A colored Petri nets-based framework for modeling and simulating biological systems

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Outline

- Motivation
- Colored Petri nets-based framework
- Functionalities and features
- Example
Motivation
Low-level Petri nets

- Low-level Petri nets do not scale,
- Mainly restricted to relatively small models,
- Difficult to manage and understand large-scale nets,
- Increasing risk of modeling errors for large-scale nets.
Colored Petri nets

- Compact and readable representation,
- Increasing net size = increasing color sets,
- Analysis techniques of low-level Petri nets by automatic unfolding,
- Analysis techniques of high-level Petri nets.
Colored Petri nets-based framework
Colored Petri nets-based framework

![Diagram showing the relationship between time-free and timed, quantitative Petri nets, SPN^C and CPN^C, in the context of discrete and continuous state spaces.]

- **QPN^C**: Time-free
- **SPN^C**: Timed, Quantitative
- **CPN^C**: Continuous State Space
- **Discrete State Space**
Colored qualitative Petri net ($QPN^C$)

- A colored extension of extended P/T net,
  e.g., inhibitor arc and read arc,

- Predefined data types for color set definition:
  - Basic types: integer, string, Boolean, enumeration, index,
  - Structured types: product, union.
An example: Cooperative binding of oxygen to hemoglobin

Hb(O2)4Lo → Hb(O2)4Hi
Hb(O2)3Lo → Hb(O2)3Hi
Hb(O2)2Lo → Hb(O2)2Hi
Hb(O2)1Lo → Hb(O2)1Hi
Hb(O2)0Lo → Hb(O2)0Hi
An example: Cooperative binding of oxygen to hemoglobin
An example: Cooperative binding of oxygen to hemoglobin

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\text{Fei Liu (BTU)}
\]
Declarations for the $QPN^C$ models of the cooperative ligand binding

Declarations

```
colorset Dot = dot;
colorset HbO2 = int with 0-4;
colorset Level = enum with H,L;
colorset P = product with HbO2 × Level;
variable x: HbO2;
variable y: Level;
```
Colored stochastic Petri net ($SPN^C$)

- A colored extension of biochemically interpreted extended stochastic Petri nets,
- Many features helpful for modeling biological systems, e.g., initial marking definition, rate function definition.
Functionalities and features
Functionalities

- Colored Petri net models as drawn as usual, and checking the syntax of declarations and expressions automatically.
- Automatic animation, and single-step animation by manually choosing a binding.
- Simulation is done on an automatically unfolded Petri net.
- Simulation results for colored or uncolored places/transitions are given together or separately.
- Several simulation algorithms to simulate $SPN^C$, including the Gillespie stochastic simulation algorithm (SSA).
- $QPN^C$ and $SPN^C$ are exported to different net formalisms.
Features for modeling biological systems

- Concise specification of initial markings,
- Specifying a rate function for each instance of a colored transition,
- Supporting several special arc types:
  - inhibitor arc,
  - read arc,
  - reset arc,
  - modifier arc,
- Supporting extended rate functions:
  - stochastic transitions with freestyle rate functions
  - immediate firing,
  - deterministic firing delay,
  - scheduled firing.
Specification of initial markings

- Specifying colors and their corresponding tokens as usual,
- Specifying a set of colors with the same number of tokens,
- Using a predicate to choose a set of colors and then specifying a same number of tokens,
- Using the `all()` function to specify all colors with a specified number of tokens.

<table>
<thead>
<tr>
<th>Color/Predicate/Function</th>
<th>marking</th>
</tr>
</thead>
<tbody>
<tr>
<td>all()</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4,5,7</td>
<td>2</td>
</tr>
<tr>
<td>( x &gt; 10 )</td>
<td>2</td>
</tr>
</tbody>
</table>

Colorset \( CS = \text{int with 1-100}; \)
Supporting special arc types

Declarations:
Colorset CS=int with 1,2;
Variable x:CS;
Specifying a rate function for each instance of a colored transition

Declarations:
Colorset CS = int with 1-2;
Variable x : CS;

[x=1] MassAction( 0.01 )
[x=2] LevelInterpretation(0.1,16)
Example
Stochastic Petri net model for the repressilator
Colored stochastic Petri net model for the repressilator

Transition Rate function

generate 0.1 * gene
block 1.0 * proteine
unblock 0.0001 * blocked
degraded 0.001 * proteine
Colored stochastic Petri net model for the repressilator

Increasing net size = increasing color set.
Thank You!

Begin to demonstrate $QPN^C / SPN^C$