Biochemical Space Language
in Relation to Multiset Rewriting Systems

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Abstract. This technical report relates Biochemical Space Language (BCSL) [4] to Multiset rewriting systems (MRS) [3]. For a BCSL model, the semantics are defined in terms of transition systems, while for an MRS, they are defined in terms of a set of runs. In this report, we relate BCSL to MRS by first showing how the transition system is related to a set of runs and consequently showing how for every BCSL model, an MRS can be constructed such that both represent the same set of runs. The motivation of this step is to establish BCSL in the context of a more general rewriting system and benefit from properties shown for them. Finally, we show that regulations defined for MRS can be consequently used in the BCSL model.

1 Multiset rewriting systems

This section recalls some definitions and known results about multisets and rewriting systems over them. Intuitively, a multiset is a set of elements with allowed repetitions. A multiset rewriting rule describes how a particular multiset is transformed into another one. A multiset rewriting system consists of a set of rewriting rules, defining how the system can evolve, and an initial multiset, representing the starting point for the rewriting.

Definition 1. Multiset
Let \( S \) be a finite set of elements. A multiset over \( S \) is a total function \( \mu : S \rightarrow \mathbb{N} \) (where \( \mathbb{N} \) is the set of natural numbers including 0). For each \( a \in S \) the multiplicity (the number of occurrences) of \( a \) is the number \( \mu(a) \).

Operations and relations over multisets are defined in a standard way, taking into account the repetition of elements.

Definition 2. Operations and relations over multisets
- Union: \( \forall a \in S. (\mu_1 \cup \mu_2)(a) = \mu_1(a) + \mu_2(a) \)
- Difference: \( \forall a \in S. (\mu_1 \setminus \mu_2)(a) = \begin{cases} \mu_1(a) - \mu_2(a) & \text{if } \mu_2(a) \leq \mu_1(a) \\ 0 & \text{otherwise} \end{cases} \)
- Intersection: \( \forall a \in S. (\mu_1 \cap \mu_2)(a) = \min\{\mu_1(a), \mu_2(a)\} \)
- Submultiset: \( \forall a \in S. \mu_1(a) \leq \mu_2(a) \)
- Equality: \( \mu_1 = \mu_2 : \forall a \in S. \mu_1(a) = \mu_2(a) \)
- Occurrence \( \forall a \in \mathbb{M} : \exists a \in S. \mu(a) \geq 1 \)

Definition 3. Multiset rewriting rule
A multiset rewriting rule over \( S \) is a pair \( \mu = (\bullet \mu, \mu^*) \) of multisets over \( S \), usually written as \( \mu : \bullet \mu \rightarrow \mu^* \) for convenience.

The rule rewrites elements specified in the left-hand multiset \( \bullet \mu \) to elements specified in the right-hand multiset \( \mu^* \).

Definition 4. Multiset rewriting system
A multiset rewriting system (MRS) over \( S \) is a pair \( \mathcal{M} = (\mathcal{X}, \mathcal{M}_0) \), where \( \mathcal{X} \) is a finite set of multiset rewrite rules and \( \mathcal{M}_0 \) is the initial multiset (state), both over \( S \).

We denote by MRS the class of multiset rewriting systems.

Definition 5. Enabled rule
Let \( \mathcal{M} = (\mathcal{X}, \mathcal{M}_0) \) be an MRS, both over \( S \). A rule \( \mu \in \mathcal{X} \) is enabled at \( \mathcal{M} \) if \( \bullet \mu \subseteq \mathcal{M} \).

Definition 6. Rule application
The application of an enabled rule \( \mu \in \mathcal{X} \) to \( \mathcal{M} \), written \( \mathcal{M} \xrightarrow{\mu} \mathcal{M}' \), creates a multiset \( \mathcal{M}' = (\mathcal{M} \setminus \bullet \mu) \cup \mu^* \).
Definition 7. Run
A run $\pi$ of $M$ is an infinite sequence of multisets $\pi = M_0 M_1 M_2 \ldots$ such that for any step $i > 0$ holds that $M_{i-1} \rightarrow_\mu M_i$ for some $\mu \in X$. We denote by $\pi[i]$ the multiset created in step $i$.

Definition 8. Run label
A run label $\pi$ of a run $\pi$ is an infinite sequence of rules $\pi = \mu_1 \mu_2 \mu_3 \ldots$ such that for any step $i > 0$ holds that $\pi[i-1] \rightarrow_\mu \pi[i]$. We denote by $\pi[i]$ the rule applied in step $i$.

Definition 9. Semantics
The semantics of system $M$ is an (infinite) set $L(M)$ of all possible runs such that $\forall \pi \in L(M). \pi[0] = M_0$ (i.e. runs start in the initial multiset).

To ensure the infiniteness of runs, we implicitly assume the presence of a special empty rule $\varepsilon = (\emptyset, \emptyset)$. We require that this rule can be applied only when no other rule of the system is enabled. It also ensures that the set of rules $X$ is always non-empty.

2 BioChemical Space Language

In this section we provide declarative definition of BioChemical Space Language. A constructive (or imperative) version of the definition is available in [4].

Let $V_\delta, V_a, V_s, V_c$ be mutually exclusive finite sets of names of features, names of atomic and structure components, and compartments, respectively.

| Term        | Satisfying axioms |
|-------------|-------------------|
| multisets   | $M_1 + M_2 \equiv M_2 + M_1$  |
|             | $M + \emptyset \equiv M$      |
| chains      | chain.component \equiv component.chain |
| compositions| composition, atomic \equiv atomic, composition  |
|             | $\emptyset$, composition \equiv composition  |

Table 2: Table defining axioms of structural congruence $\equiv$ for particular terms from BCSL grammar.

In Table 1 we provide a fragment of complete syntax\(^1\) of BCSL, capturing agents and multisets, where the terminal (in capitals) $\text{FEATURE} \in V_\delta$ is from given set of feature names, $\text{NAME} \in V_a$ (resp. $\text{NAME} \in V_s$) is from given set of atomic (resp. structure) component names, and $\text{COMPARTMENT} \in V_c$ is from given set of compartments. We restrict ourselves only to finite expressions and require that an atomic name occurs at most once in a composition. On top of this syntax, several syntactic extensions [4] are build providing more convenient and succinct notation.

For simplicity, we denote by $M$ a multiset and by $M$ the set of all multisets. We assume the structural congruence $\equiv$ to be the least congruence on terms from Table 2 satisfying respective axioms. That is, two multisets (or any terms) are equal if they are structurally congruent.

The structural congruence $\equiv$ allows us to formally define the algebraic multiset operations $\in, \subseteq, \cup, \cap$ and $\setminus$ on BCSL multisets. For example, $\text{agent} \in M$ corresponds to $\exists M' \in M. M \equiv \text{agent} + M'$ and $M \subseteq M'$ corresponds to $\exists M'' \in M. M' \equiv M + M''$. Moreover, by $M(\text{agent})$ we denote the number of occurrences of agent $\text{agent}$ in the multiset $M$.

\(^1\) https://github.com/sybila/eBCSgen/wiki/Model-syntax#complete-syntax
Definition 10. Signature
Atomic signature $\sigma_s : V_s \rightarrow 2^V_s$ is a function from an atomic name to a non-empty set of feature names. Set of possible atomic signatures is denoted as $\Sigma_s$. Structure signature $\sigma_s : V_s \rightarrow 2^V_s$ is a function from a structure name to a set of atomic names. Set of possible structure signatures is denoted as $\Sigma_s$.

Definition 11. Pattern
Let $V_s = V_b \cup \{\varepsilon\}$ be a set of feature names extended by a special symbol $\varepsilon$. Pattern $P$ is defined according to the same grammar as multiset but with $\text{FEATURE} \in V_s$. We denote by $\mathbb{P}$ the set of all patterns.

The two patterns are equal if they are structurally equal (the congruence relation defined on multisets does not apply). Finally, a pattern is well-formed if the atoms are alphanumerically sorted in compositions with respect to their names. From now on, we assume only well-formed patterns.

Remark 1. In the following text, there is often a situation when a pattern $P$ is compared to a multiset $M$. In such a case, we treat the pattern as a multiset too (i.e. they are equal if they are structurally congruent according to Table 2). Moreover, it holds that $\varepsilon \neq \delta$ for any $\delta \in V_b$.

Definition 12. Instantiation
An instantiation function $I : \mathbb{P} \rightarrow \mathbb{P}$ assigns to every atomic $A$ in $P$ with feature $\varepsilon$ a feature $\delta \in \sigma_s(A)$. By $I(P)$ we denote a finite set of all possible instantiations $I(P)$ of pattern $P$.

We define deatomisation of pattern $P$, written $d(P)$, as a sequence of atoms preserving the order of their occurrence in the pattern. Note that this applies to atoms in both chains and compositions.

Definition 13. Consistent instantiations
Let us have two finite patterns $P, P'$ with deatomisations $d(P) = A_1, A_2, \ldots, A_n$ and $d(P') = A'_1, A'_2, \ldots, A'_m$. Next, let us have two instantiations $I(P) \in I(P)$ and $I(P') \in I(P')$ with their deatomisations $d(I(P)) = I(A_1), I(A_2), \ldots, I(A_n)$ and $d(I(P')) = I(A'_1), I(A'_2), \ldots, I(A'_m)$. We say the instantiations $I(P), I(P')$ are consistent, written $I(P) \Delta I(P')$, if $\forall i < \min(m, n)$ holds that $A_i = A'_i \Rightarrow I(A_i) = I(A'_i)$.

Consistency of two instantiations ensures that the same features are assigned in the same positions.

Definition 14. Pattern expansion
Pattern expansion is a function $\langle \cdot \rangle : \mathbb{P} \rightarrow \mathbb{P}$ which extends a given pattern $P$ to a pattern $\langle P \rangle$ such that every occurrence of a composition of a structure is expanded by atoms whose names are not yet present in the composition and are defined in the given signature $\sigma_s(\text{structure})$. These newly added atoms have assigned feature $\varepsilon$ and are inserted to the composition in such way that they preserve the alphanumerical order.

Definition 15. BCSL rule
A BCSL rule $R$ is a pair $(P_l, P_r) \in \mathbb{P} \times \mathbb{P}$, usually written as $P_l \rightarrow P_r$.

The rule describes a structural change of a multiset defined by the difference between left-hand and right-hand patterns.

Definition 16. BCSL model
A BCSL model $B$ is a tuple $(\mathcal{R}, \sigma_s, \sigma_a, M_0)$ such that $\mathcal{R}$ is a finite set of rewrite rules, $\sigma_s \in \Sigma_s$ is a structure signature, $\sigma_a \in \Sigma_a$ is an atomic signature, and $M_0 \in M$ is an initial multiset.

Definition 17. BCSL rewriting
Let $B = (\mathcal{R}, \sigma_s, \sigma_a, M_0)$ be a BCSL model. The rewriting of the multisets is given by labelled transition relation $M_1 \xrightarrow{R} M_2$ with $M_1, M_2 \in M$ and $R : P_l \rightarrow P_r$ satisfying the following inference rule:

$$\exists I(P_l) \in I(P_l). \quad I(P_l) = M_l$$

$$\exists I(P_r) \in I(P_r). \quad I(P_r) = M_r$$

$$I(P_l) \Delta I(P_r)$$

$$M + M_l \xrightarrow{R} M + M_r$$

The rewriting of the multisets gives semantics to the model. Intuitively, for pattern $P_l$, the corresponding agents from the state are found and consequently replaced according to pattern $P_r$. Applying such an operation transitively, starting in the initial multiset, yields a labelled transition system (Definition 18). An example of an LTS is available in Figure 2, corresponding to an example model from Figure 1.

Definition 18. Labelled transition system LTS
Labelled transition system $\text{LTS}(B) = (S, T, L)$ of a BCSL model $B$ is obtained by transitive rewriting of the initial state, where $S$ is a set of states (a state is a multiset of agents), $T$ is a set of transitions (a transition corresponds to the application of a rule), and $L$ is labelling function assigning to each transition an identifier of applied rule.
#! rules
r₁_S ~ P(S{i})::cell ⇒ P(S{a})::cell
r₁_T ~ P(T{i})::cell ⇒ P(T{a})::cell
r₂ ~ P()::cell ⇒ P()::out

#! inits
1 P(S{i},T{i})::cell

Fig. 1: An example of BCSL model. A single agent P can be modified on its two active sites, S and T. Both sites can be independently activated in respective rules. Additionally, the agent can be transported to another compartment outside the cell. All rules are labelled using label ~ prefix. Initially, there is a single P agent present with both sites inactivated. Please note the signature functions do not need to be explicitly defined as they can be gathered automatically from the model (in this case, Σₐ(M) = Σₐ(T) = {i, a} and Σₐ(P) = {S, T}).

Fig. 2: Transition system of the model from Figure 1 in a tree-like representation. The double circled state is the initial state, with contents defined in inits part.

3 Systems comparison

This section shows how an MRS can be constructed for any BCSL model and that such an MRS exhibits equivalent behaviour to the original BCSL model.

3.1 MRS construction

In this section, we show how an MRS \( \mathcal{M} = (\mathcal{A}, \mathcal{M}_0) \) can be constructed from a BCSL model \( \mathcal{B} = (\mathcal{R}, \Sigma_a, \Sigma_s, S_0) \). This approach is based on grounding agents and rules (supplement the missing context – Definition 19). In particular, we need to do two steps – construct the support set of elements (Definition 20) by grounding all possible agents, and then construct the set of multiset rewriting rules by grounding each BCSL rule, creating its possible instantiations in terms of multisets (Definition 22).

The abstraction provided by BCSL rules allowing to express patterns needs to be grounded in concrete multisets. Informally, this is accomplished by supplementing the context information from the signature functions to the patterns, obtaining particular realisations of patterns. In Definition 19, there is formal definition of grounding function \( \Theta \), which uses an instantiation of patterns (Definition 12).

Definition 19. Grounding function \( \Theta \)

We define grounding function for a pattern \( P \) as a set of all its possible instantiated multisets \( \Theta(P) = \{ I(P) \mid I(P) \in I(\mathcal{P}) \} \). Applied to a rule \( r \), we obtain a set of all possible reactions using consistent instantiations \( \Theta(r) \equiv \Theta(lhs \Rightarrow rhs) = \{ I(lhs) \Rightarrow I(rhs) \mid I(lhs) \in I(lhs) \land I(rhs) \in I(rhs) \land I(lhs). \Delta I(rhs) \} \), where \( I(lhs) \) and \( I(rhs) \) are treated as multisets (Remark 1).

In Definition 20, we show how to create a set of all possible unique agents present in the model, which can be considered as the set of elements. It is constructed from initial state \( \mathcal{M}_0 \) and a set of rules \( \mathcal{R} \) with the information provided in signature functions. We assume that the initial state \( \mathcal{M}_0 \) contains agents which are already grounded.

Definition 20. Set of elements

Let \( \mathcal{S}_0 \) be a set of unique elements from initial state \( \mathcal{M}_0 \) and \( \mathcal{S}_\mathcal{R} \) be a set of all possible grounded agents present in the rules \( \mathcal{R} \) defined as \( \mathcal{S}_\mathcal{R} = \{ A \in \Theta(A') \mid A' \in \mathcal{A}(r) \land r \in \mathcal{R} \} \), where \( \mathcal{A}(r) = lhs \cup rhs \) is a set of all agents used in rule \( r = \text{lhs} \Rightarrow \text{rhs} \). Then, the set of all possible unique agents present in the model is \( \mathcal{S} = \mathcal{S}_0 \cup \mathcal{S}_\mathcal{R} \).
We show how to construct a set of MRS rewriting rules from a BCSL rule in Definition 22. The approach is straightforward since the grounding function $\Theta$ creates the set of all possible grounded rules (reactions). Then, we need to create a pair of multisets from both sides of each grounded rule. The obtained pair of multisets can be directly considered as multiset rewriting rule over support set $S$, because all the possible agents are already present in the set $S$ (follows from its construction). We call such rule MRS instantiation of the BCSL rule (Definition 21).

**Definition 21. MRS instantiation**

Let $r = \text{lhs} \Rightarrow \text{rhs}$ be a BCSL rule. We define MRS instantiation $\mu(r)$ of rule $r$ as a multiset rewriting rule $\mu(r) = (L, R)$ where $L \Rightarrow R \in \Theta(\text{lhs} \Rightarrow \text{rhs})$.

**Definition 22. Set of rules**

Let $R$ be a set of BCSL rules. The corresponding set of MRS rules $\mathcal{X}$ is defined as a set of all possible MRS instantiations $\mathcal{X} = \{\mu(r) \mid r \in R\}$.

We obtain the MRS $\mathcal{M} = (\mathcal{X}, \mathcal{M}_0)$ over the set of elements $S$ (Definition 20) by taking constructed set of multiset rewriting rules $\mathcal{X}$ (MRS instantiations) as shown in Definition 22 and the initial state $\mathcal{M}_0$. In Figure 3 there is an example of the MRS constructed from BCSL model (Figure 1) using this approach.

\[
\mathcal{S} = \begin{cases} 
S(i, T[i]) :: \text{cell}, 
S[a, T[i]] :: \text{cell}, 
S[i, T[a]] :: \text{cell}, 
\end{cases}
\]

(a) Set of all unique objects.

\[
\mathcal{M} = \begin{cases} 
\mathcal{M}_0 = \{S[i, T[i]] :: \text{cell}\}, 
\mu_{i+1} : \{S[i, T[i]] :: \text{cell}\} \rightarrow \{S[a, T[i]] :: \text{cell}\}, 
\mu_{i+2} : \{S[i, T[i]] :: \text{cell}\} \rightarrow \{S[a, T[i]] :: \text{cell}\}, 
\mu_{i+3} : \{S[i, T[i]] :: \text{cell}\} \rightarrow \{S[i, T[a]] :: \text{cell}\}, 
\mu_{i+4} : \{S[a, T[i]] :: \text{cell}\} \rightarrow \{S[i, T[a]] :: \text{cell}\}, 
\mu_{i+5} : \{S[a, T[i]] :: \text{cell}\} \rightarrow \{S[a, T[a]] :: \text{cell}\}, 
\mu_{i+6} : \{S[i, T[i]] :: \text{cell}\} \rightarrow \{S[i, T[i]] :: \text{out}\}, 
\mu_{i+7} : \{S[a, T[i]] :: \text{cell}\} \rightarrow \{S[a, T[i]] :: \text{out}\}, 
\mu_{i+8} : \{S[i, T[a]] :: \text{cell}\} \rightarrow \{S[i, T[a]] :: \text{out}\}, 
\mu_{i+9} : \{S[a, T[a]] :: \text{cell}\} \rightarrow \{S[a, T[a]] :: \text{out}\}, 
\end{cases}
\]

(b) Instantiated rules.

Fig. 3: MRS representation of a BCSL model from Figure 1. All the objects in set $S$ are unique strings representing possible forms of original BCSL agents. These are used in multiset rewriting rules and the initial multiset. For convenience, to allow identification of source rule, we label each constructed multiset rewrite rule by $\mu$ where $r$ is the label of source BCSL rule.

### 3.2 BCSL vs. MRS relationship

In subsection 3.1, we provided an approach to constructing an MRS from any BCSL model. In this section, we show that the behaviour of such a constructed MRS is equivalent to the behaviour of the original BCSL model. This is shown in Theorem 1 by considering that the type of states in both systems is the same (Remark 2), both BCSL rule and its MRS instantiation can always be applied to the same state (Lemma 1), and they can always be rewritten to the same states (Lemma 2).

The semantics of MRS are given in terms of a set of infinite runs, while the semantics of BCSL are given in terms of LTS. First, we need to relate these two constructs. We define how a set of runs corresponds to an LTS. To ensure that the LTS represents only infinite runs, we extend it to LTS$_i$ such that we add self-loops on states with no successors labelled by an empty rule $\varepsilon$.

**Definition 23. Run in LTS**

Let $\text{LTS}_i = (S, T, L)$ be a labelled transition system. $\text{LTS}_i$ generates a set of infinite runs $\Sigma(\text{LTS}_i)$ such that the infinite run $\pi = s_0, s_1, s_2, \ldots$ belongs to $\Sigma(\text{LTS}_i)$ if (i) $s_0 \in S$ and (ii) for all $i \geq 1 : (s_{i-1}, s_i) \in T$. Moreover, such a run $\pi$ has a run label $\overrightarrow{r} = l_1, l_2, \ldots, l_n$ such that for all $i \geq 1 : L((s_{i-1}, s_i)) = l_i$.

Remark 2. Multisets in constructed MRS use as elements grounded BCSL agents, and therefore the type of MRS multisets and BCSL multisets is the same and they can be freely interchanged and checked for equality.
From the construction of \(\mathcal{X}\) (Definition 22) follows that for any rule \(1\text{hs} \Rightarrow \text{rhs} \in \mathcal{R}\), the function \(\Theta\) creates grounded rules, which represent all possible instantiations. Then, for any instantiation \(L \Rightarrow \mathcal{R}, L \in \mathcal{R}\) and \(\mathcal{R}\) are used to form a multiset rewriting rule, obtaining an MRS instantiation (Definition 21).

**Lemma 1.** Let \(\mathcal{M}\) be a grounded multiset, \(\mathcal{X} = 1\text{hs} \Rightarrow \text{rhs}\) a BCSL rule, and \(\mu = (\mu, \mu^{*})\) its MRS instantiation. Then, \(\mathcal{r}\) can be applied to \(\mathcal{M}\) if \(\mu\) can be applied to \(\mathcal{M}\).

**Proof.** From construction of \(\mathcal{M}\) we know that to BCSL rules correspond their MRS instantiations.

\[\Rightarrow:\] if \(\mathcal{r}\)

(a) can be applied to \(\mathcal{M}\), then there exists \(L \in \Theta(1\text{hs})\) such that \(L \subseteq \mathcal{M}\) (follows from Definition 17). That means there has to exist an MRS instantiation \(\mu = (\mu, \mu^{*})\) in \(\mathcal{X}\) of rule \(\mathcal{r}\) such that it can be applied to \(\mathcal{M}\) because \(\mu \equiv L\) and therefore \(\mu^{*} \subseteq \mathcal{M}\) and \(\mu\) is enabled.

(b) can not be applied to \(\mathcal{M}\), then for all \(L \in \Theta(1\text{hs})\) holds that \(L \not\subseteq \mathcal{M}\) (follows from Definition 17). That means that any MRS instantiation \(\mu = (\mu, \mu^{*})\) in \(\mathcal{X}\) of rule \(\mathcal{r}\) can not be applied to \(\mathcal{M}\) because \(\mu \equiv L\) and therefore \(\mu^{*} \not\subseteq \mathcal{M}\) and \(\mu\) is not enabled.

\[\Leftarrow:\] Symmetrically, if \(\mu = (\mu, \mu^{*})\)

(a) can be applied to \(\mathcal{M}\), then \(\mu\) is enabled and therefore \(\mu^{*} \subseteq \mathcal{M}\). That means there has to exist a rule \(\mathcal{r}\)

such that \(\mu\) is its MRS instantiation with \(L \in \Theta(1\text{hs})\) where \(\mu \equiv L\). Therefore, also \(L \subseteq \mathcal{M}\) and \(\mathcal{r}\) can be applied to \(\mathcal{M}\).

(b) can not be applied to \(\mathcal{M}\), then \(\mu\) is not enabled and therefore \(\mu^{*} \not\subseteq \mathcal{M}\). That means that any rule \(\mathcal{r}\)

such that \(\mu\) is its MRS instantiation with \(L \in \Theta(1\text{hs})\) where \(\mu \equiv L\), holds that \(L \not\subseteq \mathcal{M}\) and \(\mathcal{r}\) can not be applied to \(\mathcal{M}\).

**Lemma 2.** Let \(\mathcal{M}\) be a grounded multiset, \(\mathcal{X} = 1\text{hs} \Rightarrow \text{rhs}\) a BCSL rule, and \(\mu = (\mu, \mu^{*})\) its MRS instantiation. Then, by applying \(\mathcal{r}\) to \(\mathcal{M}\), we get a set of possible multisets. Among them, there is a multiset \(\mathcal{M}'\) which can be obtained by applying \(\mu\) to \(\mathcal{M}\).

**Proof.** Follows from the definition of BCSL rewriting (Definition 17) where instantiations of both \(1\text{hs}\) and \(\text{rhs}\) of the rule are created, which corresponds to the MRS instantiation \(\mu\) (Definition 21). Then, instantiated agents from \(1\text{hs}\) are subtracted from, and \(\text{rhs}\) agents are added to the current state, which is in parallel with the MRS approach. Finally, from Remark 2 we know that states in BCSL directly correspond to multisets in MRS, which forms the same basis for both formalisms.

Having such constructed MRS \(\mathcal{M}\), we need to show that its behaviour (set of runs) corresponds to the behaviour (transition system) of the BCSL model.

**Theorem 1.**

For any BCSL model \(\mathcal{B} = (\mathcal{R}, \Sigma, \Sigma, \mathcal{M}_0)\) there exists an MRS \(\mathcal{M} = (\mathcal{X}, \mathcal{M}_0)\) with \(\Sigma(\text{LTS}_\mathcal{B}(\mathcal{B})) = \Sigma(\mathcal{M})\).

When we construct the MRS \(\mathcal{M}\) using approach described in subsection 3.1, the proof of the theorem boils down to proving that for any grounded multiset \(\mathcal{M}\) the following two implications hold:

\[\Rightarrow:\] for any BCSL rule \(\mathcal{r} \in \mathcal{R}\) it holds that if \(\mathcal{B}\) can apply \(\mathcal{r}\) to \(\mathcal{M}\) then there exists MRS rule \(\mu \in \mathcal{X}\) such that \(\mathcal{M}\) can apply \(\mu\) to \(\mathcal{M}\)

\[\Leftarrow:\] for any MRS rule \(\mu \in \mathcal{X}\) it holds that if \(\mathcal{M}\) can apply \(\mu\) to \(\mathcal{M}\) then there exists \(\mathcal{r} \in \mathcal{R}\) such that \(\mathcal{M}\) can apply \(\mathcal{r}\) to \(\mathcal{M}\)

and in both cases we obtain the same multiset \(\mathcal{M}'\).

**Proof.** Follows from construction of \(\mathcal{M}\) (construction of corresponding MRS instantiations of rules), Lemma 1 (either both rules are enabled or neither of them is) and Lemma 2 (both rules create identical results).

**4 Regulations**

BCSL models manifest strong nondeterminism, which is natural but often not desired to some extent. Additional knowledge about the described biological system can further reduce possible model behaviour scenarios. These are usually introduced by defining quantitative properties [2]. However, these properties are not always easy to define, and alternative mechanisms are needed.

In the following, we provide an introduction to regulation approaches applied to BCSL. These were introduced in [3] for MRS. To formally establish them in the context of BCSL, we assume the corresponding MRS is constructed first (Theorem 1) and the regulation is applied to it. This can be done because the constructed MRS shares rule labels with the original BCSL model and states and their content are of the same type (Remark 2).
Regular rewriting

In regular rewriting, there is given a $\omega$-regular language $\zeta$ over rules. This explicitly defines sequences of rules that can be used. Only runs with the rule sequence from this language are allowed. Typically, we define the language $\zeta$ using a regular expression.

For example, we define a regular expression $(r_1.S, r_1.T, r_2 | r_1.T, r_1.S)$ as regulation for model from Figure 1. This RE makes sure that first both activation rules are used and then the molecule is exported out of the cell, depending on the order of activation. The effect of regulation on set of runs is depicted in Figure 4.

![Fig. 4: The set of runs of the model with regular regulation.](image)

Ordered rewriting

Ordered regulation defines a partial order on rules. Then it is not allowed to apply a rule immediately after the rule which is higher in the order. Runs that violate this property are not allowed.

For example, we define a partial order $r_1.S < r_2, r_1.T < r_2$ as regulation for model from Figure 1. This order makes sure that rule $r_2$ is never used after rule $r_1.S$ neither rule $r_1.T$. The effect of regulation on set of runs is depicted in Figure 5.

![Fig. 5: The set of runs of the model with ordered regulation.](image)
Programmed rewriting

Programmed regulation defines a set of successor rules to every rule. When a particular rule is used, only its successors are allowed to be used next. Similarly to the previous regulation, Runs which violate this property are not allowed.

For example, we use successor function defined as \( \zeta(r_{1,S}) = \{r_2, r_{1,T}\} \), \( \zeta(r_{1,T}) = \{r_{1,S}\} \), and \( \zeta(r_2) = \emptyset \) as regulation for model from Figure 1. This function makes sure that rule \( r_2 \) is used only after rule \( r_{1,S} \), never after rule \( r_{1,T} \). The effect of regulation on set of runs is depicted in Figure 6.

\[ \begin{align*}
P(S(i),T{i})::cell & \quad P(S{i},T{i})::out \\
P(S{a},T{a})::cell & \quad P(S{i},T{a})::out \\
P(S{i},T{i})::cell & \quad P(S{a},T{i})::cell \\
P(S{a},T{i})::cell & \quad P(S{a},T{a})::cell \\
P(S{a},T{a})::cell & \quad P(S{i},T{a})::out \\
P(S{i},T{a})::out & \quad P(S{a},T{a})::out \end{align*} \]

**Fig. 6:** The set of runs of the model with programmed regulation. The runs correspond to the model from Figure 1 with applied programmed regulation. The runs are represented as possible paths in the tree-like graph, starting in the double circled state (the initial state). The grey states and transition are absent due to effects of the regulation.

Conditional rewriting

Conditional rewriting defines a prohibited context to each rule, that is, a multiset of grounded agents which cannot be present in the current state. Conditional regulation is based on local information and does not need any history of applied rules. Runs that violate this property are not allowed.

Please note that without loss of generality, the prohibited context can contain a set of prohibited multisets, and for then each of them it has to hold that it is not a subset of the current state.

For example, we define prohibited context \( \zeta(r_2) = \{P(S{a},T{i})::cell\} \) as regulation for model from Figure 1. This \( \zeta \) makes sure that rule \( r_2 \) is never used when agent \( P(S{a},T{i})::cell \) is present in the current state. The effect of regulation on set of runs is depicted in Figure 7.

\[ \begin{align*}
P(S(a),T(a))::out & \quad P(S(i),T(i))::out \\
P(S(a),T(a))::cell & \quad P(S(i),T(i))::cell \\
P(S(a),T(a))::cell & \quad P(S(a),T(a))::cell \\
P(S(a),T(a))::cell & \quad P(S(a),T(i))::out \\
P(S(a),T(i))::cell & \quad P(S(a),T(a))::out \\
P(S(a),T(i))::out & \quad P(S(a),T(i))::cell \end{align*} \]

**Fig. 7:** The set of runs of the model with conditional regulation. The runs correspond to the model from Figure 1 with applied conditional regulation. The runs are represented as possible paths in the tree-like graph, starting in the double circled state (the initial state). The grey states and transition are absent due to effects of the regulation.
Concurrent-free rewriting

Concurrent rules are those which consume common agents. Concurrent-free rewriting assigns a priority to one of the concurrent rules. Whenever multiple concurrent rules are applicable in a state, only the prioritised one can be used. Runs that violate this property are not allowed.

For example, we define prioritisation $\zeta = \{(r_1_S, r_2), (r_1_T, r_2)\}$ as regulation for model from Figure 1. This $\zeta$ makes sure that rules $r_1_S$ and $r_1_T$ have always priority over rule $r_2$. The effect of regulation on set of runs is depicted in Figure 8.

Fig. 8: The set of runs of the model with concurrent-free regulation. The runs correspond to the model from Figure 1 with applied concurrent-free regulation. The runs are represented as possible paths in the tree-like graph, starting in the double circled state (the initial state). The grey states and transition are absent due to effects of the regulation.

5 Summary

In this short paper, we first introduce multiset rewriting systems MRS [3] and BioChemical Space language [4]. Then, in subsection 3.1 we show how for any BCSL model, we can construct an MRS such that the corresponding set of runs are equal for both systems. Finally, we introduce regulations in the context of BCSL, formally influencing the runs of respective MRS. This way, we can use regulated BCSL models while they hold properties shown in [3].

References

1. Roger S Scowen. Generic base standards. In Proceedings 1993 Software Engineering Standards Symposium, pages 25–34. IEEE, 1993.
2. Matej Troják, David Šafraňek, Lukrécia Mertová, and Luboš Brim. Parameter synthesis and robustness analysis of rule-based models. In NASA Formal Methods Symposium, pages 41–59. Springer, 2020.
3. Matej Troják, Samuel Pastva, David Šafraňek, and Luboš Brim. Regulated multiset rewriting systems, 2021. arXiv:2111.13036.
4. Matej Troják, David Šafraňek, Luboš Brim, Jakub Šalagovič, and Jan Čerwený. Executable Biochemical Space for Specification and Analysis of Biochemical Systems. Electronic Notes in Theoretical Computer Science, 350:91–116, 2020. Proceedings of SASB 2018, the Ninth International Workshop on Static Analysis and Systems Biology, Freiburg, Germany - August 28th, 2018. doi:https://doi.org/10.1016/j.entcs.2020.06.006.