Abstract Interpretation for Probabilistic Termination of Biological Systems

Roberta Gori
Dipartimento di Informatica
Università di Pisa
Largo Pontecorvo 2
Pisa, Italy
gori@di.unipi.it

Francesca Levi
Dipartimento di Informatica
Università di Pisa
Largo Pontecorvo 2
Pisa, Italy
levifran@di.unipi.it

In [5] the authors applied the Abstract Interpretation approach for approximating the probabilistic semantics of biological systems, modeled specifically using the Chemical Ground Form calculus [3]. The methodology is based on the idea of representing a set of experiments, which differ only for the initial concentrations, by abstracting the multiplicity of reagents present in a solution, using intervals. In this paper, we refine the approach in order to address probabilistic termination properties. More in details, we introduce a refinement of the abstract LTS semantics and we abstract the probabilistic semantics using a variant of Interval Markov Chains [34, 13, 19]. The abstract probabilistic model safely approximates a set of concrete experiments and reports conservative lower and upper bounds for probabilistic termination.

1 Introduction

Process calculi, originally designed for modeling distributed and mobile systems, are nowadays one of the most popular formalisms for the specification of biological systems. In this new application domain, a great effort has been devoted for adapting traditional models to characterize the molecular and biochemical aspects of biological systems. Among them [32, 30, 2], stochastic calculi, based on π-calculus [29, 31], capture the fundamental quantitative aspect (both time and probability) of real life applications. The use of a process calculus as a specification language offers a range of well established methods for analysis and verification that could now be applied to biological system models. These techniques can be applied to complex biological systems in order to test hypotheses and to guide future in vivo experimentations. Stochastic simulators, e.g. [33, 27, 28] for π-calculus, are able to realize virtual experiments on biological system models, while model checking techniques, recently extended also to probabilistic and stochastic models [18, 21], support the validation of temporal properties.

However, the practical application of automatic tools to biological systems revealed serious limitations. One specific feature of biological processes is that they are composed by a huge number of processes with identical behavior, such as thousands of molecules of the same type. Moreover, typically the exact concentrations of molecules are not known, meaning that the hypotheses have to be tested with respect to different scenarios. Thus, different experiments have to be realized and the state space of the models to be analyzed is often very large (even infinite).

Static analysis techniques provide automatic and decidable methods for establishing properties of programs, by computing safe approximations of the (run-time) behavior. This approach has been successfully applied to purely qualitative process calculi for distributed and mobile systems, and recently also to biologically inspired process calculi, in order to validate safety as well as more complex temporal properties [1, 14, 23, 25, 13, 16, 26].
In [5] we have proposed an approximation technique, based on Abstract Interpretation [7, 8], able to address probabilistic temporal properties for a simple calculus, the Chemical Ground Form (CGF)[3]. CGF is a fragment of stochastic π-calculus which is rich enough for modeling the dynamics of biochemical reactions. The abstraction is based on the idea of approximating the information about the multiplicities of reagents, present in a solution, by means of intervals of integers [6]. The approach computes an abstract probabilistic semantics for an abstract system, which approximates the probabilistic semantics, namely the Discrete-Time Markov Chain (DTMC), for any corresponding concrete system. In particular, the validation of an abstract system gives both lower and upper bounds on the probability of temporal properties [17], for a set of concrete systems (experiments) differing only for the concentrations of reagents.

The methodology is illustrated in Fig. 1. As usual, the DTMC of a concrete system is derived from the LTS semantics, by calculating the probability of each move. The technique of abstraction is based on the definition of a suitable abstract LTS semantics for abstract systems, which support the derivation of an abstract probabilistic model, represented by an Interval Markov Chains [34, 13, 19]. In Interval Markov Chains transitions are labeled with intervals of probabilities, representing the uncertainty about the concrete probabilities; consequently, the validation of temporal properties reports lower and upper bounds, rather than exact values, which are obtained by considering the worst-case and best-case scenario w.r.t. all non-deterministic choices. Obviously, the key step of the translation from abstract LTS into the Interval Markov Chain consists in the computation of intervals of probabilities from the information reported by abstract transition labels. A quite precise approximation is achieved because the information reported by transition labels is profitably exploited in order to capture also relational information.

Unfortunately, if one is interested in proving more complex properties of biological systems, such as probabilistic termination [35], the previously proposed abstraction is not sufficiently powerful. For probabilistic termination we have to calculate the probability to reach a terminated state, e.g. a state where the probability to move in any other state is zero.

To illustrate probabilistic termination, we consider the "groupies" example proposed by Cardelli in several tutorials on biochemistry and also reported in [4]. The idea is to study how a set of entities collects behave. The behavior of a single entity is represented by the automaton in Fig. 2 it has
two possible states, $X$ and $Y$. A single automaton performs no interaction, while it may interact with other automata. Two automata in state $X$ are stable since they both offer !$a$ and ?$b$ and no interaction are possible. Analogously for two automata in state $Y$. If one automata is in state $X$ and another is in state $Y$ then either they can interact on channel $a$ and both move to state $X$ or they can interact on channel $b$ and both move to state $Y$. No matter how many automata are in state $X$ or in state $Y$ initially, eventually the groupies form a single homogeneous population of all $X$ or of all $Y$. Thus, these systems always terminate, namely they universally terminate.

The limitation of the abstract LTS semantics, defined in [5], is represented by hybrid states, namely abstract states representing concrete terminated as well as non terminated states. It should be clear that, given an abstract state, the most precise and correct intervals of probabilities, could be derived by considering the minimum and maximum exact probabilities, for each concrete move, respectively. Thus, for an hybrid state we would obtain very approximated intervals of probabilities, such as $[0, 1]$, both for the self-loop and for any other move. This information says that some concrete states may loop forever, while others may move somewhere else. As a consequence, the lower and upper bound probabilities to reach a terminated state, from an hybrid state, are typically zero and one, respectively. This is the case of example for the CGF specification of groupies example, previously commented.

In order to better capture probabilistic termination, we propose in this paper a refinement of our approach, based on a modification of the abstract LTS semantics. More in details, the abstract transition relation is refined so that terminated and non-terminated states are properly separated, and consequently hybrid states are never generated. To this aim, it may be necessary to replace a single abstract transition, corresponding to a given reaction, by a set of abstract transitions, leading to different abstract target states. Such distinct abstract transitions model the same reaction but with different concentrations of reactants. This situation induces a notion of conflict between abstract transitions; indeed, the corresponding reaction, for each concrete state, is approximated by exactly one of those abstract transitions. In this context, the labels of transitions precisely identify the interaction and can naturally be exploited to capture conflicts between abstract transitions.

Once the abstract LTS semantics has been refined, the remaining problem is to generalize the translation from the abstract LTS to the abstract probabilistic model. In order to maintain the information about conflict, recorded by abstract transition labels, we adopt a generalization of the original model, called Labeled Interval Markov Chains (IMC). In IMC the labels permit to more accurately represent the set of distributions represented by the interval of probabilities. We show that the technique of [5] for computing intervals of probabilities from abstract transition labels can be successfully generalized, by finding out a good trade-off between precision and complexity. Finally, the soundness of the proposed technique is formalized following the approach of [5] (see also [10, 11, 12, 34, 19]) which exploits suitable approximation orders, both on abstract LTS and on IMC.

The paper is organized as follows. Section 2 introduces the CGF calculus and the LTS semantics, while Section 3 shows the probabilistic semantics in terms of a DTMC. Section 4 presents the refined abstract LTS semantics. Section 5 introduces the IMC model and finally, Section 6 presents the effective method to derive the abstract probabilistic semantics.

## 2 Chemical Ground Form

The CGF calculus [3] is a fragment of stochastic $\pi$-calculus [29, 27] without communication. Basic actions are related to rates, which are the parameters of the exponential distribution. We present the labeled transition system (LTS) semantics of CGF, proposed in [5], which supports more precise abstrac-
Abstract Interpretation for Probabilistic Termination of Biological Systems

Table 1: Syntax of CGF

| Syntax          | Definition | Description                |
|-----------------|------------|----------------------------|
| $E$ ::= 0 | $X = S, E$ | Environment               |
| $S ::= 0$ | $\pi^\lambda, P + S$ | Molecules                 |
| $P ::= 0$ | $X | P$ | Solutions                 |
| $\pi ::= a_r$ | $\hat{a}_r | \tau_r$ | $r \in \mathbb{R}^+$ | Basic Actions |

Definitions with respect to the original proposal of [3]. In this approach, processes are labeled, and transitions record information about the labels of the actions which participate to the move, about their rates, and about their number of occurrences (in place of the rate of the move as in [3]).

The syntax of (labeled) CGF is defined in Table 1. We consider a set $\mathcal{N}$ (ranged over by $a, b, c, \ldots$) of names, a set $\mathcal{L}$ (ranged over by $\lambda, \mu, \ldots$) of labels, and a set $\mathcal{X}$ (ranged over by $X, Y, \ldots$) of variables (representing reagents).

A CGF is defined as a pair $(E, P)$ where $E$ is a species environment and $P$ is a solution. The environment $E$ is a (finite) list of reagent definitions $X_i = S_i$ for distinct variables $X_i$ and molecules $S_i$. We assume that the environment $E$ defines all the reagents of solution $E$. A molecule $S$ may do nothing, or may change after a delay or may interact with other reagents. A standard notation is adopted: $\tau_r$ represents a delay at rate $r$; $a_r$ and $\hat{a}_r$ model, respectively, the input and output on channel $a$ at rate $r$. A solution $P$ is a parallel composition of variables, that is a finite list of reagents.

Labels are exploited in order to distinguish the actions which participate to a move. To this aim, we consider CGF $(E, P)$, where $E$ is well-labeled, meaning that the labels of basic actions are all distinct. Moreover, given a label $\lambda \in \mathcal{L}$, we use the notation $E.X.\lambda$ to indicate the process $\pi^\lambda.P$ provided that $X = \ldots + \pi^\lambda.P + \ldots$ is the definition of $X$ occurring in $E$. We may also use $\mathcal{L}(E.X)$ for the set of labels appearing in the definition of $X$ in $E$.

The semantics is based on the natural representation of solutions as multisets of reagents. A multiset is a function $M : \mathcal{X}^{-} \rightarrow \mathbb{N}$. In the following, we use $\mathcal{M}$ for the set of multisets and we use $[[P]]$ for the multiset of reagents corresponding to a solution $P$. Moreover, we call $M(X)$ the multiplicity of reagent $X$ in the multiset $M$. We may also represent multisets as sets of pairs $(m, X)$, where $m$ is the multiplicity of reagent $X$, using a standard notation, where the pairs with multiplicity 0 are omitted. Over multisets we use the standard operations of sum and difference $\oplus$ and $\ominus$, such that $\forall X \in \mathcal{X} : M + N(X) = M(X) + N(X)$ and $M - N(X) = \widehat{M(X)} - \widehat{N(X)}$ where $n - m = n - m$ if $n - m \geq 0$, 0 otherwise.

The evolution of a solution (w.r.t. a given environment $E$) is described by a labeled transition relation of the form

$$M \xrightarrow{\Theta, \Delta_r} M'$$

where $r \in \mathbb{R}^+$ is a rate, $\Theta \in \widehat{\mathcal{L}} = \mathcal{L} \cup (\mathcal{L} \times \mathcal{L})$, $\Delta \in \widehat{\mathcal{Q}} = \mathbb{N} \cup (\mathbb{N} \times \mathbb{N})$ such that $arity(\Theta) = arity(\Delta)$. Here, $\Theta$ reports the label (the labels) of the basic action (the basic actions), which participate to the move, $\Delta$ reports consistent information about the multiplicity, and $r$ is the related rate.

The transition relation for multisets is defined by the rules Table 2 (we are tacitly assuming to reason w.r.t. a given environment $E$). Rule (Delay) models the move of a process $\tau_r^\lambda.Q$ appearing in the definition of a reagent $X$. The transition records the label $\lambda$ together with the multiplicity of $X$ (e.g $M(X)$) as well as the rate $r$. Rule (Sync) models the synchronization between two complementary processes $a_r^\lambda.Q_1$ and $\hat{a}_r^\mu.Q_2$ appearing in the definition reagents $X$ and $Y$ (that may even coincide). The transition records the labels $\lambda$ and $\mu$ together with the multiplicities of $X$ and $Y$ (e.g $M(X)$ and $M(Y)$) as well as the rate $r$.

We denote with $\text{LTS}((E, M_0)) = (S, \rightarrow, M_0, E)$ the LTS, obtained as usual by transitive closure, start-
We introduce the probabilistic model of DTMC and we briefly discuss the notion of probabilistic semantics. In DTMC state transitions are equipped with probabilities, e.g. moving from state \( M \) to state \( M' \) has probability \( \rho(M \rightarrow M') \). Notice that we adopt a labeled version of the model in order to simplify the correspondence with the abstract models; the labels do not modify the probability distributions in the concrete model. We use \( \mathcal{L}:\mathcal{T}:\mathcal{S} \) to denote the set of LTS.

In the following, given a transition \( t = \Theta:\Delta \rightarrow M \rightarrow M' \) we use \( \text{label}(t) \) to denote its label \( \Theta \), and \( \text{source}(t), \text{target}(t) \) to denote its source state \( M \) and target \( M' \), respectively. Similarly, for a set of transitions \( TS \), we use \( \text{label}(TS) = \bigcup_{t \in TS} \text{label}(t) \). We also use \( TS_M(M,M') = \{ t | \text{source}(t) = M \ \text{and} \ \text{target}(t) = M' \} \) and \( TS_M(M) = \{ t | \text{source}(t) = M \} \) for describing the transitions from a multiset \( M \) to a multiset \( M' \), and all transitions leaving from multiset \( M \), respectively.

### 3 Probabilistic Semantics

We introduce the probabilistic model of DTMC and we briefly discuss the notion of probabilistic termination [35]. We also introduce the probabilistic semantics of CGF proposed in [5].

**Discrete-Time Markov Chains.**

Given a finite or countable set of states \( S \subseteq \mathcal{M} \) we denote with

\[
\text{SDistr}(S) = \{ \rho | \rho : S \rightarrow [0,1] \}, \quad \text{Distr}(S) = \{ \rho | \rho \in \text{SDistr}(S) \ \text{and} \ \sum_{M \in S} \rho(M) = 1 \}
\]

the set of (discrete) probability pseudo-distributions and of distributions on \( S \), respectively.

**Definition 3.1 (DTMC)** A DTMC is a tuple \( (S, P, L, M_0) \) where: (i) \( S \subseteq \mathcal{M} \) is a finite or countable set of states, \( M_0 \in S \) is the initial state; (ii) \( P : S \rightarrow \text{Distr}(S) \) is the probability transition function; (iii) \( L : S \rightarrow (S \rightarrow \rho(\mathcal{L})) \) is a labeling function.

In DTMC state transitions are equipped with probabilities, e.g. \( P(M)(M') \) reports the probability of moving from state \( M \) to state \( M' \). In addition, \( L(M)(M') \) reports the set of labels corresponding to the moves from state \( M \) to state \( M' \). Notice that we adopt a labeled version of the model in order to simplify the correspondence with the abstract models; the labels do not modify the probability distributions in the concrete model. We use \( \mathcal{M}' \mathcal{C} \) for the set of DTMC.

We are interested in probabilistic termination, e.g. on the probability to reach a state, which is terminated. Given a DTMC \( (S, P, L, M_0) \), we say that a state \( M \in S \) is terminated iff \( P(M)(M') = 0 \), for each \( M' \in S \) with \( M' \neq M \).

The probability to reach a terminated state can be formalized by associating a probability measure to paths of a DTMC. Let \( (S, P, L, M_0) \) be a DTMC. A path \( \pi \) is a non-empty sequence of states of \( S \). We denote the \( i \)-th state in a path \( \pi \) by \( \pi[i] \), and the length of \( \pi \) by \( |\pi| \). The set of (resp. finite) paths over \( S \) is denoted by (resp. \( \text{FPaths}(S) \)) \( \text{Paths}(S) \), while \( C(M) \) denotes the set of paths starting from the state...
\( M \in S \). In the following, for \( M \in S \) and \( \Pi \in C(M) \), \( P_M(\Pi) \) stands for the probability of the sets of paths \( \Pi \) (see [20] for the standard definition).

**Definition 3.2 (Probabilistic Termination)** Let \( mc = (S, P, L, M_0) \) be a DTMC. The probability of reaching a terminated state, from \( M \in S \), is \( \text{Reach}_{mc}(M) = P_M(\{ \pi \in C(M) \mid \pi[|\pi|] \text{ is terminated, and } \forall j, 0 \leq j \leq |\pi|, \pi[j] \text{ is non-terminated} \}) \).

**Derivation of the DTMC.**

The derivation of a DTMC from the LTS is based on the computation of the probability of moving from \( M \to M' \), for any \( M \) and \( M' \). To this aim, we extract the rate corresponding to the move from \( M \) to \( M' \) by exploiting the information reported by transition labels.

Formally, for a transition \( t = M \xrightarrow{\Theta, \Delta, r} M' \) we define the corresponding *rate* as follows,

\[
\text{rate}(t) = \begin{cases} 
  n \cdot r & \Theta = \lambda, \Delta = n, \\
  n \cdot (m-1) \cdot r & \Theta = (\lambda, \mu), \Delta = (n,m), \mu \in \mathcal{L}(E.X), \\
  n \cdot m \cdot r & \Theta = (\lambda, \mu), \Delta = (n,m), \lambda \in \mathcal{L}(E.X), \mu \in \mathcal{L}(E.Y), X \neq Y.
\end{cases}
\]

As usual, for computing \( \text{rate}(t) \) it is necessary to take into account the number of distinct transitions \( t \) that may occur in the multiset \( M \). Thus, the rate of the basic action (actions related to \( \Theta \)) is multiplied by the number of distinct combinations appearing in \( M \) (by exploiting the information recorded by \( \Delta \)).

Then, we introduce functions \( \mathbf{R} : S \times S \to \mathbb{R}^\geq 0 \) and \( \mathbf{E} : S \to \mathbb{R}^\geq 0 \), such that

\[
\mathbf{R}(M, M') = \sum_{t \in \text{Ts}(M, M')} \text{rate}(t) \quad \mathbf{E}(M) = \sum_{M' \in S} \mathbf{R}(M, M').
\]

Intuitively, \( \mathbf{R}(M, M') \) reports the rate corresponding to the move from \( M \) to \( M' \), while \( \mathbf{E}(M) \) is the *exit rate*. Finally, the probability of moving from \( M \) to \( M' \) is computed from \( \mathbf{R}(M, M') \) and from the exit rate \( \mathbf{E}(M) \), in a standard way.

**Definition 3.3** We define a probabilistic translation function \( \mathbf{H} : \mathcal{L} \mathcal{T} \mathcal{S} \to \mathcal{M} \mathcal{S} \) such that \( \mathbf{H}((S, \to, M_0, E)) = (S, P, L, M_0) \), where

1. \( P : S \to \text{Dist}(S) \) is the probability transition function, such that for each \( M, M' \in S \):
   a) if \( \mathbf{E}(M) > 0 \), then \( P(M)(M') = \mathbf{R}(M, M') / \mathbf{E}(M) \);
   b) if \( \mathbf{E}(M) = 0 \), then \( P(M)(M') = 1 \), and \( P(M)(M') = 0 \) for \( M' \neq M \).

2. \( L : S \to (S \to \phi(\mathcal{L})) \) is a labeling function, such that, for each \( M, M' \in S \), \( L(M, M') = \text{label}(\{ t \in \text{Ts}(M, M') \mid \text{rate}(t) > 0 \}) \).

Due to the particular labeling of the LTS semantics, also the DTMC, modeling the probabilistic semantics of a CGF process, satisfies the properties that all transitions leaving from a state, are decorated by distinct labels.

**Example 3.4** The example of groupies, commented in the Introduction, can be formalized by the following environment, \( E ::= X = a^\lambda X + b^\rho Y, Y = a^\mu X + b^\nu Y \).

Reagents \( X \) and \( Y \) may interact together in two possible ways: either along channel \( a \) or along channel \( b \); both reactions have the same rate \( r \). The former case models a duplication of \( X \), while the latter case models a duplication of \( Y \).
Fig. 3 illustrates the LTS and the corresponding DTMC, for the CGF \((E, M_0)\), where \(M_0 = \{(1,X),(2,Y)\} M_1 = \{(2,X),(1,Y)\} M_2 = \{(3,X)\} M_3 = \{(3,Y)\} \)

The LTS reports for each state, except for states \(M_2\) and \(M_3\), two transitions: label \((\lambda,\mu)\) models the duplication of \(X\), while label \((\delta,\eta)\) models the duplication of \(Y\). The transitions record also the multiplicities of reagents \(X\) and \(Y\) and the corresponding rate. As a consequence, in the DTMC, states \(M_2\) and \(M_3\) are terminated. By contrast, the states \(M_0\) and \(M_1\) have two different moves with the same probability. By calculating the probability to reach a terminated state from \(M_0\) we obtain exactly 1. Indeed, the probability to be stuck in the loop \(M_0\)-\(M_1\) is zero.

\[ \square \]

4 Abstract LTS

The abstract LTS semantics uses the same abstraction of multisets of [5], based on the approximation of the multiplicity of reagents by means of intervals of integers [6]. Instead, the abstract transition relation is refined, and the related notions, needed for expressing soundness, are adapted accordingly.

**Abstraction of states.**

We adopt intervals of integers, \(\mathcal{I} = \{[m,n] | m \in \mathbb{N}, n \in \mathbb{N} \cup \{\infty\} \wedge m \leq n\} \). Over intervals we consider the standard order \(\subseteq\), such that \(I \subseteq J\) iff \(\min(I),\max(I) \in J\). Moreover, we use \(\sqcup I\) for the corresponding l.u.b.

The abstract states are defined by replacing multiplicities with intervals of multiplicities. Therefore, an abstract state is a function \(M^\circ : \mathcal{X} \rightarrow \mathcal{I}\). We also use \(\mathcal{M}^\circ\) for the set of abstract states.

Obvious, given a multiset \(M\), there exists an abstract multiset \(M^\circ\), which is its most precise approximation. Indeed, each multiplicity, such as \(n\), can be replaced with the exact interval \([n,n]\); for simplicity, we may even use \(n\) as a shorthand of \([n,n]\). In the following, \(\alpha(M)\) stands for the best abstraction of a multiset \(M\). Moreover, we use \(M^\circ[I/X]\) for denoting the abstract state where the abstract multiplicity of reagent \(X\) is replaced by the interval \(I \in \mathcal{I}\). We adopt abstract operations of sum and difference, such that \(\forall X \in \mathcal{X}\),

\[
\begin{align*}
M^\circ \oplus \circ N^\circ(X) &= M^\circ(X) + N^\circ(X), \quad I + J = [\min(I) + \min(J),\max(I) + \max(J)] \\
M^\circ \ominus \circ N^\circ(X) &= M^\circ(X) - N^\circ(X), \quad I - J = [\min(I) - \max(J),\max(I) - \min(J)]
\end{align*}
\]

It is immediate to define the following approximation order over abstract states.

**Definition 4.1 (Order on States)** Let \(M_1^\circ, M_2^\circ \in \mathcal{M}^\circ\), we say that \(M_1^\circ \sqsubseteq M_2^\circ\) iff, for each reagent \(X \in \mathcal{X}\), \(M_1^\circ(X) \subseteq_I M_2^\circ(X)\).
The relation between multisets and abstract states is formalized as a Galois connection \[^8\]. The abstraction function \(\alpha: \mathcal{P}(\mathcal{M}) \rightarrow \mathcal{M}^\circ\) reports the best approximation for each set of multisets \(S\); the l.u.b. (denoted by \(\sqcup^\circ\)) of the best abstraction of each \(M \in S\). Its counterpart is the concretization function \(\gamma: \mathcal{M}^\circ \rightarrow \mathcal{P}(\mathcal{M})\) which reports the set of multisets represented by an abstract state. We refer the reader to \[^5\] for the properties of functions \((\alpha, \gamma)\).

**Definition 4.2** We define \(\alpha: \mathcal{P}(\mathcal{M}) \rightarrow \mathcal{M}^\circ\) and \(\gamma: \mathcal{M}^\circ \rightarrow \mathcal{P}(\mathcal{M})\) such that, for each \(S \in \mathcal{P}(\mathcal{M})\) and \(M^\circ \in \mathcal{M}^\circ\): (i) \(\alpha(S) = \bigsqcup_{M \in S} \alpha(M)\); (ii) \(\gamma(M^\circ) = \{M' \mid \alpha(M') \sqsubseteq^\circ M^\circ\}\).

**Abstract transitions.**

The semantics of \[^5\] uses abstract transitions of the form \(M_1^\circ \xrightarrow{\Theta \Delta^\circ, r} M_2^\circ\) where \(\Theta \in \mathcal{L}, \Delta^\circ \in \mathcal{Q}^\circ = \mathcal{I} \cup (\mathcal{I} \times \mathcal{I}), \) with \(\text{arity}(\Theta) = \text{arity}(\Delta^\circ)\). Similarly as in the concrete case, \(\Theta\) reports the label (the labels) of the basic action (actions), \(\Delta^\circ\) reports consistent information about the possible multiplicities, while \(r\) is the rate.

In the proposed approach, such a transition is intended to approximate all the concrete moves, corresponding to label \(\Theta\), for each multiset \(M_1\) approximated by the abstract state \(M_1^\circ\). This means that there exists a concrete transition \(M_1 \xrightarrow{\Theta \Delta, r} M_2\), where the multiplicity (multiplicities) \(\Delta\) is included in the interval (intervals) \(\Delta^\circ\); and \(M_2\) is approximated by the abstract state \(M_2^\circ\).

Let us consider the environment \(E\) commented in Example \[^3, 4\] and a very simple abstract state such as \(M_0^\circ = \{(\{1, 2\}, X), (\{1, 2\}, Y)\}\). The abstract state \(M_0^\circ\) describes a set of experiments; thus, the abstract semantics has to model the system described by \(E\), w.r.t. different initial concentrations. For approximating the duplication of \(X\), i.e. the synchronization between \(X\) and \(Y\) along channel \(a\), we would obtain

\[
M_0^\circ \xrightarrow{a} M_0'^\circ \quad \text{with} \quad M_0'^\circ = \{(\{2, 3\}, X), (\{0, 1\}, Y)\}.
\]

In this way, however, a hybrid state \(M_0'^\circ\) is introduced. Actually, \(M_0'^\circ\) represents terminated multisets, where the concentration of reagent \(Y\) is zero, as well as non terminated multisets, where reagent \(Y\) is still available.

It should be clear that the moves corresponding to \((\lambda, \mu)\) could be better approximated by adopting two different abstract transitions,

\[
M_0^\circ \xrightarrow{\Theta \Delta, \{1, 2\}, r} M_1^\circ \quad \text{or} \quad M_0^\circ \xrightarrow{\Theta \Delta, \{2, 2\}, r} M_2^\circ
\]

where \(M_1^\circ = \{(\{2, 3\}, X), (\{1, 1\}, Y)\}\) and \(M_2^\circ = \{(\{2, 3\}, X), (\{0, 0\}, Y)\}\). In this representation the labels capture a relevant information because they express a conflict. Actually, each multiset represented by \(M_0^\circ\), realizes a move corresponding to \((\lambda, \mu)\) which is abstracted either by transition (a) or by transition (b).

Table \[^3\] presents the refined abstract transition rules (as usual, w.r.t. a given environment \(E\)). The rules are derived from the concrete ones, by replacing multiplicities with intervals of multiplicities. The following operators are applied both to the target state and to the intervals, appearing in the transition labels, in order to properly split the intervals, such as \([0, n]\).

For \(X \in \mathcal{X}^\circ\), we define \(\mathcal{R}(X) = \{(X = 0), (X > 0)\}\). Then, given an abstract state \(M^\circ \in \mathcal{M}\) and \(\sharp \in \mathcal{R}(X)\) we define

\[
\nabla^\sharp(M^\circ) = \begin{cases} M^\circ[0, 0]/X & \text{if } \sharp = (X = 0), M^\circ(X) = [0, n], n > 0 \\ M^\circ[1, n]/X & \text{if } \sharp = (X > 0), M^\circ(X) = [0, n], n > 0 \\ M^\circ & \text{otherwise} \end{cases}
\]
With an abuse of notation, we may write $\nabla^{21,22}(M^\circ)$ in place of $\nabla^{21}(\nabla^{12}(M^\circ))$. Similarly, for an interval $I = [n, m] \in \mathcal{I}$ and $\sharp \in \mathbb{R}(X)$,

$$I^\sharp = \begin{cases} 
[n, 1] & \text{if } \sharp = (X = 0), n \leq 1, \\
[2, m] & \text{if } \sharp = (X > 0), n \leq 1, m \geq 2, \\
I & \text{otherwise.}
\end{cases}$$

In the following we use $\mathcal{L}\mathcal{T}\mathcal{S}^\circ$ to denote the set of abstract LTS. We also assume that all notations defined for LTS are adapted in the obvious way. Hence, we write $\text{LTS}^\circ((E, M_0^\circ)) = (S^\circ, \rightarrow^\circ, M_0^\circ, E)$ for the abstract LTS, obtained for the initial abstract state $M_0^\circ$ by transitive closure.

For the sake of simplicity we have presented an approximation where the number of states may be infinite. Further approximations can be easily derived by means of widening operators (see [5]).

**Soundness.**

In the style of [5], we introduce an approximation order $\sqsubseteq^\circ_{lts}$ over abstract LTS. In this way, we can say that an abstract LTS $lts^\circ$ is a sound approximation of a LTS $lts$ provided that $\alpha_{lts}(lts^\circ) \sqsubseteq^\circ_{lts} lts^\circ$; as usual, $\alpha_{lts}(lts)$ is the best approximation of $lts$.

**Definition 4.3 (Best Abstraction of LTS)** We define $\alpha_{lts} : \mathcal{L}\mathcal{T}\mathcal{S} \rightarrow \mathcal{L}\mathcal{T}\mathcal{S}^\circ$, such that $\alpha_{lts}((S, \rightarrow, M_0, E)) = (\{\alpha(M)\}_{M \in S}, \alpha(\rightarrow), \alpha(M_0), E)$ where $\alpha(\rightarrow) = \{\alpha(M) \xrightarrow{\Theta_{\Delta^r}} \alpha(M_1) | M \xrightarrow{\Theta_{\Delta^r}} M_1 \in \rightarrow\}$ and $\Delta^\circ$ is the best abstraction of $\Delta$, derived component-wise.

In the following, we assume to extend the order $\sqsubseteq$ over intervals to pairs of intervals; $\Delta^\circ_1 \sqsubseteq \Delta^\circ_2$ is defined component-wise.

**Definition 4.4 (Order on abstract LTS)** Let $\text{lts}^\circ_1 = (S^\circ_1, \rightarrow^\circ_1, M^\circ_0, E)$ with $i \in \{1, 2\}$ be abstract LTS. For $M^\circ_1 \in S^\circ_1, M^\circ_2 \in S^\circ_2$, we say that $M^\circ_1 \preceq_{lts} M^\circ_2$ if and only if there exists a surjective function $H_r : \text{Ts}(M^\circ_1) \rightarrow \text{Ts}(M^\circ_2)$ such that, for each $t^\circ_1 \in \text{Ts}(M^\circ_1), t^\circ_2 \in \text{Ts}(M^\circ_2), t^\circ_1 = M^\circ_1 \xrightarrow{\Theta_{\Delta^r}} N^\circ_1$ and $H_r(t^\circ_1) = t^\circ_2$ where $t^\circ_2 = M^\circ_2 \xrightarrow{\Theta_{\Delta^r}} N^\circ_2$, $\Delta^\circ_1 \sqsubseteq \Delta^\circ_2$ and $\Delta^\circ_1 \sqsubseteq \Delta^\circ_2$. We say that $\text{lts}^\circ_1 \preceq_{lts} \text{lts}^\circ_2$ if $M^\circ_{0,1} \preceq_{lts} M^\circ_{0,2}$.

The approximation order for abstract LTS is based on a simulation between abstract states. More in details, we say that $M^\circ_2$ simulates $M^\circ_1$ ($M^\circ_2 \preceq_{lts} M^\circ_1$) whenever $M^\circ_2$ approximates $M^\circ_1$, and there exists a surjective function $H^\circ_1 : \text{Ts}(M^\circ_1) \rightarrow \text{Ts}(M^\circ_2)$ between the transitions of $M^\circ_1$ and $M^\circ_2$. In particular, each move $M^\circ_1 \xrightarrow{\Theta_{\Delta^r}} N^\circ_1$ has to be matched by a move $M^\circ_2 \xrightarrow{\Theta_{\Delta^r}} N^\circ_2$, related to the same label $\Theta$, and such that $\Delta^\circ_1 \sqsubseteq \Delta^\circ_2$, showing that the multiplicities are properly approximated.
Examples 3.4 and 4.6. As it is illustrated in the LTS of Fig. 4, the reachable states from this information is not adequate for our abstraction. Let us consider again the system, commented in Theorem 4.5 (Soundness).

\[
\alpha_{\text{LTS}}(E, M) \subseteq_{\text{hs}} \alpha_{\text{LTS}}(E, \gamma(M)).
\]

Splitting hybrid states by means of the \( \nabla^d \) operator, in order to distinguish terminated and non-terminated states may, in general, increase drastically the number of abstract states. For example the abstract LTS, starting from the state \( M^0_6 = \{([1,2], X), ([1,2], Y)\} \) w.r.t. to the environment \( E \) of Example 3.4 would have 14 abstract states.

It is worth noting, however, that for modeling probabilistic termination we don’t need to be too fine in distinguishing different non-terminated states. For this reason we can apply the following widening operator to each abstract transition step: we approximate the new abstract state \( M^o \), result of the application of the transition relation of Table 3, with an abstract state \( M^o_1 \), if \( M \sqsubseteq^{\circ} M^o_1 \) and \( M^o_1 \) was already generated in a previous derivation step. This will reduce the number of new generated abstract states as it is shown in the next example.

For these reasons in the following we always assume the application of the previous widening operator.

Example 4.6 Fig. 4 shows the complete abstract LTS for the abstract state \( M^o_6 = \{([1,2], X), ([1,2], Y)\} \) w.r.t. to the environment \( E \) of Example 3.4 where

\[
M^o_1 = \{([2,3], X), ([1,1], Y)\} \quad M^o_2 = \{([3,4], X), ([0,0], Y)\} \quad M^o_3 = \{([2,3], X), ([0,0], Y)\}
\]

\[
M^o_4 = \{([0,0], X), ([2,3], Y)\} \quad M^o_5 = \{([1,1], X), ([2,3], Y)\} \quad M^o_6 = \{([0,0], X), ([3,4], Y)\}
\]

5 Abstract Probabilistic Semantics

In standard Interval Markov Chains [34, 13] transitions report intervals of probabilities, representing a lower and upper bound on the concrete probabilities, e.g. a set of possible distributions. Unfortunately, this information is not adequate for our abstraction. Let us consider again the system, commented in Examples 3.4 and 4.6. As it is illustrated in the LTS of Fig. 4, the reachable states from \( M^o_6 \) are \( M^o_1, M^o_3, M^o_5 \) and \( M^o_2 \) (see also Fig. 5(c)).
Figure 5: The interval of probabilities and of multiplicities for $M_0^\circ$’s transitions.

In order to reason on the interval of probabilities we could safely assign to each transition leaving from $M_0^\circ$, it is useful to examine the set of concrete probability distributions, for each multiset $M_0$, represented by $M_0^\circ$. The DTMC corresponding to one of experiments represented by $M_0^\circ$ is described in Fig. 3; the other cases show analogous behaviors. Actually, for each $M_0$, there are two possible synchronizations between reagents $X$ and $Y$: one corresponding to the duplication of $X$ and the other one corresponding to the duplication of $Y$. These two alternative moves always have the same probability.

Moreover, each solution $M_0$, when there is a duplication of $X$, evolves into a solution, which is represented either by $M_1^\circ$ (where reagent $Y$ is still available) or by $M_3^\circ$ (where the concentration of $Y$ is 0). Analogously, for the duplication of $Y$ and the abstract states $M_4^\circ$ and $M_5^\circ$. Thus, the abstract distributions representing the concrete distributions are:

\[
\begin{align*}
\rho_1(M_3) &= 1/2, \rho_1(M_1) = 0, \rho_1(M_5) = 1/2, \rho_1(M_4) = 0, \\
\rho_2(M_3) &= 1/2, \rho_2(M_1) = 0, \rho_2(M_5) = 0, \rho_2(M_4) = 1/2, \\
\rho_3(M_3) &= 0, \rho_3(M_1) = 1/2, \rho_3(M_5) = 1/2, \rho_3(M_4) = 0, \\
\rho_4(M_3) &= 0, \rho_4(M_1) = 1/2, \rho_4(M_5) = 0, \rho_4(M_4) = 1/2.
\end{align*}
\]

It should be clear that the most precise intervals of probabilities representing the previous distributions, could be obtained by considering the minimum and maximum probability, for each move. The intervals we would obtain in this way, are illustrated in Fig5(a). This representation introduces a clear loss of information. For instance, the intervals include a distribution such as $\rho(M_1) = 1/2, \rho(M_3) = 1/2, \rho(M_5) = 0$, which does not correspond to any concrete behavior. Actually, states $M_1^\circ$ and $M_3^\circ$ are in conflict.

Since labels are suitably exploited in the abstract LTS in order to represent conflict, we introduce a generalization of the original model, called Labeled Interval Markov Chains (IMC). The model permits to more accurately represent the set of distributions represented by intervals of probability by means of labels.

**Labeled Interval Markov Chains.**

**Definition 5.1 (IMC)** A IMC is a tuple $(S^\circ, P^-, P^+, L, M_0^\circ)$ where

1. $S^\circ \subseteq \mathcal{M}^\circ$ is a countable set of abstract states and $M_0^\circ \in S^\circ$ is the initial state;
2. $P^-, P^+: S^\circ \rightarrow SDistr(S^\circ)$ are the lower and upper bounds on probabilities, such that for each $M_1^\circ, M_2^\circ \in S^\circ$, $P^-(M_1^\circ)(M_2^\circ) \leq P^+(M_1^\circ)(M_2^\circ)$;
3. $L: S^\circ \rightarrow (S^\circ \rightarrow 2^{\mathcal{L}})$ is a labeling function.
In the following we use $\mathcal{I} \mathcal{M} \mathcal{C}$ to denote the set of IMC. As in the standard model, $P^-(M_1^0)(M_2^0)$ and $P^+(M_1^0)(M_2^0)$ define the lower and upper bound, for the move from $M_1^0$ to $M_2^0$, respectively. In addition, $L(M_1^0)(M_2^0)$ reports the set of labels corresponding to the move. Intervals represent set of admissible distributions; the notion of admissible distribution has to be slightly adapted in order to handle the conflict between (sets of) labels.

**Definition 5.2 (Conflict of Labels)** Let $\alpha, \beta \in \mathcal{L}$ be sets of labels. We say that $\alpha$ is in conflict with $\beta$ iff there exists $\vartheta \in \mathcal{L}$ such that $\alpha = \{ \vartheta \} = \beta$.

The notion of conflict between labels obviously induces a corresponding notion of conflict between states. Let $(S^0, P^-, P^+, L, M_0^0)$ be an IMC and $M^0 \in S^0$. We say that $NS^0 \subseteq S^0$ is a set of no-conflict states w.r.t. $M^0$ iff it is maximal and, for each $M_1^0, M_2^0 \in NS^0$, there is no conflict between $L(M^0)(M_1^0)$ and $L(M^0)(M_2^0)$.

**Definition 5.3 (Admissible Distribution)** Let $mc^0 = (S^0, P^-, P^+, L, M_0^0)$ be an IMC and let $M^0 \in S^0$. We say that a distribution $\rho \in \text{Distr}(S^0)$ is admissible for $M^0$ iff there exists a set of no-conflict states $NS^0$ such that, for each $M_1^0 \in NS^0$, if $M_1^0 \in NS^0$, then $P^-(M^0)(M_1^0) \leq \rho(M_1^0) \leq P^+(M^0)(M_1^0)$; $\rho(M_1^0) = 0$, otherwise. We use $\text{ADistr}_{mc^0}(M^0)$ for the set of admissible distributions for $M^0$.

Intuitively, an admissible distribution $\rho$ corresponds to a set of no-conflict states $NS^0$, and reports a value included in the interval, for each state of $NS^0$, and zero otherwise. As an example, the IMC illustrated in Fig 5(b) reports four non-conflict set of states w.r.t. $M_0^0$: (1) $\{M_3^0, M_4^0\}$, (2) $\{M_3^0, M_5^0\}$; (3) $\{M_1^0, M_4^0\}$ and (4) $\{M_1^0, M_5^0\}$. As a consequence, the admissible distributions, corresponding to (1)-(4) are exactly the distributions $\rho_1 - \rho_4$, discussed at the beginning of the Section. This shows that the IMC of Fig. 5(b) is a sound and very precise approximation of the probabilistic semantics, for each multiset represented by $M_0^0$.

Once defined admissible distributions the concept of scheduler follows the same guidelines of [5]. The notion of path and cylinder for IMC are analogous to that presented for DTMC.

**Definition 5.4 (Scheduler)** Let $mc^0 = (S^0, P^-, P^+, L, M_0^0)$ be an IMC, a scheduler is a function $A : \text{FPaths}(S^0) \rightarrow \text{Distr}(S^0)$ such that $A(\pi^0) \in \text{ADistr}_{mc^0}(\pi^0 \mid \pi^0)$ for any abstract path $\pi^0 \in \text{FPaths}(S^0)$. We use $\text{Adv}(mc^0)$ to denote the set of schedulers.

Given a scheduler a probability space over paths can be defined analogously as for DTMC. In the following, $P_{mc}^\Pi$ stands for the probability starting from $M^0$ w.r.t. the scheduler $\Pi \in \text{Adv}(mc^0)$.

An IMC gives both under and over approximations of the probability of reachability properties, that can be computed by considering the worst and best probabilities w.r.t. all the schedulers. For approximating probabilistic termination, we have to define terminated abstract states. A state $M^0 \in S^0$ of a IMC $mc^0 = (S^0, P^-, P^+, L, M_0^0)$ is $\exists$-terminated iff $P^+(M^0)(M^0) = 1$, and is $\forall$-terminated iff $P^-(M^0)(M^0) = 1$.

**Definition 5.5 (Probabilistic Termination)** Let $mc^0 = (S^0, P^-, P^+, L, M_0^0)$ be an IMC. The lower and upper bound of probabilistic termination, starting from $M^0 \in S^0$, are

\[
\text{Reach}_{mc^0}^-(M^0) = \inf_{\Pi \in \text{Adv}(mc^0)} P_{mc}^\Pi (\{ \pi^0 \in C(M^0) \mid \pi^0[i] \text{ is } \exists\text{-terminated for some } i \geq 0 \})
\]

\[
\text{Reach}_{mc^0}^+(M^0) = \sup_{\Pi \in \text{Adv}(mc^0)} P_{mc}^\Pi (\{ \pi^0 \in C(M^0) \mid \pi^0[i] \text{ is } \forall\text{-terminated for some } i \geq 0 \})
\]

Finally, we observe that the problem of model checking the IMC can be reduced, as in the case of Markov Interval Chains, to the verification of a Markov Decision Process (MDP), by considering the so
called feasible solutions. The complexity of this reduction is comparable to the one for a standard Markov Interval Chains with the same number of states. Analogously, more efficient iterative algorithms which construct a basic feasible solution on-the-fly can also be used to model check our IMC (see [34, 13]).

Soundness and precision of approximations.

We introduce a notion of best abstraction of a DTMC based on an approximation order on IMC. Here, for a lack of space, we give just an intuitive definition of such an order. The reader can refer to [5] for the formal definition.

Definition 5.6 (Best Abstraction) We define \( \alpha_{MC} : \mathcal{M} \to \mathcal{M}^o \) such that \( \alpha_{MC}((S,P,L,M_0)) = (\{\alpha(M)\}_{M \in S}, P_a^-, P_a^+, L, \alpha(M_0)) \), where \( P_a^- (\alpha(M_1), \alpha(M_2)) = P_a^+ (\alpha(M_1), \alpha(M_2)) = P(M_1)(M_2) \).

The order on IMC is based on a sort of probabilistic simulation. Intuitively, \( M_2^o \) simulates \( M_1^o \) \( (M_1^o \preceq_{mc} M_2^o) \) whenever: (i) \( M_2^o \) approximates \( M_1^o \); (ii) each distribution of \( M_1^o \) is matched by a corresponding distribution of \( M_2^o \), where the probabilities of the target states are eventually summed up.

This simulation provides sufficient conditions for the preservation of extremum probabilities, as stated by the following theorem.

Theorem 5.7 (Soundness of the order) Let \( mc_i^o = (S_i^o, P_i^-, P_i^+, L_i, M_0_{i,0}) \) be two IMC and let \( M_i^o \in S_i^o \), for \( i \in \{1,2\} \). If \( M_1^o \preceq_{mc} M_2^o \), then \( \text{Reach}_{mc_2^o}(M_2^o) \leq \text{Reach}_{mc_1^o}(M_1^o) \leq \text{Reach}_{mc_1^o}(M_1^o) \leq \text{Reach}_{mc_2^o}(M_2^o) \).

6 Derivation of IMC

We define a systematic method for deriving an IMC from an abstract LTS. Obviously, the crucial part of the translation consists of the calculation of intervals of probabilities from the information reported on abstract transitions labels. The approach, proposed in [5], suggests a methodology similar to the one applied in the concrete case, based on the calculation of abstract rates, e.g. intervals of rates.

The idea is to derive from abstract transition labels the interval of rates \( (t^o) \) corresponding to any abstract transition \( t^o \). Then, by "summing up" the abstract rates \( (t^o) \) of all transitions \( t^o \in Ts(M_i^o, M_2^o) \), we can obtain the abstract rate \( R^o(M_i^o, M_2^o) \) for the complete move from \( M_i^o \) to \( M_2^o \). Analogously, we can also obtain the abstract exit rate \( E^o(M_i^o) \) corresponding to all the moves from \( M_i^o \). Finally, both lower and upper bounds of the probability of moving from \( M_i^o \) to \( M_2^o \) can easily be computed by minimizing and maximizing the solution of \( R^o(M_i^o, M_2^o) \) and \( E^o(M_i^o) \), resp..

However, the refined abstract LTS semantics presents a relevant difference: the labels represent a notion of conflict between abstract transitions. As an example, Fig. 5(c) reports the abstract transitions (see also Example 4.5 and Fig. 4) for the abstract state \( M_0^o \). Notice that just four combinations of transitions are possible: (a) (1) and (3); (b) (1) and (4); (c) (2) and (3); (d) (2) and (4). It should be clear that each combination \( i \in \{(a)-(d)\} \) leads to a different abstract exit rate for \( M_0^o, E^o(M_i^o) \). As a consequence, in order to generalize the approach of [5], we could minimize and maximize the solution of \( R^o(M_i^o, M_2^o) \) and \( E^o(M_i^o) \), for each combination \( i \in \{(a)-(d)\} \), resp..

It should be clear that this naive generalization of the approach would be very computationally expensive. Therefore, we propose a more efficient approximated calculation. The idea is to compute a different exit rate \( E^o_{M_2^o}(M_i^o) \) for \( M_0^o \), w.r.t. each \( M_2^o \), reporting the abstract rate of all transitions which may appear in parallel with a transition of \( Ts(M_i^o, M_2^o) \). This represents obviously an approximation of the exit rates that we would obtain by considering all combinations involving a transition of \( Ts(M_i^o, M_2^o) \).

In the style of [5], the abstract rates (intervals of rates) are represented by symbolic expressions on reagent variables, such as \( e \in \mathcal{E} \) is an expression over variables \( \mathcal{E} \); (ii) \( c \in \mathcal{C} \) is a set of
membership constraints of the form $X \in I$. This approach permits to more accurately exploit the information recorded by abstract transition labels. Moreover, for $op \in \{+,-,\}$ we use: (a) $(e_1,c_1)op^\circ (e_2,c_2) = (e_1 op e_2, c_1 \cup c_2)$; (b) $(e,c_1)\cup^\circ (e,c_2) = (e, c_1 \cup c_2)$, where $c_1 \cup c_2 = \bigcup_{X \in \mathcal{X}} (X \in \bigcup_{l \in I \cap c_1 \cup c_2}(l)\).

The abstract rate of a transition $t^\circ = M_1^\circ \xrightarrow{\Theta, \lambda, \mu} M_2^\circ$ can be defined as follows:

\[
\text{rate}^\circ(t^\circ) = \begin{cases} 
(X \cdot r, \{X \in I\}) & \Theta = \lambda, \lambda \in \mathcal{L}(E,X), \Delta^\circ = I, \\
(X \cdot (X \cdot \cdot r, \{X \in I\}) & \Theta = (\lambda, \mu), \Delta^\circ = (I, I), \lambda, \mu \in \mathcal{L}(E,X), \\
(X \cdot Y \cdot r, \{X \in I_1, Y \in I_2\}) & \Theta = (\lambda, \mu), \Delta^\circ = (I_1, I_2), \lambda \in \mathcal{L}(E,X), \mu \in \mathcal{L}(E.Y), X \neq Y.
\end{cases}
\]

Then, we define $E_{M_2^\circ}(M_1^\circ)$ and $R^\circ(M_1^\circ, M_2^\circ)$, where $Ts^\circ \subseteq Ts(M_1^\circ)$,

\[
E_{M_2^\circ}(M_1^\circ) = \sum_{(e,c) \in \text{rate}(Ts_{M_2^\circ}(M_1^\circ) \cup Ts(M_1^\circ \setminus M_2^\circ))}(e,c) \quad R^\circ(M_1^\circ, M_2^\circ) = \sum_{(r, (e, c) \in \text{rate}(r^\circ))}(e,c)
\]

Then, we define $\hat{\text{rate}}(r^\circ) = \begin{cases} 
(e, c \cup \{X \in [0,0] \mid X \in \text{Vars}(e)\}) & \text{if } \text{rate}^\circ(r^\circ) = (e, c) \text{ and } \text{label}(r^\circ) \in \text{label}(Ts_{M_1^\circ}(M_1^\circ)), \\
\text{otherwise}.
\end{cases}
\]

$\text{rate}(Ts^\circ) = \{r_0 \mid \Theta \in \hat{\mathcal{L}}, r_0 = \bigcup_{(e, c) \in \text{rate}(r^\circ)}(e, c) \}

\text{rate}(T s^\circ) = \{r_0 \mid \Theta \in \hat{\mathcal{L}}, r_0 = \bigcup_{(e, c) \in \text{rate}(r^\circ)}(e, c) \}

T s_{M_1^\circ}(M_1^\circ) = \{t^\circ \in Ts(M_1^\circ) \mid \text{rate}(r^\circ) \neq M_2^\circ, \text{label}(r^\circ) \not\in \text{Conflict with label}(Ts(M_1^\circ, M_2^\circ)) \}

Here, $T s_{M_1^\circ}(M_1^\circ) \subseteq Ts(M_1^\circ)$ reports the transitions which may appear in parallel with a transition of $T s(M_1^\circ, M_2^\circ)$. In the calculation of $E_{M_1^\circ}(M_2^\circ)$ the abstract rates of transitions with the same label are merged (namely approximated) by taking the union of the membership constraints.

Finally, both lower and upper bounds of the probability of moving from $M_1^\circ$ to $M_2^\circ$ can be derived by minimizing and maximizing the solution of $R^\circ(M_1^\circ, M_2^\circ) / E_{M_1^\circ}(M_2^\circ)$, respectively. This reasoning has to be properly combined with two special cases when $\max(E_{M_1^\circ}(M_2^\circ)) = 0$ or $\min(E_{M_1^\circ}(M_2^\circ)) = 0$.

**Definition 6.1** The abstract probabilistic translation function $H^\circ: \mathcal{L}(T, I, \circ) \rightarrow I \mathcal{M}^\circ$ such that $H^\circ((S^\circ, -\circ, M_1^\circ, E)) = (S^\circ, P^-, P^+, L, M_2^\circ)$, and $P^-, P^+: S^\circ \rightarrow SDist(S^\circ)$ are the lower and upper probability functions, such that for each $M_1^\circ \in S^\circ$:

a) for each $M_2^\circ \in S^\circ$, such that $\max(E_{M_1^\circ}(M_1^\circ)) > 0$, $\min(R^\circ(M_1^\circ, M_2^\circ)) = 0$, then also $P^-(M_1^\circ)(M_2^\circ) = 0$;

b) if, for each $M_2^\circ \in S^\circ$, $\max(E_{M_1^\circ}(M_1^\circ)) = 0$, then $P^+ = P^-$, $P^+(M_1^\circ)(M_2^\circ) = 1$, and $\forall M_2^\circ \neq M_1^\circ$,

P^+(M_1^\circ), (M_2^\circ) = 0;

c) if, $\exists M_2^\circ \in S^\circ$, such that $\max(E_{M_1^\circ}(M_1^\circ)) > 0$ and $\min(R^\circ(M_1^\circ, M_2^\circ)) = 0$, then $P^+(M_1^\circ)(M_2^\circ) = 1$, and $P^-(M_1^\circ), (M_2^\circ) = 0$.

L : $S^\circ \rightarrow (S^\circ \rightarrow \circ(\hat{\mathcal{L}}))$ is a labeling function defined as $\forall M_1^\circ, M_2^\circ \in S^\circ$, $L(M_1^\circ, M_2^\circ) = \text{label}((t^\circ \in Ts(M_1^\circ, M_2^\circ) \mid \max(\text{rate}(r^\circ)) > 0))$.

The following theorems state the soundness of our approach.

**Theorem 6.2** Let $lts_1^\circ = (S_1^\circ, \rightarrow_1^\circ, M_0_1^\circ, E)$ be two abstract LTS. If $lts_1^\circ \sqsubseteq lts_2^\circ, then H^\circ(lts_1^\circ) \sqsubseteq H^\circ(lts_2^\circ)$.

\(^1\)We require that, $\forall X \in \text{Vars}(e)$, there exists exactly one constraint $X \in I$ in $c$.}
Theorem 6.3 Let $E$ be an environment and $M_0 \in \mathcal{M}$ be a multiset.
We have $\alpha_{\text{MC}}(H(\text{LTS}((E,M_0)))) \subseteq \alpha_{\text{LTS}}(\text{LTS}((E,M_0)))$.

Example 6.4 Fig. 6 describes the IMC, obtained from the abstract LTS of Fig. 4 for the abstract state $M_0^0 = \{(\{1,2\},X),([1,2],Y)\}$ (see also Examples 3.4 and 4.6).
Note that the result is very precise. For $M_0^0$ we derive precisely the approximation, discussed in Fig. 5(b); namely, four admissible distributions corresponding to the combinations of labels not in conflict. For the other states there is exactly one admissible distribution. In particular, $M_2, M_3, M_4$ and $M_5$ are $\forall$-terminated. By computing lower and upper bounds for probabilistic termination, from $M_0^0$, we obtain exactly one in both cases. For the maximum, it is enough to choose the admissible distributions which reach terminated states as soon as possible. This is obviously represented by the distribution for $M_0^0$, reporting probability $1/2$ to move in $M_3$ and $M_4$. By contrast, for the minimum, it is enough to choose the admissible distributions which do not reach terminated states, every time this is possible. This is obviously represented by the choice of the distribution for $M_0^0$, reporting probability $1/2$ to move in $M_1$ and $M_2$. Thus, we obtain a DTMC, and the reasoning is similar to that discussed in Example 5.4.

This proves that each experiment, represented by $M_0^0$, leads to a terminated state with probability one, e.g. universally terminates. Note that here we have examined a very small example for sake of simplicity; however, it should be clear that the result could be generalized to any concentration of reagents $X$ and $Y$.

7 Conclusions

The methodology proposed in this paper is substantially different from most of the approaches, proposed in literature \cite{11,13,19,24,22,13}, in order to abstract probabilistic models, based on abstract interpretation or partitioning of the concrete state space. Actually, our goal is to represent by means of the IMC of an abstract system a set of concrete systems, each corresponding to a different DTMC. In this setting it is therefore essential to develop an effective method (even for infinite state systems) for computing the abstract probabilistic model, directly from the abstract LTS. The main contribution of the approach consists in the calculation of the intervals of probabilities from the information reported on abstract transition labels, without building all the concrete distributions. We have also shown that the technique of
can be successfully generalized to the refined abstract LTS, by finding out a good trade-off between precision and complexity. For this reason, a probabilistic model such as a Markov Decision Process is not adequate.

An advantage of our framework is that other kinds of uncertainties of biological systems could be handled in a similar way. For example, the approach could be easily adapted in order to model (even infinite) sets of concrete systems with different values for the rates. Another advantage of our framework, based on abstract interpretation, is that new analyses could be easily designed by introducing new abstract LTS semantics. For example, we would like to investigate the application of more precise numerical domains able to model also relational information, such as the domain of convex polyhedra. We leave to the future work the extension of the framework to the full calculus with communication as well as the extension to Continuous-Time Markov Chains.

References

[1] C. Bodei, P. Degano, F. Nielson and H. Riis Nielson. Static Analysis for the Pi-Calculus with Applications to Security. Information and Computation, 168: 68-92, 2001.
[2] L. Cardelli. Brane Calculi. Proc. of CMSB ‘04, LNCS 3082, 257–278, 2004.
[3] L. Cardelli. On Process Rate Semantics. Theoretical Computer Science, 391 190–215, 2008.
[4] L. Cardelli. Algorithmic Bioprocesses. In A. Condon, D. Harel, J. N. Kok, A. Salomaa, E. Winfree (Eds.), Springer, 2009
[5] A. Coletta and R. Gori and F. Levi. Approximating probabilistic behaviours of biological systems using abstract interpretation. Proc. of FBTC ’08, ENTCS 229 (1), 165–182, 2009.
[6] P. Cousot and R. Cousot. Static Determination of Dynamic Properties of Programs. Proc. of POPL’76 , 106–130, 1976.
[7] P. Cousot and R. Cousot. Abstract Interpretation: A Unified Lattice Model for Static Analysis of Programs by Construction or Approximation of Fixpoints. Proc. of POPL’77, 238–252, 1977.
[8] P. Cousot and R. Cousot. Systematic Design of Program Analysis Frameworks. Proc. of POPL’79 , 269–282, 1979.
[9] P. Cousot and R. Cousot. Comparing the Galois Connection and Widening/Narrowing Approaches to Abstract Interpretation. Proc. of PLILP’92, LNCS 631, 269–295, 1992.
[10] D. Dams, R. Gerth and O. Grumberg. Abstract Interpretation of Reactive Systems. TOPLAS, 19(2), 253-291, 1997.
[11] P. D’Argenio, B. Jeannet, H. Jensen and K. Larsen. Reachability Analysis of Probabilistic Systems by Successive Refinements. Proc. of PAPM-PROMIV’01, LNCS 2165, 39–56, 2001.
[12] P. D’Argenio, B. Jeannet, H. Jensen and K. Larsen. Reduction and Refinement Strategies for Probabilistic Analysis. Proc. of PAPM-PROMIV’02, LNCS 2399, 57–76, 2002.
[13] H. Fecher, M. Leucker and V. Wolf. Don’t Know in Probabilistic Systems. Proc. of SPIN’06, LNCS 3925, 71–88, 2006.
[14] J. Feret. Abstract Interpretation-Based Static Analysis of Mobile Ambients. Proc. of SAS’01, LNCS 2126, 412-430, Springer Verlag, 2001.
[15] R. Gori and F. Levi. A new occurrence Counting analysis for BioAmbients. Proc. of APLAS ’05, LNCS 3780, 381–400, 2005.
[16] R. Gori and F. Levi. An Analysis for proving Temporal Properties of Biological Systems. Proc. of APLAS ’06, LNCS 4279, 234–252, 2006.
[17] H. Hansson and B. Jonsson. A Logic for Reasoning about Time and Probability. Formal Aspects of Computing, 6(5), 512–535, 1994.
[18] A. Hinton, M. Kwiatkowska, G. Norma and D. Parker. PRISM: a tool for automatic verification of probabilistic systems. Proc. of TACAS’06, LNCS 3920, 441-444, Springer-Verlag, 2006.

[19] M. Huth. On finite-state approximants for probabilistic computation tree logic. Theoretical Computer Science, 346(1), 113–134, 2005.

[20] J.G. Kemeny, J.L. Snell and A.W. Knapp. Denumerable Markov Chains. Springer, 1976.

[21] M. Kwiatkowska. Model checking for probability and time: from theory to practice. Proc. of LICS’ 03, 351–360, 2003.

[22] M. Kwiatkowska, G. Norman and D. Parker. Game-based Abstraction for Markov Decision Processes. Proc. of QEST’06, 157–166, 2006.

[23] F. Levi and S. Maffeis. On Abstract Interpretation of Mobile Ambients. Information and Computation 188, 179–240, 2004.

[24] D. Monniaux. Abstract interpretation of programs as Markov Decision Processes. Science of Computer Programming, 58(1-2), 179–205, 2005.

[25] F. Nielson, H.R. Nielson, R.R. Hansen. Validating firewalls using flow logics. Theoretical Computer Science, 283(2), 381-418, 2002.

[26] F. Nielson, H.R. Nielson and H. Pilegaard. Spatial Analysis of BioAmbients. Proc. of SAS’04, LNCS 3148, pp. 69–83, Springer-Verlag, 2004.

[27] A. Phillips and L. Cardelli. A Correct Abstract Machine for the Stochastic Pi-calculus. Proc. of BioCONCUR ’04, ENTCS, 2004.

[28] A. Phillips and L. Cardelli. Efficient, Correct Simulation of Biological Processes in the Stochastic Pi-calculus. Proc. of CMSB ’07, LNCS 4695, 184–199, 2007.

[29] C.Priami. Stochastic π-calculus. The Computer Journal, 38, 578–589,1995.

[30] C.Priami and P. Quaglia. Beta binders for biological interactions. Proc. of CMSB’04, LNCS 3082,20–33,2005.

[31] C. Priami, A. Regev, W. Silverman and E. Shapiro. Application of a stochastic name-passing calculus to representation and simulation of molecular processes. Information Processing Letters, 80 (1), 25–31, 2001.

[32] A. Regev, E. M. Panina, W. Silverman, L. Cardelli and E. Shapiro. BioAmbients: an Abstraction for Biological Compartments. Theoretical Computer Science, 325, 141–167, 2004.

[33] A. Regev, W. Silverman and E. Shapiro. Representation and Simulation of Biochemical Processes using the pi-calculus process algebra. Proc. of the Pacific Symposium on Biocomputing 2001, 6, 459–470, 2001.

[34] K. Sen, M. Viswanathan and G. Agha. Model Checking Markov Chains in the Presence of Uncertainties. Proc. of TACAS’06, LNCS 3920, 394-410, 2006.

[35] G. Zavattaro and L. Cardelli. Termination Problems in Chemical Kinetics. Proc. of CONCUR’08, LNCS 5201, 477-491, 2008.