rPrism – A software for reactive weighted state transition models

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PRISM.

PRISM is a probabilistic model checker to study model with random or probabilistic behaviors.

A model in PRISM is composed by integer variables; and actions, which alter the value of variables. Actions can have guards and rates assigned to them.

PRISM allows us to simulate as well as use their linear logics to describe and check properties of the system.

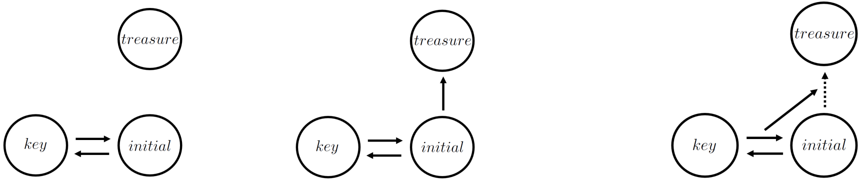
Probabilistic automata can be encoded using PRISM by relating states to variables and actions to edges.

Many examples of applications can be found in literature.

Switch graphs.

A switch graph is a pair (W, S) where W is a non empty set of worlds (states) and S is a set of generalized edges defined as:

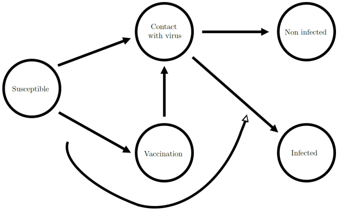
- $S_0 \subseteq W \times W$
- $S_{n+1} \subseteq S_0 \times S_n \times \{\bullet, \circ\}$
- $S = \bigcup_n S_n$



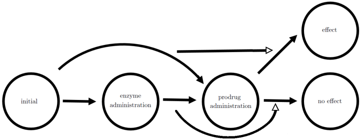
Switch graphs.

Biochemical examples

Vaccination



Prodrugs



Introducing weights.

The biological systems are not as deterministic as the examples shown before:

- A person does not usually become absolutely immune to a virus with vaccination.
- The biochemical molecular processes within human body follow stochastic rules that can be thought as deterministic due to the law of large numbers.

For many biological systems, probabilities or rates should be considered.

Stochastic processes should be considered for many biological systems.

Introducing weights.

One-level weighted switch graphs

We introduce a new notion of graph to accommodate weights.

Definition

A *one-level weighted switch graph* is a pair (W, S) with $W \neq \{\}$ and $S = S_0 \cup S_1$ such that:

- $S_0 \subseteq W \times W$
- $S_1 \subseteq S_0 \times S_0$

along with an initial *instantiation* $I_0 : S \to \mathcal{W}$, where $\mathcal{W}$ is the set of weights.

We note that this is not a complete generalization of switch graph since it only considers a level of higher-level edges.

Introducing weights.

One-level weighted switch graphs

Given a one-level switch graph (W, S) and an instantiation I, we say that an arc $s \in S$ has weight $I(s)$.

The evolution of a one-level weighted switch graph is given as the updates of the instantiation.

Definition.

Consider a one-level weighted switch graph (W, S) and an instantiation I, when some edge $s \in W \times W$ is crossed we update the actual instantiation I to I^+ in the following way:

- $I^+(t) = \begin{cases} I(t), & \text{if } (s,t) \notin S \\ I(s,t), & \text{otherwise.} \end{cases}$

An edge $(s, t) \in S_1$ assign its weight to t whenever s is crossed.

Introducing weights.

Biological example.

We consider a model for circadian rhythm of a cyanobacteria as described by M. Chaves & M. Preto.

In their work, they consider a system for circadian rhythm with three proteins – KaiA, KaiB and KaiC.

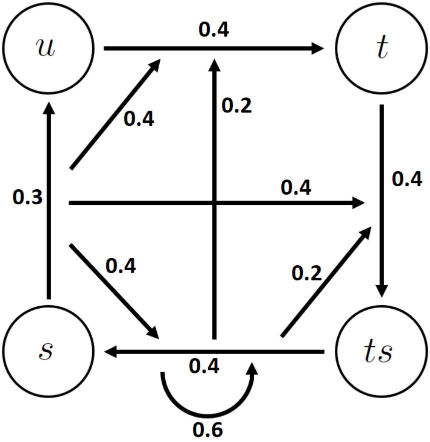
A model considering variables for the concentration of KaiA and four forms of KaiC is obtained – one unphosphorylated form and three phosphorylated forms.

In this way they build a model considering the following variables:

- a for KaiA
- u for the unphosphorylated form of KaiC
- t, ts, and s for the phosphorylated forms of KaiC.

Introducing weights.
Biological example.

We use the reactivity of our models to represent the effect of KaiA i the system. Thus, we obtain a model without the variable *a*:



Simulating using PRISM.

The reactive models presented can be, indeed simulated using PRISM (whenever they have finite vertices and any-level edges).

Considering the set of admissible instantiations, we can consider a family of weighted state transition graphs with fixed weights.

Thus, for a weighted one-level reactive model, we can generate a larger but non-reactive weighted state transition model by considering each state of our generated model as a pair (x, i) where x identifies the state, as usual, and i relates to the instantiation.

Not every state is attainable at all instantiations.

A finite one-level reactive model (finite number of components and edges of any level) generates a finite model with no reactivity.

Simulating using rPrism.

Using this idea we can generate a model which can be analyzed with rPrism.

Moreover, PRISM does not need to generate non-attainable states.

Recall the example of circadian rhythm presented before. We have a model where the component KaiA was removed and switched for a reactive behavior.

We know that, in practice, we obtain a periodic behavior for the concentrations of the components.

With rPrism we are able to obtain a stochastic simulation. Since we understand weights as rates, we use "cmtc" (Continuous time Markov chain).

Simulating using rPrism.

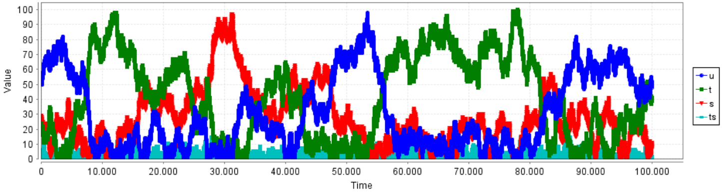
```
NS {
N s 0 100 25 {
u 0.3;
}
N ts 0 100 25 {
s 0.4;
}
N t 0 100 25 {
ts 0.4;
}
N u 0 100 25 {
t 0.4;
}
}
```

```
H1 {
s:u u:t 0.4;
s:u ts:s 0.4;
s:u t:ts 0.4;
ts:s u:t 0.2;
ts:s t:ts 0.2;
ts:s ts:s 0.6;
}

options simtime 100000;
output all;
sim cmtc;
```

Simulating using rPrism.

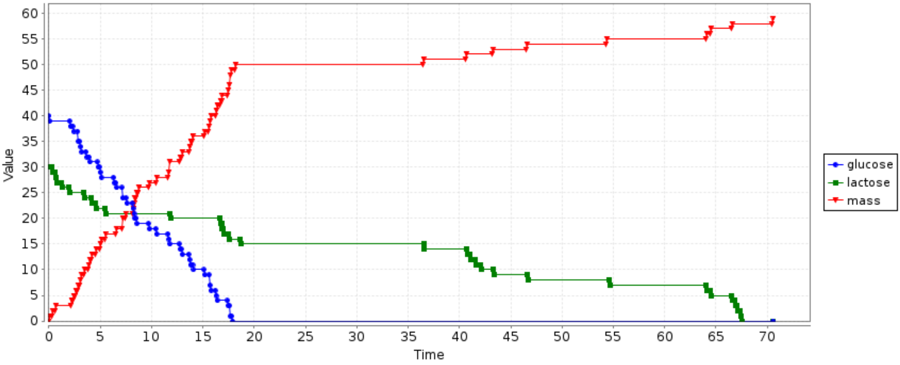
From rPrism, it was possible to obtain the following results:



In particular, the periodic behavior is recovered.

Simulating using rPrism.

Lac. Operon



Conclusions and future work.

We proposed some new reactive models using weights.

We showed that they can be studied using rPrism.

In future, we intend to continue this study with particular focus on the following topics:

- Expand rPrism functionalities in order to enable the use of linear logic to perform model check.
- Formally describe reactive graphs with probabilities;
- Use PRISM to study specific reactive boolean networks with probabilities;

Definition.

A *weighted switch graph* is a pair (X, S) with $X \neq \{\}$ and $S = \bigcup_{i \geq 0} S_k$ such that:

- $S_0 \subseteq W \times W$
- $S_{n+1} \subseteq S_0 \times S_n \times \{\bullet, \circ\}$, for $n \geq 0$

along with an initial *instantiation* $I_0 : S \to \mathcal{W} \cup \{\circledcirc\}$.

We say that an arc $s \in S$ is inhibited if $I(s) = \circledcirc$ and an inhibited edge $s \in W \times W$ cannot be crossed.

If $I(s) \neq \circledcirc$, we say that the edge s is active and with weight $I(s)$.

The evolution of the weighted switch graph when some edge $s \in W \times W$ is crossed is given in the following way:

$$I^{+}(t) = \begin{cases} I(t), & \text{if } (s,t,*) \notin S \ \vee \ I(s,t,*) = \circledcirc, \text{ for any } * \in \{\bullet, \circ\} \\ \circledcirc, & \text{if } (s,t,\circ) \in S \text{ and } I(s,t,\circ) \neq \circledcirc \\ I(s,t,\bullet), & \text{otherwise.} \end{cases}$$

In the example of this presentation, we consider the one-level weighted switch graphs which are a particular case of weighted switch graphs.

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