Enhancing reaction systems: a process algebraic approach

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Abstract. In the area of Natural Computing, reaction systems are a qualitative abstraction inspired by the functioning of living cells, suitable to model the main mechanisms of biochemical reactions. This model has already been applied and extended successfully to various areas of research. Reaction systems interact with the environment represented by the context, and pose problems of implementation, as it is a new computation model. In this paper we consider the `link`-calculus, which allows to model multiparty interaction in concurrent systems, and show that it allows to embed reaction systems, by representing the behaviour of each entity and preserving faithfully their features. We show the correctness and completeness of our embedding. We illustrate our framework by showing how to embed a *lac* operon regulatory network. Finally, our framework can contribute to increase the expressiveness of reaction systems, by exploiting the interaction among different reaction systems.

Keywords: Process algebras · Reaction systems · Multi-party interaction.

1 Introduction

Natural Computing is an emerging area of research which has two main aspects: human designed computing inspired by nature, and computation performed in nature. Reaction Systems (RSs) [9] are a rewriting formalism inspired by the way biochemical reactions take place in living cells. This theory has already shown to be relevant in several different fields, such as computer science [17], biology [2,15,1,3], and molecular chemistry [18]. Reaction Systems formalise the mechanisms of biochemical systems, such as *facilitation* and *inhibition*. As a qualitative approximation of the real biochemical reactions, they consider if a necessary reagent is or not present, and likewise they consider if an inhibiting molecule is or not present. The possible reactants and inhibitors are called

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'entities'. RSs model in a direct way the interaction of a living cell with the environment (called 'context'). However, two RSs are seen as independent models and do not interact.

In this paper, we present an encoding from RSs, to the open multiparty process algebra cCNA[4], a variant of the `link`-calculus [5,8] without name mobility. This formalism allows several processes to synchronise and communicate altogether, at the same time, with a new communicating mechanism based on links and link chains. Our initial motivation for introducing this mechanism was to encode Mobile Ambients [12], obtaining a much stronger operational correspondence than any one available in the literature, such as the one in [10]. This allowed us to easily encode calculi for biology equipped with membranes, as in [6]. Process calculi have been used successfully to model biological processes, see [4] for a recent survey. We illustrate our embedding by means of some simple basic examples, and then we consider a more complex example, by modeling a RS representing a regulatory network for *lac* operon, presented in [15]. We also show that our embedding preserves the main features of RSs, and prove its correctness and completeness. Our main contributions are as follows:

- the behaviour of the context, for each single entity, can be specified in a recursive way as an ordinary process;
- our translation results in a cCNA system where from each state only one transition can be generated, thus the cCNA computation is fully deterministic as that of the encoded RS;
- we can express the behaviour of entity mutation, in such a way that the mutated entity s' can take part to only a subset of rules requiring entity s;
- with a little coding effort, two RSs can communicate; i.e. a subset of those entities that the context can provide, are then provided by a second RS.

The main drawback of our proposal, is that the cCNA translation is verbose. Nevertheless it is clear that our translation can be automatised by means of a proper front-end in an implementation of the `link`-calculus.

As we have remarked, in our translation, Reaction Systems get the ability to interact between them in a synchronized manner. This interaction is not foreseen in the basic RS framework, as it can only happen with the context. By exploiting recursion, the kind of interactions which can be defined can be complex and expressive. Example 3 and more in general the discussion in Section 6 show that the interaction between RSs can help to model new scenarios.

Structure of the paper. Section 2 describes RSs and their semantics (interactive processes). Section 3 describes briefly the cCNA process algebra and its operational semantics. Section 4 defines the embedding of RSs in cCNA processes and shows some simple examples to illustrate it. Section 5 shows a more complex example taken from the literature on RSs and illustrates a *lac* operon. Section 6 presents some features and advantages of our embedding for the compositionality of RSs. Finally, Section 7 discusses future work and concludes.

[4] After 'chained Core Network Algebra'.

2 Reaction Systems

Natural Computing is concerned with human-designed computing inspired by nature as well as with computation taking place in nature. The theory of Reaction Systems [9] was born in the field of Natural Computing to model the behaviour of biochemical reactions taking place in living cells. Despite its initial aim, this formalism has shown to be quite useful not only for modeling biological phenomena, but also for the contributions given to computer science [17], theory of computing, mathematics, biology [2,15,1,3], and molecular chemistry [18]. Here we briefly review the basic notions of RSs, see [9] for more details.

The mechanisms that are at the basis of biochemical reactions and thus regulate the functioning of a living cell, are *facilitation* and *inhibition*. These mechanisms are reflected in the basic definitions of Reaction Systems.

Definition 1 (Reaction). *A reaction is a triplet $a = (R, I, P)$, where R, I, P are finite, non empty sets and $R \cap I = \emptyset$. If S is a set such that $R, I, P \subseteq S$, then a is a reaction in S.*

The sets R, I, P are also written R_a, I_a, P_a and called the *reactant set* of a, the *inhibitor set* of a, and the *product set* of a, respectively. All reactants are needed for the reaction to take place. Any inhibitor blocks the reaction if it is present. Products are the outcome of the reaction. Also, $R_a \cup I_a$ is the set of the resources of a and $rac(S)$ denotes the set of all reactions in S. Because R and I are non empty, all products are produced from at least one reactant and every reaction can be inhibited in some way. Sometimes artificial inhibitors are used that are never produced by any reaction. For the sake of simplicity, and without loss of generality, in some examples, we will allow I to be empty.

Definition 2 (Reaction System). *A Reaction System (RS) is an ordered pair $\mathcal{A} = (S, A)$ such that S is a finite set, and $A \subseteq rac(S)$.*

The set S is called the *background set* of $\mathcal{A}$, its elements are called *entities*, and they represent molecular substances (e.g., atoms, ions, molecules) that may be present in the states of a biochemical system. The set A is the set of *reactions* of $\mathcal{A}$. Since S is finite, so is A: we denote by $|A|$ the number of reactions in A.

Definition 3 (Reaction Result). *Given a finite set of entities S, let $T \subseteq S$.*

1. *Let $a \in rac(S)$ be a reaction. Then a is enabled by T, denoted by $en_a(T)$, if $R_a \subseteq T$ and $I_a \cap T = \emptyset$.*
2. *Let $a \in rac(S)$ be a reaction. The result of a on T, denoted by $res_a(T)$, is defined by: $res_a(T) = P_a$ if $en_a(T)$, and $res_a(T) = \emptyset$ otherwise.*
3. *Let $A \subseteq rac(S)$ be a finite set of reactions. The result of A on T, denoted by $res_A(T)$, is defined by: $res_A(T) = \bigcup_{a \in A} res_a(T)$.*

The theory of Reaction Systems is based on the following assumptions.

– **No permanency.** An entity of a set T vanishes unless it is sustained by a reaction. This reflects the fact that a living cell would die for lack of energy, without chemical reactions.

- **No counting.** The basic model of RSs is very abstract and qualitative, i.e. the quantity of entities that are present in a cell is not taken into account.
- **Threshold nature of resources.** From the previous item, we assume that either an entity is available and there is enough of it (i.e. there are no conflicts), or it is not available at all.

The dynamic behaviour of a RS is formalized in terms of *interactive processes*.

Definition 4 (Interactive Process). *Let $\mathcal{A} = (S, A)$ be a RS and let $n \geq 0$. An n-step* interactive process *in $\mathcal{A}$ is a pair $\pi = (\gamma, \delta)$ of finite sequences s.t. $\gamma = \{C_i\}_{i\in[0,n]}$ and $\delta = \{D_i\}_{i\in[0,n]}$ where $C_i, D_i \subseteq S$ for any $i \in [0, n]$, $D_0 = \emptyset$, and $D_i = res_{\mathcal{A}}(D_{i-1} \cup C_{i-1})$ for any $i \in [1, n]$.*

Living cells are seen as open systems that continuously react with the external environment, in discrete steps. The sequence γ is the *context sequence* of π and represents the influence of the environment on the Reaction System. The sequence δ is the *result sequence* of π and it is entirely determined by γ and A. The sequence $\tau = W_0, \ldots, W_n$ with $W_i = C_i \cup D_i$, for any $i \in [0, n]$ is called a *state sequence*. Each state W_i in a state sequence is the union of two sets: the context C_i at step i and the result of the previous step.

For technical reasons, we extend in a straightforward way the notion of an interactive process to deal with infinite sequences.

Definition 5 (extended interactive process). *Let $\mathcal{A} = (S, A)$ be a RS, and let $\pi = (\gamma, \delta)$ be an n-step interactive process, with $\gamma = \{C_i\}_{i\in[0,n]}$ and $\delta = \{D_i\}_{i\in[0,n]}$. Then, let $\pi' = (\gamma', \delta')$ be the extended interactive process of $\pi = (\gamma, \delta)$, defined as $\gamma' = \{C'_i\}_{i\in\mathbb{N}}$, $\delta' = \{D'_i\}_{i\in\mathbb{N}}$, where $C'_j = C_j$ for $j \in [0, n]$ and $C'_j = \emptyset$ for $j > n$, $D'_0 = D_0$ and $D'_j = res_A(D'_{j-1} \cup C'_{j-1})$ for $j \geq 1$.*

The next example shows that the functioning of the interacting processes is deterministic, once the context is fixed.

Example 1. Let $\mathcal{A} = (S, A)$ be a RS with $S = \{s_1, s_2, s_3, s_4\}$, and $A = \{a_1, a_2\}$, where $a_1 = (\{s_1\}, \{s_3\}, \{s_1\})$, $a_2 = (\{s_2\}, \{s_4\}, \{s_2\})$. Now, we show the first three steps of an interacting process $\pi = (\gamma, \delta)$ where the context provides entities as follows: $\gamma = \{C_0 = \{s_1, s_2\}, C_1 = \{s_3\}, C_2 = \{s_1, s_4\}, C_3 = \emptyset, C_4, \ldots, C_n\}$. Initally $D_0 = \emptyset$ and from $C_0 \cup D_0 = \{s_1, s_2\}$ we get to $C_1 \cup D_1 = \{s_1, s_2, s_3\}$ by applying a_1, a_2 (they both are enabled); after that we get to $C_2 \cup D_2 = \{s_1, s_2, s_4\}$, by applying a_2 only (a_1 is not enabled); finally we get to $C_3 \cup D_3 = \{s_1\}$ by applying a_1 (a_2 is not enabled). Thus $\delta = \{D_0 = \emptyset, D_1 = \{s_1, s_2\}, D_2 = \{s_2\}, D_3 = \{s_1\}, D_4, \ldots, D_n\}$. We remark that at every state $C_i \cup D_i$ all the reactions which are enabled are applied, so the computation is deterministic.

3 Chained CNA (cCNA)

In this section we introduce the syntax and operational semantics of a variant of the `link`-calculus [5], the cCNA (chained CNA), where the prefixes are link chains.

Link Chains. Let $\mathcal{C}$ be the set of channels, ranged over by $a, b, ...$, and let $\mathcal{N} = \mathcal{C} \cup \{\tau\} \cup \{\Box\}$ be the set of actions, ranged over by $\alpha, \beta, ...$, where the symbol τ denotes a *silent* action, while the symbol $\Box$ denotes a *virtual* (non-specified) action. A *link* is a pair $\ell = {}^{\alpha}\backslash_{\beta}$; it is *solid* if $\alpha, \beta \neq \Box$; the link ${}^{\Box}\backslash_{\Box}$ is called *virtual*; the link ${}^{\tau}\backslash_{\tau}$ is called *silent*. A link is *valid* if it is solid or virtual. A *link chain* is a finite sequence $v = \ell_1 ... \ell_n$ of valid links $\ell_i = {}^{\alpha_i}\backslash_{\beta_i}$ such that:

1. for any $i \in [1, n-1]$, $\begin{cases} \beta_i, \alpha_{i+1} \in \mathcal{C} & \text{implies } \beta_i = \alpha_{i+1} \\ \beta_i = \tau & \text{iff } \alpha_{i+1} = \tau \end{cases}$
2. $\exists i \in [1, n].\ \ell_i \neq {}^{\Box}\backslash_{\Box}$.

A link chain whose links are silent is also called silent. Virtual links ${}^{\Box}\backslash_{\Box}$ represent missing elements of a chain. The equivalence $\bowtie$ models expansion and contraction of virtual links to adjust the length of a link chain.

Definition 6 (Equivalence $\bowtie$). *We let $\bowtie$ be the least equivalence relation over link chains closed under the axioms (whenever both sides are well defined):*

$$v\,{}^{\Box}\backslash_{\Box} \bowtie v \qquad v_1\,{}^{\Box}\backslash^{\Box}_{\Box}\backslash_{\Box} v_2 \bowtie v_1\,{}^{\Box}\backslash_{\Box} v_2$$
$${}^{\Box}\backslash_{\Box} v \bowtie v \qquad v_1\,{}^{\alpha}\backslash^{a}_{a}\backslash_{\beta} v_2 \bowtie v_1\,{}^{\alpha}\backslash^{\Box}_{a}\backslash^{a}_{\Box}\backslash_{\beta} v_2$$

Two link chains of equal length can be merged whenever each position occupied by a solid link in one chain is occupied by a virtual link in the other chain and solid links in adjacent positions match. Positions occupied by virtual links in both chains remain virtual. Merging is denoted by $v_1 \bullet v_2$. For example, given $v_1 = {}^{a}\backslash^{\Box}_{b}\backslash^{\Box}_{\Box}\backslash_{\Box}$ and $v_2 = {}^{\Box}\backslash^{b}_{\Box}\backslash^{\Box}_{c}\backslash_{\Box}$ we have $v_1 \bullet v_2 = {}^{a}\backslash^{b}_{b}\backslash^{\Box}_{c}\backslash_{\Box}$.

Some names in a link chain can be restricted as non observable and transformed into silent actions τ. This is possible only if they are matched by some adjacent link. Restriction is denoted by $(\nu\, a)v$. For example, given $v = {}^{a}\backslash^{b}_{b}\backslash^{\Box}_{c}\backslash_{\Box}$ we have $(\nu\, b)v = {}^{a}\backslash^{\tau}_{\tau}\backslash^{\Box}_{c}\backslash_{\Box}$.

Syntax. The cCNA processes are generated by the following grammar:

$$P, Q ::= \textstyle\sum_{i \in I} v_i.P_i \ \mid\ P|Q \ \mid\ (\nu\, a)P \ \mid\ P[\phi] \ \mid\ A$$

where v_i is a link chain, ϕ is a channel renaming function, and A is a process identifier for which we assume a definition $A \triangleq P$ is available in a given set Δ of (possibly recursive) process definitions. We let $\mathbf{0}$, the inactive process, denote the empty summation.

The syntax of cCNA extends that of CNA [8] by allowing to use link chains as prefixes instead of links. This extension was already discussed in [8] and it preserves all the main formal properties of CNA. For the rest it features nondeterministic choice, parallel composition, restriction, relabelling and possibly recursive definitions of the form $A \triangleq P$ for some constant A. Here we do not consider name mobility, which is present instead in the `link`-calculus.

$$\frac{v \bowtie v_j \quad j \in I}{\sum_{i\in I} v_i.P_i \xrightarrow{v} P_j}\ (Sum) \qquad \frac{P \xrightarrow{v} P' \qquad (A \triangleq P) \in \Delta}{A \xrightarrow{v} P'}\ (Ide)$$

$$\frac{P \xrightarrow{v} P'}{P[\phi] \xrightarrow{\phi(v)} P'[\phi]}\ (Rel) \qquad \frac{P \xrightarrow{v} P'}{(\nu\, a)P \xrightarrow{(\nu\, a)v} (\nu\, a)P'}\ (Res)$$

$$\frac{P \xrightarrow{v} P'}{P|Q \xrightarrow{v} P'|Q}\ (Lpar) \qquad \frac{P \xrightarrow{v'} P' \qquad Q \xrightarrow{v} Q'}{P|Q \xrightarrow{v\bullet v'} P'|Q'}\ (Com)$$

Fig. 1: SOS semantics of the cCNA (rules (*Rel*) and (*Rpar*) omitted).

Semantics. The operational semantics of cCNA is defined in the SOS style by the inference rules in Fig.1. The rules are reminiscent of those for Milner's CCS and they essentially coincide with those of CNA in [8], except for the presence of prefixes that are link chains instead of single links. Briefly: rule (*Sum*) selects one alternative and uses, as a label, a possible contraction/expansion v of the link chain v_j in the selected prefix; rule (*Ide*) selects one transition of the process defined by a constant; rule (*Rel*) renames the channels in the label as indicated by ϕ; rule (*Res*) restricts some names in the label (it cannot be applied when $(\nu\, a)v$ is not defined); rules (*Lpar*) and (*Rpar*) account for interleaving in parallel composition; rule (*Com*) synchronises interactions (it cannot be applied when $v \bullet v'$ is not defined). Analogously to CNA, the operational semantics of cCNA satisfies the so called Accordion Lemma: whenever $P \xrightarrow{v} Q$ and $v' \bowtie v$ then $P \xrightarrow{v'} Q$. As a matter of notation, we write $P \to Q$ when $P \xrightarrow{v} Q$ for some silent link chain v and call it a *silent transition*. Similarly, a sequence of j silent transitions is denoted $P \to^j Q$.

3.1 Notation for link chains

Hereafter we make use of some new notations for link chains that will facilitate the presentation of our translation.

Definition 7 (Replication). *Let υ be a link chain. Its n times replication υ^n is defined recursively by letting $\upsilon^0 = \epsilon$ (i.e. the empty chain) and $\upsilon^n = \upsilon^{n-1}\upsilon$, with the hypothesis that all the links in the resulting link chains match.*

For example, the expression $({}^{a}\backslash{}^{\square}_{b}\backslash_{\square})^3$ denotes the chain ${}^{a}\backslash{}^{\square}_{b}\backslash{}^{a}_{\square}\backslash{}^{\square}_{b}\backslash{}^{a}_{\square}\backslash{}^{\square}_{b}\backslash_{\square}$. We introduce the *half link* that will be used in conjunction with the *open block of chain* to form regular link chains. Let ${}^{a}\backslash$ denote the *half left link* of a link ${}^{a}\backslash_{x}$, and conversely let $\backslash_{a}$ denote the *half right link* of ${}^{x}\backslash_{a}$.

Definition 8 (Open block). *Let R be a totally ordered, finite set of names. We define an* open block *as $\left(\bigbackslash_{c\,\in\,R}{}^{\square}_{c_i}\backslash{}^{c_o}_{\square}\right)$, where c_i and c_o are annotated version of the name c, as follows*

set	*open block expression*	*result*
$R = \emptyset$	$\left(\lVert_{c \in R} \overset{\square}{c_i} \backslash \overset{c_o}{\square}\right)$	ϵ
$R = \{a\}$	$\left(\lVert_{c \in R} \overset{\square}{c_i} \backslash \overset{c_o}{\square}\right)$	$\overset{\square}{a_i} \backslash \overset{a_o}{\square}$
$R = \{a\} \uplus R'$ *with* $a = \min R$	$\left(\lVert_{c \in R} \overset{\square}{c_i} \backslash \overset{c_o}{\square}\right)$	$\overset{\square}{a_i} \backslash \overset{a_o}{\square} \backslash \left(\lVert_{c \in R'} \overset{\square}{c_i} \backslash \overset{c_o}{\square}\right)$

We then combine half links and open blocks to form regular link chains. For example, for $R = \{a, b\}$ the expression $\left(\lVert_{c \in R} \overset{\square}{c_i} \backslash \overset{c_o}{\square}\right)$ denotes the block of chains $\overset{\square}{a_i} \backslash \overset{a_o}{\square} \backslash \overset{\square}{b_i} \backslash \overset{b_o}{\square}$; and the expression $\overset{r_1}{} \backslash \left(\lVert_{c \in R} \overset{\square}{c_i} \backslash \overset{c_o}{\square}\right) \backslash_{r_2}$ denotes the chain $\overset{r_1}{} \backslash \overset{\square}{a_i} \backslash \overset{a_o}{\square} \backslash \overset{\square}{b_i} \backslash \overset{b_o}{\square} \backslash_{r_2}$.

4 From Reaction Systems to cCNA

Here we present a translation from Reaction Systems to cCNA. The idea is to define separated processes for representing the behaviour of each entity, each reaction, and for the provisioning of each entity by the context.

Processes for entities. Given an entity $s \in S$, we exploit four different names for the interactions over s: names s_i, s_o are used to test the presence of s in the system; names $\hat{s}_i$, $\hat{s}_o$ are used to test the provisioning of s from the context; names $\tilde{s}_i$, $\tilde{s}_o$ are used to test the production of s by some reaction; names $\overline{s}_i$, $\overline{s}_o$ are used to test the absence of s in the system; and names $\underline{s}_i$, $\underline{s}_o$ are used to test the absence of s from the context. We let P_s be the process implementing the presence of s in the system, and $\overline{P_s}$ its absence. They are defined below:

$$
\begin{aligned}
P_s \triangleq\ & \textstyle\sum_{h \geq 0, k \geq 0} \left(\overset{s_i}{} \backslash \overset{\square}{s_o} \backslash_{\square}\right)^h \ \overset{\hat{s}_i}{} \backslash \overset{\square}{\hat{s}_o} \backslash_{\square} \left(\overset{\tilde{s}_i}{} \backslash \overset{\square}{\tilde{s}_o} \backslash_{\square}\right)^k . P_s \\
& + \\
& \textstyle\sum_{h \geq 0, k \geq 1} \left(\overset{s_i}{} \backslash \overset{\square}{s_o} \backslash_{\square}\right)^h \ \overset{\underline{s}_i}{} \backslash \overset{\square}{\underline{s}_o} \backslash_{\square} \left(\overset{\tilde{s}_i}{} \backslash \overset{\square}{\tilde{s}_o} \backslash_{\square}\right)^k . P_s \\
& + \\
& \textstyle\sum_{h \geq 0} \left(\overset{s_i}{} \backslash \overset{\square}{s_o} \backslash_{\square}\right)^h \ \overset{\underline{s}_i}{} \backslash_{\underline{s}_o} . \overline{P_s}
\end{aligned}
$$

$$
\begin{aligned}
\overline{P_s} \triangleq\ & \textstyle\sum_{h \geq 0, k \geq 0} \left(\overset{\overline{s}_i}{} \backslash \overset{\square}{\overline{s}_o} \backslash_{\square}\right)^h \ \overset{\hat{s}_i}{} \backslash \overset{\square}{\hat{s}_o} \backslash_{\square} \left(\overset{\tilde{s}_i}{} \backslash \overset{\square}{\tilde{s}_o} \backslash_{\square}\right)^k . P_s \\
& + \\
& \textstyle\sum_{h \geq 0, k \geq 1} \left(\overset{\overline{s}_i}{} \backslash \overset{\square}{\overline{s}_o} \backslash_{\square}\right)^h \ \overset{\underline{s}_i}{} \backslash \overset{\square}{\underline{s}_o} \backslash_{\square} \left(\overset{\tilde{s}_i}{} \backslash \overset{\square}{\tilde{s}_o} \backslash_{\square}\right)^k . P_s \\
& + \\
& \textstyle\sum_{h \geq 0} \left(\overset{\overline{s}_i}{} \backslash \overset{\square}{\overline{s}_o} \backslash_{\square}\right)^h \ \overset{\underline{s}_i}{} \backslash_{\underline{s}_o} . \overline{P_s}
\end{aligned}
$$

The first line of P_s accounts for the case where s is tested for presence by h reactions and produced by k reactions, while being provided by the context $\left(\overset{\hat{s}_i}{} \backslash_{\hat{s}_o}\right)$. Thus, s will be present at the next step (the continuation is P_s). Here h and k are not known a priori and therefore any combination is possible. By knowing the number of reactions that test s, we can bound the maximum values of h and k. The second line accounts for the analogous case where s is not provided by the context $\left(\overset{\underline{s}_i}{} \backslash_{\underline{s}_o}\right)$. The condition $k \geq 1$ guarantees that s will

remain present (the continuation is P_s). The third line accounts for the case where s is tested for presence by h reactions, but it is neither produced nor provided by the context. Therefore, in the next step s will be absent in the system (the continuation is $\overline{P_s}$). Note that in the case of $\overline{P_s}$ the test for presence of s in the system is just replaced by the test for its absence. As before, s will be present again in the system if s will be produced (rows 1 and 2 in $\overline{P_s}$ code), or if the context will provide it (row 1 in $\overline{P_s}$ code).

Processes for reactions. We assume that each reaction a is assigned a progressive number j. The process for reaction $a_j = (R_j, I_j, P_j)$ must assert either the possibility to apply the reaction or its impossibility. The first case happens when all its reactants are present (the link ${}^{s_i}\backslash_{s_o}$ is requested for any $s \in R_j$) and all its inhibitors are absent (the link ${}^{\overline{e}_i}\backslash_{\overline{e}_o}$ is requested for any $e \in I_j$), then the product set is released (the link ${}^{\tilde{c}_i}\backslash_{\tilde{c}_o}$ is requested for any $c \in P_j$). The next case can happen for two reasons: one of the reactants is absent (the link ${}^{\overline{s}_i}\backslash_{\overline{s}_o}$ is requested for some $s \in R_j$) or one of the inhibitors is present (the link ${}^{e_i}\backslash_{e_o}$ is requested for some $e \in I_j$). The process is recursive so that reactions can be applied at any step.

$$
\begin{aligned}
P_{a_j} \triangleq\ & {}^{r_j}\backslash \Big(\Big\backslash\!\Big\backslash_{s \in R_j} {}^{\square}\backslash^{s_o}_{s_i}\Big)\backslash \Big(\Big\backslash\!\Big\backslash_{e \in I_j} {}^{\square}\backslash^{\overline{e}_o}_{\overline{e}_i}\Big)\backslash^{\square}_{r_{j+1}} \backslash^{p_j}_{\square} \backslash \Big(\Big\backslash\!\Big\backslash_{c \in P_j} {}^{\square}\backslash^{\tilde{c}_o}_{\tilde{c}_i}\Big)\backslash_{p_{j+1}}.P_{a_j} && \{a_j \text{ is applicable}\} \\
& + \\
& \textstyle\sum_{s \in R_j} {}^{r_j}\backslash^{\square}_{\overline{s}_i}\backslash^{\overline{s}_o}_{\square}\backslash^{\square}_{r_{j+1}} \backslash^{p_j}_{\square}\backslash_{p_{j+1}}.P_{a_j} && \{a_j \text{ is not applicable}\} \\
& + \\
& \textstyle\sum_{e \in I_j} {}^{r_j}\backslash^{\square}_{e_i}\backslash^{e_o}_{\square}\backslash^{\square}_{r_{i+1}} \backslash^{p_j}_{\square}\backslash_{p_{j+1}}.P_{a_j} && \{a_j \text{ is not applicable}\}
\end{aligned}
$$

Formally speaking, the definition of the case when a_j is applicable (row 1) requires R_j, I_j and P_j to be totally ordered, because open block expressions are used. It is worth noting that the chosen orders are inessential for exploiting P_{a_j} in the encoding of a RS, but they are needed to disambiguate its definition. Without loss of generality, we assume that all the entities are enumerated, likewise reactions, so that R_j, I_j and P_j inherit the same order. We exploit names r_j, p_j to join the chains provided by the application of all the reactions. Channels r_j and r_{j+1} enclose the enabling/disabling condition of reaction a_j. Channels p_i and p_{j+1} enclose the links related to the entities produced by a_j. We will see that all the link chain labels of transitions follow the same schema: first we find all the reactions limited to the reactants and inhibitors (chained using r_j channels), then all the supplies by the contexts (chained using cxt_j channels, to be introduced next), and finally the products for all the reactions (chained using p_j channels). In the following there is an example explaining this schema.

Processes for contexts. For each entity $s \in S$, we introduce another process Cxt_s, participating in each transition and determining whether the entity s is provided by the context or not. As already said, we assume that entities are enumerated and use the names cxt_j to concatenate the chains formed by the application of all the contexts. For each entity s with number j, at step $n > 0$ there are two

possible behaviours:

$$Cxt_s^n \triangleq \begin{cases} cxt_j \backslash^{\square}_{\hat{s}_i} \backslash^{\hat{s}_o}_{\square} \backslash_{cxt_{j+1}}.Cxt_s^{n+1} & \text{if the context provides } s \text{ at the } n\text{-th step} \\ cxt_j \backslash^{\square}_{\underline{s}_i} \backslash^{\underline{s}_o}_{\square} \backslash_{cxt_{j+1}}.Cxt_s^{n+1} & \text{otherwise} \end{cases}$$
$$Cxt_s \triangleq Cxt_s^1$$

We only consider Cxt_s^n with $n > 0$, as the entities such that $s \in C_0$ (resp. $s \notin C_0$) are modeled by the P_s processes (resp. $\overline{P_s}$) in the initial cCNA process. The intrinsic modularity of cCNA allows us to run different context behaviours for the same system by changing the definitions of Cxt_s^n.

Definition 9 (Translation). *Let $\mathcal{A} = (S, A)$ be a RS, and let $\pi = (\gamma, \delta)$ be an extended interactive process in $\mathcal{A}$, with $\gamma = \{C_i\}_{i \in \mathbb{N}}$. We define its cCNA translation $[\![\mathcal{A}, \gamma]\!]$ as follows:*

$$[\![\mathcal{A}, \gamma]\!] = (\nu\, reacts, cxts, ents, prods)(\Pi_{s \in C_0} P_s | \Pi_{s \notin C_0} \overline{P_s} | \Pi_{a \in A} P_a | \Pi_{s \in S} Cxt_s),$$

with $reacts$ be the set of reaction names r_j, $cxts$ the set of context names cxt_j, $ents$ the set of decorated entity names $\{s_i, s_o, \hat{s}_i, \hat{s}_o, \tilde{s}_i, \tilde{s}_o, \overline{s}_i, \overline{s}_o, \underline{s}_i, \underline{s}_o | s \in S\}$, and $prods$ be the set of names p_j associated to each reaction. In the following, we set $names = reacts \cup cxts \cup ents \cup prods$. For notational convenience, we fix that $r_1 = \tau$, $r_{u+1} = cxt_1$ for u the number of reacts, and $cxt_{w+1} = p_1$ $p_{u+1} = \tau$ for w the number of entities.

It is important to observe that, for each transition, our cCNA encoding requires all the processes P_a, with $a \in A$, and Cxt_s and P_s, with $s \in S$, be interacting in that transition. This is due to the fact that all the channels r_j, p_j, cxt_j, and s_i, and s_o are restricted. Each reaction defines a pattern to be satisfied, i.e. each reaction inserts as many virtual links as the number of reactants, inhibitors, and products, as required by the corresponding reaction.

Lemma 1. *Let $\mathcal{A} = (S, A)$ be a RS and let $\pi = (\gamma, \delta)$ be an extended interactive process in $\mathcal{A}$. Let $P = [\![\mathcal{A}, \gamma]\!]$ its cCNA translation. If there exists P' such that $t = (P \xrightarrow{(\nu\, names)\upsilon} P')$ is a transition of P, then*

1. *for each reaction $a_j \in A$, the corresponding channels r_j and p_j appear in υ; for each entity $s_h \in S$ (where h is the identifying number of s), the corresponding channel s_h (suitably decorated), and the corresponding channel cxt_h appear in υ;*
2. *for each reaction $a \in A$ and each entity $s \in S$, each virtual link offered by processes P_a and Cxt_s is overlapped by exactly one solid link offered by processes representing entities.*

Example 2. Let $\mathcal{A}$ be a RS whose specification contains two entities, $s1$ and $s2$, and, among the others, the reaction $a = (\{s1\}, \{\dots\}, \{s1\})$ that guarantees the persistence of the entity $s1$ once it is present in the system. Note that we use here a dummy inhibitor $(\dots)$ which will never be present. Then, we assume an

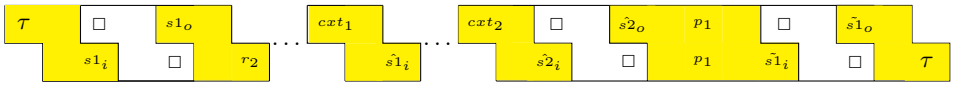

Fig. 2: The link chain structure arising from reactions and context processes.

extended interactive process $\pi = (\gamma, \delta)$ where the context γ provides $s1$ and $s2$. Our translation includes the processes:

$$P_a \triangleq \tau\backslash^{\square}_{s1_i}\backslash^{s1_o}_{\square}\backslash^{\square}_{r_2}\backslash^{p_1}_{\square}\backslash^{\square}_{\tilde{s1}_i}\backslash^{\tilde{s1}_o}_{\square}\backslash_{p_2}.P_a + \ldots;$$

$$P_{s1} \triangleq s1_i\backslash^{\square}_{s1_o}\backslash^{\hat{s1}_i}_{\square}\backslash^{\square}_{\hat{s1}_o}\backslash^{\tilde{s1}_i}_{\square}\backslash_{\tilde{s1}_o}.P_{s1} + \ldots; \qquad P_{s2} \triangleq \hat{s2}_i\backslash_{\hat{s2}_o}.P_{s2} + \ldots;$$

$$Cxt_{s1} \triangleq cxt_1\backslash^{\square}_{\hat{s1}_i}\backslash^{\hat{s1}_o}_{\square}\backslash_{cxt_2}.Cxt_{s1} \qquad Cxt_{s2} \triangleq cxt_2\backslash^{\square}_{\hat{s2}_i}\backslash^{\hat{s2}_o}_{\square}\backslash_{p_1}.Cxt_{s2}$$

Now, we assume that $s1$ is in the initial state of $\mathcal{A}$, and in Figure 2 we show the structure of a link chain label related to the execution of a transition of the cCNA system: $(\nu\, names)(P_{s1}|P_{s2}|P_a|\ldots|Cxt_{s1}|Cxt_{s2})$. The yellow blocks are referred to the processes encoding the reactions (P_a, in our case) and the contexts (Cxt_{s1} and Cxt_{s2}). As the figure puts in evidence, these two kinds of processes determine the structure of the link chain, from end to end, i.e. from the left τ to the right one. We could say that these processes form the *backbone* of the interaction. In contrast, the processes encoding the entities (P_{s1}, and P_{s2}, in our case) provides the solid links to overlap the virtual links of the backbone.

Example 2 outlines two different roles of the processes defining the translation of an interactive process: those processes encoding the reactions and the context provide the backbone of each transition, whereas the processes encoding the entities provide the resources needed for the communication to take place.

With the next proposition, we analyse the structure of a cCNA process encoding of a reactive process after one step transition. In the following four statements, for brevity, we let $\mathcal{A} = (S, A)$ be a RS, and let $\pi = (\gamma, \delta)$ be an extended interactive process in A, with $\gamma = \{C_i\}_{i\in\mathbb{N}}$ and $\delta = \{D_i\}_{i\in\mathbb{N}}$. Moreover, we denote by π^j the shift of π starting at the j-th state sequence; formally we let $\pi^j = (\gamma^j, \delta^j)$ with $\gamma^j = \{C'_i\}_{i\in\mathbb{N}}$, $\delta^j = \{D'_i\}_{i\in\mathbb{N}}$ such that $C'_0 = C_j \cup D_j$, $D'_0 = \emptyset$, and $C'_i = C_{i+j}$, $D'_i = D_{i+j}$ for any $i \geq 1$.

Proposition 1 (Correctness 1). *Let $P = [\![\mathcal{A}, \gamma]\!]$ with*

$$P = (\nu\, names)(\Pi_{a\in A}P_a|\Pi_{s\in S}Cxt^1_s|\Pi_{s\in C_0}P_s|\Pi_{s\notin C_0}\overline{P}_s).$$

If $P \xrightarrow{v} Q$, then v is a silent action and $Q = [\![\mathcal{A}, \gamma^1]\!]$, namely

$$Q = (\nu\, names)(\Pi_{a\in A}P_a|\Pi_{s\in S}Cxt^2_s|\Pi_{s\in C_1\cup D_1}P_s|\Pi_{s\notin C_1\cup D_1}\overline{P}_s).$$

Now, we extend the previous result to a series of transitions.

Corollary 1 (Correctness 2). *Let $P = [\![\mathcal{A}, \gamma]\!]$ and $j \geq 1$. If there exists Q such that $P \rightarrow^j Q$, then $Q = [\![\mathcal{A}, \gamma^j]\!]$.*

Conversely, we prove that the cCNA process $[\![\mathcal{A}, \gamma]\!]$ can simulate all the evolutions of the underlying interactive process.

Proposition 2 (Completeness 1). $[\![\mathcal{A}, \gamma]\!] \rightarrow [\![\mathcal{A}, \gamma^1]\!]$.

Now, we extend the previous result to a series of transitions.

Corollary 2 (Completeness 2). $[\![\mathcal{A}, \gamma]\!] \rightarrow^j [\![\mathcal{A}, \gamma^j]\!]$.

5 Example: *lac* operon

In this section we present the encoding of a RS example taken from [15].

5.1 The *lac* operon

An operon is a cluster of genes under the control of a single promoter. The *lac* operon is involved in the metabolism of lactose in *Escherichia coli* cells; it is composed by three adjacent structural genes (plus some regulatory components): $lacZ$, $lacY$ and $lacA$ encoding for two enzymes Z and A, and a transporter Y, involved in the digestion of the *lactose*. The main regulations are:

- the gene $lacI$ encodes a repressor protein I;
- the DNA sequence, called *promoter*, is recognised by a RNA polymerase to iniziate the transcription of the genes $lacZ$, $lacY$ and $lacA$;
- a DNA segment, called the *operator* (OP), obstructs the RNA polymerase functionality when the repressor protein I is bound to it forming I-OP;
- a short DNA sequence, called the CAP-*binding site*, when it is bound to the complex composed by the protein CAP and the signal molecule $cAMP$, acts as a promoter for the interaction between the RNA polymerase and the promoter.

The functionality of the *lac* operon depends on the integration of two control mechanisms, one mediated by *lactose*, and the other one mediated by *glucose*.

In the first control mechanism, an effect of the absence of the *lactose* is that I is able to bind the operator sequence preventing the *lac* operon expression. If lactose is available, I is unable to bind the operator sequence, and the *lac* operon can be potentially expressed.

In the second control mechanism, when glucose is absent, the molecule $cAMP$ and the protein CAP increase the *lac* operon expression, thanks to the fact that the binding between the molecular complex $cAMP$-CAP and the CAP-*binding site* increases. In summary, the condition promoting the operon gene expression is when the *lactose* is present and the *glucose* is absent.

In the following we report the description of the *lac* operon mechanism in the reaction system formalism and then show its encoding in cCNA.

5.2 The RS formalization

The reaction system for the *lac* operon is defined as $A_{lac} = (S, A)$, where the set S represents the main biochemical components involved in this genetic system, while the reaction set A contains the biochemical reactions involved in the regulation of the *lac* operon expression. Formally, the *lac* operon reaction system is defined as follows: S is the set

$$\{lac, Z, Y, A, lacI, I, I\text{-}OP, cya, cAMP, crp, CAP, cAMP\text{-}CAP, lactose, glucose\},$$

and A consists of the following 10 reactions:

$$\begin{array}{ll}
a_1 = (\{lac\}, \{...\}, \{lac\}), & a_6 = (\{cya\}, \{...\}, \{cAMP\}), \\
a_2 = (\{lacI\}, \{...\}, \{lacI\}), & a_7 = (\{crp\}, \{...\}, \{crp\}), \\
a_3 = (\{lacI\}, \{...\}, \{I\}), & a_8 = (\{crp\}, \{...\}, \{CAP\}), \\
a_4 = (\{I\}, \{lactose\}, \{I\text{-}OP\}), & a_9 = (\{cAMP, CAP\}, \{glucose\}, \{cAMP\text{-}CAP\}), \\
a_5 = (\{cya\}, \{...\}, \{cya\}), & a_{10} = (\{lac, cAMP\text{-}CAP\}, \{I\text{-}OP\}, \{Z, Y, A\}).
\end{array}$$

The default context (DC) is composed by those entities that are always present in the system $DC = \{lac, lacI, I, cya, cAMP, crp, CAP\}$, whereas the *lactose* and the *glucose* are given non-deterministically by the context.

5.3 The RS encoding

For the sake of readability, the encoding we propose exploits the specific features of the example in hand to perform some simplifications:

- for the entities in the default context, $s \in DC$, as they are persistent, we do not provide the $\overline{P_s}$ processes and the Cxt_s processes;
- for the reactions requiring the presence of entities $s \in DC$, we do not provide the reaction alternative behaviour when s is absent;
- the Cxt_s processes are specified only for those entitiess that are really provided by the context.

Moreover, we do not model the *dummy* entity that is specified by dots ($\ldots$) by the RS reactions in Section 5.2. Finally, we exclude the *duplication reactions* (a_1, a_2, a_5, a_7), and renumber the remaining reactions :

old	new	reactions
a_3	a_1	$= (\{lacI\}, \{...\}, \{I\})$,
a_4	a_2	$= (\{I\}, \{lactose\}, \{I\text{-}OP\})$,
a_6	a_3	$= (\{cya\}, \{...\}, \{cAMP\})$,
a_8	a_4	$= (\{crp\}, \{...\}, \{CAP\})$,
a_9	a_5	$= (\{cAMP, CAP\}, \{glucose\}, \{cAMP\text{-}CAP\})$,
a_{10}	a_6	$= (\{lac, cAMP\text{-}CAP\}, \{I\text{-}OP\}, \{Z, Y, A\})$.

Expression reactions. First we define the parametric process

$$P_i(s1, s2) \triangleq {}^{r_i}\!\!\setminus^{\square}_{s1_i} \setminus^{s1_o}_{\square} \setminus^{\square}_{r_{i+1}} \setminus^{p_i}_{\square} \setminus^{\square}_{\tilde{s2}_i} \setminus^{\tilde{s2}_o}_{\square} \setminus_{p_{i+1}}.P_i(s1, s2)$$

Then, we let $P_{a1} \triangleq P_1(lacI, I)$, $P_{a3} \triangleq P_3(cya, cAMP)$, and $P_{a4} \triangleq P_4(crp, CAP)$.

Regulation reactions.

$$P_{a2} \triangleq {}^{r_2}\backslash^{\Box}_{I_i}\backslash^{I_o}_{\Box}\backslash^{\Box}_{\overline{lactose}_i}\backslash^{\overline{lactose}_o}_{\Box}\backslash^{\Box}_{r_3}\backslash^{p_2}_{\Box}\backslash^{\Box}_{\widetilde{I\text{-}OP}_i}\backslash^{\widetilde{I\text{-}OP}_o}_{\Box}\backslash_{p_3}.P_{a2}$$
$$+$$
$${}^{r_2}\backslash^{\Box}_{lactose_i}\backslash^{lactose_o}_{\Box}\backslash^{\Box}_{r_3}\backslash^{p_2}_{\Box}\backslash_{p_3}.P_{a2} \;+\; {}^{r_2}\backslash^{\Box}_{\overline{I}_i}\backslash^{\overline{I}_o}_{\Box}\backslash^{\Box}_{r_3}\backslash^{p_2}_{\Box}\backslash_{p_3}.P_{a2}$$

$$P_{a5} \triangleq {}^{r_5}\backslash^{\Box}_{cAMP_i}\backslash^{cAMP_o}_{\Box}\backslash^{\Box}_{CAP_i}\backslash^{CAP_o}_{\Box}\backslash^{\Box}_{\overline{glucose}_i}\backslash^{\overline{glucose}_o}_{\Box}\backslash^{\Box}_{r_6}\backslash^{p_5}_{\Box}\backslash^{\Box}_{\widetilde{cAMP\text{-}CAP}_i}\backslash^{\widetilde{cAMP\text{-}CAP}_o}_{\Box}\backslash_{p_6}.P_{a5}$$
$$+$$
$${}^{r_5}\backslash^{\Box}_{glucose_i}\backslash^{glucose_o}_{\Box}\backslash^{\Box}_{r_6}\backslash^{p_5}_{\Box}\backslash_{p_6}.P_{a5}$$
$$+$$
$${}^{r_5}\backslash^{\Box}_{\overline{cAMP}_i}\backslash^{\overline{cAMP}_o}_{\Box}\backslash^{\Box}_{r_6}\backslash^{p_5}_{\Box}\backslash_{p_6}.P_{a5} \;+\; {}^{r_5}\backslash^{\Box}_{\overline{CAP}_i}\backslash^{\overline{CAP}_o}_{\Box}\backslash^{\Box}_{r_6}\backslash^{p_5}_{\Box}\backslash_{p_6}.P_{a5}$$

$$P_{a6} \triangleq {}^{r_6}\backslash^{\Box}_{lac_i}\backslash^{lac_o}_{\Box}\backslash^{\Box}_{cAMP\text{-}CAP_i}\backslash^{cAMP\text{-}CAP_o}_{\Box}\backslash^{\Box}_{\overline{I\text{-}OP}_i}\backslash^{\overline{I\text{-}OP}_o}_{\Box}\backslash^{\Box}_{cxt_1}\backslash^{p_6}_{\Box}\backslash^{\Box}_{\tilde{z}_i}\backslash^{\tilde{z}_o}_{\Box}\backslash^{\Box}_{\tilde{y}_i}\backslash^{\tilde{y}_o}_{\Box}\backslash^{\Box}_{\tilde{A}_i}\backslash^{\tilde{A}_o}_{\Box}\backslash_{\tau}.P_{a6}$$
$$+$$
$${}^{r_6}\backslash^{\Box}_{I\text{-}OP_i}\backslash^{I\text{-}OP_o}_{\Box}\backslash^{\Box}_{cxt_1}\backslash^{p_6}_{\Box}\backslash_{\tau}.P_{a6}$$
$$+$$
$${}^{r_6}\backslash^{\Box}_{\overline{lac}_i}\backslash^{\overline{lac}_o}_{\Box}\backslash^{\Box}_{cxt_1}\backslash^{p_6}_{\Box}\backslash_{\tau}.P_{a6} \;+\; \backslash^{\Box}_{\overline{cAMP\text{-}CAP}_i}\backslash^{\overline{cAMP\text{-}CAP}_o}_{\Box}\backslash^{\Box}_{cxt_1}\backslash^{p_6}_{\Box}\backslash_{\tau}.P_{a6}$$

Processes for the entities. We exploit the specificity of the example in hand to optimise the code, and we specify exactly the number of solid links that each process encoding an entity must offer. For the always present entities we let:

$$P_{cya} \triangleq {}^{cya_i}\backslash_{cya_o}.P_{cya} \qquad P_{crp} \triangleq {}^{crp_i}\backslash_{crp_o}.P_{crp}$$
$$P_{lacI} \triangleq {}^{lacI_i}\backslash_{lacI_o}.P_{lacI} \qquad P_{lac} \triangleq {}^{lac_i}\backslash_{lac_o}.P_{lac}$$

For the entities always produced (i.e. not present only at the first step), we provide a parametric definition $P_e(s) \triangleq {}^{s_i}\backslash^{\Box}_{s_o}\backslash^{\tilde{s}_i}_{\Box}\backslash_{\tilde{s}_o}.P_e(s) + {}^{\tilde{s}_i}\backslash_{\tilde{s}_o}.P_e(s)$.
There are three entities of the second type:

$$P_{cAMP} \triangleq P_e(cAMP) \qquad P_{CAP} \triangleq P_e(CAP) \qquad P_I \triangleq P_e(I).$$

The entity *I-OP* can be either produced (by a_2) or tested for absence (by a_6). Correspondingly, the process $P_{I\text{-}OP}$ is defined as follows:

$$P_{I\text{-}OP} \triangleq \textstyle\sum_{h=0}^{1}({}^{I\text{-}OP_i}\backslash^{\Box}_{I\text{-}OP_o}\backslash_{\Box})^h \, {}^{\widetilde{I\text{-}OP}_i}\backslash_{\widetilde{I\text{-}OP}_o}.P_{I\text{-}OP} \;+\; {}^{I\text{-}OP_i}\backslash_{I\text{-}OP_o}.\overline{P_{I\text{-}OP}}$$
$$\overline{P_{I\text{-}OP}} \triangleq \textstyle\sum_{h=0}^{1}({}^{\overline{I\text{-}OP}_i}\backslash^{\Box}_{\overline{I\text{-}OP}_o}\backslash_{\Box})^h \, {}^{\widetilde{I\text{-}OP}_i}\backslash_{\widetilde{I\text{-}OP}_o}.P_{I\text{-}OP} \;+\; {}^{\overline{I\text{-}OP}_i}\backslash_{\overline{I\text{-}OP}_o}.\overline{P_{I\text{-}OP}}$$

The process $P_{cAMP\text{-}CAP}$ is similar to $P_{I\text{-}OP}$, as it is produced by a_5 and tested for presence by a_6. Its code is omitted.

The *lactose* is provided by the context and tested for absence by a_2.

$$P_{lactose} \triangleq \sum_{h=0}^{1} (^{lactose_i}\backslash^{\Box}_{lactose_o}\backslash\Box)^h \ \widehat{^{lactose_i}\backslash_{lactose_o}}.P_{lactose} + \sum_{h=0}^{1} (^{lactose_i}\backslash^{\Box}_{lactose_o}\backslash\Box)^h \ \underline{^{lactose_i}\backslash_{lactose_o}}.\overline{P_{lactose}}$$

$$\overline{P_{lactose}} \triangleq \sum_{h=0}^{1} (^{\overline{lactose_i}}\backslash^{\Box}_{\overline{lactose_o}}\backslash\Box)^h \ \widehat{^{lactose_i}\backslash_{lactose_o}}.P_{lactose} + \sum_{h=0}^{1} (^{\overline{lactose_i}}\backslash^{\Box}_{\overline{lactose_o}}\backslash\Box)^h \ \underline{^{lactose_i}\backslash_{lactose_o}}.\overline{P_{lactose}}$$

The process $P_{glucose}$ is similar to $P_{lactose}$ and tested for absence by a_5. Its code is omitted.

The entity z can only be produced by rule a_6, while it is never provided by the context. Moreover, there is no rule for testing its presence or absence.

$$P_z \triangleq \tilde{z}_i\backslash^{\Box}_{\tilde{z}_o}\backslash^{z_i}_{\Box}\backslash_{\underline{z_o}}.P_z \ + \ \underline{^{z_i}\backslash_{z_o}}.\overline{P_z} \qquad \overline{P_z} \triangleq \tilde{z}_i\backslash^{\Box}_{\tilde{z}_o}\backslash^{z_i}_{\Box}\backslash_{\underline{z_o}}.\overline{P_z} \ + \ \underline{^{z_i}\backslash_{z_o}}.\overline{P_z}$$

The entities y and A are treated likewise z. Their processes are omitted.

Context. The entities in DC are assumed always present by default, so no context process is needed for them. The entities z, y, and A are assumed never provided by the context:

$$Cxt_z \triangleq {}^{cxt_1}\backslash^{\Box}_{\underline{z_i}}\backslash^{z_o}_{\Box}\backslash_{cxt_2}.Cxt_z \qquad Cxt_y \triangleq {}^{cxt_2}\backslash^{\Box}_{\underline{y_i}}\backslash^{y_o}_{\Box}\backslash_{cxt_3}.Cxt_y$$
$$Cxt_A \triangleq {}^{cxt_3}\backslash^{\Box}_{\underline{A_i}}\backslash^{A_o}_{\Box}\backslash_{cxt_4}.Cxt_A$$

Also, for the sake of presentation, we assume that the *glucose* is never provided and *lactose* is always provided by the context:

$$Cxt_{lactose} \triangleq {}^{cxt_4}\backslash^{\Box}_{\widehat{lactose_i}}\backslash^{\widehat{lactose_o}}_{\Box}\backslash_{cxt_5}.Cxt_{lactose}$$
$$Cxt_{glucose} \triangleq {}^{cxt_5}\backslash^{\Box}_{\underline{glucose}_i}\backslash^{\overline{glucose}_o}_{\Box}\backslash_{p_1}.Cxt_{glucose}$$

In the following we let $CXT \triangleq Cxt_z|Cxt_y|Cxt_A|Cxt_{lactose}|Cxt_{glucose}$ be the processes for context. The whole system is as follows:

$$lacOp \triangleq (\nu\, names)(\Pi_{i=1}^{6} P_{ai}|\Pi_{s\in DC}P_s|\Pi_{s\in S\setminus DC}\overline{P}_s|CXT)$$

Execution. Now, we show the execution of two transitions. After the first transition, the entity *cAMP-CAP* is produced due to the absence of *glucose*(see P_{a5}), while the presence of *lactose* inhibits the production of *I-OP* (see P_{a2}): $lacOp \xrightarrow{(\nu\, names)v} lacOp'$, where

$$v = {}^{\tau}\backslash_{lac_i}\ldots{}^{lactose_o}\backslash_{r3}\ldots{}^{r_5}\backslash_{cAMP_i}\ldots{}^{\overline{glucose}_o}\backslash_{r_6}\ldots{}^{p_5}\backslash_{\widehat{cAMP\text{-}CAP}_i}\ldots{}^{p_6}\backslash_{\tau}$$
$$lacOp' \triangleq (\nu\, names)(\Pi_{i=1}^{6} P_{ai}|\Pi_{s\in AP}P_s|\Pi_{s\in S\setminus AP}\overline{P}_s|CXT)$$

with $AP = DC \cup \{cAMP\text{-}CAP\}$ the actual context.
After the second step the entities z, y and A are produced, due to the presence of

$cAMP\text{-}CAP$ and the absence of $I\text{-}OP$ (see P_{a6}), thus $lacOp' \xrightarrow{(\nu\, names)v'} lacOp''$ where:

$$v' = {}^{\tau}\backslash_{lac_i} \dots {}^{lac_o}\backslash_{cAMP-CAP_i} \dots {}^{\overline{I-OP}_o}\backslash^{\dots}_{cxt_1} \underline{glucose}_o \backslash^{p_1}_{p_1} \backslash^{p_6}_{\dots} \backslash^{\tilde{z}_i}_{\tilde{z}_i} \backslash^{\tilde{z}_o}_{\tilde{z}_o} \backslash^{\tilde{y}_i}_{\tilde{y}_i} \backslash^{\tilde{y}_o}_{\tilde{y}_o} \backslash^{\tilde{A}_i}_{\tilde{A}_i} \backslash^{\tilde{A}_o}_{\tilde{A}_o} \backslash_{\tau}$$

$$lacOp'' \triangleq (\nu\, names)(\Pi_{i=1}^{6} P_{ai} | \Pi_{s \in AP'} P_s | \Pi_{s \in S \setminus AP'} \overline{P}_s | CXT)$$

with $AP' = DC \cup \{z, y, A\}$.

6 Enhanced Reaction Systems

Our encoding increases the expressivity of RS concerning: the behaviour of the context, the possibility of alternative behaviour of mutated entities and the communication between two different reaction systems. It is important to note that our encoding guarantees that from each state, in the cCNA transition system, only one transition comes out, as the dynamics is totally deterministic.

6.1 Recursive contexts

In RS, the behaviour of the context is finite. For the first n steps, it is specified which are the entities that are provided from the context. Using cCNA we can describe in a natural way the behaviour of the context in a recursive way. Then, the context behaviour would not necessarily end after n steps, and could be infinite. For example, in an extended interactive process, we may want that the entity s is intermittently provided by the context every two steps:

$$\begin{array}{lll}
Cxt_s \triangleq {}^{cxt_j}\backslash^{\square}_{\hat{s}_i}\backslash^{\hat{s}_o}_{\square}\backslash_{cxt_{j+1}}.Cxt_{s'}, & \text{context provides } s; \\
Cxt_{s'} \triangleq {}^{cxt_j}\backslash^{\square}_{\underline{s}_i}\backslash^{\underline{s}_o}_{\square}\backslash_{cxt_{j+1}}.Cxt_{s''}, & \text{context doesn't provide } s; \\
Cxt_{s''} \triangleq {}^{cxt_j}\backslash^{\square}_{\underline{s}_i}\backslash^{\underline{s}_o}_{\square}\backslash_{cxt_{j+1}}.Cxt_{s}, & \text{context doesn't provide } s.
\end{array}$$

6.2 Mutating entities

In RS, when an entity is present, it can potentially be involved in each reaction where it is required. With a few more lines of code, in cCNA it is possible to describe the behaviour of a mutation of an entity, in a way that the mutated version of the entity can take part to only a subset of the rules requiring the *normal version* of the entity. For example, let us assume that entity $s1$ is consumed by reactions $a1$ and $a2$. Reaction $a1$ produces $s1$ if $s2$ is present, otherwise $a1$ produces a mutated version of $s1$, say $s1'$. When $s1'$ is produced, reaction $a1$ behaves in the same way as if $s1$ would be absent, whereas $a2$ recognises the presence of $s1'$ and behaves in the same way as if $s1$ would be present. Technically, in both cases it is enough to add one more non deterministic choice in the code of P_{a1} and P_{a2}.

$rs1$	$rs2$
$a_1 = (s, \ , x)$	$a_2 = (y, \ , s)$

Table 1: The two reaction systems $rs1$ and $rs2$.

6.3 Communicating reaction systems

We sketch how it is possible to program two RS encodings, in a way that the entities that usually come from context of one RS will be provided instead from the other RS.

Example 3. Let $rs1$ and $rs2$ be two RSs, defined by the rules in Table 1.
Now, we set our example such that the two contexts, for $rs1$ and $rs2$, do not provide any entities. We also assume that entity s in $rs1$ is provided by $rs2$, as $rs2$ produces a quantity of s that is enough for $rs1$ and $rs2$. For technical reasons, we can not use the same name for s in both the two RSs, then we use the name ss in $rs2$. We need to modify our translation technique to suite this new setting. As we do not model contexts, we introduce *dummy* channel names dx and dss to model the case x and ss are not produced. Also, thanks to the simplicity of the example, we can leave out the use of the p_i channels. This streamlining does not affect the programming technique we propose to make two RSs communicate. First, we translate the reaction in $rs1$:

$$[\![a_1]\!] \triangleq P_{a_1} \triangleq {}^{\tau}\backslash^{\square}_{s_i}\backslash^{s_o}_{\square}\backslash^{\square}_{\tilde{x}_i}\backslash^{\tilde{x}_o}_{\square}\backslash_{a_2}.P_{a_1} + {}^{\tau}\backslash^{\square}_{\overline{s}_i}\backslash^{\overline{s}_o}_{\square}\backslash^{\square}_{dx_i}\backslash^{dx_o}_{\square}\backslash_{a_2}.P_{a_1}$$

Please note, that prefixes of process P_{a_1} end with the channel name a_2, as the link chain is now connected with the reaction of $rs2$. The translation for the entities follows.

$$[\![s]\!] \triangleq \begin{array}{l} P_s \triangleq {}^{s_i}\backslash^{\square}_{s_o}\backslash^{\hat{s}_i}_{\square}\backslash_{\hat{s}_o}.P_s + {}^{s_i}\backslash_{s_o}.\overline{P_s} \\ \overline{P_s} \triangleq {}^{\overline{s}_i}\backslash^{\square}_{\overline{s}_o}\backslash^{\hat{s}_i}_{\square}\backslash_{\hat{s}_o}.P_s + {}^{\overline{s}_i}\backslash_{\overline{s}_i}.\overline{P_s} \end{array} \qquad [\![x]\!] \triangleq \begin{array}{l} P_x \triangleq {}^{\tilde{x}_i}\backslash_{\tilde{x}_o}.P_x + {}^{dx_i}\backslash_{dx_o}.\overline{P_x} \\ \overline{P_x} \triangleq {}^{\tilde{x}_i}\backslash_{\tilde{x}_o}.P_x + {}^{dx_i}\backslash_{dx_o}.\overline{P_x} \end{array}$$

The translation for the $rs2$ follows.

$$[\![a_2]\!] \triangleq P_{a_2} \triangleq {}^{a_2}\backslash^{\square}_{y_i}\backslash^{y_o}_{\square}\backslash^{\square}_{\tilde{s}s_i}\backslash^{\tilde{s}s_o}_{\square}\backslash_{\tau}.P_{a_2} + {}^{a_2}\backslash^{\square}_{\overline{y}_i}\backslash^{\overline{y}_o}_{\square}\backslash^{\square}_{dss_i}\backslash^{dss_o}_{\square}\backslash_{\tau}.P_{a_2}$$

In the translation of the entities in $rs2$, we introduce the mechanism that allows the entity s (ss in $rs2$) to be provided in $rs1$. Every time ss is produced in $rs2$, a virtual link is created to synchronise with $rs1$ on link ${}^{\hat{s}_i}\backslash_{\hat{s}_o}$:

$$[\![ss]\!] \triangleq \begin{array}{l} P_{ss} \triangleq {}^{\tilde{s}s_i}\backslash^{\square}_{\hat{s}_i}\backslash^{\hat{s}_o}_{\square}\backslash_{\tilde{s}s_o}.P_{ss} + {}^{dss_i}\backslash_{dss_o}.\overline{P_{ss}} \\ \overline{P_{ss}} \triangleq {}^{\tilde{s}s_i}\backslash^{\square}_{\hat{s}_i}\backslash^{\hat{s}_o}_{\square}\backslash_{\tilde{s}s_o}.P_{ss} + {}^{dss_i}\backslash_{dss_o}.\overline{P_{ss}} \end{array} \qquad [\![y]\!] \triangleq \begin{array}{l} P_y \triangleq {}^{y_i}\backslash_{y_o}.\overline{P_y} \\ \overline{P_y} \triangleq {}^{\overline{y}_i}\backslash_{\overline{y}_o}.\overline{P_y} \end{array}$$

We now assume that the initial system is $S \triangleq (\nu\, names)(P_{a_1}|P_{a_2}|P_s|P_y|\overline{P_x}|\overline{P_{ss}})$, i.e. only entities s and y are present. Now, the only possible transition has the following label (that we report without restriction):

$$\tau\backslash^{s_i}_{s_i}\backslash^{s_o}_{s_o}\backslash^{\tilde{x}_i}_{\tilde{x}_i}\backslash^{\tilde{x}_o}_{\tilde{x}_o}\backslash^{a_2}_{a_2}\backslash^{y_i}_{y_i}\backslash^{y_o}_{y_o}\backslash^{\tilde{s}s_i}_{\tilde{s}s_i}\backslash^{\hat{s}_i}_{\hat{s}_i}\backslash^{\hat{s}_o}_{\hat{s}_o}\backslash^{\tilde{s}s_o}_{\tilde{s}s_o}\backslash_{\tau},$$

where the black links belong to the prefixes of P_{a_1}, and P_{a_2}, the blue links belong to P_s, the gray links belong to P_y, and $\overline{P_x}$ and the red links belong to $\overline{P_{ss}}$. After the execution, the entity s is still present in $rs1$ as it has been provided by $rs2$.

As we have briefly sketched, our model of two *communicating reaction systems* can enable the study of the behaviour of one RS in relation to another one. Thus, the products of the reactions of one RS can become the input for another one. This could allow for a modular approach to modeling complex systems, by composing different Reaction Systems.

7 Conclusion

In this paper we have exploited a variant of the `link`-calculus where prefixes are link chains and no more single links. This variant was already briefly discussed by the end of [8]. This variant allowed us to define an elegant embedding of reaction systems, an emerging formalism to model computationally biochemical systems. This translation shows several benefits. For instance, the context behaviour can also be expressed recursively; entity mutations can be expressed easily; reaction systems can communicate between them.

We believe that our embedding can contribute to extend the applications of reaction systems to diverse fields of computer science, and life sciences. As we have already mentioned, the evolution of each process resulting from our embedding is deterministic, thus we do not have the problem of having infinitely many transitions in the produced labelled transition system. In any case, we can exploit the implementation of the symbolic semantics of the `link`-calculus [11] that is available at [19].

As future work, we plan to implement a prototype of our framework, with an automatic translation from RSs to the `link`-calculus. We believe that our work can also help to extend the framework of RSs towards a model which can improve the communication between different RSs. We also believe that our work can make possible to investigate how to apply formal techniques to prove properties of the modeled systems [13,20,7,16,14].

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