Reaction Mining for Reaction Systems

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Additional Declarations: No competing interests reported.

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Abstract

Reaction systems are a formal model for computational processing in which reactions operate on sets of entities (molecules) providing a framework for dealing with qualitative aspects of biochemical systems. This paper is concerned with reaction systems in which entities can have discrete concentrations, and so reactions operate on multisets rather than sets of entities. The resulting framework allows one to deal with quantitative aspects of reaction systems, and a bespoke linear-time temporal logic allows one to express and verify a wide range of key behavioural system properties.

In practical applications, a reaction system with discrete concentrations may only be partially specified, and the possibility of an effective automated calculation of the missing details provides an attractive design approach. With this idea in mind, the current paper discusses parametric reaction systems with parameters representing unknown parts of hypothetical reactions. The main result is a method aimed at replacing the parameters in such a way that the resulting reaction system operating in a specified external environment satisfies a given temporal logic formula.

This paper provides an encoding of parametric reaction systems in SMT, and outlines a synthesis procedure based on bounded model checking for solving the synthesis problem. It also reports on the initial experimental results demonstrating the feasibility of the novel synthesis method.

1

1 Introduction

The seminal paper [1] introduced the *reaction systems* model for computational processes inspired by the functioning of a living cell. Reaction systems can capture in a very simple set-theoretic way the basic mechanisms underpinning the dynamic behaviour of a living cell. A key feature of reaction systems is that they can model interactions of biochemical reactions based on the mechanisms of facilitation and inhibition, i.e., the products of reactions may facilitate or inhibit each other. The original reaction system model represents the reactions, states, and dynamic processes using (tuples of) finite sets, and so it directly captures the qualitative aspects of systems. Having said that, more involved structural concepts can be introduced on top of the basic ones.

Several papers on reaction systems have been motivated by biological issues or by the need to understand computations/processes underlying the dynamic behaviour of reaction systems (see, e.g., [2, 3]). There are also significant extensions of reaction systems, e.g., reaction systems with time [4], reaction systems with durations [5], and quantum and probabilistic reaction systems [6]. Mathematical properties of reaction systems were investigated in, e.g., [7–16].

Notable examples of applications of reaction systems to modelling of systems include, e.g., [17, 18], and the verification of reaction systems was adressed in, e.g., [19–24]. The papers [25, 26] introduced reaction systems with discrete concentrations of entities and reactions operating on multisets of entities, resulting in a model allowing direct quantitative modelling. Although there are other approaches supporting the modelling of complex dependencies of concentration levels and their changes, e.g., chemical reaction networks theory based on [27] or non-linear biochemical control networks theory [28], reaction systems provide much simpler framework (including interactions with the external environment). Discrete concentrations can be simulated in the original qualitative reaction systems, but reaction systems with discrete concentrations provide much more succinct representations in terms of the number of entities being used, and allow for more efficient verification [25]. The properties being verified can be expressed in rsLTL which is a version of the linear-time temporal logic tailored for reaction systems.

In practical applications, a reaction system with discrete concentrations may have only partially specified reactions, and a reaction mining i.e., a computationally effective method of filling in the missing details could provide an attractive design approach.

In the domain of discrete concurrent systems, which encompass reaction systems as well as closely related related membrane systems [29] and tissue systems [30], *synthesis* usually refers to one of two methods for constructing a blueprint for a system's design. The first method includes transformations from system designs in one formalism to (behaviourally) equivalent designs in another formalism. The other method includes transformations of (desired) descriptions of system behaviour into (behaviourally) equivalent system designs. Both approaches have been applied in the fields of reaction

systems, membrane systems, and tissue systems. Examples of the first approach include [17] presenting the design a reaction system model for the heat shock response in such a way that the qualitative behavior of the result correlates well with the quantitative behavior of the corresponding ODE model of the heat shock response, and [31] developing a reaction system model inspired by the mechanistic model of within-cell signal transduction networks of [32]. Examples of the second approach include [33, 34] presenting automated synthesis from behavioural specifications into membrane systems which are a computational model carrying out calculations in cells using a biologically inspired abstraction, and [35, 36] discussing tissue systems which provide a computational abstraction of biological reactions and transport of molecules in a tissue. In both cases the problem addressed was that of synthesising systems from specifications of observed or desired behaviour given in the form of transition systems. The results obtained in [33–36] were underpinned by strong connections between biologically inspired computational abstractions and Petri nets [37] and were based on methods based on the theory of regions [38]. Yet another strand of recently proposed work aimed at building reaction systems is to provide facilities allowing synthesising of complex designs using established programming constructs as well as the concepts related to asynchrony in real-life system behaviours [39]. A preliminary version of the current paper [40] extended the scope of synthesis to reaction systems in which entities can have discrete concentrations and reactions operate on multisets of entities, providing a succinct framework for dealing with quantitative aspects of biological systems. It introduced reaction systems with parameters representing the unknown parts of the reactions. The main result was a method to replace these parameters in such a way that the resulting reaction system operating in a given external environment satisfied a given temporal logic formula. Following the approach based on reaction mining, this paper discusses reaction systems with parameters representing the unknown parts of the reactions. The main result is a methodology which replaces these parameters in such a way that the resulting reaction system satisfies a given *rsLTL formula* when operating in a given external *environment*. Intuitively, the rsLTL formula might correspond to a several observations of the behaviour of a partially specified system. The environment is given by a *context automaton* representing the influence of an encompassing system. The current paper provides an encoding of parametric reaction systems in SMT, and proposes a synthesis procedure based on bounded model checking. It also reports on the successful preliminary experimental results demonstrating the scalability of the new synthesis method.

It is important to emphasize that this paper not only introduces a method for parameter synthesis for reaction systems, but it also extends previous results for rsLTL published in [26]. Our paper provides a complexity result for rsLTL model checking as well as correctness analysis for the SMT encoding. Additionally, it shows how model checking for rsLTL can be translated into a corresponding problem for LTL. Last but not least, it proposes a method for reaction mining, for which a parametric extension of reaction systems is introduced.

The paper is organised in the following way. The next section recalls the basic notations and definitions used by reaction systems with discrete concentrations. Section 3

introduces reaction systems with concentrations, while rsLTL for specifying their properties is defined in Section 4. An smt-based encoding for both formalisms is defined in the following section. Section 6 introduces parametric reaction systems and Section 7 provides their smt-based encoding. Experimental evaluation of the proposed synthesis approach is presented in Section 8.

2 Preliminaries

2.1 Multisets

A *multiset* over a set X is a mapping $\mathbf{b} : X \to \mathbb{N}$, and the *empty* multiset $\varnothing_X$ (or simply $\varnothing$) is the constant function which always returns 0. The *carrier* of a multiset $\mathbf{b}$ is the set $carr(\mathbf{b}) = \{x \in X \mid \mathbf{b}(x) > 0\}$. By $\mathcal{B}(X)$ we denote the set of all multisets over X, hence $\mathbf{b} \in \mathcal{B}(X)$ means that $\mathbf{b}$ is a multiset over X. We define the union $⋈$ of multisets in a standard way. For a finite set $\mathbf{B}$ of multisets over X, $⋈(\mathbf{B})(x) = \max(\{\mathbf{b}(x) \mid \mathbf{b} \in \mathbf{B}\})$, for every $x \in X$. For two multisets, $\mathbf{b}$ and $\mathbf{b}'$, we denote $\mathbf{b} \le \mathbf{b}'$ if $\mathbf{b}(x) \le \mathbf{b}'(x)$, for every $x \in X$.

In what follows, we us the notation $x \mapsto i$ to indicate the multiplicity of an element x in a multiset over X. For example, $\{x \mapsto 2, y \mapsto 1\}$ is a multiset with two copies of x, one copy of y, and nothing else. If the multiplicity of an element is 1, we may also simply omit the value as in, e.g., $\{x \mapsto 2, y\}$.

2.2 Reaction systems

Definition 1 (reaction system)**.** *A reaction system is a pair $\mathcal{R} = (S, A)$, where S is a finite* background *set and A is a set of* reactions *over S. A reaction is a triple*

$$a = (R, I, P) = (R_a, I_a, P_a),$$

where R, I, P are nonempty subsets of S such that $R \cap I = \varnothing$, called respectively the reactant, inhibitor, *and* product set.

Definition 2 (reaction system behaviour)**.** *Given a reaction system $\mathcal{R} = (S, A)$, a reaction $a \in A$ is* enabled *by $T \subseteq S$, denoted $en_a(T)$, if $R_a \subseteq T$ and $I_a \cap T = \varnothing$. The* result *of a on T is given by $res_a(T) = P_a$ if $en_a(T)$ holds, and by $res_a(T) = \varnothing$ otherwise. Moreover, the* result *of A on T is*

$$res_A(T) = \bigcup \{res_a(T) \mid a \in A\} = \bigcup \{P_a \mid a \in A \text{ and } en_a(T)\} \,.$$

The set T in Definition 2 represents the current state of a biochemical system being modelled by listing all present biochemical entities. A reaction is enabled and can take place if all its reactants are present and none of its inhibitors is present. The system reaches the next state $res_A(T)$ by executing all the reactions enabled in T.

Example 1. *Let $(S, A) = (\{1, 2, 3, 4\}, \{a_1, a_2, a_3, a_4\})$ be a reaction system, where:*

$$a_1 = (\{1, 4\}, \{2\}, \{1, 2\}), \quad a_2 = (\{2\}, \{3\}, \{1, 3, 4\}),$$
$$a_3 = (\{1, 3\}, \{2\}, \{1, 2\}), \quad a_4 = (\{3\}, \{2\}, \{1\}).$$

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In the state $T = \{1, 3, 4\}$ reactions a_1, a_3, and a_4 are enabled, while a_2 is not. Hence

$$res_A(T) = res_{a_1}(T) \cup res_{a_3}(T) \cup res_{a_4}(T) = \{1,2\} \cup \{1,2\} \cup \{1\} = \{1,2\} \ . \quad \square$$

A reaction system is a finite state system as each each state is a subset of the finite background set, and its state transformations are deterministic since there are no conflicts between enabled reactions. This changes after introducing the external environment, represented by a context automaton, in order to reflect the fact that the living cell is an open system.

Definition 3 (context automaton)**.** *A context automaton* over a set Σ is a triple

$$\mathfrak{A} = (\mathcal{Q}, \mathfrak{q}^{init}, R),$$

where $\mathcal{Q}$ is a finite set of states, *$\mathfrak{q}^{init} \in \mathcal{Q}$ is the* initial state, *and $R \subseteq \mathcal{Q} \times \Sigma \times \mathcal{Q}$ is a* transition relation *labelled with the elements of Σ.*
We assume that for all $\mathfrak{q} \in \mathcal{Q}$ there exists $c \in \Sigma$ and $\mathfrak{q}' \in \mathcal{Q}$ such that $(\mathfrak{q}, c, \mathfrak{q}') \in R$.

Definition 4 (context restricted reaction system)**.** *A context restricted reaction system is a pair*

$$CR\text{-}\mathcal{R} = (\mathcal{R}, \mathfrak{A})$$

such that $\mathcal{R} = (S, A)$ is a reaction system, and $\mathfrak{A} = (\mathcal{Q}, \mathfrak{q}^{init}, R)$ is a context automaton *over 2^S.*

The dynamic behaviour of a context restricted reaction system is captured by the state sequences of its interactive processes.

Definition 5 (interactive process)**.** *An* interactive process *in a context restricted reaction system $CR\text{-}\mathcal{R} = (\mathcal{R}, \mathfrak{A})$, where $\mathcal{R} = (S, A)$ and $\mathfrak{A} = (\mathcal{Q}, \mathfrak{q}^{init}, R)$, is a triple $\pi = (\zeta, \gamma, \delta)$ such that:*

- $\zeta = (z_0, z_1, \ldots, z_n)$, $\gamma = (C_0, C_1, \ldots, C_n)$, *and* $\delta = (D_0, D_1, \ldots, D_n)$
- $z_0, z_1, \ldots, z_n \in Q$ *with* $z_0 = \mathfrak{q}^{init}$
- $C_0, C_1, \ldots, C_n, D_0, D_1, \ldots, D_n \subseteq S$ *with* $D_0 = \varnothing$
- $(z_i, C_i, z_{i+1}) \in R$, *for every* $i \in \{0, \ldots, n-1\}$
- $D_i = res_A(D_{i-1} \cup C_{i-1})$, *for every* $i \in \{1, \ldots, n\}$.

Then the state sequence *of π is*

$$tau = (W_0, \ldots, W_n) = (C_0 \cup D_0, \ldots, C_n \cup D_n).$$

Intuitively, the state sequence of π captures the observed behaviour of CR-$\mathcal{R}$ by recording the successive states of the evolution of the reaction system $\mathcal{R}$ in the environment represented by the context automaton $\mathfrak{A}$. Note that in Definition 5 it is required that for each context set C_i there exists in the automaton a transition from its current state.

3 Reaction systems with discrete concentrations

In practice, the *concentration levels* of the reactant and inhibitor molecules/entities can be more useful than simply using binary values representing their presence or

absence. This can be addressed by introducing an explicit representation of the discrete concentration levels of entities using multisets rather than sets. In concrete terms, we will represent the kth level of concentration of an entity x by including in the multiset of entities exactly k copies of x.

Definition 6 (reaction system with discrete concentrations [25]). *A reaction system with discrete concentrations is a pair $\mathcal{C} = (S, A)$ such that:*

- *S is a finite* background *set; and*
- *A is a nonempty finite set of* c-reactions *over the background set, where a* c-reaction *is a triple $a = (\mathbf{r}, \mathbf{i}, \mathbf{p})$ such that $\mathbf{r}$, $\mathbf{i}$, $\mathbf{p}$ are multisets over S with $\mathbf{r}(e) < \mathbf{i}(e)$, for every $e \in carr(\mathbf{i})$.*

The multisets $\mathbf{r} = \mathbf{r}_a$, $\mathbf{i} = \mathbf{i}_a$, and $\mathbf{p} = \mathbf{p}_a$ in Definition 6 are the *reactant, inhibitor,* and *product* concentration levels, respectively. Moreover, an entity e is an inhibitor of a whenever $e \in carr(\mathbf{i}_a)$.

Similarly as in the case of basic reaction systems recalled in Section 2.2, a c-reaction a is *enabled* by $\mathbf{t} \in \mathcal{B}(S)$ if it is facilitated by reactants (their concentrations are high enough) and not inhibited by inhibitors (their concentrations are below specified threshold).

Definition 7 (behaviour of reaction system with discrete concentrations [25]). *Given a reaction system with discrete concentrations $\mathcal{C} = (S, A)$, a c-reaction $a \in A$ is* enabled *by $\mathbf{t} \in \mathcal{B}(S)$ (denoted by $en_a(\mathbf{t})$) if $\mathbf{r}_a \leq \mathbf{t}$ and $\mathbf{t}(e) < \mathbf{i}_a(e)$, for every $e \in carr(\mathbf{i}_a)$. The* result *of a on $\mathbf{t}$ is $res_a(\mathbf{t}) = \mathbf{p}_a$ if $en_a(\mathbf{t})$, and $res_a(\mathbf{t}) = \varnothing_S$ otherwise. Then the* result *of A on $\mathbf{t}$ is:*

$$res_A(\mathbf{t}) = \Cup\{res_a(\mathbf{t}) \mid a \in A\} = \Cup\{\mathbf{p}_a \mid a \in A \text{ and } en_a(\mathbf{t})\}.$$

The $\mathbf{t}$ in Definition 7 can be regarded as a *state* of a biochemical system, where $\mathbf{t}(e)$ is the *concentration level* of each entity e. In particular, $\mathbf{t}(e) = 0$ indicates the absence of e is in the current state, while $\mathbf{t}(e) = 1$ indicates that e is present in a current state at its lowest observable concentration level.

Definition 8 (context restricted reaction system with discrete concentrations [26]). *A* context restricted reaction system with discrete concentrations *is a pair*

$$\text{CR-}\mathcal{C} = (\mathcal{C}, \mathfrak{A})$$

such that $\mathcal{C} = (S, A)$ is a reaction system with discrete concentrations, and $\mathfrak{A} = (\mathcal{Q}, \mathfrak{q}^{init}, R)$ is a context automaton *over $\mathcal{B}(S)$.*

To capture the dynamic behaviours a context restricted reaction system with discrete concentrations, we next introduce interactive process using state sequences.

Definition 9 (interactive process [26]). *An* interactive process *in a context restricted reaction system with discrete concentrations $\text{CR-}\mathcal{C} = (\mathcal{C}, \mathfrak{A})$, where $\mathcal{C} = (S, A)$ and $\mathfrak{A} = (\mathcal{Q}, \mathfrak{q}^{init}, R)$, is a triple $\pi = (\zeta, \gamma, \delta)$ such that:*

- *$\zeta = (\mathfrak{q}_0, \mathfrak{q}_1, \ldots, \mathfrak{q}_n)$, $\gamma = (\mathbf{c}_0, \mathbf{c}_1, \ldots, \mathbf{c}_n)$, and $\delta = (\mathbf{d}_0, \mathbf{d}_1, \ldots, \mathbf{d}_n)$*
- *$\mathfrak{q}_0, \mathfrak{q}_1, \ldots, \mathfrak{q}_n \in \mathcal{Q}$ with $\mathfrak{q}_0 = \mathfrak{q}^{init}$*
- *$\mathbf{c}_0, \mathbf{c}_1, \ldots, \mathbf{c}_n, \mathbf{d}_0, \mathbf{d}_1, \ldots, \mathbf{d}_n \in \mathcal{B}(S)$ with $\mathbf{d}_0 = \varnothing_{\mathcal{B}(S)}$*
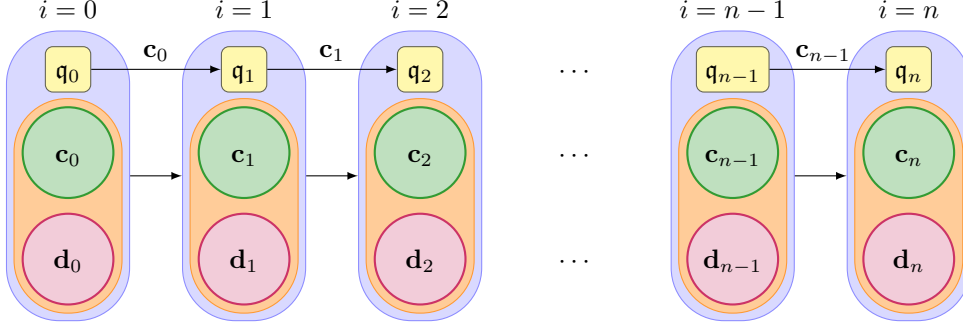
Fig. 1 Interactive process in context restricted reaction system with discrete concentrations

- $\mathfrak{q}_i, \mathbf{c}_i, \mathfrak{q}_{i+1}) \in R$, *for every* $i \in \{0, \ldots, n-1\}$
- $\mathbf{d}_i = res_A(\mathbb{M}\{\mathbf{d}_{i-1}, \mathbf{c}_{i-1}\})$, *for every* $i \in \{1, \ldots, n\}$.

Then the state sequence *of* π *is*

$$\tau = (\mathbf{w}_0, \ldots, \mathbf{w}_n) = (\mathbb{M}\{\mathbf{c}_0, \mathbf{d}_0\}, \ldots, \mathbb{M}\{\mathbf{c}_n, \mathbf{d}_n\}).$$

An diagrammatic representation of an interactive process in a context restricted reaction system with discrete concentrations is depicted in Figure 1.

Note that a context restricted reaction system with discrete concentrations CR-$\mathcal{C} = (\mathcal{C}, \mathfrak{A})$ comprises finitely many c-reactions. Since we also have finitely many multisets labelling on the arcs of its context automaton, CR-$\mathcal{C}$ is a finite state system. We can demonstrate this more precisely by showing that there exists a context restricted reaction system which simulates the behaviour of CR-$\mathcal{C}$. Let $\#_{\text{CR-}\mathcal{C}}(e)$ be such that $\mathbf{w}(e) \leq \#_{\text{CR-}\mathcal{C}}(e)$, for all $e \in S$ and all the states occurring in the state sequences of the interactive processes in CR-$\mathcal{C}$. (Note that such a bound can be obtained by taking the maximum integer assigned to $e \in S$ in all the multisets of entities occurring in both $\mathcal{C}$ and $\mathfrak{A}$.)

To construct a reaction system that simulates CR-$\mathcal{C}$, for every multiset $\mathbf{t} \in \mathcal{B}(S)$, we define two <u>sets</u> of entities:

$$\Gamma(\mathbf{t}) = \{e.i \mid e \in S \wedge \mathbf{t}(e) = i > 0\} \quad and \quad \Gamma_{all}(\mathbf{t}) = \{e.i \mid e \in S \wedge 1 \leq i \leq \mathbf{t}(e)\}.$$

The set Γ contains all the entities provided by the transition $\mathbf{t}$ together with their concentration, while Γ_{all} is the *downward-closure* of Γ (i.e., if $e.i \in \Gamma(\mathbf{t})$ and $i > 1$, then $e.1, \ldots, e.(i\text{-}1) \in \Gamma_{all}(\mathbf{t})$). In fact, Γ_{all} is a bijection from the set of all multisets over S to all the downward-closed sets of entities, and its inverse Γ_{all}^{-1} is given by $\Gamma_{all}^{-1}(Z)(e) = \max\{\{0\} \cup \{i \mid e.i \in Z\}\}$, for every $e \in S$. In what follows, Γ_{all} and Γ_{all}^{-1} will be applied component-wise to sequences of respectively multisets and downward-closed sets. We define the context restricted reaction system corresponding to CR-$\mathcal{C}$ as

$$\Theta(\text{CR-}\mathcal{C}) = (\mathcal{R}, \mathfrak{A}) = ((S', A'), (\mathcal{Q}, \mathfrak{q}^{init}, R'))$$

where:

- $S' = \{e.i \mid e \in S \text{ and } 1 \le i \le \#_{\text{CR-}\mathcal{C}}(e)\}$,
- $A' = \{(\Gamma(\mathbf{r}), \Gamma(\mathbf{i}), \Gamma_{all}(\mathbf{p})) \mid (\mathbf{r}, \mathbf{i}, \mathbf{p}) \in A\}$, and
- $R' = \{(z, \Gamma_{all}(\mathbf{c}), z') \mid (z, \mathbf{c}, z') \in R\}$.

It is straightforward to see that $\Theta(\text{CR-}\mathcal{C})$ is well-defined.

Let us discuss the complexity of the translation. The sizes of the set of reactions, the set of states and the set of transitions remain the same. The representations of reactions and inhibitors are of the same order. However, the sizes of the background set as well as the representations of products and contexts are increas by the factor $\max\{\#_{\text{CR-}\mathcal{C}}(e) \mid e \in S\}$ in the worst case.

Let us look at a relationship between $\Theta(\text{CR-}\mathcal{C})$ and $\text{CR-}\mathcal{C}$. First, we observe that, by the definitions of A' and R', all sets of entities occurring in the interactive processes of $\Theta(\text{CR-}\mathcal{C})$ are downward-closed. Theorems 1 and 2 below demonstrate that all interactive processes of $\text{CR-}\mathcal{C}$ can be simulated by $\Theta(\text{CR-}\mathcal{C})$ and all interactive processes of $\Theta(\text{CR-}\mathcal{C})$ simulate those of $\text{CR-}\mathcal{C}$.

Theorem 1 ([26])**.** *If $\pi = (\zeta, \gamma, \delta)$ is an interactive process in $\text{CR-}\mathcal{C}$, then*

$$\pi' = (\zeta, \Gamma_{all}(\gamma), \Gamma_{all}(\delta))$$

is an interactive process in $\Theta(\text{CR-}\mathcal{C})$.

Theorem 2 ([26])**.** *If $\pi = (\zeta, \gamma, \delta)$ is an interactive process in $\Theta(\text{CR-}\mathcal{C})$, then*

$$\pi' = (\zeta, \Gamma_{all}^{-1}(\gamma), \Gamma_{all}^{-1}(\delta))$$

is an interactive process in $\text{CR-}\mathcal{C}$.

In this way, we have obtained a bisimulation between the interactive processes in $\Theta(\text{CR-}\mathcal{C})$ and $\text{CR-}\mathcal{C}$.

Remark 1. *We can redefine Γ_{all} as:*

$$\Gamma'_{all}(\mathbf{t}) = \Gamma(\mathbf{t}) \cup \left(\Gamma_{all}(\mathbf{t}) \cap \bigcup_{a \in A} \Gamma(\mathbf{r}_a) \cup \Gamma(\mathbf{i}_a)\right)$$

and then only use those concentration levels which are important from the point of view of enabling the c-relations.

Note that syntactically context restricted reaction system are a subclass of context restricted reaction system with discrete concentrations such that all the concentration levels are binary, i.e., for all $\mathbf{t} \in \mathcal{B}(S)$ and $e \in carr(\mathbf{t})$, we have $\mathbf{t}(e) = 1$.

4 Linear-time temporal logic for reaction systems

In this section we recall from [26] a linear-time temporal logic tailored to reaction systems and we evaluate its expressiveness.

Consider the following grammar of *multiset expressions* over a background set S:

$$\mathfrak{a} ::= true \mid e \sim c \mid e \sim e \mid \neg \mathfrak{a} \mid \mathfrak{a} \vee \mathfrak{a},$$

where $\sim \in \{<, \leq, =, \geq, >\}$, $e \in S$, and $c \in \mathbb{N}$. The set of all the multiset expressions over S is denoted by $BE(S)$.

Let $\mathbf{b}$ be a multiset over S. By $\mathbf{b} \models_b \mathfrak{a}$ we denote that $\mathfrak{a}$ holds in $\mathbf{b}$. The relation $\models_b$ is defined as follows:

$$
\begin{array}{lll}
\mathbf{b} \models_b \mathit{true} & \text{for any } \mathbf{b} \in \mathcal{B}(S), \\
\mathbf{b} \models_b e_1 \sim c & \text{iff} & \mathbf{b}(e_1) \sim c, \\
\mathbf{b} \models_b e_1 \sim e_2 & \text{iff} & \mathbf{b}(e_1) \sim \mathbf{b}(e_2), \\
\mathbf{b} \models_b \neg\mathfrak{a} & \text{iff} & \mathbf{b} \not\models_b \mathfrak{a}, \\
\mathbf{b} \models_b \mathfrak{a}_1 \vee \mathfrak{a}_2 & \text{iff} & \mathbf{b} \models_b \mathfrak{a}_1 \text{ or } \mathbf{b} \models_b \mathfrak{a}_2.
\end{array}
$$

Note that the conjunction $\mathfrak{a}_1 \wedge \mathfrak{a}_2$ can be derived as $\neg(\neg\mathfrak{a}_1 \vee \neg\mathfrak{a}_2)$.

The language of *reaction systems linear-time temporal logic* (rsLTL, for short) is give by the following grammar, where $\mathfrak{a} \in BE(S)$:

$$
\phi ::= \mathfrak{a} \mid \phi \wedge \phi \mid \phi \vee \phi \mid \mathsf{X}_\mathfrak{a}\phi \mid \phi\mathsf{U}_\mathfrak{a}\phi \mid \phi\mathsf{R}_\mathfrak{a}\phi
$$

The logic captures constraints imposed on paths in the model of a context restricted reaction system with discrete concentrations. Intuitively, $\mathsf{X}_\mathfrak{a}\phi$ means 'following an action satisfying $\mathfrak{a}$, ϕ holds in the next state', $\phi_1\mathsf{U}_\mathfrak{a}\phi_2$ means 'ϕ_2 holds eventually, and ϕ_1 must hold at every preceding state, following only actions satisfying $\mathfrak{a}$', and $\phi_1\mathsf{R}_\mathfrak{a}\phi_2$ means 'following only actions satisfying $\mathfrak{a}$, ϕ_2 holds up to and including the first state where ϕ_1 holds'.

In order to define the semantics of the introduced operators, we need to define the model of a given CR-$\mathcal{C}$.

Definition 10 ([26])**.** *Let* CR-$\mathcal{C} = (\mathcal{C}, \mathfrak{A})$ *be a context restricted reaction system with discrete concentrations, where* $\mathcal{C} = (S, A)$ *and* $\mathfrak{A} = (\mathcal{Q}, \mathfrak{q}^{init}, R)$. *Then, the model for* CR-$\mathcal{C}$ *is a triple* $\mathcal{M} = (\mathbb{W}, \mathtt{w}_0, \longrightarrow)$, *where:*

- $\mathbb{W} = \mathcal{B}(S) \times \mathcal{Q}$ *is the set of states,*
- $\mathtt{w}^{init} = (\varnothing, \mathfrak{q}^{init})$ *is the initial state,*
- $\longrightarrow \subseteq \mathbb{W} \times \mathcal{B}(S) \times \mathbb{W}$ *is the transition relation such that for all* $\mathbf{w}, \mathbf{w}', \alpha \in \mathcal{B}(S)$, $\mathfrak{q}, \mathfrak{q}' \in \mathcal{Q}$: $\big((\mathbf{w}, \mathfrak{q}), \alpha, (\mathbf{w}', \mathfrak{q}')\big) \in \longrightarrow$ *iff:* $(\mathfrak{q}, \alpha, \mathfrak{q}') \in R$ *and* $\mathbf{w}' = res_A(\bigwedge\{\mathbf{w}, \alpha\})$. *Each element* $(\mathtt{w}, \alpha, \mathtt{w}') \in \longrightarrow$ *is denoted* $\mathtt{w} \xrightarrow{\alpha} \mathtt{w}'$.

Assuming the notation as in Definition 10, the paths in rsLTL are defined as alternating sequences of states and actions (*context multisets*).

Definition 11 ([26])**.** *A path is an infinite sequence* $\sigma = (\mathtt{w}_0, \alpha_0, \mathtt{w}_1, \alpha_1, \dots)$ *of states and actions such that:* $\mathtt{w}_i \xrightarrow{\alpha_i} \mathtt{w}_{i+1}$ *and* $\alpha_i \in \mathcal{B}(S)$, *for* $i \geq 0$.

Let σ be a path as in Definition 11. By $\sigma_s(i)$ and $\sigma_a(i)$ we denote the ith state $\mathtt{w}_i$ and the ith action α_i of the path σ, respectively. Let $\sigma_s(i) = (\mathbf{w}_i, q_i)$, for each $i \geq 0$. Then $\mathbf{w}_i$ is denoted by $\sigma_b(i)$, while q_i is denoted by $\sigma_{ca}(i)$. If $i \geq 0$, then σ^i denotes the suffix of σ such that

$$
\sigma^i = (\sigma_s(i), \sigma_a(i), \sigma_s(i+1), \sigma_a(i+1), \dots),
$$

i.e., $\sigma_s^i(j) = \sigma_s(j+i)$ and $\sigma_a^i(j) = \sigma_a(j+i)$, for each $j \geq 0$. By $\Pi_{\mathcal{M}}$ we denote the set of all the paths of the model $\mathcal{M}$, whereas by $\Pi_{\mathcal{M}}(\mathtt{w})$ we denote the set of all the paths that start in $\mathtt{w} \in \mathbb{W}$, that is, $\Pi_{\mathcal{M}}(\mathtt{w}) = \{\sigma \in \Pi \mid \sigma_s(0) = \mathtt{w}\}$.

Definition 12 ([26])**.** *Let $\mathcal{M} = (\mathbb{W}, \mathtt{w}^{init}, \longrightarrow)$ be a model as in Definition 10, and $\sigma \in \Pi_{\mathcal{M}}$ be a path of $\mathcal{M}$. The fact that ϕ holds over σ is denoted by $\mathcal{M}, \sigma \models \phi$ (or $\sigma \models \phi$ if $\mathcal{M}$ is understood), where the relation $\models$ is defined as follows:*

$$
\begin{array}{lll}
\sigma \models \mathfrak{a} & \textit{iff} & \sigma_b(0) \models_b \mathfrak{a}, \\
\sigma \models \phi_1 \vee \phi_2 & \textit{iff} & \sigma \models \phi_1 \textit{ or } \sigma \models \phi_2, \\
\sigma \models \phi_1 \wedge \phi_2 & \textit{iff} & \sigma \models \phi_1 \textit{ and } \sigma \models \phi_2, \\
\sigma \models \mathsf{X}_{\mathfrak{a}}\phi_1 & \textit{iff} & \sigma_a(0) \models_b \mathfrak{a} \textit{ and } \sigma^1 \models \phi_1, \\
\sigma \models \phi_1 \mathsf{U}_{\mathfrak{a}}\phi_2 & \textit{iff} & (\exists j \geq 0)(\sigma^j \models \phi_2 \\
& & \quad \textit{and } (\forall 0 \leq l < j)(\sigma^l \models \phi_1 \textit{ and } \sigma_a(l) \models_b \mathfrak{a})), \\
\sigma \models \phi_1 \mathsf{R}_{\mathfrak{a}}\phi_2 & \textit{iff} & (\forall j \geq 0)\big((\sigma^j \models \phi_2 \textit{ and } (\forall 0 \leq l < j)(\sigma_a(l) \models_b \mathfrak{a})) \\
& & \quad \textit{or } (\exists 0 \leq l < j)(\sigma^l \models \phi_1)\big).
\end{array}
$$

Note that one can easily derive the following operators:

$$
\mathfrak{a} \Rightarrow \phi \stackrel{def}{\equiv} \neg\mathfrak{a} \vee \phi, \qquad \mathsf{G}_{\mathfrak{a}}\phi \stackrel{def}{\equiv} false\mathsf{R}_{\mathfrak{a}}\phi, \qquad \mathsf{F}_{\mathfrak{a}}\phi \stackrel{def}{\equiv} true\mathsf{U}_{\mathfrak{a}}\phi.
$$

Moreover, we assume $\mathfrak{a} = true$ when $\mathfrak{a}$ is unspecified for any of the rsLTL operators, e.g., $\mathsf{F}\phi$ is the same as $\mathsf{F}_{true}\phi$. The fragment of rsLTL where $\mathfrak{a} = true$ for all the multiset expressions $\mathfrak{a}$ is called LTL. And, if the exact concentration levels are irrelevant, we may simply write e for $e > 0$ and $\neg e$ for $e = 0$.

An rsLTL formula holds (holds existentially) in a model iff it holds in all the paths (at least one path) starting in the initial state. More precisely, $\mathcal{M} \models \phi$ iff $\sigma \models \phi$ for all $\sigma \in \Pi_{\mathcal{M}}(\mathtt{w}^{init})$, and $\mathcal{M} \models_{\exists} \phi$ iff there exists $\sigma \in \Pi_{\mathcal{M}}(\mathtt{w}^{init})$ such that $\sigma \models \phi$.

Given a context restricted reaction system with discrete concentrations CR-$\mathcal{C}$ and an rsLTL formula ϕ, *rsLTL model checking* is the problem of deciding whether $\mathcal{M} \models \phi$, where $\mathcal{M}$ is the model for CR-$\mathcal{C}$. The existential rsLTL model checking problem is the problem of deciding whether $\mathcal{M} \models_{\exists} \phi$.

To carry out the complexity analysis of rsLTL, we need additional technical notions and notations.

Definition 13. *Let $\mathfrak{a} \in BE(S)$. Then $|\mathfrak{a}|$ – the size of $\mathfrak{a}$ – is defined as follows:*

- *if $\mathfrak{a} = true$, then $|\mathfrak{a}| = 1$,*
- *if $\mathfrak{a} = e_1 \sim c$ or $\mathfrak{a} = e_1 \sim e_2$, where $e_1, e_2 \in S$ and $c \in \mathbb{N}$, then $|\mathfrak{a}| = 2$,*
- *if $\mathfrak{a} = \neg\mathfrak{a}'$, then $|\mathfrak{a}| = |\mathfrak{a}'| + 1$,*
- *if $\mathfrak{a} = \mathfrak{a}' \vee \mathfrak{a}''$, then $|\mathfrak{a}| = |\mathfrak{a}'| + |\mathfrak{a}''|$.*

Definition 14. *Let ϕ be an rsLTL formula. Then $\mathsf{op}(\phi)$ – the number of operators used in ϕ – is defined as follows:*

- *if $\phi = \mathfrak{a}$, where $\mathfrak{a} \in BE(S)$, then $\mathsf{op}(\phi) = 0$,*
- *if $\phi = \mathsf{X}_{\mathfrak{a}}\phi_1$, then $\mathsf{op}(\phi) = \mathsf{op}(\phi_1) + 1$,*
- *if $\phi \in \{\phi_1 \vee \phi_2, \phi_1 \wedge \phi_2, \phi_1 \mathsf{U}_{\mathfrak{a}}\phi_2, \phi_1 \mathsf{R}_{\mathfrak{a}}\phi_2\}$, then $\mathsf{op}(\phi) = \mathsf{op}(\phi_1) + \mathsf{op}(\phi_2) + 1$.*

Definition 15. *Let ϕ be an rsLTL formula. Then* $\mathsf{mbe}(\phi)$ *– the size of the largest expression* $\mathfrak{a} \in BE(S)$ *with respect to* $|\mathfrak{a}|$ *used in* ϕ *– is defined as follows:*

- *if $\phi = \mathfrak{a}$, where $\mathfrak{a} \in BE(S)$, then $\mathsf{mbe}(\phi) = 0$,*
- *if $\phi \in \{\phi_1 \vee \phi_2, \phi_1 \wedge \phi_2\}$, then $\mathsf{mbe}(\phi) = max(\{\mathsf{mbe}(\phi_1), \mathsf{mbe}(\phi_2)\})$,*
- *if $\phi = \mathsf{X}_{\mathfrak{a}}\phi_1$, then $\mathsf{mbe}(\phi) = max(\{|\mathfrak{a}|, \mathsf{mbe}(\phi_1)\})$,*
- *if $\phi \in \{\phi_1\mathsf{U}_{\mathfrak{a}}\phi_2, \phi_1\mathsf{R}_{\mathfrak{a}}\phi_2\}$, then $\mathsf{mbe}(\phi) = max(\{|\mathfrak{a}|, \mathsf{mbe}(\phi_1), \mathsf{mbe}(\phi_2)\})$.*

4.1 rsltl as ltl

We now demonstrate how the model checking problem for rsLTL can be translated into LTL model checking.

Let ϕ be an rsLTL formula and CR-$\mathcal{C} = (\mathcal{C}, \mathfrak{A})$ be a context restricted reaction system with discrete concentrations, where $\mathfrak{A} = (\mathcal{Q}, \mathfrak{q}^{init}, R)$ and $R = \{t_1, \ldots, t_m\}$. The aim of the translation is to define a context restricted reaction system with discrete concentrations CR-$\mathcal{C}'$ and an LTL formula ϕ' such that $\mathcal{M} \models \phi$ iff $\mathcal{M}' \models \phi'$, where $\mathcal{M}$ and $\mathcal{M}'$ are the models for CR-$\mathcal{C}$ and CR-$\mathcal{C}'$, respectively.

The translation defines a context restricted reaction system with discrete concentrations that for each context entity provided by the context automaton produces the corresponding entity. These entities indicate which context entities were provided immediately before the system transitioned to a given state, i.e., via which context the current state was reached. Then, the original rsLTL formula is translated into an LTL formula where all the multiset expressions restricting contexts are expressed as constraints on the states.

First, we define a set of entities corresponding to the transitions of $\mathfrak{A}$:

$$S_{\star} = \{\star_i \mid t_i \in R\}.$$

Next, we define the set of the entities that are used to distinguish the ordinary entities from the entities that were supplied by the context:

$$S_c = \{\tilde{e} \mid e \in S\}.$$

Note that this set can be made smaller by only selecting the entities that are used in the context automaton, i.e.,

$$S_c = \{\tilde{e} \mid (\exists t \in R)(t = (\mathfrak{q} \xrightarrow{\mathbf{c}} \mathfrak{q}') \wedge e \in carr(\mathbf{c}))\}$$

Let CR-$\mathcal{C}' = (\mathcal{C}', \mathfrak{A}')$, then $\mathcal{C}' = (S', A')$, where $S' = S \cup S_{\star} \cup S_c$. The set of reactions of $\mathcal{C}'$ is defined as $A' = A \cup A_c$ where the set A_c consists of the following reactions defined for each transition $t_i \in R$:

$$(\{\star_i \mapsto 1\}, \varnothing_{S'}, \{\tilde{e} \mapsto \mathbf{c}(e) \mid t_i = (\mathfrak{q} \xrightarrow{\mathbf{c}} \mathfrak{q}') \wedge e \in carr(\mathbf{c})\}).$$

The context automaton uses a modified transition relation and is defined as $\mathfrak{A}' = (\mathcal{Q}, \mathfrak{q}^{init}, R')$ where:

$$R' = \{\mathfrak{q} \xrightarrow{\mathbf{c}} \mathfrak{q}' \mid (\exists t_i \in R)(t_i = (\mathfrak{q}_i \xrightarrow{\mathbf{c}_i} \mathfrak{q}_i') \wedge \mathbf{c} = \bigwedge(\mathbf{c}_i, \{\star_i \mapsto 1\}))\}.$$

Finally, we define the translation of multiset expressions interpreted over the context sets with $repl(\mathfrak{a})$ denoting the expression $\mathfrak{a}$, where each occurrence of $e \in S$ in $\mathfrak{a}$ is replaced with $\tilde{e}$. For an rsLTL formula ϕ we define the translation $tr^{\text{LTL}}(\phi)$ such that $tr^{\text{LTL}}(\phi)$ is an LTL formula.

- if $\phi = \mathfrak{a}$ and $\mathfrak{a} \in BE(S)$, then $tr^{\text{LTL}}(\phi) = \phi$,
- if $\phi = \phi_1 \vee \phi_2$, then $tr^{\text{LTL}}(\phi) = tr^{\text{LTL}}(\phi_1) \vee tr^{\text{LTL}}(\phi_2)$,
- if $\phi = \phi_1 \wedge \phi_2$, then $tr^{\text{LTL}}(\phi) = tr^{\text{LTL}}(\phi_1) \wedge tr^{\text{LTL}}(\phi_2)$,
- if $\phi = \mathsf{X}_\mathfrak{a}\phi_1$, then $tr^{\text{LTL}}(\phi) = \mathsf{X}(repl(\mathfrak{a}) \wedge tr^{\text{LTL}}(\phi_1))$,
- if $\phi = \phi_1 \mathsf{U}_\mathfrak{a}\phi_2$, then $tr^{\text{LTL}}(\phi) = (repl(\mathfrak{a}) \wedge tr^{\text{LTL}}(\phi_1))\mathsf{U}\, tr^{\text{LTL}}(\phi_2)$,
- if $\phi = \phi_1 \mathsf{R}_\mathfrak{a}\phi_2$, then $tr^{\text{LTL}}(\phi) = tr^{\text{LTL}}(\phi_1)\mathsf{R}\,(repl(\mathfrak{a}) \wedge tr^{\text{LTL}}(\phi_2))$.

The construction of $S_\star$, A_c, and $\mathfrak{A}'$ requires $\mathcal{O}(|R|)$ steps, while the set S_c can be built in $\mathcal{O}(|S|)$ steps. The translation of the formula ϕ runs in $\mathcal{O}(\mathsf{op}(\phi) \cdot \mathsf{mbe}(\phi))$, since for each temporal operator the associated expression $\mathfrak{a} \in BE(S)$ needs to be re-written using the entities of S_c, each rsLTL operator has a constant number of arguments, and $\mathsf{mbe}(\phi)$ is the largest $\mathfrak{a}$ used in ϕ. Therefore, the translation runs in $\mathcal{O}(|R| + |S| + \mathsf{op}(\phi) \cdot \mathsf{mbe}(\phi))$.

The verification method presented in Section 5 encodes context restricted reaction systems with discrete concentrations and rsLTL directly and does not use the above translation.

4.2 Complexity analysis

In this section, our aim is to show that rsLTL model checking is PSPACE-complete. First, we define the reachability problem for context restricted reaction system with discrete concentrations.

Let $n \geq 0$ be an integer. A result $\mathbf{d} \in \mathcal{B}(S)$ is *n-step reachable* in CR-$\mathcal{C}$ if there exists an interactive process $\pi = (\zeta, \gamma, \delta)$ in CR-$\mathcal{C}$ such that $\delta = (\mathbf{d}_0, \mathbf{d}_1, \dots, \mathbf{d}_n)$ and $\mathbf{d}_n = \mathbf{d}$. We say that $\mathbf{d}$ is *reachable* in CR-$\mathcal{C}$ if there is $n \geq 0$ such that $\mathbf{d}$ is *n-step* reachable in CR-$\mathcal{C}$.

Lemma 3. *The reachability problem for context restricted reaction systems with discrete concentrations is PSPACE-hard.*

Proof. The proof is by reduction of a PSPACE-complete problem to the reachability problem for context restricted reaction systems with discrete concentrations. Let us take the problem of reachability of configurations of polynomial-space Turing machines, which is a PSPACE-complete problem [41]. The presented reduction is similar to those in [42] and [43].

Let $TM = (Q, \Sigma, \Gamma, \delta, q_I, q_F)$ be a deterministic single-tape Turing machine, where $Q = \{q_1, \dots, q_m\}$ is the set of states, $\Sigma = \{0, 1\}$ is the input alphabet, $\Gamma = \Sigma \cup \{\triangleright\}$ is the tape alphabet, and $q_I, q_F \in Q$ are, respectively, the initial and the accepting

state of *TM*. The transition function is defined as $\delta : Q \times \Gamma \longrightarrow Q \times \Gamma \times \{-1, 0, 1\}$. The input string always starts with the symbol $\triangleright$ that is never written or changed by *TM*, i.e., for all the transitions $\delta(q, \gamma) = (q, \gamma', d)$ we have $\gamma = \triangleright$ iff $\gamma' = \triangleright$. Moreover, if $\gamma = \triangleright$, then the tape head moves right, i.e., $d = 1$. A *configuration* of *TM* is a tuple $C = (q, x, pos)$, where $q \in Q$ is a state, $x \in \Sigma^*$ is the tape content and *pos* is the head position. The *initial configuration* of *TM* is defined as $C_{init} = (q_I, \gamma_1 \ldots \gamma_N, 1)$, where the current state of *TM* is q_I, the tape head is at position 1, and $\gamma_1 \ldots \gamma_N \in \Sigma^*$ is an input string of length N. We also assume *TM* is polynomially space-bounded [44], i.e., there is a polynomial P such that for an input $\gamma_1 \ldots \gamma_N \in \Sigma^*$ the machine visits at most the first $P(N)$ cells of the tape. We assume $P(N) \geq N$.

The aim of this construction is to define CR-$\mathcal{C} = ((S, A), \mathfrak{A})$ that preserves the following property: a configuration C is reachable in *TM* from C_{init} iff the state of CR-$\mathcal{C}$ corresponding to the configuration C is reachable in CR-$\mathcal{C}$.

We begin by introducing the background set $S = \{e, h, w_1, \ldots, w_{P(N)}\}$. The concentration levels of e are used to encode the states of Q: we define a bijection $\mathsf{c} : Q \longrightarrow \{1, \ldots, m\}$ assigning concentration levels to the states, i.e., $\{e \mapsto \mathsf{c}(q)\}$ encodes $q \in Q$. The concentration of h denotes the position of the tape head (the concentration level values for h are taken from the set $\{0, \ldots, P(N) + 1\}$). The entities $w_1, \ldots, w_{P(N)}$ encode the symbols on the tape, i.e., tape contents.

Configurations of TM. Let $n \leq P(N)$. The configuration $C = (q, \gamma_1 \ldots \gamma_n, pos)$ is encoded in CR-$\mathcal{C}$ as follows:

$$conf_{\text{CR-}\mathcal{C}}(C) = \left(\{e \mapsto \mathsf{c}(q), h \mapsto pos\} \cup \bigcup_{j \in \{1, \ldots, n\}} \{w_j \mapsto \gamma_j\} \right). \tag{1}$$

Next, we define the reactions of A that aim to emulate the steps of *TM* in CR-$\mathcal{C}$.
Transition function. For each transition $\delta(q, \gamma) = (r, \gamma', d)$ and each tape head position $pos \in \{1, \ldots, P(N)\}$ we define the following reaction:

$$(\{e \mapsto \mathsf{c}(q), h \mapsto pos, w_{pos} \mapsto \gamma\},$$
$$\{e \mapsto (\mathsf{c}(q) + 1), h \mapsto (pos + 1), w_{pos} \mapsto (1 - \gamma)\},$$
$$\{e \mapsto c(r), h \mapsto (pos + d), w_{pos} \mapsto \gamma'\}).$$

The reactants encode the concentration levels encoding the state, the head position, and the symbol for the transition to be enabled. The inhibitors are used to enforce exact concentration levels by not allowing concentrations higher than specified by the reactants. Finally, the products encode the successor state, the new head position, and the symbol written on the tape.

Tape contents. For all $i, pos \in \{1, \ldots, P(N)\}$ such that $i \neq pos$, we define reactions that preserve the ith symbol of the tape if the tape head is at a different position *pos*.

$$(\{w_i \mapsto 1, h \mapsto pos\}, \{h \mapsto (pos + 1)\}, \{w_i \mapsto 1\}).$$

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Tape boundaries. If the tape reaches $\triangleright$, then the enforced move right is encoded using the following reaction:

$$(\{e \mapsto 1\}, \{h \mapsto 1\}, \{h \mapsto 1\}).$$

The reaction is enabled in any state $q \in Q$ as there is no upper bound on the concentration level of e. We do not need to handle the remaining boundary of the tape since we assume *TM* visits only the first $P(N)$ cells of the tape; however if the head reaches the position $P(N) + 1$ the computation halts since no transitions are enabled when the tape head at the position $P(N) + 1$.

Context automaton. We define $\mathfrak{A} = (\{\mathfrak{q}_0, \mathfrak{q}_1\}, \mathfrak{q}_0, R)$ with the following transition relation:

$$R = \{\mathfrak{q}_0 \xrightarrow{C_{init}} \mathfrak{q}_1, \mathfrak{q}_1 \xrightarrow{\varnothing_S} \mathfrak{q}_1\}.$$

The role of the context automaton is to provide the encoded initial configuration as the initial context and allow for the subsequent computation steps by providing transitions with empty contexts.

The reduction runs in polynomial time since the encoding of the transition function requires $\mathcal{O}(P(N) \cdot |\delta|)$ reactions[1] and the encoding of the preservation of the tape contents requires $\mathcal{O}(P(N)^2)$ reactions. The construction of CR-$\mathcal{C}$ ensures that a configuration C is reachable in *TM* iff $conf_{\text{CR-}\mathcal{C}}(C)$ is reachable in CR-$\mathcal{C}$. Therefore, the reachability problem for context restricted reaction systems with discrete concentrations is PSPACE-hard. $\qquad\square$

The reachability of $\mathbf{d} \in \mathcal{B}(S)$ can be expressed in terms of existential rsLTL model checking using the following formula:

$$\mathsf{F}\left(\bigwedge_{e \in carr(\mathbf{d})} (e = \mathbf{d}(e))\right).$$

Therefore, from Lemma 3 we also get the following result.

Corollary 1. *The existential rsLTL model checking problem is PSPACE-hard.*

Let ϕ be an rsLTL formula, CR-$\mathcal{C}$ be a context restricted reaction system with discrete concentrations, and $\mathcal{M}$ be the model for CR-$\mathcal{C}$. The existential decision problem yields *true* if $\mathcal{M} \models_\exists \phi$, and *false* otherwise. Since $\mathcal{M} \models \phi$ iff $\mathcal{M} \not\models_\exists \neg\phi$, the universal decision problem yields *true* iff the existential variant of the problem for $\neg\phi$ yields *false*.

Therefore, from the PSPACE-hardness of the existential rsLTL model checking problem we get PSPACE-hardness of its universal variant. This follows from the fact that the complement of a PSPACE-hard problem is also PSPACE-hard [41].

Corollary 2. *The rsLTL model checking problem is PSPACE-hard.*

Now, we can give the complexity result of the model checking problem for rsLTL.

Lemma 4. *The rsLTL model checking problem is in PSPACE.*

Proof. Since there is a polynomial translation of the rsLTL model checking problem to the LTL model checking problem, it is sufficient to show the LTL model checking problem for context restricted reaction systems is in PSPACE.

---

[1]The size of the transition function δ is denoted by $|\delta|$.

The proof follows the same reasoning as the one for Lemma 5.47 in [44]. It gives a nondeterministic polynomial space-bounded algorithm solving the existential LTL model checking problem. The algorithm nondeterministically guesses a path in $TS \otimes \mathcal{G}_\phi$, i.e., in the product of, respectively, a finite transition system and a generalised nondeterministic Büchi automaton for the verified LTL formula ϕ.

However, here TS is not given as the input and needs to be obtained from context restricted reaction system. In fact, it only must be possible to obtain a successor state in polynomial space and a method for that is demonstrated in the proof of Lemma 6.2 for rsCTL in [21]. □

The next result follows directly from Corollary 2 and Lemma 4.

Theorem 5. *The rsLTL model checking problem is PSPACE-complete.*

4.3 Bounded semantics

Bounded model checking has proven its usefulness in a range of successful applications [45]. Motivated by this, we focus on the bounded model checking approach defined for finite prefixes of paths. Accordingly, we can limit ourselves to consider only a finite number of states and actions that belong to the prefix of the considered path and check whether specified formula holds there.

Definition 16 ([26])**.** *A path $\sigma = (\mathtt{w}_0, \alpha_0, \mathtt{w}_1, \alpha_1, \dots)$ is a (k,l)-loop (or k-loop) if there exist $k \geq l > 0$ such that $\mathtt{w}_{l-1} = \mathtt{w}_k$ and $\sigma = (\mathtt{w}_0, \alpha_0, \dots, \alpha_{l-2}, \mathtt{w}_{l-1})(\alpha_l, \mathtt{w}_{l+1}, \alpha_{l+1}, \dots, \alpha_{k-1}, \mathtt{w}_k)^\omega$.*

Note that considering a sufficiently large and finite fragment of a path we may conclude that a given formula holds in that path. To address this issue, the bounded semantics for rsLTL is defined for finite path prefixes, and we define a satisfiability relation for a given path considering only its first k states and $k-1$ actions.

Definition 17 ([26])**.** *The fact that a formula ϕ holds in a path σ with bound $k \in \mathbb{N}$ is denoted by $\sigma \models^k \phi$. Then, $\sigma \models^k \phi$ if:*

- *σ is a (k,l)-loop for some $0 < l \leq k$ and $\sigma \models \phi$, or*
- *$\sigma \models_{nl} \phi$, where:*

$$
\begin{aligned}
\sigma \models_{nl} \mathfrak{a} \quad &\textit{iff} \quad \sigma_s(0) \models_b \mathfrak{a}, \\
\sigma \models_{nl} \phi_1 \wedge \phi_2 \quad &\textit{iff} \quad \sigma \models_{nl} \phi_1 \text{ and } \sigma \models_{nl} \phi_2, \\
\sigma \models_{nl} \phi_1 \vee \phi_2 \quad &\textit{iff} \quad \sigma \models_{nl} \phi_1 \text{ or } \sigma \models_{nl} \phi_2, \\
\sigma \models_{nl} \mathsf{X}_\mathfrak{a}\phi \quad &\textit{iff} \quad k > 0, \ \sigma_a(0) \models_b \mathfrak{a}, \text{ and } \sigma^1 \models_{nl} \phi, \\
\sigma \models_{nl} \phi_1 \mathsf{U}_\mathfrak{a}\phi_2 \quad &\textit{iff} \quad (\exists 0 \leq j \leq k)\big(\sigma^j \models_{nl} \phi_2 \\
&\qquad \text{and } (\forall 0 \leq l < j)(\sigma^l \models_{nl} \phi_1 \text{ and } \sigma_a(l) \models_b \mathfrak{a})\big) \\
\sigma \models_{nl} \phi_1 \mathsf{R}_\mathfrak{a}\phi_2 \quad &\textit{iff} \quad (\exists 0 \leq j \leq k)\big(\sigma^j \models_{nl} \phi_1 \text{ and } ((\forall 0 \leq l \leq j)(\sigma^l \models_{nl} \phi_2) \\
&\qquad \text{and } (\forall 0 \leq l < j)(\sigma_a(l) \models_b \mathfrak{a}))\big)
\end{aligned}
$$

For the sake of completeness, we now recall facts related with the compatibility of the bounded semantics with the general semantics of rsLTL.

Lemma 6 ([26])**.** *Let $k \in \mathbb{N}$, ϕ be an rsLTL formula, and σ be a path. Then, $\sigma \models^k \phi$ implies $\sigma \models \phi$.*

Lemma 7 ([26]). *Let ϕ be an rsLTL formula and $\mathcal{M}$ be a model. Then, $\mathcal{M} \models \phi$ implies that there exists $k \in \mathbb{N}$ such that $\mathcal{M} \models^k \phi$.*

The ideas of proofs for these lemmas derive from [46], where similar facts for LTL are proven. The only difference is related to the augmented temporal operators that impose additional restrictions on the considered path by using multiset expressions.

We define the relation $\models^k_\exists$ (where $k \in \mathbb{N}$ is a given bound) for models as follows: $\mathcal{M} \models^k_\exists \phi$ iff there exists $\sigma \in \Pi_\mathcal{M}(\mathtt{w}^{init})$ such that $\sigma \models^k \phi$. Given a bound $k \in \mathbb{N}$, an rsLTL formula ϕ, and a model $\mathcal{M}$, the *bounded model checking problem* for rsLTL is defined as the decision problem of checking whether $\mathcal{M} \models^k_\exists \phi$ for a given bound $k \in \mathbb{N}$.

Finally, we are ready to state the main theorem, following from Lemmas 6 and 7.

Theorem 8. *Let ϕ be an rsLTL formula and $\mathcal{M}$ be a model. Then, $\mathcal{M} \models_\exists \phi$ iff there exists $k \in \mathbb{N}$ such that $\mathcal{M} \models^k_\exists \phi$.*

5 smt-based encoding

In this section, we explain how the bounded model checking problem for rsLTL can be mapped to Satisfiability Modulo Theory (SMT) [45] within the context of integer arithmetic theory. SMT presents a broader perspective on the Boolean satisfiability problem by allowing certain functions and predicate symbols to have interpretations based on the foundational theory they stem from.

Let CR-$\mathcal{C} = (\mathcal{R}, \mathfrak{A})$ be a context restricted reaction system with discrete concentrations where $\mathcal{R} = (S, A)$ and $\mathfrak{A} = (\mathcal{Q}, \mathfrak{q}^{init}, R)$, and let $\mathcal{M}$ be the model for CR-$\mathcal{C}$ and an rsLTL formula ϕ . For an integer $k \geq 0$ we construct a formula $[\mathcal{M}, \phi, k]$ such that $\mathcal{M} \models^k_\exists \phi$ iff $[\mathcal{M}, \phi, k]$ is satisfiable. We encode all the paths of the model $\mathcal{M}$ that are bounded with k. The entities of S are denoted by $e_1, \ldots, e_m$, where $m = |S|$. For each $i \in \{0, \ldots, k\}$ we introduce the following sets of positive integer variables used in the encoding:

$$\mathbf{P}_i = \{\mathtt{p}_{i,1}, \ldots, \mathtt{p}_{i,m}\} \quad and \quad \mathbf{P}_i^\mathcal{E} = \{\mathtt{p}_{i,1}^\mathcal{E}, \ldots, \mathtt{p}_{i,m}^\mathcal{E}\}.$$

Let σ be a path of $\mathcal{M}$. Then, $\mathtt{p}_{i,1}, \ldots, \mathtt{p}_{i,m}$ and $\mathtt{p}_{i,1}^\mathcal{E}, \ldots, \mathtt{p}_{i,m}^\mathcal{E}$ encode $\sigma_b(i)$ and $\sigma_a(i)$, respectively. We also introduce the variables $\mathtt{q}_0, \ldots, \mathtt{q}_k$ which are used to encode the locations of $\mathfrak{A}$. The location $\sigma_{ca}(i)$ of the context automaton is then encoded with $\mathtt{q}_i$. Then, we define $\overline{\mathbf{p}}_i = (\mathtt{p}_{i,1}, \ldots, \mathtt{p}_{i,m})$ and $\overline{\mathbf{p}}_i^\mathcal{E} = (\mathtt{p}_{i,1}^\mathcal{E}, \ldots, \mathtt{p}_{i,m}^\mathcal{E})$. With $\overline{\mathbf{p}}_i[j]$ and $\overline{\mathbf{p}}_i^\mathcal{E}[j]$ we denote, respectively, $\mathtt{p}_{i,j}$ and $\mathtt{p}_{i,j}^\mathcal{E}$. Then, we also define $\mathbf{P} = \bigcup_{i=0}^k \mathbf{P}_i$ and $\mathbf{P}^\mathcal{E} = \bigcup_{i=0}^k \mathbf{P}_i^\mathcal{E}$.

We define the subsequent functions that associate entities within the background set with the corresponding variables used in the encoding: for all $0 \leq i \leq k$ we define $\mathtt{t}_i : S \to \mathbf{P}_i$ and $\mathtt{t}_i^\mathcal{E} : S \to \mathbf{P}_i^\mathcal{E}$ such that $\mathtt{t}_i(e_j) = \mathtt{p}_{i,j}$, $\mathtt{t}_i^\mathcal{E}(e_j) = \mathtt{p}_{i,j}^\mathcal{E}$ for all $1 \leq j \leq m$. To map states of the context automaton to the corresponding natural values used in the encoding we use the function $\mathtt{e} : \mathcal{Q} \to \{0, \ldots, |\mathcal{Q}| - 1\}$. The set of the reactions that are capable of producing $e \in S$ is $Prod(e) = \{a \in A \mid \mathbf{p}_a(e) > 0\}$. Let f_1, f_2, f_3 be expressions over $\mathbf{P} \cup \mathbf{P}^\mathcal{E}$, then we define the *if-then-else* operator:

$$f_1 \to f_2 \mid f_3 = (f_1 \wedge f_2) \vee (\neg f_1 \wedge f_3).$$

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To define the SMT encoding of the paths we need auxiliary functions that correspond to elements of the encoding.

The encoding of the reactions is defined in two steps: (i) we define a formula encoding the condition for when a reaction is enabled, and (ii) a formula encoding what that reaction produces when it is enabled.

The enabledness of a reaction $a \in A$ is encoded as follows:

$$\mathsf{En}_a\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}\big) = \bigwedge_{e \in S} \big(\mathbf{t}_i(e) \geq \mathbf{r}_a(e) \vee \mathbf{t}_i^{\mathcal{E}}(e) \geq \mathbf{r}_a(e)\big)$$

$$\wedge \bigwedge_{e \in S} \big(\mathbf{t}_i(e) < \mathbf{i}_a(e) \wedge \mathbf{t}_i^{\mathcal{E}}(e) < \mathbf{i}(e)\big).$$

The formula encodes the conditions for $a \in A$ to be enabled, i.e., in the current state and in the context, the concentration levels of the reactants specified in $\mathbf{r}_a$ need to be sufficient and the concentration levels of all its inhibitors need to be below the threshold specified by $\mathbf{i}_a$.

To encode the produced entity concentration level of an entity $e \in S$ we take all the reactions that have e in their products, i.e., all the reactions of $Prod(e)$ and order them with respect to the produced concentration levels of e. Let $a_1, a_2, \ldots, a_w \in Prod(e)$ and assume $\mathbf{p}_{a_j} \leq \mathbf{p}_{a_{j+1}}$ for all $1 \leq j < w$. First, we encode the produced concentration level of entity e where $j \in \{1, \ldots, w\}$ when there exist reactions producing e, i.e., $w > 0$, and at least one such reaction is enabled (the remaining cases are handled later). The encoding is defined as follows:

$$\mathsf{C}_e^j\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \overline{\mathbf{p}}_{i+1}\big) =$$
$$\begin{cases} \mathsf{En}_{a_j}\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}\big) \to \big(\mathbf{t}_{i+1}(e) = \mathbf{p}_{a_j}\big) \mid \mathsf{C}_e^{j-1}\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \overline{\mathbf{p}}_{i+1}\big) & \text{if } 1 < j \leq w, \\ \mathsf{En}_{a_j}\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}\big) \wedge \big(\mathbf{t}_{i+1}(e) = \mathbf{p}_{a_j}\big) & \text{if } j = 1. \end{cases}$$

In the definition of $\mathsf{C}_e^j\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \overline{\mathbf{p}}_{i+1}\big)$ with the use of the *if-then-else* operator we always encode the highest available concentration of e if the corresponding reaction producing e with that concentration level is enabled. Finally, we define the complete entity concentration encoding for all the reactions:

$$\mathsf{C}_e\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \overline{\mathbf{p}}_{i+1}\big) =$$
$$\begin{cases} \mathbf{t}_{i+1}(e) = 0 & \text{if } w = 0, \\ \mathsf{C}_e^w\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \overline{\mathbf{p}}_{i+1}\big) \vee \left(\left(\bigwedge_{a \in Prod(e)} \neg\mathsf{En}_a\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}\big)\right) \wedge \big(\mathbf{t}_{i+1}(e) = 0\big)\right) & \text{if } w > 0. \end{cases}$$

In the above, we handle the remaining cases: (1) when $w = 0$, i.e., if there are no reactions producing e, and (2) there are reactions producing e or (3) none of them are enabled. In (1) and (3) the entity e is produced with the concentration level equal 0. In (2) the encoding of $\mathsf{C}_e^w\big(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \overline{\mathbf{p}}_{i+1}\big)$ ensures production of e and selection

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of its maximal concentration level by starting the encoding from a_w, i.e., the reaction producing the highest concentration level of e.

Let $\mathbf{c} \in \mathcal{B}(S)$ be a multiset of context entities. The encoding of $\mathbf{c}$ is defined as follows:

$$\mathsf{Ct}_{\mathbf{c}}(\overline{\mathbf{p}}_i^{\mathcal{E}}) = \bigwedge_{e \in S} (\mathsf{t}_i^{\mathcal{E}}(e) = \mathbf{c}(e)).$$

The encoding of the transition relation of the context automaton is a disjunction of the encodings for each transition:

$$\mathsf{Tr}_{\mathfrak{A}}(\mathsf{q}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \mathsf{q}_{i+1}) = \bigvee_{(\mathsf{q}, \mathbf{c}, \mathsf{q}') \in R} \left(\mathsf{q}_i = \mathsf{e}(\mathsf{q}) \wedge \mathsf{Ct}_{\mathbf{c}}(\overline{\mathbf{p}}_i^{\mathcal{E}}) \wedge \mathsf{q}_{i+1} = \mathsf{e}(\mathsf{q}') \right).$$

We build a conjunction by combining the generated concentration levels for all entities and the transition relation of the context automaton. This conjunction serves to encode the transition relation of the model:

$$\mathsf{Tr}_{\text{CR-}\mathcal{C}}(\overline{\mathbf{p}}_i, \mathsf{q}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \overline{\mathbf{p}}_{i+1}, \mathsf{q}_{i+1}) = \left(\bigwedge_{e \in S} \mathsf{C}_e(\overline{\mathbf{p}}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \overline{\mathbf{p}}_{i+1}) \right) \wedge \mathsf{Tr}_{\mathfrak{A}}(\mathsf{q}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \mathsf{q}_{i+1}).$$

To encode the initial state of the model where all the concentration levels are set to zero and the context automaton is in its initial state we define the following formula:

$$\mathtt{Init}(\overline{\mathbf{p}}_i, \mathsf{q}_i) = \bigwedge_{e \in S} (\mathsf{t}_i(e) = 0) \wedge \left(\mathsf{q}_i = \mathsf{e}(\mathsf{q}^{init}) \right).$$

We encode the paths of $\mathcal{M}$ that are bounded with k by unrolling the transition relation up to k and combining it with the encoding of the initial state of the model as follows:

$$\mathsf{Paths}^k = \mathsf{Init}(\overline{\mathbf{p}}_0, \mathsf{q}_0) \wedge \bigwedge_{i=0}^{k-1} \mathsf{Tr}_{\text{CR-}\mathcal{C}}(\overline{\mathbf{p}}_i, \mathsf{q}_i, \overline{\mathbf{p}}_i^{\mathcal{E}}, \overline{\mathbf{p}}_{i+1}, \mathsf{q}_{i+1}).$$

Following the fixed point encoding for LTL in [47], we translate the rsLTL formulae into an SMT encoding.

In rsLTL, instead of employing propositional variables found in conventional LTL formulas, we utilize multiset expressions. Let $\mathfrak{a}$ be a multiset expression. By $enc_i^b(\mathfrak{a})$ and $enc_i^{ct}(\mathfrak{a})$ we denote the encoding of $\mathfrak{a}$ using the variables of $\overline{\mathbf{p}}_i$ and $\overline{\mathbf{p}}_i^{\mathcal{E}}$, respectively. The former refers to states of RSC, while the latter refers to actions (or contexts). We are defining a translation into SMT, hence the encodings of multisets can be defined in a straightforward way. We introduce an integer variable $\mathtt{L}$, which is utilized to handle (k, l)-loops as follows. When $\mathtt{L} = l$ holds for a path then the path is a (k, l)-loop:

$$\mathsf{Loops}^k = \neg(\mathtt{L} = 0) \wedge \bigwedge_{i=1}^{k} \left((\mathtt{L} = i) \Rightarrow \mathsf{E}(\overline{\mathbf{p}}_{i-1}, \mathsf{q}_{i-1}, \overline{\mathbf{p}}_k, \mathsf{q}_k) \right),$$

where E encodes the equivalence of two states of the model:

$$\mathsf{E}(\overline{\mathbf{p}}_i, \mathsf{q}_i, \overline{\mathbf{p}}_j, \mathsf{q}_j) = (\mathsf{q}_i = \mathsf{q}_j) \wedge \bigwedge_{c=1}^{m} (\overline{\mathbf{p}}_i[c] = \overline{\mathbf{p}}_j[c]).$$

The encoding of an rsLTL formula ϕ at the position $i \in \{0, \ldots, k\}$ is defined as $\llbracket \phi \rrbracket_i^k$. We start with introducing the encoding for propositional formulae:

$\llbracket \phi \rrbracket_i^k$	$0 \le i \le k$
$\llbracket \mathfrak{a} \rrbracket_i^k$	$enc_i^b(\mathfrak{a})$
$\llbracket \phi_1 \wedge \phi_2 \rrbracket_i^k$	$\llbracket \phi_1 \rrbracket_i^k \wedge \llbracket \phi_2 \rrbracket_i^k$
$\llbracket \phi_1 \vee \phi_2 \rrbracket_i^k$	$\llbracket \phi_1 \rrbracket_i^k \vee \llbracket \phi_2 \rrbracket_i^k$

We follow up with the encoding for temporal formulae. Here we follow the fixed point encoding for CTL [48] and introduce an auxiliary translation $\langle\!\langle \phi \rangle\!\rangle_i^k$ to cope with the until and release operators.

$\llbracket \phi \rrbracket_i^k$	$0 \le i < k$
$\llbracket \mathsf{X}_\mathfrak{a} \phi_1 \rrbracket_i^k$	$\llbracket \phi_1 \rrbracket_{i+1}^k \wedge enc_i^{ct}(\mathfrak{a})$
$\llbracket \phi_1 \mathsf{U}_\mathfrak{a} \phi_2 \rrbracket_i^k$	$\llbracket \phi_2 \rrbracket_i^k \vee \left(\llbracket \phi_1 \rrbracket_i^k \wedge (\llbracket \phi_1 \mathsf{U}_\mathfrak{a} \phi_2 \rrbracket_{i+1}^k \wedge enc_i^{ct}(\mathfrak{a})) \right)$
$\llbracket \phi_1 \mathsf{R}_\mathfrak{a} \phi_2 \rrbracket_i^k$	$\llbracket \phi_2 \rrbracket_i^k \wedge \left(\llbracket \phi_1 \rrbracket_i^k \vee (\llbracket \phi_1 \mathsf{R}_\mathfrak{a} \phi_2 \rrbracket_{i+1}^k \wedge enc_i^{ct}(\mathfrak{a})) \right)$
	$i = k$
$\llbracket \mathsf{X}_\mathfrak{a} \phi_1 \rrbracket_i^k$	$\bigvee_{j=1}^{k} ((\mathsf{L} = j) \wedge \llbracket \phi_1 \rrbracket_j^k) \wedge enc_i^{ct}(\mathfrak{a})$
$\llbracket \phi_1 \mathsf{U}_\mathfrak{a} \phi_2 \rrbracket_i^k$	$\llbracket \phi_2 \rrbracket_i^k \vee \left(\llbracket \phi_1 \rrbracket_i^k \wedge (\bigvee_{j=1}^{k} ((\mathsf{L} = j) \wedge \langle\!\langle \phi_1 \mathsf{U}_\mathfrak{a} \phi_2 \rangle\!\rangle_j^k) \wedge enc_i^{ct}(\mathfrak{a})) \right)$
$\llbracket \phi_1 \mathsf{R}_\mathfrak{a} \phi_2 \rrbracket_i^k$	$\llbracket \phi_2 \rrbracket_i^k \wedge \left(\llbracket \phi_1 \rrbracket_i^k \vee (\bigvee_{j=1}^{k} ((\mathsf{L} = j) \wedge \langle\!\langle \phi_1 \mathsf{R}_\mathfrak{a} \phi_2 \rangle\!\rangle_{i+1}^k) \wedge enc_i^{ct}(\mathfrak{a})) \right)$
$\langle\!\langle \phi \rangle\!\rangle_i^k$	$0 \le i < k$
$\langle\!\langle \phi_1 \mathsf{U}_\mathfrak{a} \phi_2 \rangle\!\rangle_i^k$	$\llbracket \phi_2 \rrbracket_i^k \vee \left(\llbracket \phi_1 \rrbracket_i^k \wedge (\langle\!\langle \phi_1 \mathsf{U}_\mathfrak{a} \phi_2 \rangle\!\rangle_{i+1}^k \wedge enc_i^{ct}(\mathfrak{a})) \right)$
$\langle\!\langle \phi_1 \mathsf{R}_\mathfrak{a} \phi_2 \rangle\!\rangle_i^k$	$\llbracket \phi_2 \rrbracket_i^k \wedge \left(\llbracket \phi_1 \rrbracket_i^k \vee (\langle\!\langle \phi_1 \mathsf{R}_\mathfrak{a} \phi_2 \rangle\!\rangle_{i+1}^k \wedge enc_i^{ct}(\mathfrak{a})) \right)$
	$i = k$
$\langle\!\langle \phi_1 \mathsf{U}_\mathfrak{a} \phi_2 \rangle\!\rangle_i^k$	$\llbracket \phi_2 \rrbracket_i^k$
$\langle\!\langle \phi_1 \mathsf{R}_\mathfrak{a} \phi_2 \rangle\!\rangle_i^k$	$\llbracket \phi_2 \rrbracket_i^k$

We consider separately the cases for $\llbracket \phi \rrbracket_i^k$ when $i = k$. When (k, j)-loop exists ($\mathsf{L} = j$), the additional transitions for $j \in \{1, \ldots, k\}$ need to be encoded. Unlike the LTL encoding in [47], we necessitate that all transitions are subject to constraints imposed by the parameter $\mathfrak{a}$, which is encoded using $enc_i^{ct}(\mathfrak{a})$.

Finally, we reduce the bounded model checking problem for rsLTL to the satisfiability checking, i.e., to verify if $\mathcal{M} \models_\exists^k \phi$ we check the satisfiability of the following formula:

$$[\mathcal{M}, \phi, k] = \mathsf{Paths}^k \wedge \mathsf{Loops}^k \wedge \llbracket \phi \rrbracket_0^k.$$

We conclude this section with the following theorem, confirming the correctness of the presented procedure.

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Theorem 9. *Let CR-$\mathcal{C} = (\mathcal{C}, \mathfrak{A})$ be a context restricted reaction system with discrete concentrations, $\mathcal{M}$ be its model and ϕ an rsLTL formula. For any $k \in \mathbb{N}$, the formula $[\mathcal{M}, \phi, k]$ is satisfiable iff $\mathcal{M} \models^k_\exists \phi$.*

Proof. Let $k \in \mathbb{N}$. Then $[\mathcal{M}, \phi, k]$ is satisfiable iff there exists a valuation of the variables used in the encoding such that the formula is satisfied. The valuation then represents the path prefix of a path in $\mathcal{M}$ for which the formula ϕ holds. We first show that Paths^k encodes path prefixes of paths in $\mathcal{M}$. There exists a path σ in $\mathcal{M}$ and σ^k is its prefix of length k iff there exists a valuation representing σ^k that satisfies Paths^k. Let $i \in \{0, \ldots, k-1\}$. We observe the formula $\mathsf{Tr}_{\text{CR-}\mathcal{C}}$ is satisfied for the valuation encoding $\sigma_s(i)$, $\sigma_a(i)$ and $\sigma_s(i+1)$ iff $\sigma_s(i) \xrightarrow{\sigma_a(i)} \sigma_s(i+1)$. This follows from the encoding of C_e and $\mathsf{Tr}_{\mathfrak{A}}$. Let us recall that $\sigma_s(i) = (\sigma_b(i), \sigma_{ca}(i))$. For an entity $e \in S$ it is clear from the construction that the formula C_e is satisfied iff the valuation encodes the concentration level of the entity e in $\sigma_b(i+1)$ that is produced by the reactions enabled in $\sigma_b(i)$ with the context $\sigma_a(i)$. The encoding C_e is applied to all $e \in S$, i.e., the valuation must encode in $\sigma_b(i+1)$ the concentration levels of all the entities of S. The formula $\mathsf{Tr}_{\mathfrak{A}}$ is satisfied iff the valuation encodes a transition $(\mathfrak{q}, \mathbf{c}, \mathfrak{q}') \in R$ such that $\mathfrak{q} = \sigma_{ca}(i)$, $\mathbf{c} = \sigma_a(i)$ and $\mathfrak{q}' = \sigma_{ca}(i+1)$. Then, the formula Paths^k is satisfied iff the valuation encodes a path prefix σ^k such that the state $\sigma_s(0)$ of $\mathcal{M}$ is the initial state and $\sigma_s(i) \xrightarrow{\sigma_a(i)} \sigma_s(i+1)$ for all $i \in \{0, \ldots, k-1\}$.

It remains to be shown that $\mathsf{Loops}^k \wedge [\![\phi]\!]^k_0$ restricts the valuation so that the formula $[\mathcal{M}, \phi, k]$ is satisfiable iff it encodes a path prefix of a path in which ϕ holds. To show this we apply the same reasoning as for LTL in [47, Theorem 3.1], which follows by induction on the structure of the LTL formula. $\qquad\square$

6 Parametric reaction systems

In *parametric reaction systems* reactions can be defined partially, i.e., reactants, inhibitors, and products can be replaced with *parameters*.

Definition 18 (parametric reaction system)**.** *A parametric reaction system is a triple $\mathcal{P} = (S, P, A)$, where:*

- *S is a finite* background *set,*
- *P is a finite set of elements called* parameters*, and*
- *A is a nonempty finite set of* parametric reactions *over S, where each parametric reaction is a triple $a = (\mathfrak{r}, \mathfrak{i}, \mathfrak{p})$ such that $\mathfrak{r}, \mathfrak{i}, \mathfrak{p} \in \mathcal{B}(S) \cup P$.*

The elements $\mathfrak{r}$, $\mathfrak{i}$, and $\mathfrak{p}$ are respectively denoted by $\mathfrak{r}_a$, $\mathfrak{i}_a$, and $\mathfrak{p}_a$ and called the *reactants*, *inhibitors*, and *products* of parametric reaction a.

Definition 19. *Let $\mathcal{P} = (S, P, A)$ be a parametric reaction system. A* parameter valuation *of $\mathcal{P}$ is a function $\mathtt{v} : P \cup \mathcal{B}(S) \to \mathcal{B}(S)$ such that $\mathtt{v}(\mathfrak{b}) = \mathfrak{b}$ if $\mathfrak{b} \in \mathcal{B}(S)$.*

We also write $\mathfrak{b}^{\leftarrow \mathtt{v}}$ for $\mathtt{v}(\mathfrak{b})$. The set of all the parameter valuations for $\mathcal{P}$ is denoted by $\mathsf{PV}_\mathcal{P}$. Let $\mathtt{v} \in \mathsf{PV}_\mathcal{P}$. For any subset $X \subseteq A$ of reactions of $\mathcal{P}$ we define:

$$X^{\leftarrow \mathtt{v}} = \{(a_\mathfrak{r}^{\leftarrow \mathtt{v}}, a_\mathfrak{i}^{\leftarrow \mathtt{v}}, a_\mathfrak{p}^{\leftarrow \mathtt{v}}) \mid a \in X\}.$$

By $\mathcal{P}^{\leftarrow \mathtt{v}}$ we denote the structure $(S, A^{\leftarrow \mathtt{v}})$ where all the parameters in A are substituted according to the parameter valuation $\mathtt{v}$. We say that $\mathtt{v} \in \mathtt{PV}_\mathcal{P}$ is a *valid parameter valuation* if $\mathcal{P}^{\leftarrow \mathtt{v}}$ yields a reaction system with discrete concentrations.

Definition 20 (context-restricted parametric reaction system)**.** *A context-restricted parametric reaction system is a pair* CR-$\mathcal{P} = (\mathcal{P}, \mathfrak{A})$ *such that* $\mathcal{P} = (S, P, A)$ *is a parametric reaction system and* $\mathfrak{A} = (\mathcal{Q}, \mathfrak{q}^{init}, R)$ *is a context automaton over S.*

For $\mathtt{v} \in \mathtt{PV}_\mathcal{P}$ we define CR-$\mathcal{P}^{\leftarrow \mathtt{v}} = (\mathcal{P}^{\leftarrow \mathtt{v}}, \mathfrak{A})$.

Example 2. *We consider a simple parametric reaction system for a simplified abstract genetic regulatory system based on [2]. The system contains two (abstract) genes x and y expressing proteins X and Y, respectively, and a protein complex Q formed by X and Y. The background set is defined as $S = \{x, \widehat{x}, X, y, \widehat{y}, Y, h, Q\}$, where $\widehat{x}$ and $\widehat{y}$ denote RNA polymerase attached to the promoter of genes x and y, respectively. Here h is used as an abstract inhibitor. Finally, the set of parametric reactions consists of the following subsets:*

- $A_x = \{(\{x\}, \{h\}, \{x\}), (\{x\}, \{h\}, \{\widehat{x}\}), (\{x, \widehat{x}\}, \{h\}, \{X\})\}$,
- $A_y = \{(\{y\}, \{h\}, \lambda_1), (\lambda_2, \{h\}, \{\widehat{y}\}), (\{y, \widehat{y}\}, \{h\}, \lambda_3)\}$,
- $A_Q = \{(\{X, Y\}, \{h\}, \{Q\})\}$.

Notice that the reactions of A_y use parameters $\lambda_1, \lambda_2, \lambda_3$ to define expression of the protein Y.

Suppose that we investigate the processes starting from the states that already contain x and y. This leads to the following definition of the context automaton: $\mathfrak{A} = (\{\mathfrak{q}_0, \mathfrak{q}_1\}, \mathfrak{q}_0, R)$, *where:* $R = \{\mathfrak{q}_0 \xrightarrow{\{x,y\}} \mathfrak{q}_1, \mathfrak{q}_1 \xrightarrow{\varnothing} \mathfrak{q}_1, \mathfrak{q}_1 \xrightarrow{\{h\}} \mathfrak{q}_0)\}$. *When the context set contains the entity h, $\mathfrak{A}$ reverts back to the initial location, while for the empty context the automaton remains in $\mathfrak{q}_1$.*

Finally, the constrained restricted parametric reaction system is defined as CR-$\mathcal{P} = ((S, P, A), \mathfrak{A})$, *where:* $P = \{\lambda_1, \lambda_2, \lambda_3\}$ *and* $A = A_x \cup A_y \cup A_Q$. □

We focus on the synthesis of a parameter valuation, given n observations of the behaviour of the system that are expressed with rsLTL formulae.

Let CR-$\mathcal{P} = (\mathcal{P}, \mathfrak{A})$ be a constrained restricted parametric reaction system and $F = \{\phi_1, \ldots, \phi_n\}$ be a set of rsLTL formulae. The aim of *parameter synthesis* for constrained restricted parametric reaction system is to find a valid parameter valuation $\mathtt{v}$ of CR-$\mathcal{P}$ such that:

$$\big(\mathcal{M}(\text{CR-}\mathcal{P}^{\leftarrow \mathtt{v}}) \models_\exists \phi_1\big) \wedge \cdots \wedge \big(\mathcal{M}(\text{CR-}\mathcal{P}^{\leftarrow \mathtt{v}}) \models_\exists \phi_n\big).$$

Each formula of F corresponds to an interactive process observed in the analysed system via, e.g., experiments or simulations. Therefore, for each such process we expect an individual path in $\mathcal{M}(\text{CR-}\mathcal{P}^{\leftarrow \mathtt{v}})$ and we solve the n model checking problem instances for rsLTL in one instance. However, the parameter valuation v is shared among all instances, which allows us to calculate v for which all the properties of F are satisfied.

Example 3. *Let us assume we performed an experiment on the system from Example 2 where protein Y was expressed, and we collected the following observations related to the expression of Y:*

- *when the current state contains y, then y and $\widehat{y}$ are present in the next state:*

$$\phi_1^c = \mathsf{G}_{\neg h}(y \Rightarrow \mathsf{X}(y \wedge \widehat{y})),$$

- *when y and $\widehat{y}$ are present, then Y is finally produced:*

$$\phi_2^c = \mathsf{G}_{\neg h}((y \wedge \widehat{y}) \Rightarrow \mathsf{F}Y),$$

- *the entities y, $\widehat{y}$, and Y are eventually produced:*

$$\phi^r = (\mathsf{F}_{\neg h}y) \wedge (\mathsf{F}_{\neg h}\widehat{y}) \wedge (\mathsf{F}_{\neg h}Y).$$

These observations are made assuming h is not provided in the context set. Additionally, we observe that the protein Q is not present in the first three steps of the execution and then, after an arbitrary number of steps, it is finally produced:

$$\phi^d = \neg Q \wedge \mathsf{X}(\neg Q \wedge \mathsf{X}(\neg Q \wedge \mathsf{F}Q)).$$

The observations are related to a single interactive process (or an experiment), therefore we constrain the problem using the conjunction of all the observations. Finally, the observations are expressed using the following rsLTL formula:

$$\phi_y = \phi^r \wedge \phi_1^c \wedge \phi_2^c \wedge \phi^d.$$

We perform parameter synthesis for $F = \{\phi_y\}$, that is, we obtain a valid parameter valuation $\mathbf{v}$ such that $\mathcal{M}(\mathrm{CR}\text{-}\mathcal{P}^{\leftarrow \mathbf{v}}) \models_{\exists} \phi$. In fact, it may be possible to obtain more than one such valuation. A parameter valuation $\mathbf{v}_1$ such that
$$\lambda_1^{\leftarrow \mathbf{v}_1} = \{y\},\ \lambda_2^{\leftarrow \mathbf{v}_1} = \{y\},\ \lambda_3^{\leftarrow \mathbf{v}_1} = \{Y\}$$
is valid and satisfies the requirements of our observations. A parameter valuation $\mathbf{v}_2$ such that
$$\lambda_1^{\leftarrow \mathbf{v}_2} = \{X, y\},\ \lambda_2^{\leftarrow \mathbf{v}_2} = \{x, \widehat{x}, y\},\ \lambda_3^{\leftarrow \mathbf{v}_2} = \{X, y, \widehat{y}, Y, Q\}$$
is an another example of a valid valuation which satisfies the requirements. $\square$

Example 4. *We introduce an additional unknown into the system declared in Example 2. That is, we add a parameter λ_4 and re-define the reactions of A_x in such a way that one of them uses the newly introduced parameter:*

$$A_x = \{(\{x\}, \{h\}, \{x\}), (\lambda_4, \{h\}, \{\widehat{x}\}), (\{x, \widehat{x}\}, \{h\}, \{X\})\}.$$

Let us assume that in another experiment we observed when the current state contains x, then x and $\widehat{x}$ are found in the next state. This is expressed with the formula $\phi_x = \mathsf{G}_{\neg h}(x \Rightarrow \mathsf{X}(x \wedge \widehat{x}))$. Next, we perform parameter synthesis for $F = \{\phi_x, \phi_y\}$, where ϕ_y is the formula from Example 3. We use two rsLTL formulae in F since our observations were gathered in two separate experiments and may be related to separate interactive processes. A parameter valuation $\mathbf{v}$ such that
$$\lambda_1^{\leftarrow \mathbf{v}} = \{X, y\},\ \lambda_2^{\leftarrow \mathbf{v}} = \{y\},\ \lambda_3^{\leftarrow \mathbf{v}} = \{\widehat{x}, Y\},\ \lambda_4^{\leftarrow \mathbf{v}} = \{Q\}$$
is valid and satisfies the requirements of our observations. $\square$

The parameter valuation v_2 obtained in Example 3 and the valuation from Example 4 do not result in the same reactions as the original ones from [2]. This might be undesired, depending on the application of the synthesis and the knowledge of the system under analysis. To address this issue, in the following section we introduce parameter constraints which allow for providing additional restrictions on the parameters used in the synthesis.

6.1 Parameter constraints

In some cases restricting parameter valuations using only RSLTL formulae may prove to be less efficient than constraining the valuation using specialised constraints for the parameters of a parametric reaction system.

Definition 21. *The grammar of the parameter constraints for $\mathcal{P} = (S, P, A)$ is defined as follows:*

$$\mathfrak{c} ::= true \mid \lambda[e] \sim c \mid \lambda[e] \sim \lambda[e] \mid \neg\mathfrak{c} \mid \mathfrak{c} \vee \mathfrak{c},$$

where $\lambda \in P$, $e \in S$, $c \in \mathbb{N}$, and $\sim \in \{<, \leq, =, \geq, >\}$.

The set of all the parameter constraints for $\mathcal{P}$ is denoted by $PC(\mathcal{P})$. Intuitively, $\lambda[e]$ can be used to refer to the concentration of $e \in S$ in the multisets corresponding to the valuations of λ.

Definition 22. *Let v be a parameter valuation of $\mathcal{P}$. The fact that a parameter constraint $\mathfrak{c}$ holds in v is denoted by $v \models_p \mathfrak{c}$ and defined as follows:*

$$
\begin{array}{ll}
v \models_p true & \text{for every } v, \\
v \models_p \lambda[e] \sim c & \text{iff } \lambda^{\leftarrow v}(e) \sim c, \\
v \models_p \lambda_1[e_1] \sim \lambda_2[e_2] & \text{iff } \lambda_1^{\leftarrow v}(e_1) \sim \lambda_2^{\leftarrow v}(e_2), \\
v \models_p \neg\mathfrak{c} & \text{iff } v \not\models_p \mathfrak{c}, \\
v \models_p \mathfrak{c}_1 \vee \mathfrak{c}_2 & \text{iff } v \models_p \mathfrak{c}_1 \text{ or } v \models_p \mathfrak{c}_2.
\end{array}
$$

Definition 23 (constrained parametric reaction system)**.** *A constrained parametric reaction system is a tuple $\mathcal{CP} = (S, P, A, \mathfrak{c})$ such that $\mathcal{P} = (S, P, A)$ is a parametric reaction system and $\mathfrak{c} \in PC(\mathcal{P})$.*

For $v \in PV_{\mathcal{P}}$, we then define $\mathcal{CP}^{\leftarrow v} = \mathcal{P}^{\leftarrow v}$. A parameter valuation $v \in PV_{\mathcal{P}}$ is *valid* in $\mathcal{CP}$ if it is valid in $\mathcal{P}$ and $v \models_p \mathfrak{c}$.

Definition 24 (context-restricted parametric reaction system)**.** *A context-restricted parametrised reaction system is a pair $\text{CR-}\mathcal{CP} = (\mathcal{CP}, \mathfrak{A})$ such that $\mathcal{CP} = (S, P, A, \mathfrak{c})$ is a constrained parametric reaction system and $\mathfrak{A}$ is a context automaton over S.*

We also denote $\text{CR-}\mathcal{CP}^{\leftarrow v} = (\mathcal{CP}^{\leftarrow v}, \mathfrak{A})$.

Example 5. *Let us consider the system used in Example 4. We might want to assume that the parameters used in the reactions of A_y do not use any of the entities used in the reactions of A_x. Let $E = \{x, \widehat{x}, X\}$ be the set of entities we want to exclude and that are used in A_x. The desired restriction can be expressed using the following parameter constraint:*

$$\bigwedge_{i \in \{1,\ldots,3\}} \bigwedge_{e \in E} (\lambda_i[e] = 0)$$

Similarly,

$$\bigwedge_{e \in (S \setminus E)} (\lambda_4[e] = 0).$$

can express that the parameter λ_4 used in the reaction of A_x is only allowed to use the entities of E. $\qquad\square$

Example 6. *It is possible to constrain multisets corresponding to parameters. Suppose $\lambda_1, \lambda_2, \lambda_3 \in P$. To constrain $\lambda_1^{\leftarrow \mathtt{v}}$ to be a sub-multiset of $\lambda_2^{\leftarrow \mathtt{v}}$ (i.e., $\lambda_1^{\leftarrow \mathtt{v}} \subseteq \lambda_2^{\leftarrow \mathtt{v}}$, for all $\mathtt{v}$), we define:*

$$submset(\lambda_1, \lambda_2) = \bigwedge_{e \in S} (\lambda_1[e] \leq \lambda_2[e]).$$

To constrain $\lambda_3^{\leftarrow \mathtt{v}}$ to be the intersection of $\lambda_1^{\leftarrow \mathtt{v}}$ and $\lambda_2^{\leftarrow \mathtt{v}}$ (i.e., $\lambda_1^{\leftarrow \mathtt{v}} \cap \lambda_2^{\leftarrow \mathtt{v}} = \lambda_3^{\leftarrow \mathtt{v}}$, for all $\mathtt{v}$), we define:

$$intersect(\lambda_1, \lambda_2, \lambda_3) = \bigwedge_{e \in S} \Big(((\lambda_1[e] > \lambda_2[e]) \wedge (\lambda_3[e] = \lambda_2[e]))$$
$$\vee \, ((\lambda_1[e] \leq \lambda_2[e]) \wedge (\lambda_3[e] = \lambda_1[e])) \Big). \quad \square$$

The parameter synthesis problem for context-restricted parametric reaction systems is defined similarly as for context-restricted parametric reaction system. Let $\text{CR-}\mathcal{CP} = (\mathcal{CP}, \mathfrak{A})$ be a context-restricted parametric reaction system, and $F = \{\phi_1, \ldots, \phi_n\}$ be a set of rsLTL formulae. The aim of *parameter synthesis* for context-restricted parametric reaction systems is to find a valid parameter valuation $\mathtt{v}$ of $\text{CR-}\mathcal{CP}$ such that:

$$(\mathcal{M}(\text{CR-}\mathcal{CP}^{\leftarrow \mathtt{v}}) \models_\exists \phi_1) \wedge \ldots \wedge (\mathcal{M}(\text{CR-}\mathcal{CP}^{\leftarrow \mathtt{v}}) \models_\exists \phi_n). \tag{2}$$

Next, we define the *nonemptiness checking* problem, which is a decision problem related to the problem of parameter synthesis. The nonemptiness checking problem consists in checking if there exists a valuation $\mathtt{v}$ such that the condition (2) holds.

6.2 Complexity analysis

Theorem 10. *The nonemptiness checking problem for context-restricted parametric reaction systems and rsLTL is PSPACE-complete.*

Proof. The lower bound follows directly from Corollary 1, hence the problem is PSPACE-hard.

For the upper bound we need to show the problem is in PSPACE. To show this we define a nondeterministic space-bounded algorithm and use Lemma 4. Algorithm 1 presents an outline for the nonemptiness checking procedure. First, the algorithm nondeterministically generates a valuation $\mathtt{v} \in \text{PV}_\mathcal{P}$. If $\mathtt{v}$ is valid in $\text{CR-}\mathcal{CP}$, then it proceeds to verifying the rsLTL formulae. For all the formulae $\phi \in F$ the algorithm performs existential rsLTL model checking in $\mathcal{M}(\text{CR-}\mathcal{CP}^{\leftarrow \mathtt{v}})$. From Lemma 4 and the fact that PSPACE is closed under complementation, i.e., PSPACE = coPSPACE, the existential variant of the rsLTL model checking problem is also in PSPACE. The nonemptiness checking algorithm requires the space needed by the algorithm for rsLTL model checking. Since all the $|F|$ model checking instances are constructed independently and the algorithm only stores the overall result R, the algorithm requires space for at most one instance at any given time. Additionally, the algorithm requires

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Algorithm 1 Nondeterministic procedure for nonemptiness checking

1: guess $\mathbf{v} \in \mathrm{PV}_{\mathcal{P}}$
2: **if** $\mathbf{v} \models_p \mathfrak{c}$ **then**
3:     $R := true$
4:     **for all** $\phi \in F$ **do**
5:         $R := (\mathcal{M}(\mathrm{CR}\text{-}\mathcal{CP}^{\leftarrow \mathbf{v}}) \models_{\exists} \phi) \wedge R$
6:     **end for**
7:     **if** $R = true$ **then return** $true$
8:     **end if**
9: **end if**

space $\mathcal{O}(|A| \cdot |S|)$ to store the valuation $\mathbf{v}$ and $\mathcal{O}(1)$ for the verification result R. Therefore, the problem remains in PSPACE and given the lower bound we conclude the problem is PSPACE-complete. $\qquad \square$

In the following section we show how the synthesis problem can be solved using an incremental approach, which amounts to checking

$$(\mathcal{M}(\mathrm{CR}\text{-}\mathcal{CP}^{\leftarrow \mathbf{v}}) \models_{\exists}^{k} \phi_1) \wedge \ldots \wedge (\mathcal{M}(\mathrm{CR}\text{-}\mathcal{CP}^{\leftarrow \mathbf{v}}) \models_{\exists}^{k} \phi_n)$$

for $k \geq 0$, by increasing the value of k until a valid parameter valuation is found.

7 smt-based encoding for parametric reaction systems

In this section, we provide a translation of the parameter synthesis problem for context-restricted parametric reaction systems and rsLTL into SMT with the integer arithmetic theory.

Let $\mathrm{CR}\text{-}\mathcal{CP} = ((S, P, A, \mathfrak{c}), (\mathcal{Q}, \mathfrak{q}^{init}, R))$ be a context-restricted parametric reaction system, and $F = \{\phi_1, \ldots, \phi_n\}$ be a set of rsLTL formulae. We encode the model $\mathcal{M}_{\mathrm{CR}\text{-}\mathcal{CP}^{\leftarrow \mathbf{v}}}$, where $\mathbf{v}$ is a valid parameter valuation of $\mathrm{CR}\text{-}\mathcal{CP}$.

Let $k \geq 0$ be an integer, then for each $f \in \{1, \ldots, n\}$ we encode any possible path prefix of $\mathcal{M}_{\mathrm{CR}\text{-}\mathcal{CP}^{\leftarrow \mathbf{v}}}$. The encoded path prefixes are bounded with k. That is, for each formula ϕ_f we encode a separate path prefix representing its witness. The entities of S are denoted by $e_1, \ldots, e_m$, where $m = |S|$. For each $\phi_f \in F$ and $i \in \{0, \ldots, k\}$, we introduce sets of positive integer variables:

$$\mathbf{P}_{f,i} = \{\mathbf{p}_{f,i,1}, \ldots, \mathbf{p}_{f,i,m}\}, \quad \mathbf{P}_{f,i}^{\mathcal{E}} = \{\mathbf{p}_{f,i,1}^{\mathcal{E}}, \ldots, \mathbf{p}_{f,i,m}^{\mathcal{E}}\}, \quad \text{and} \quad \mathbf{Q}_f = \{\mathbf{q}_{f,0}, \ldots, \mathbf{q}_{f,k}\}.$$

Let $\mathtt{ta} : A \to \{1, \ldots, |A|\}$ be a bijection mapping all the reactions to integers. For each $a \in A$, we introduce the set of variables encoding the products:

$$\mathbf{P}_{f,i,a}^{p} = \{\mathbf{p}_{f,i,\mathtt{ta}(a),1}^{p}, \ldots, \mathbf{p}_{f,i,\mathtt{ta}(a),m}^{p}\}.$$

Let $\sigma.f$ be a path of $\mathcal{M}(\mathrm{CR}\text{-}\mathcal{CP}^{\leftarrow \mathbf{v}})$, then

$$\overline{\mathbf{p}}_{f,i} = (\mathbf{p}_{f,i,1}, \ldots, \mathbf{p}_{f,i,m}) \quad \text{and} \quad \overline{\mathbf{p}}_{f,i}^{\mathcal{E}} = (\mathbf{p}_{f,i,1}^{\mathcal{E}}, \ldots, \mathbf{p}_{f,i,m}^{\mathcal{E}})$$

are used to encode $(\sigma.f)_b(i)$ and $(\sigma.f)_a(i)$, respectively. With $\overline{\mathbf{p}}_{f,i}[j]$ and $\overline{\mathbf{p}}^{\mathcal{E}}_{f,i}[j]$ we denote, respectively, $\mathsf{p}_{f,i,j}$ and $\mathsf{p}^{\mathcal{E}}_{f,i,j}$. For each $i \geq 1$, we define:

$$\overline{\mathbf{p}}^p_{f,i} = (\mathsf{p}^p_{f,i,1,1}, \ldots, \mathsf{p}^p_{f,i,1,m}, \ldots, \mathsf{p}^p_{f,i,|A|,1}, \ldots, \mathsf{p}^p_{f,i,|A|,m}).$$

The following functions map the background set entities to the corresponding variables of the encoding: for all $i \in \{0, \ldots, k\}$, we define $\mathsf{t}_{f,i} : S \to \mathbf{P}_{f,i}$ and $\mathsf{t}^{\mathcal{E}}_{f,i} : S \to \mathbf{P}^{\mathcal{E}}_{f,i}$ such that $\mathsf{t}_{f,i}(e_j) = \mathsf{p}_{f,i,j}$ and $\mathsf{t}^{\mathcal{E}}_{f,i}(e_j) = \mathsf{p}^{\mathcal{E}}_{f,i,j}$, for all $j \in \{1, \ldots, m\}$. For all $i \in \{0, \ldots, k\}$ and $a \in A$, we define $\mathsf{t}^p_{f,i,a} : S \to \mathbf{P}^p_{f,i,a}$ such that: $\mathsf{t}^p_{f,i,a}(e_j) = \mathsf{p}^p_{f,i,\mathtt{ta}(a),j}$, for all $j \in \{1, \ldots, m\}$.

The bijection $\mathsf{e} : \mathcal{Q} \to \{1, \ldots, |\mathcal{Q}|\}$ maps the states of the context automaton to the integers used in the encoding. Let $\mathsf{tp} : P \to \{1, \ldots, |P|\}$ be a bijection mapping all the parameters to their corresponding integers. We define:

$$\overline{\mathbf{p}}^{par} = (\mathsf{p}^{par}_{1,1}, \ldots, \mathsf{p}^{par}_{1,m}, \ldots, \mathsf{p}^{par}_{|P|,1}, \ldots, \mathsf{p}^{par}_{|P|,m}).$$

For each parameter $\lambda \in P$, we define:

$$\mathbf{P}^{par}_{\lambda} = \{\mathsf{p}^{par}_{\mathsf{tp}(\lambda),1}, \ldots, \mathsf{p}^{par}_{\mathsf{tp}(\lambda),m}\}$$

and $\mathsf{pm}_{\lambda} : S \to \mathbf{P}^{par}_{\lambda}$ such that $\mathsf{pm}_{\lambda}(e_j) = \mathsf{p}^{par}_{\mathsf{tp}(\lambda),j}$. Let $a \in A$ and $\mathfrak{s} \in \{\mathfrak{r}_a, \mathfrak{i}_a, \mathfrak{p}_a\}$. Then, $re^{\mathfrak{s}}(e_j)$ denotes $\mathsf{pm}_{\mathfrak{s}}(e_j)$ if $\mathfrak{s} \in P$, and $\mathfrak{s}(e_j)$ otherwise. To define the SMT encoding of the paths we need auxiliary functions that correspond to elements of the encoding.

To encode the initial state of the model for $\phi_f \in F$, we define

$$\mathtt{Init}(\overline{\mathbf{p}}_{f,i}, \mathsf{q}_{f,i}) = \left(\bigwedge_{e \in S} \mathsf{t}_{f,i}(e) = 0 \right) \wedge \mathsf{q}_{f,i} = \mathsf{e}(\mathsf{q}^{init}),$$

where all the concentration levels are set to zero, and the context automaton is in its initial state.

With $\mathsf{PC}(\overline{\mathbf{p}}^{par})$ we encode the parameter constraints, require that the concentration levels of the reactants are always lower than the concentration levels of the inhibitors, and ensure that all the multisets corresponding to the parameters are non-empty, i.e., for each parameter, at least one entity must a have positive concentration level:

$$\mathsf{PC}(\overline{\mathbf{p}}^{par}) = enc_{\mathfrak{c}}(\overline{\mathbf{p}}^{par}) \wedge \left(\bigwedge_{a \in A} \bigwedge_{e \in S} re^{\mathfrak{i}_a}(e) > 0 \Rightarrow (re^{\mathfrak{r}_a}(e) < re^{\mathfrak{i}_a}(e)) \right) \wedge$$

$$\left(\bigwedge_{\lambda \in P} \bigvee_{e \in S} \mathsf{pm}_{\lambda}(e) > 0 \right),$$

where $enc_{\mathfrak{c}}(\overline{\mathbf{p}}^{par})$ is the encoding of $\mathfrak{c}$ and it is defined over the variables of $\overline{\mathbf{p}}^{par}$. The encoding follows directly from the semantics of parameter constraints.

The parametric reactions $a \in A$ are encoded with

$$\mathsf{Rct}_a(\overline{\mathbf{p}}_{f,i}, \overline{\mathbf{p}}_{f,i}^{\mathcal{E}}, \overline{\mathbf{p}}_{f,i+1}^{p}, \overline{\mathbf{p}}^{par}) = \bigwedge_{e \in S} ((\mathsf{t}_{f,i}(e) \geq re^{\mathtt{r}_a}(e) \vee \mathsf{t}_{f,i}^{\mathcal{E}}(e) \geq re^{\mathtt{r}_a}(e)) \wedge$$
$$(\mathsf{t}_{f,i}(e) < re^{\mathtt{i}_a}(e) \wedge \mathsf{t}_{f,i}^{\mathcal{E}}(e) < re^{\mathtt{i}_a}(e)) \wedge (\mathsf{t}_{f,a,i+1}^{p}(e) = re^{\mathtt{p}_a}(e))).$$

With the following formula we encode the selection of the maximal concentration levels produced for each entity by all the reactions:

$$\mathsf{Results}(\overline{\mathbf{p}}_{f,i}, \overline{\mathbf{p}}_{f,i}^{p}) = \left(\bigwedge_{e \in S} \mathsf{t}_{f,i+1}(e) = max(\{0\} \cup \bigcup_{a \in A} \{\mathsf{t}_{f,a,i+1}^{p}(e)\}) \right).$$

We encode the local state changes of $\mathcal{CP}$ with the following function:

$$\mathsf{Tr}_{\mathcal{CP}}(\overline{\mathbf{p}}_{f,i}, \overline{\mathbf{p}}_{f,i}^{\mathcal{E}}, \overline{\mathbf{p}}_{f,i+1}^{p}, \overline{\mathbf{p}}_{f,i+1}, \overline{\mathbf{p}}^{par}) = \left(\bigwedge_{a \in A} \mathsf{Rct}_a(\overline{\mathbf{p}}_{f,i}, \overline{\mathbf{p}}_{f,i}^{\mathcal{E}}, \overline{\mathbf{p}}_{f,i+1}^{p}, \overline{\mathbf{p}}^{par}) \right) \wedge$$
$$\mathsf{Results}(\overline{\mathbf{p}}_{f,i+1}, \overline{\mathbf{p}}_{f,i+1}^{p}).$$

To encode a multiset $\mathbf{c} \in \mathcal{B}(S)$ of context entities we define the following function:

$$\mathsf{Ct}_{\mathbf{c}}(\overline{\mathbf{p}}_{f,i}^{\mathcal{E}}) = \bigwedge_{e \in S} \mathsf{t}_{f,i}^{\mathcal{E}}(e) = \mathbf{c}(e)$$

The encoding of the transition relation of the context automaton is a disjunction of the encoded transitions:

$$\mathsf{Tr}_{\mathfrak{A}}(\mathsf{q}_{f,i}, \overline{\mathbf{p}}_{f,i}^{\mathcal{E}}, \mathsf{q}_{f,i+1}) = \bigvee_{(\mathfrak{q}, \mathbf{c}, \mathfrak{q}') \in R} \left(\mathsf{q}_{f,i} = \mathsf{e}(\mathfrak{q}) \wedge \mathsf{Ct}_{\mathbf{c}}(\overline{\mathbf{p}}_{f,i}^{\mathcal{E}}) \wedge \mathsf{q}_{f,i+1} = \mathsf{e}(\mathfrak{q}') \right).$$

The transition relation of the model for CR-$\mathcal{CP}$ is a conjunction of the encoded transition relations for $\mathcal{CP}$ and $\mathfrak{A}$:

$$\mathsf{Tr}_{\text{CR-}\mathcal{CP}}(\overline{\mathbf{p}}_{f,i}, \mathsf{q}_{f,i}, \overline{\mathbf{p}}_{f,i}^{\mathcal{E}}, \overline{\mathbf{p}}_{f,i+1}^{p}, \overline{\mathbf{p}}_{f,i+1}, \overline{\mathbf{p}}^{par}) =$$
$$\mathsf{Tr}_{\mathcal{CP}}(\overline{\mathbf{p}}_{f,i}, \overline{\mathbf{p}}_{f,i}^{\mathcal{E}}, \overline{\mathbf{p}}_{f,i+1}^{p}, \overline{\mathbf{p}}_{f,i+1}, \overline{\mathbf{p}}^{par}) \wedge \mathsf{Tr}_{\mathfrak{A}}(\mathsf{q}_{f,i}, \overline{\mathbf{p}}_{f,i}^{\mathcal{E}}, \mathsf{q}_{f,i+1}).$$

Finally, to encode the paths of $\mathcal{M}_{\text{CR-}\mathcal{CP}\leftarrow\text{v}}$ that are bounded with k, we unroll the transition relation up to k and combine it with the encoding of the initial state of the model:

$$\mathsf{Paths}_f^k = \mathsf{Init}\left(\overline{\mathbf{p}}_{f,0}, \mathsf{q}_{f,0}\right) \wedge \bigwedge_{i=0}^{k-1} \mathsf{Tr}_{\text{CR-}\mathcal{CP}}(\overline{\mathbf{p}}_{f,i}, \mathsf{q}_{f,i}, , \overline{\mathbf{p}}_{f,i}^{\mathcal{E}}, \overline{\mathbf{p}}_{f,i+1}^{p}, \overline{\mathbf{p}}_{f,i+1}, \overline{\mathbf{p}}^{par}).$$

The encoded rsLTL formula ϕ_f at a position $i \in \{0, \ldots, k\}$ is denoted by $[\![\phi_f]\!]_i^k$. To encode the formula $[\![\phi_f]\!]_i^k$, we use our translation presented in Section 5. However, for each formula $\phi_f \in F$, we use independent sets of encoding variables corresponding to its path, i.e., the variables indexed with f. The encoding Loops_f^k for the loop positions is defined for each formula $\phi_f \in F$. Finally, we perform the synthesis of the parameter valuation $\mathtt{v}$ by testing the satisfiability of the following formula:

$$[\mathcal{M}_{\text{CR-}\mathcal{CP}\leftarrow\mathtt{v}}, F, k] = \bigwedge_{\phi_f \in F} \left(\mathsf{Paths}_f^k \wedge \mathsf{Loops}_f^k \wedge [\![\phi_f]\!]_0^k \right) \wedge \mathsf{PC}(\overline{\mathbf{p}}^{par}). \tag{3}$$

The presented encoding differs from that for the context restricted reaction systems with discrete concentrations and rsLTL (Section 5) in the way the transition relation is encoded. Here, we use an additional step that encodes the concentration levels of each entity produced by the individual reactions.

These results are then used to select the maximal concentration level produced for a given entity. This is required because some reactions produce parameters for which we do not have concrete values at the encoding stage. Therefore, it is not possible to use the technique demonstrated in Section 5, where the reactions are ordered and effectively only that producing the maximal concentration level is enabled.

We can then establish the correctness of the proposed encoding for a given valid parameter valuation.

Theorem 11. *Let* CR-$\mathcal{CP} = (\mathcal{CP}, \mathfrak{A})$ *be a context-restricted parametric reaction system,* $\mathtt{v} \in \mathsf{PV}_{CR\text{-}\mathcal{CP}}$ *be a valid parameter valuation,* $\mathcal{M}_{CR\text{-}\mathcal{CP}\leftarrow\mathtt{v}}$ *be its model, and* F *be a set of rsLTL formulae. For any* $k \in \mathbb{N}$*, the formula* $[\mathcal{M}_{CR\text{-}\mathcal{CP}\leftarrow\mathtt{v}}, F, k]$ *is satisfiable iff* $\bigwedge_{\phi \in F} \left(\mathcal{M}_{CR\text{-}\mathcal{CP}\leftarrow\mathtt{v}} \models_\exists^k \phi \right)$.

Proof. Since we assume a valid parameter valuation $\mathtt{v}$, to obtain a context-restricted parametric reaction system we can perform the substitution of all the parameters that occur in context-restricted parametric reaction system. Then, the proof is similar to the one of Theorem 9 for context restricted reaction systems with discrete concentrations and rsLTL. The formula $\mathsf{PC}(\overline{\mathbf{p}}^{par})$ applies only to the encoding of parameters and after performing the substitution we can simply assume that it is *true* as it does not constrain anything. The formula $[\mathcal{M}_{CR\text{-}\mathcal{CP}\leftarrow\mathtt{v}}, F, k]$ encodes $|F|$ bounded model checking instances (similar to what was described in Section 5). Let us consider $\phi_f \in F$. We assume an arbitrary $k \in \mathbb{N}$ and focus on the satisfiability of Paths_f^k, since the encoding of this formula differs from the corresponding one in the encoding for CR-$\mathcal{C}$. There exists a path $\sigma.f$ in $\mathcal{M}_{CR\text{-}\mathcal{CP}\leftarrow\mathtt{v}}$ and $(\sigma.f)^k$ is its prefix of length k iff there exists a valuation that represents $(\sigma.f)^k$ which satisfies Paths_f^k. Let $i \in \{0, \ldots, k-1\}$. We observe the formula $\mathsf{Tr}_{CR\text{-}\mathcal{CP}}$ is satisfied for the valuation encoding $(\sigma.f)_s(i)$, $(\sigma.f)_a(i)$ and $(\sigma.f)_s(i+1)$ iff $(\sigma.f)_s(i) \xrightarrow{(\sigma.f)_a(i)} (\sigma.f)_s(i+1)$. This follows from the encoding of $\mathsf{Tr}_{\mathcal{CP}}$ and $\mathsf{Tr}_{\mathfrak{A}}$. Let us first recall that $(\sigma.f)_s(i) = ((\sigma.f)_b(i), (\sigma.f)_{ca}(i))$. The formula $\mathsf{Tr}_{\mathcal{CP}}$ is satisfied iff the valuation satisfies $\mathsf{Results}$ and Rct_a for each $a \in A$. The formula Rct_a encodes the produced concentration levels for all the entities $e \in S$ by $a \in A$ using the intermediate variables of $\mathbf{P}_{f,i,a}^p$. Then, $\mathsf{Results}$ ensures the maximal produced concentration levels for each entity and each reaction are encoded using the variables of $\mathbf{P}_{f,i+1}$. It follows

from the construction that Results and Rct_a are satisfied iff the valuation encodes the concentration levels of the entities in the successor state $(\sigma.f)_b(i+1)$ that are produced by the reactions from the state $(\sigma.f)_b(i)$ combined with the context $(\sigma.f)_a(i)$. The formula $\mathsf{Tr}_{\mathfrak{A}}$ is satisfied iff the valuation encodes a transition $(\mathfrak{q}, \mathbf{c}, \mathfrak{q}') \in R$ such that $\mathfrak{q} = (\sigma.f)_{ca}(i)$, $\mathbf{c} = (\sigma.f)_a(i)$ and $\mathfrak{q}' = (\sigma.f)_{ca}(i+1)$. Then, the formula Paths_f^k is satisfied iff the valuation encodes a path prefix $(\sigma.f)^k$ such that the state $(\sigma.f)_s(0)$ of $\mathcal{M}_{\mathrm{CR}\text{-}\mathcal{CP}\leftarrow v}$ is the initial state and $(\sigma.f)_s(i) \xrightarrow{(\sigma.f)_a(i)} (\sigma.f)_s(i+1)$ for all $i \in \{0, \ldots, k-1\}$. The rest of the proof for Loops_f^k and $[\![\phi_f]\!]_0^k$ follows as for Theorem 9.

Now it is easy to see that $\mathsf{Paths}_f^k \wedge \mathsf{Loops}_f^k \wedge [\![\phi_f]\!]_0^k$ is satisfiable iff $\mathcal{M}_{\mathrm{CR}\text{-}\mathcal{CP}\leftarrow v} \models_{\exists}^k \phi_f$. Finally, we conclude that $[\mathcal{M}_{\mathrm{CR}\text{-}\mathcal{CP}\leftarrow v}, F, k]$ is satisfiable iff $\mathcal{M}_{\mathrm{CR}\text{-}\mathcal{CP}\leftarrow v} \models_{\exists}^k \phi_f$ for all $\phi_f \in F$. $\qquad\square$

In practice, the encoding $[\mathcal{M}_{\mathrm{CR}\text{-}\mathcal{CP}\leftarrow v}, F, k]$ is intended to be satisfiable for any valid parameter valuation v such that $\bigwedge_{\phi \in F} (\mathcal{M}_{\mathrm{CR}\text{-}\mathcal{CP}\leftarrow v} \models_{\exists}^k \phi)$. The constraints that enforce the valuation to be valid are expressed using the encoding of PC. We extract the valuation of the parameters of P when the formula (3) is satisfiable. For the satisfied formula we obtain its model, i.e., the valuations of the variables used in the formula. Let $V(\mathbf{p})$ denote the valuation of a variable $\mathbf{p}$ used in our encoding. The parameter valuations are defined as follows: $\lambda^{\leftarrow v}(e) = V(\mathtt{pm}_\lambda(e))$ for each $e \in S$ and $\lambda \in P$.

8 Experimental evaluation

In this section, we present the results of experimental evaluation of the translation presented in Section 7. We tested the method on a parametric version (PMUTEX) of the reaction system model introduced in [21] for a mutual exclusion protocol.

The system we consider consists of $n \geq 2$ processes competing for an exclusive access to the critical section. The background set of the context restricted reaction system with discrete concentrations modelling the mutual exclusion protocol is defined as $S = \bigcup_{i=1}^n S_i$, with the set of background entities corresponding to the i-th process given by:
$$S_i = \{\, out_i, req_i, in_i, act_i, lock, done, s \,\},$$
where the entities $lock$, $done$, and s are shared amongst all the processes.

We start by defining the context automaton $\mathfrak{A}$. Initially, all the processes are outside of their critical sections and are not requesting access, which is indicated by the presence of out_i, for each $i \in \{1, \ldots, n\}$. Next, we assume that $\mathfrak{A}$ may supply any $C \subseteq \{act_1, \ldots, act_n\}$ such that $|C| \leq 2$, allowing at most two simultaneously active processes – we assume that if the context contains act_i then the ith process is to perform an action. This leads to the following definition of the context automaton: $\mathfrak{A} = (\{\mathfrak{q}_0, \mathfrak{q}_1\}, \mathfrak{q}_0, R)$, where:

$$R = \{\mathfrak{q}_0 \xrightarrow{\{out_1, \ldots, out_n\}} \mathfrak{q}_1\} \cup \{\mathfrak{q}_1 \xrightarrow{C} \mathfrak{q}_1 \mid C \subseteq \{act_1, \ldots, act_n\} \text{ and } |C| \leq 2\}.$$

We allow at most two active processes at a time to avoid encoding in the context automaton all the 2^n transitions with the subsets of $\{act_1, \ldots, act_n\}$.

The ith process requests access to its critical section by producing req_i. Then, it is possible for the process to enter the critical section when it is allowed to perform an action and the critical section is not locked (the *lock* entity is not present). In the case of entering a critical section, to avoid the situation where two processes enter their critical sections synchronously, the assumption on act_i is stricter: only one act_i, for some $i \in \{1, \ldots, n\}$, is allowed to be present for the process to enter the critical section. When a process enters the critical section, the critical section is locked, i.e., the *lock* entity is produced. The *lock* entity is preserved until the entity *done* appears, which is produced when the process leaves the critical section. Any reaction in the system may be inhibited by the s entity.

This version of the mutual exclusion protocol implementation differs from that presented in [21] by the use of concentration levels. Each process after requesting access to its critical section must wait at least one step before it is allowed to gain access and, after entering the critical section, the process performs computations which take two steps.

Let A_i be the set of reactions of the ith process, for $i \in \{1, \ldots, n\}$. Then, the set A_i consists of the following reactions:

- $(\{out_i \mapsto 1, act_i \mapsto 1\}, \{s \mapsto 1\}, \{req_i \mapsto 1\})$,
- $(\{out_i \mapsto 1\}, \{act_i \mapsto 1\}, \{out_i \mapsto 1\})$,
- $(\{req_i \mapsto 1, act_i \mapsto 1, act_j \mapsto 1\}, \{s \mapsto 1\}, \{req_i \mapsto 1\})$ for each $j \in \{1, \ldots, n\}$ s.t. $i \neq j$,
- $(\{req_i \mapsto 1\}, \{act_i \mapsto 1\}, \{req_i \mapsto 2\})$,
- $(\{req_i \mapsto 2, act_i \mapsto 1\}, \{act_j \mapsto 1 \mid j \in \{1, \ldots, n\} \text{ and } j \neq i\} \cup \{lock \mapsto 1\}, \{in_i \mapsto 3, lock \mapsto 1\})$,
- $(\{in_i \mapsto 3, act_i \mapsto 1\}, \{s \mapsto 1\}, \{in_i \mapsto 2\})$,
- $(\{in_i \mapsto 2, act_i \mapsto 1\}, \{s \mapsto 1\}, \{in_i \mapsto 1\})$,
- $(\{in_i \mapsto 1, act_i \mapsto 1\}, \{s \mapsto 1\}, \{out_i \mapsto 1, done \mapsto 1\})$,
- $(\{in_i \mapsto 1\}, \{s \mapsto 1\}, \{in_i \mapsto 1\})$.

Next, we assume here that the system is open and we allow for introducing new processes that participate in the communication to gain access to the critical section. Let us assume that we are allowed to modify the behaviour of an additional process (the nth process) only by introducing an additional reaction. Such an assumption could be justified by a mechanism that accepts new processes to participate in the protocol only if they contain the reactions of A_i, for $i \in \{1, \ldots, n\}$, while the remaining reactions could be performing some computation outside of the critical section.

Our aim is to violate the property of mutual exclusion by making the first and the nth process enter their critical sections simultaneously. The additional (malicious) reaction uses the parameters of $P = \{\lambda_r, \lambda_i, \lambda_p\}$ and is defined as follows:

$$A_p = \{(\lambda_r, \lambda_i, \lambda_p)\}$$

The set of reactions is defined as:

$$A = \left(\bigcup_{i=1}^{n} A_i \right) \cup A_p \cup \left\{ (\{lock \mapsto 1\}, \{done \mapsto 1\}, \{lock \mapsto 1\}) \right\}.$$

Finally, we define the CRRSC modelling PMUTEX as: CR-$\mathcal{C}_M = ((S, P, A, \mathfrak{c}), \mathfrak{A})$, where:

$$\mathfrak{c} = \left((\lambda_p[in_n] = 0) \wedge \bigwedge_{\lambda \in P, e \in S \setminus S_n} (\lambda[e] = 0) \right).$$

The constraint $\mathfrak{c}$ constrains the additional reaction by requiring that it may produce only entities related to the nth process and it cannot produce in_n. This is to avoid trivial solutions. Then, we need to synthesise a parameter valuation $\mathtt{v}$ of CR-$\mathcal{CP}_M$ which gives the rsLTL property $\phi = \mathsf{F}((in_1 > 0) \wedge (in_n > 0))$, i.e., $\mathcal{M}(\text{CR-}\mathcal{CP}_M^{\leftarrow \mathtt{v}}) \models_\exists \phi$.
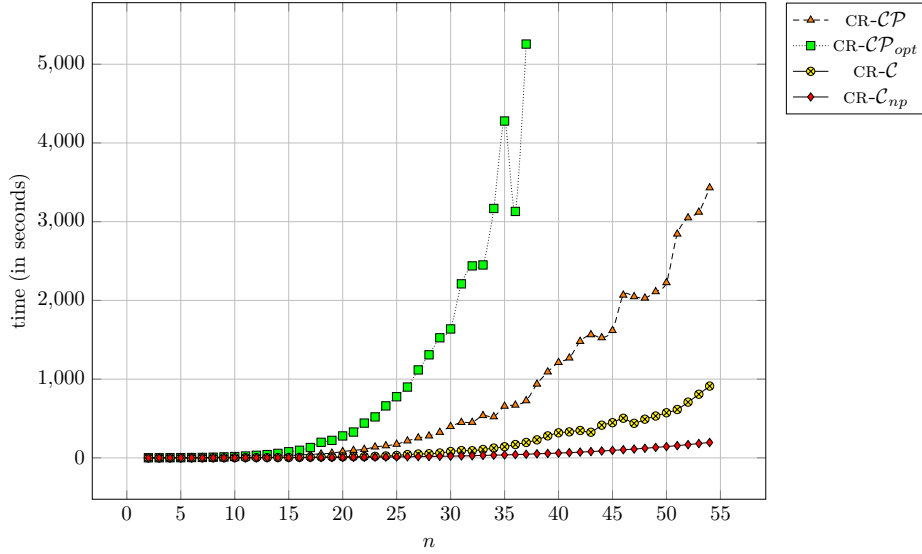
Fig. 2 Synthesis results for PMUTEX: execution time

The verification tool was implemented in Python and it used Z3 4.12.2 [49] for SMT-solving. We implemented an incremental approach, i.e., in a single SMT instance, we increase the length of the encoded interactive processes by unrolling their encoding until witnesses for all the verified formulae are found. Then, the corresponding parameter valuation is extracted. The verification results presented in Fig. 2–3 compare the implementation of the encoding from Section 7 (CR-$\mathcal{CP}$) and its extension (CR-$\mathcal{CP}_{opt}$) that optimises the obtained parameter valuations by using OptSMT provided with Z3. We also use the same encoding for the verification of the rsLTL property (CR-$\mathcal{C}$), i.e., we replace all the parameters with the obtained parameter valuations and test
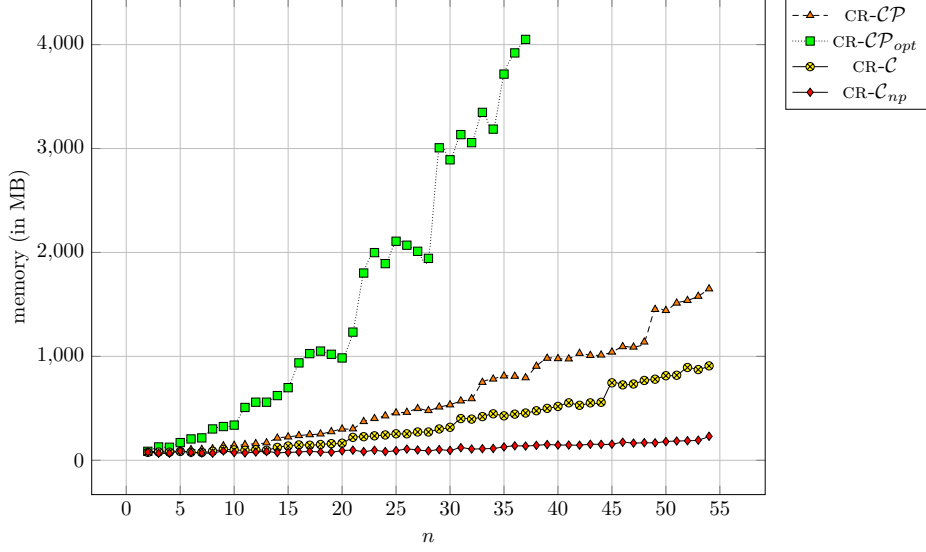
31

Fig. 3 Synthesis results for PMUTEX: memory consumption

the formula ϕ in the same way as it is possible with the method defined in Section 5. Next, we compare our results with those obtained using the non-parametric method (CR-$\mathcal{C}_{np}$) defined in Section 5.

The experimental implementation provides a valuation $\mathtt{v}$ which allows to violate the mutual exclusion property, where $\lambda_r^{\leftarrow\mathtt{v}} = \{out_n \mapsto 1\}$, $\lambda_i^{\leftarrow\mathtt{v}} = \{s \mapsto 1\}$, and $\lambda_p^{\leftarrow\mathtt{v}} = \{req_n \mapsto 2, done \mapsto 1\}$, for all the values $n \geq 2$ tested. This valuation was obtained using CR-$\mathcal{CP}_{opt}$.

The difference in time and memory consumption between the parametric (CR-$\mathcal{CP}$) and the non-parametric (CR-$\mathcal{C}$) approach is minor, while CR-$\mathcal{C}_{np}$ is the most efficient of all the approaches tested. The difference between the performance of CR-$\mathcal{C}_{np}$ and CR-$\mathcal{C}$ shows the potential for optimisations of our parametric encoding as CR-$\mathcal{C}$ uses a simpler encoding. However, the performance of CR-$\mathcal{CP}_{opt}$ shows that the cost of minimising parameter valuations can be high and for $n = 37$ our implementation consumed 4050MB of memory, while the variant without the optimisation required only 794MB. For this reason we did not obtain results for $n > 37$.

9 Concluding remarks

In this paper, we introduced a method for reaction mining that allows for calculating parameter valuations for partially defined reactions of reaction systems. We then demonstrated how the proposed method can be used for the synthesis of an attack in which one injects an additional instruction represented by a reaction, and used rsLTL to express the goal of such an attack. Furthermore, we extended our results for rsLTL [26] showing that rsLTL model checking is PSPACE-complete, and provided a translation of rsLTL model checking to LTL model checking for reaction systems.

Assuming there is a finite set of allowed concentration levels for the parameters, the method introduced here allows for enumerating all the possible parameter valuations for fixed-length processes. This can be achieved by adding an additional constraint blocking the parameter valuation obtained in the preceding step.

When dealing with parameter synthesis, the parameters could be associated with the model [50, 51] or with the formalism used to express its properties [52, 53]. We focused on the synthesis of the parameters which appear in the reaction system. One could also consider extending this approach to include parameters in the context automaton. This might allow one to synthesise the behaviour of the environment which would lead to the satisfaction of the verified rsLTL property. Having said that, in the implementation of our approach, when the verified formula is satisfied, we also obtain the witness which contains the entire context sequence generated by the context automaton. This sequence represents the behaviour of the environment which leads to satisfaction of the rsLTL formula.

Note also that parameters could be introduced in the rsCTL or rsLTL formulae leading to parametric variants of both logics, e.g., by introducing parameters in place of the families of sets of entities (or the multiset expressions for rsLTL).

Declarations

Ethical Approval

Not applicable.

Competing interests

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

Authors' contributions

All authors have contributed equally.

Funding

Availability of data and materials

Our experimental results can be reproduced by cloning the repository with Reactics (https://github.com/arturmeski/reactics/) and running the shell script from the `experiments/reaction_mining_mutex` directory.

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