

A Framework for Modular Modeling and Analysis of Signaling Networks

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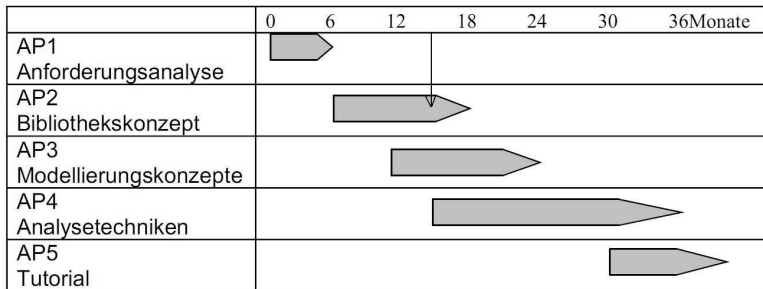
MOPS meeting, Kassel
May 21, 2010

Project Milestones

Project milestones

- WP1 - Requirements analysis
- WP2 - Library approach for generic model components
- WP3 - Modeling concepts for dealing with model alternatives
- WP4 - Analysis techniques for identification and behavior comparison of model components
- WP5 - Tutorial

Schedule



Project Results

January 2010 – May 2010

Overview of main results

- Improvement of QPN^C and SPN^C prototypes
- Construction of colored Petri net models
- Case studies

Functionalities

- Rich data types for color set definition: integer, string, Boolean, enumeration, index, product and union.
- 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 different types of transitions:
 - ▶ stochastic transitions with freestyle rate functions
 - ▶ immediate firing,
 - ▶ deterministic firing delay,
 - ▶ scheduled firing.

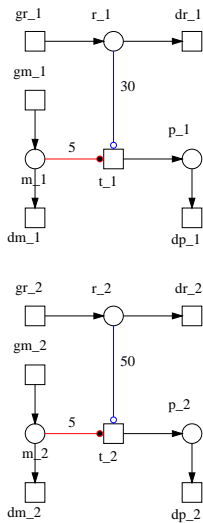
Specification of initial markings

- 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.

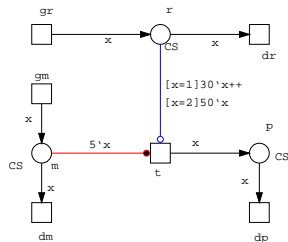
Color/Predicate/Function	marking
<i>all()</i>	2
1	2
4,5,7	2
$x > 10$	2

Colorset CS = int with 1-100;

Supporting special arc types

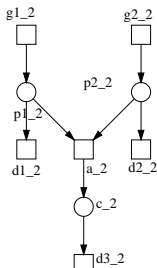
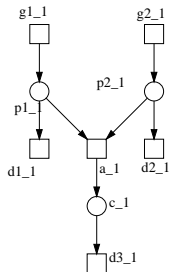


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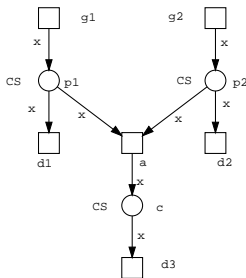


Declarations:
 Colorset CS=int with 1,2;
 Variable x:CS;

Specifying a rate function for each instance of a colored transition



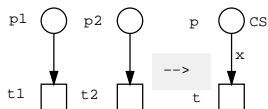
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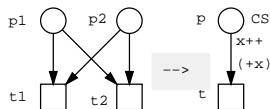
Declarations:
Colorset CS = int with 1-2;
Variable x : CS;

[x=1] MassAction(0.01)
[x=2] LevelInterpretation(0.1,16)

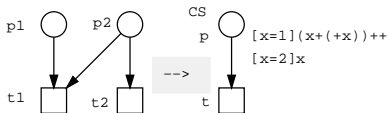
Construction of colored Petri net models



(a)



(b)

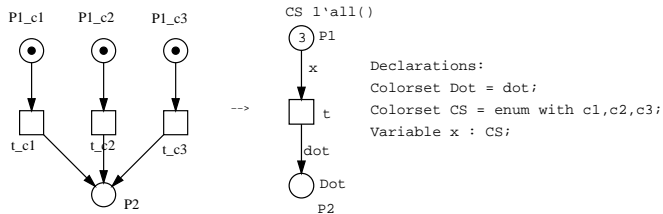


(c)

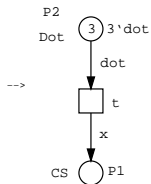
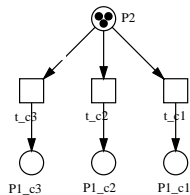
Declarations:
 colorset CS = int with 1,2;
 variable x : CS ;

(d)

Construction of colored Petri net models



Construction of colored Petri net models



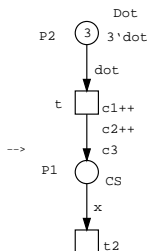
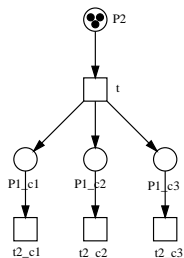
Declarations:

```
Colorset Dot = dot;
```

```
Colorset CS = enum with c1,c2,c3;
```

```
Variable x : CS;
```

Construction of colored Petri net models



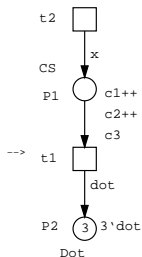
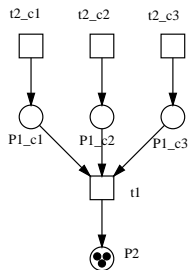
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Construction of colored Petri net models



Declarations:

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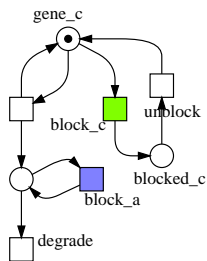
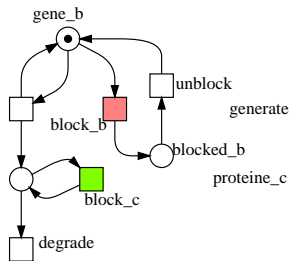
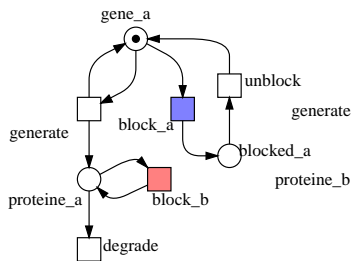
```
Colorset CS = enum with c1,c2,c3;
```

```
Variable x : CS;
```

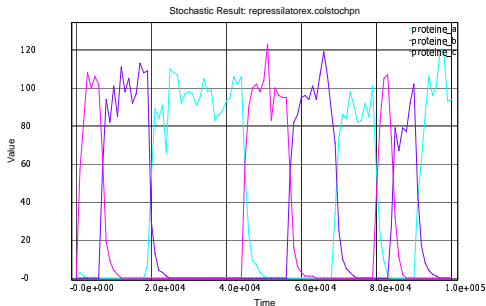
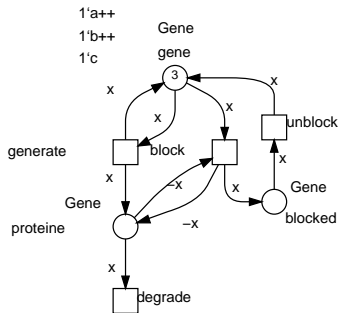

Case studies

- QPN^C model for the cooperative ligand binding,
- QPN^C model for the *C. elegans* vulval development,
- QPN^C and SPN^C models for the repressilator,
- SPN^C model for the halobacterium phototaxis,
- QPN^C and SPN^C model for the pain switch.

Stochastic Petri net model for the repressilator



Colored stochastic Petri net model for the repressilator



Transition Rate function

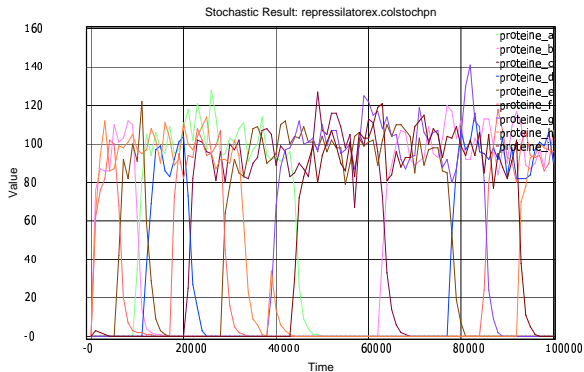
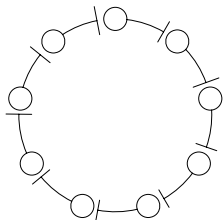
generate $0.1 * gene$

block $1.0 * proteine$

unblock $0.0001 * blocked$

degrade $0.001 * proteine$

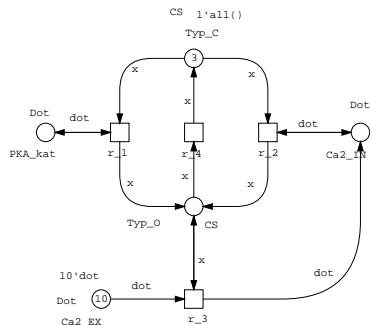
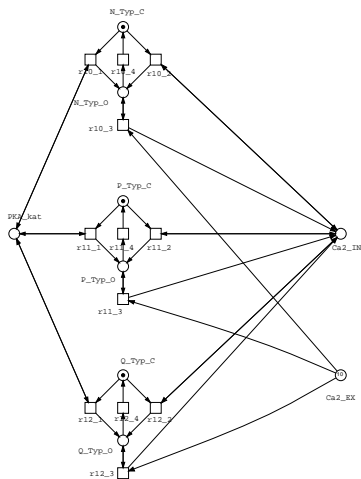
Colored stochastic Petri net model for the repressilator



Increasing net size = increasing color set.

Pain switch models

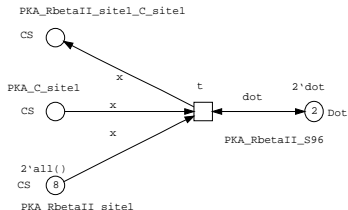
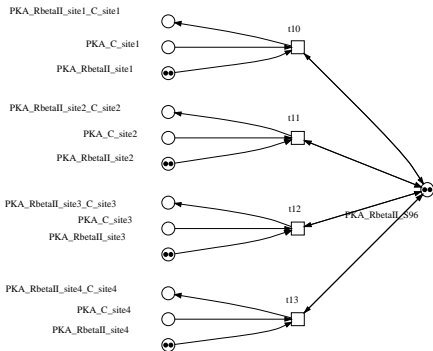
Colored Petri net model for E1, E2 and E3



Declarations:
Colorset CS=int with 1-3;
Variable x:CS;

Pain switch models

Colored Petri net model for PKA - regulation2



Declarations:
Colorset CS=int with 1-4;
Variable x:CS;

Next Steps

Next steps

- Continue to color pain switch models,
- Working on a manual for colored Petri nets (35 pages finished),
- Making a case study: the size of the underlying net is about 110,000 places and 135,000 transitions,
- Develop analysis techniques for colored stochastic Petri nets,
- Coupling with the database developed by M2,
needs to be discussed.

Thank You !

Begin to demonstrate QPN^C/SPN^C