matrix of the reaction graph $\mathcal{R}_N$ of N.

Lemma 2.1 (Section 6 of [9]) *Let $N = (S, R, F)$ be a CRN. Then $\mathcal{I}_N = \mathcal{Y}_N \mathcal{R}_N$.*

In the above equality, $\mathcal{R}_N$ denotes the incidence matrix $\mathcal{R}_N$ and not the graph.

Proof Let $V = \{\text{in}(r) \mid r \in R\} \cup \{\text{out}(r) \mid r \in R\}$. Let $s \in S$ and $r \in R$. Then $\mathcal{I}_N(s,r) = (\text{out}(r) - \text{in}(r))(s) = \mathcal{Y}_N(s, \text{out}(r)) \cdot 1 + \mathcal{Y}_N(s, \text{in}(r)) \cdot (-1) = \sum_{x \in V} \mathcal{Y}_N(s,x)\mathcal{R}_N(x,r) = \mathcal{Y}_N \mathcal{R}_N$. □

As a corollary to Lemma 2.1, we have the following.

Corollary 2.1 ([11]) *Let $N = (S, R, F)$ be a CRN. Then* $\ker(\mathcal{R}_N) \subseteq \ker(\mathcal{I}_N)$.

The vectors v of $\ker(\mathcal{R}_N) \cap \mathbb{N}^R$, which are T-invariants by Corollary 2.1, are called *closed* T-invariants [3]. Recall that the vectors v of $\ker(\mathcal{R}_N) \cap \mathbb{N}^R$ describe the cycles of $\mathcal{R}_N$, and so for each closed T-invariant v of N, $\text{supp}(v)$ does not contain any bridge of $\mathcal{R}_N$. Since each of the entries of a T-invariant is nonnegative, the linear space $\ker(\mathcal{I}_N)$ does not necessarily have a basis consisting of only T-invariants, see Example 2.5 below.

The *deficiency* $\delta(N)$ of a CRN N is $r(\mathcal{R}_N) - r(\mathcal{I}_N)$. By Corollary 2.1, $\delta(N)$ is non-negative. Thus, one may view $\delta(N)$ as a measure of the difference in dimensions between $\ker(\mathcal{R}_N)$ and $\ker(\mathcal{I}_N)$. The former is determined only by the structure of the reaction graph (ignoring the identity of the vertices), while the latter also incorporates the relations that rely on the identities of the vertices of the reaction graph.

Recall from Subsection 2.1 that $r(\mathcal{R}_N) = |V(\mathcal{R}_N)| - c(\mathcal{R}_N)$. Hence, we have $\delta(N) = |V(\mathcal{R}_N)| - c(\mathcal{R}_N) - r(\mathcal{I}_N)$ [10, 8]. Note that if $\delta(N) = 0$, then every T-invariant of N is closed and $\ker(\mathcal{R}_N) = \ker(\mathcal{I}_N)$.

Example 2.5 In the running example, $\ker(\mathcal{R}_{N_1})$ only contains the zero vector, while $\ker(\mathcal{I}_{N_1})$ contains all scalar multiples of the vector w with $w(a) = w(b) = 1$. Thus $\ker(\mathcal{I}_{N_1})$ has a basis consisting of only T-invariants. Moreover, $\delta(N_1) = 1$. Alternatively, the reaction graph $\mathcal{R}_{N_1}$ has 4 vertices and 2 connected components and $r(\mathcal{I}_{N_1}) = 1$. Thus, $\delta(N_1) = 4 - 2 - 1 = 1$.

If we consider the CRN N_2 of Figure 5, then $\ker(\mathcal{R}_{N_2})$ also only contains the zero vector, while $\ker(\mathcal{I}_{N_2})$ contains all scalar multiples of the vector w with $w(a) = -w(b) = 1$. Again, $\delta(N_2) = 1$, however the only T-invariant of $\ker(\mathcal{I}_{N_2})$ is the zero vector.

3 Dominance and non-closed T-invariants

In this section we prove the main results and discuss their consequences. First we collect various notions in Subsection 3.1.

3.1 Dominance and auxiliary notions

Note that there is a natural partial order for the set of SCCs of a graph: for SCCs X and Y, we have $X \preccurlyeq Y$ if there is a path from a vertex of Y to a vertex of X. We now consider a different partial order, denoted by $\leq_d$, for the SCCs of a reaction graph of a CRN.

Let N be a CRN and let $\leq_{sd}$ be the relation on the SCCs of $\mathcal{R}_N$ such that for all SCCs X and Y of $\mathcal{R}_N$, $X \leq_{sd} Y$ if and only if there are vertices x of X and y of Y such that $x \leq y$. We now define $\leq_d$ to be the transitive closure of $\leq_{sd}$.

Lemma 3.1 *Let $N = (S, R, F)$ be a structurally-bounded CRN. Then the $\leq_d$ relation between SCCs of $\mathcal{R}_N$ is a partial order.*

Proof The $\leq_d$ relation is obviously reflexive and transitive. To show that $\leq_d$ is antisymmetric, let $X \leq_d Y$ and $Y \leq_d X$ for some SCCs X and Y of $\mathcal{R}_N$. Hence there are vertices x_1 and x_2 of X and y_1 and y_2 of Y such that $x_1 \leq y_1$ and $y_2 \leq x_2$. Let π_1 be a path from x_1 to x_2 and let π_2 be a path from y_2 to y_1 in $\mathcal{R}_N$. Then $x_1 + y_2 \rightarrow^{\pi_1} x_2 + y_2 \rightarrow^{\pi_2} x_2 + y_1$. If $X \neq Y$, then $x_1 < y_1$ and $y_2 < x_2$. Thus we have $x_1 + y_2 < x_2 + y_1$, and so N is not structurally bounded — a contradiction. □

For SCCs X and Y we write $X <_d Y$ if $X \leq_d Y$ and $X \neq Y$, and similarly for $<_{sd}$. We say that X *dominates* Y when $X <_d Y$. For a set $\mathcal{S}$ of SCCs, we let $\min_{\leq_d}(\mathcal{S}) \subseteq \mathcal{S}$ be the set of elements of $\mathcal{S}$ that are minimal with respect to the $\leq_d$ relation among all the elements of $\mathcal{S}$.

Note that if a CRN N is structurally-bounded and $x \rightarrow^* y$ for some configurations x and y, then $x \not< y$. Consequently, for any path of some vertex v to some vertex w in $\mathcal{R}_N$, we have $v \not< w$. As a result, for distinct SCCs X and Y, if $X \preccurlyeq Y$, then $Y \not\leq_d X$. In other words, the relation $\preccurlyeq \cup \leq_d$ (i.e., for SCCs X and Y, we have $(X, Y) \in \preccurlyeq \cup \leq_d$ if and only if $X \preccurlyeq Y$ or $X \leq_d Y$) is acyclic modulo reflexivity, that is, it represents a directed acyclic graph where "acyclic" is meant modulo self-loops.

For a SCC X of $\mathcal{R}_N$, we denote by $\mathrm{out}(X)$ the set of edges of $\mathcal{R}_N$ going out of X. In other words, $\mathrm{out}(X) = \{r \in E(\mathcal{R}_N) \mid \mathrm{in}(r) \in V(X), \mathrm{out}(r) \notin V(X)\}$. We call X *terminal* if X has no outgoing edges (i.e., $\mathrm{out}(X) = \emptyset$). We call a reaction r (complex x, resp.) *terminal* if $r \in E(X)$ ($x \in V(X)$, resp.) for some terminal SCC X of $\mathcal{R}_N$.

Before we can state the main technical lemma of this paper in the next subsection, we need one more notion. Let B be the set of bridges of $\mathcal{R}_N$. An *exit set* of a set $\mathcal{S}$ of non-terminal SCCs, is a set $Z \subseteq B$ with both $|Z| = |\mathcal{S}|$ and $|Z \cap \mathrm{out}(X)| = 1$ for all $X \in \mathcal{S}$. In other words, Z contains exactly one bridge of $\mathrm{out}(X)$ for each $X \in \mathcal{S}$. Note that an exit set exists for any set $\mathcal{S}$ of non-terminal SCCs.

3.2 Main technical lemma

The main technical lemma of this paper essentially relates the recurrent configurations of the configuration graph CG_N with the terminal vertices of the reaction graph $\mathcal{R}_N$. Recall that the recurrent configurations of CG_N are the vertices that belong to SCCs of CG_N without outgoing edges. Similarly, the terminal vertices

of $\mathcal{R}_N$ are those that belong to SCCs of $\mathcal{R}_N$ without outgoing edges. Thus, this lemma compares the SCCs without outgoing edges of the graphs CG_N (which represents the behavior of N) and $\mathcal{R}_N$ (which represents the structure of N). In this way, the long-term behavior of a CRN is related to a structural property of the CRN. As such, this lemma can be seen as a model-checking tool for CRNs.

Assuming the existence of a non-terminal reaction that can fire for some recurrent configuration c, the main technical lemma of this paper ensures the existence of certain sequences τ with $c' \to^\tau c'$ for some configuration c' reachable from c. For each exit set Z, there exists such a τ that avoids all bridges outside Z and, at the same time, uses the bridges of Z whenever possible. As a consequence, each of the sequences τ corresponds to a T-invariant $v = \Phi(\tau)$ that have zero entries for the bridges outside Z and nonzero entries for some of the bridges inside Z. This necessary condition translates into a sufficient condition for CRNs to have the property that only terminal reactions can fire for any of its recurrent configurations (cf. Theorem 3.1).

Notice that if a reaction r can fire for some configuration c, then any path in the reaction graph $\mathcal{R}_N$ beginning with r corresponds to a path in the configuration graph CG_N. The proof of the next lemma repeatedly exploits this idea of simultaneously walking in $\mathcal{R}_N$ and CG_N. The proof idea is the following. Let us start with a recurrent configuration c. While traversing CG_N by applying a sequence of reactions starting from c corresponding to a path in $\mathcal{R}_N$, we need never choose a bridge of $\mathcal{R}_N$ going out of a SCC X that is dominated by some SCC. Indeed, if $x \in V(X)$ and $y \in V(Y)$ with $y < x$, then we may walk inside X to x and $y < x$ implies that any reaction r with $\mathrm{in}(r) = y$ can fire for x. In this way we also avoid taking a reaction r' with $\mathrm{in}(r') = x$. Walking out of a SCC that is not dominated by any SCC can be done by taking any of the bridges. We choose the one from the exit set Z. Now, eventually, our path inside $\mathcal{R}_N$ will lead to a terminal vertex. However, since c is recurrent, we can go back to c. If a non-terminal reaction can fire for c, then this means that we can iterate this process (walking along bridges, etc.). Structural boundedness finally ensures that the set of configurations reachable from c is finite and so, we must eventually repeat a configuration that closes the "circuit".

We are now ready to formulate the main technical lemma of this paper.

Lemma 3.2 *Let $N = (S, R, F)$ be a structurally-bounded CRN, and let $\mathcal{X} = \min_{\leq_d}(\mathcal{N})$, where $\mathcal{N}$ is the set of non-terminal SCCs of $\mathcal{R}_N$. Let B be the set of bridges of $\mathcal{R}_N$. Let L be the set of all non-terminal reactions r of $\mathcal{R}_N$ such that there is a non-terminal reaction r' of $\mathcal{R}_N$ with $\mathrm{in}(r') < \mathrm{in}(r)$.*

If some non-terminal reaction can fire for some recurrent configuration c, then for each exit set Z of $\mathcal{X}$, there is a $\tau \in R^*$ such that

1. *τ contains no reactions from $(B \setminus Z) \cup L$,*
2. *τ contains at least one reaction from Z, and*
3. *$c' \to^\tau c'$ for some recurrent configuration c' reachable from c.*

Proof Assume that some non-terminal reaction r_1 can fire for some recurrent configuration c. Let $Z \subseteq B$ be an exit set of $\mathcal{X}$.

Let Y be the SCC containing the vertex $v_1 = \mathrm{in}(r_1)$. We distinguish two cases.

(1) If $Y \notin \mathcal{X}$, then there is a $X <_{sd} Y$. Thus, there are $v_2 \in V(X)$ and $y \in V(Y)$ with $v_2 < y$. Let $\alpha_1 \in R^*$ be a shortest path in Y from v_1 to y. Observe that $\mathrm{supp}(\alpha_1) \cap L = \emptyset$ (if $r_1 \in L$, then α_1 is the empty string).

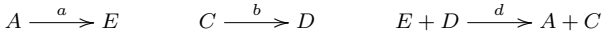

Fig. 6 The reaction graph of the CRN N_3 of Example 3.1.

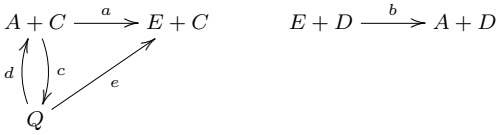

Fig. 7 The reaction graph of the CRN N_4 of Example 3.2.

(2) If $Y \in \mathcal{X}$, then let $\alpha_1 = p_1 b_Y \in R^*$ be a path in $\mathcal{R}_N$ such that p_1 is a path in Y from v and $b_Y \in Z \cap \mathrm{out}(Y)$. Let $v_2 = \mathrm{out}(b_Y)$.

In both cases we have that *(i)* α_1 can fire for c, *(ii)* if $c \to^{\alpha_1} c'$, then $v_2 \leq c'$, and *(iii)* v_2 is in a different SCC than v_1. If vertex v_2 is non-terminal, then we repeat this procedure starting with vertex v_2. In this way, we obtain by iteration a sequence $\pi_1 = \alpha_1 \cdots \alpha_l$ that can fire for c and such that the obtained vertex v_{l+1} is a terminal vertex. Indeed, since the relation $\leq_d \cup \preccurlyeq$ is acyclic (modulo reflexivity), the vertices $v_1, v_2, \ldots$ belong to mutually distinct SCCs of $\mathcal{R}_N$ and so we must eventually reach a terminal SCC. Since c is recurrent, there is a sequence σ_1 of terminal reactions such that $\tau_1 = \pi_1 \sigma_1$ has the property that $c \to^{\tau_1} c''$ where some non-terminal reaction r_2 can fire for c''. Note that τ_1 contains no reactions from $(B \setminus Z) \cup L$ and at least one reaction from Z.

We repeat the above described procedure (that constructed τ_1) for configuration c'' and vertex $\mathrm{in}(r_2)$, to obtain (by iteration) an infinite sequence $\tau = \tau_1 \tau_2 \cdots$. Since τ is infinite and N is structurally bounded, there is a configuration c_r such that $c \to^{\tau_{\mathrm{pre}}} c_r \to^{\tau_{\mathrm{loop}}} c_r$ and $\tau_{\mathrm{loop}} = \tau_i \cdots \tau_j$ for some $i < j$. Note that, by the construction of τ, τ_{loop} contains no reactions from $(B \setminus Z) \cup L$ and at least one reaction from Z, and so we are done. □

We illustrate Lemma 3.2 through a couple of examples.

Example 3.1 Consider the CRN N_3 of Figure 6. It is easy to verify that $c = A + C$ is a recurrent configuration. Moreover, there is a non-terminal reaction r that can fire for this configuration (take $r = a$ or $r = b$). Note that there is only one exit set Z for $\mathcal{X}$, which is $Z = B = \{a, b, d\}$. By Lemma 3.2, there is a $\tau \in R^*$ such that (1) τ contains no reactions from $(B \setminus Z) \cup L$, (2) τ contains at least one reaction from Z, and (3) $c' \to^{\tau} c'$ for some recurrent configuration c' reachable from c. Indeed, we can choose, e.g., $\tau = abd$ and $c' = c$.

We now give another example.

Example 3.2 Consider the CRN N_4 of Figure 7. It is easy to verify that $c = Q + D$ is a recurrent configuration. Moreover, there is a non-terminal reaction r that can fire for this configuration (take $r = d$ or $r = e$). We have that $B = \{a, b, e\}$ and there are two exits set $Z_1 = \{a, b\}$ and $Z_2 = \{b, e\}$ for $\mathcal{X}$. We notice that $\tau = dabc$ and $c' = c$ for Z_1 and $\tau = ebc$ and $c' = c$ for Z_2 satisfy the conditions of Lemma 3.2.

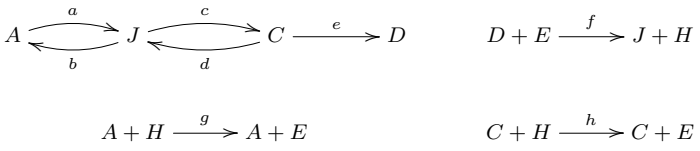

Fig. 8 The reaction graph of the CRN N_5 of Example 3.3.

3.3 Main result

Considering the non-closed T-invariant $v = \Phi(\tau)$ with τ from Lemma 3.2, we have the following corollary to Lemma 3.2. It is the main result of this paper.

Theorem 3.1 *Let N, $\mathcal{X}$, B, and L be as in Lemma 3.2.*

Assume there is an exit set Z of $\mathcal{X}$ such that there is no non-closed T-invariant v with (1) $v(x) = 0$ for all $x \in (B \setminus Z) \cup L$ and (2) $v(z) \neq 0$ for some $z \in Z$.

Then no non-terminal reaction can fire for any recurrent configuration of N.

Note that since closed T-invariants v cannot contain bridges, we may without loss of generality remove the condition that v is "non-closed" in Theorem 3.1.

We use Theorem 3.1 to determine whether no non-terminal reaction can fire for any recurrent configuration of a CRN. While non-closed T-invariants have a central role in Theorem 3.1, curiously, this notion from [3] has been given only modest attention in both the Petri net theory and the CRN theory.

For a given exit set Z of $\mathcal{X}$, one can verify using linear programming in polynomial time whether or not there is a non-closed T-invariant v with the properties of Theorem 3.1. While in general there may be an exponential number of exit sets (exponential in the number of reactions) to check, in many cases the number of exit sets is severely constrained and in these cases the sufficient condition of Theorem 3.1 is computationally efficient.

We now give some examples to illustrate Theorem 3.1.

Example 3.3 Consider the CRN N_5 of Figure 8. This CRN is a simplification of a CRN from biology studied in [16] (see also [1]). We have

$$\mathcal{I}_{N_5} = \begin{array}{c} \\ A \\ J \\ C \\ D \\ E \\ H \end{array} \begin{array}{c} \begin{array}{cccccccc} a & b & c & d & e & f & g & h \end{array} \\ \begin{pmatrix} -1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & -1 & -1 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -1 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & -1 & -1 \end{pmatrix} \end{array}.$$

It is easy to verify that the sum of the rows of $\mathcal{I}_{N_5}$ is the zero vector and so N_5 is conservative. Consequently, N_5 is structurally bounded. It turns out that $\ker(\mathcal{I}_{N_5})$ is of dimension 4 and is spanned by T-invariants. In fact, one can verify that $\ker(\mathcal{I}_{N_5})$ is spanned by the two closed T-invariants $w_1 = \Phi(ab)$ and $w_2 = \Phi(cd)$ together with the two non-closed T-invariants $v_1 = \Phi(gfce)$ and $v_2 = \Phi(hfce)$. We remark that $A + H + D \to^{gfce} A + H + D$ and $C + H + D \to^{hfce} C + H + D$. Thus $\delta(N_5) = 2$. Note that $B = \{e, f, g, h\}$ is the set of bridges of $\mathcal{R}_{N_5}$. Let $\mathcal{X}$

$$A + B \xrightarrow{a} 2B \qquad B + C \xrightarrow{b} A + C$$

Fig. 9 The reaction graph of the CRN N_6 of Example 3.4.

be the set of non-terminal SCCs of $\mathcal{R}_{N_5}$ that are minimal with respect to $\leq_d$. We notice that $Z = \{e, f\}$ is the only exit set of $\mathcal{X}$. Also $L = \{g, h\}$. Now, by the structure of the non-closed T-invariants v_1 and v_2, there is no non-closed T-invariant v with both (1) $v(g) = v(h) = 0$ (note that $(B \setminus Z) \cup L = \{g, h\}$) and (2) either $v(e)$ or $v(f)$ nonzero. By Theorem 3.1, for every recurrent configuration no non-terminal reaction can fire. Since every reaction is non-terminal, for every recurrent configuration no reaction can fire.

Lemma 3.2 and Theorem 3.1 become weaker, but are more simple to state when we ignore domination, i.e., when we set $\mathcal{X} = \mathcal{N}$ and $L = \emptyset$. Below is the formulation for Theorem 3.1 where we set $\mathcal{X} = \mathcal{N}$ and $L = \emptyset$.

Corollary 3.1 *Let $N = (S, R, F)$ be a structurally-bounded CRN.*

Assume there is an exit set Z of the set of non-terminal SCCs of $\mathcal{R}_N$ such that there is no non-closed T-invariant v with (1) $v(x) = 0$ for all $x \in B \setminus Z$ and (2) $v(z) \neq 0$ for some $z \in Z$, where B is the set of bridges of $\mathcal{R}_N$.

Then no non-terminal reaction can fire for any recurrent configuration of N.

The next example shows that the converse of Lemma 3.2 does not hold.

Example 3.4 Consider the CRN N_6 of Figure 9. We show that no reaction can fire for any recurrent configuration of N_6. Let c be a recurrent configuration. If c does not contain any C, then we can fire reaction a until we obtain a configuration c' for which no more reactions can fire. Since c is recurrent, $c = c'$ and we are done. If c contains at least one C, then we can apply reaction b until we obtain a configuration c'' with only A's and C's. Hence no reaction can fire for c''. Since c is recurrent, we have $c = c''$ and we are done.

However, for $c = A + B + C$ we have $c \to^\tau c$ with $\tau = ab$. We notice that $Z = \{a, b\}$ is the only exit set of $\mathcal{X}$ and $(B \setminus Z) \cup L = \emptyset$. Thus τ trivially contains no reactions from $(B \setminus Z) \cup L$ and τ contains reactions from Z. This shows that the converse of Lemma 3.2 does not hold.

We remark that if we remove species C from reaction b, then Theorem 3.1 (and Lemma 3.2) would have been applicable to show that no (non-terminal) reaction can fire for any recurrent configuration of N_6.

3.4 Deficiency one

We now consider the case where the deficiency is 1. This severely restricts the structure of the non-closed T-invariants.

Lemma 3.3 *Let $N = (S, R, F)$ be a consistent CRN with $\delta(N) = 1$. Assume moreover that $\ker(\mathcal{R}_N)$ has a basis consisting of T-invariants (i.e., consisting of cycles of $\mathcal{R}_N$). Then for all non-closed T-invariants v, $\mathrm{supp}(v)$ contains every bridge of $\mathcal{R}_N$.*

Proof Let B be the set of bridges of $\mathcal{R}_N$. Since $\ker(\mathcal{R}_N)$ has a basis consisting of cycles of $\mathcal{R}_N$, $\mathrm{supp}(z) \cap B = \emptyset$ for all $z \in \ker(\mathcal{R}_N)$. Since $\delta(N) = 1$, we have that $\mathrm{supp}(v) \cap B = \mathrm{supp}(w) \cap B$ for all $v, w \in \ker(\mathcal{I}_N) \setminus \ker(\mathcal{R}_N)$. In other words, $\mathrm{supp}(v) \cap B = \mathrm{supp}(w) \cap B$ for all non-closed T-invariants v and w. Since N is consistent, there is a T-invariant v with $\mathrm{supp}(v) = R \supseteq B$. So $B \subseteq \mathrm{supp}(w)$ for all non-closed T-invariants w. □

The next result follows directly from Lemma 3.2 and Lemma 3.3.

Corollary 3.2 *Let N be a structurally-bounded and consistent CRN with $\delta(N) = 1$. Assume moreover that $\ker(\mathcal{R}_N)$ has a basis consisting of T-invariants. If there are non-terminal vertices x and y such that $x < y$, then for all recurrent configurations c, none of the non-terminal reactions can fire.*

Proof Assume there are non-terminal vertices x and y such that $x < y$ and assume to the contrary that some non-terminal reaction r can fire for some recurrent configuration c. By Lemma 3.3, for all non-closed T-invariants v, $\mathrm{supp}(v)$ contains every bridge of $\mathcal{R}_N$. Hence, by Lemma 3.2, every non-terminal SCC of $\mathcal{R}_N$ is minimal with respect to $\leq_d$ among the non-terminal SCCs of $\mathcal{R}_N$ — a contradiction by the existence of x and y (note that x and y cannot be vertices of the same SCC since N is structurally bounded). □

Corollary 3.2 is essentially a special case of Theorem 3.5 of the supplementary material of [1]. The latter result is stronger in that it does not assume $\ker(\mathcal{R}_N)$ to have a basis consisting of T-invariants. The interesting aspect of Corollary 3.2 is its proof: it is obtained using different techniques than in [1] — the latter is stated and proved in terms of notions from mass-action kinetics and stochastics.

Example 3.5 Consider the CRN N_1 of the running example of Section 2. Recall from Example 2.4 that N_1 is conservative and consistent. Since N_1 is conservative, it is structurally bounded. Also recall from Example 2.5 that $\delta(N_1) = 1$ and that $\ker(\mathcal{R}_N)$ only contains the zero vector (and so trivially $\ker(\mathcal{R}_N)$ has a basis consisting of T-invariants). By Corollary 3.2, no non-terminal reaction can fire for any recurrent configuration c of N_1. Since all reactions of N_1 are non-terminal, no reaction can fire for any recurrent configuration c of N_1.

4 Using rates

This paper is inspired by the main technical result of [1] (cf. Theorem 3.3 of the supplementary material of [1]). In this section we recall its result. First we recall a particular matrix. Let $\mathbb{R}_{\geq 0}$ ($\mathbb{R}_{>0}$, resp.) be the set of nonnegative (positive, resp.) real numbers.

Definition 4.1 Let $N = (S, R, F)$ be a CRN. Let $V = V(\mathcal{R}_N)$ and let $\kappa \in \mathbb{R}^R_{>0}$. We denote by $\mathcal{K}_{N,\kappa}$ the $S \times V$ matrix where for each $x \in V$ the column of $\mathcal{K}_{N,\kappa}$ belonging to x is equal to $\sum_{r \in R, \mathrm{in}(r) = x} \kappa(r) \cdot (\mathrm{out}(r) - \mathrm{in}(r))$.

The value $\kappa(r)$ in Theorem 4.1 may be interpreted as the "rate" of reaction r. Note that the definition of $\mathcal{K}_{N,\kappa}$ is closely related to the definition of $\mathcal{I}_N$ (Definition 2.3).

We are now ready to formulate the main technical result of [1].

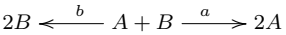

Fig. 10 The reaction graph of the CRN N_7 of Example 4.1.

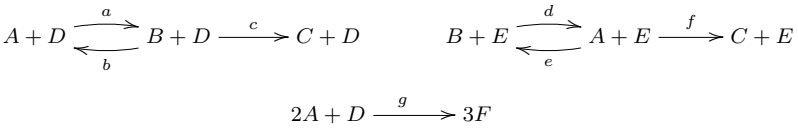

Fig. 11 The reaction graph of the CRN N_8 of Example 4.2.

Theorem 4.1 ([1]) *Let $N = (S, R, F)$ be a conservative CRN and $V = V(\mathcal{R}_N)$. Let L be the set of non-terminal vertices v of $\mathcal{R}_N$ such that there is a non-terminal vertex v' of $\mathcal{R}_N$ with $v' < v$. Assume that $L \neq \emptyset$.*

If some non-terminal reaction can fire for some recurrent configuration c, then for all $\kappa \in \mathbb{R}^R_{>0}$, there is a $w \in \ker(\mathcal{K}_{N,\kappa}) \cap \mathbb{R}^V_{\geq 0}$ with $\mathrm{supp}(w) \cap L = \emptyset$ and there is a non-terminal vertex x with $x \in \mathrm{supp}(w)$.

Theorem 4.1 is proved in [1] using both intricate probabilistic arguments and methods from mass action kinetics. In [1], the theorem is unnecessarily stated in a probabilistic fashion using the notion of "positive recurrent configuration" for stochastically modeled CRNs: it can be stated in a deterministic way (see Theorem 4.1 above) by realizing that the configuration space is finite for a given initial configuration in a structurally-bounded CRN. This deterministic formulation and the discrete model (in contrast to mass action) triggered the search in this paper for a combinatorial explanation of this result. We invite the reader to compare the proof techniques used to prove Theorem 4.1 in [1] and Lemma 3.2 in this paper.

Note that if $L = \emptyset$, then Theorem 4.1 is silent. We now show an example with $L = \emptyset$ where Theorem 3.1 can be applied.

Example 4.1 Consider the CRN N_7 of Figure 10. Note that N_7 is conservative with $w(A) = w(B) = 1$ as a witness. The only T-invariants v of N_7 are those where $v(a) = v(b)$. Let $Z = \{a\}$ be an exit set of $\mathcal{X}$. Then there is no non-closed T-invariant v with $v(b) = 0$ and $v(a) \neq 0$. By Theorem 3.1, no non-terminal reaction can fire for any recurrent configuration c of N_7. Since all reactions of N_7 are non-terminal, no reaction can fire for any recurrent configuration c of N_7. Indeed, one observes that the recurrent configurations of N_7 are those configurations containing either only A's or only B's, for which a and b cannot fire.

We conjecture that the assumption $L \neq \emptyset$ can be removed from Theorem 4.1. In case $L \neq \emptyset$ is removed from Theorem 4.1, then Theorem 4.1 also predicts that no non-terminal reaction can fire for any recurrent configuration of the CRN of Example 4.1. Next, we give an example with $L \neq \emptyset$, where Theorem 3.1 can be applied but Theorem 4.1 is silent.

Example 4.2 Consider the CRN N_8 of Figure 11. Note that N_8 is conservative with $w(X) = 1$ for all species X as a witness. Note that $A + D < 2A + D$ and so $L \neq \emptyset$

in Theorem 4.1. Let $\kappa \in \mathbb{R}^R_{>0}$. We have $\mathcal{K}_{N_8,\kappa} =$

$$\begin{array}{c} \\ A \\ B \\ C \\ D \\ E \\ F \end{array} \begin{array}{c} \begin{array}{cccccccc} A+D & B+D & B+E & A+E & 2A+D & C+D & C+E & 3F \end{array} \\ \begin{pmatrix} -\kappa(a) & \kappa(b) & \kappa(d) & -\kappa(e)-\kappa(f) & -2\kappa(g) & 0 & 0 & 0 \\ \kappa(a) & -\kappa(b)-\kappa(c) & -\kappa(d) & \kappa(e) & 0 & 0 & 0 & 0 \\ 0 & \kappa(c) & 0 & \kappa(f) & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\kappa(g) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 3\kappa(g) & 0 & 0 & 0 \end{pmatrix} \end{array}.$$

Let $w \in \mathbb{R}^V_{\geq 0}$ with $\kappa(a)w(A+D) = \kappa(d)w(B+E) > 0$ and $w(x) = 0$ for all other $x \in V$. Then $w \in \ker(\mathcal{K}_{N_8,\kappa}) \cap \mathbb{R}^V_{\geq 0}$ with $x \in \operatorname{supp}(w)$ for some non-terminal vertex x and $\operatorname{supp}(w) \cap L = \emptyset$. Thus Theorem 4.1 is silent. On the other hand, none of the non-closed T-invariants of N_8 contains a bridge and so by Theorem 3.1, no non-terminal reaction can fire for any recurrent configuration of N_8.

Conversely, despite trying numerous examples, we could not find an example where Theorem 4.1 predicts that no non-terminal reaction can fire for any recurrent configuration, but where Theorem 3.1 is silent.

5 Discussion

Based on structural properties of CRNs, the main result of this paper (cf. Theorem 3.1) provides a sufficient condition to analyze the long-term behavior of CRNs. While its proof is using basic combinatorial arguments, the result is powerful enough to apply to a large class of CRNs. Also, the sufficient condition is computationally efficient to verify for many CRNs. Another such sufficient condition is shown in [1], cf. Theorem 4.1. We have shown examples of CRNs where Theorem 3.1 is applicable while Theorem 4.1 is silent.

Given that discrete CRNs are equivalent to Petri nets, it is curious that the corresponding research areas of CRN theory and Petri net theory have evolved almost independently. In this paper we have shown that notions from Petri net theory (in particular, T-invariance) are useful for CRN theory. Similarly, notions such as deficiency, originating from CRN theory, are useful for Petri net theory. At the interface of these two notions is the scarcely studied notion of non-closed T-invariant, which is crucial in the sufficient condition of Theorem 3.1. This illustrates that both research areas can significantly profit from each other.

An open problem is resolving whether Theorem 4.1 is indeed a special case of Theorem 3.1. Another open problem is to somehow strengthen Theorem 3.1 (or Lemma 3.2) in a natural way to make it applicable for CRNs such as the one presented in Example 3.4.

A further research direction is to incorporate probabilities. One may associate a probability to each T-invariant by multiplying the probabilities of the corresponding reactions. An open problem is to find a probabilistic version of Theorem 3.1 to make predictions about long-term behavior of probabilistic computational models of CRNs, such as the models of [6, 7, 17].

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