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

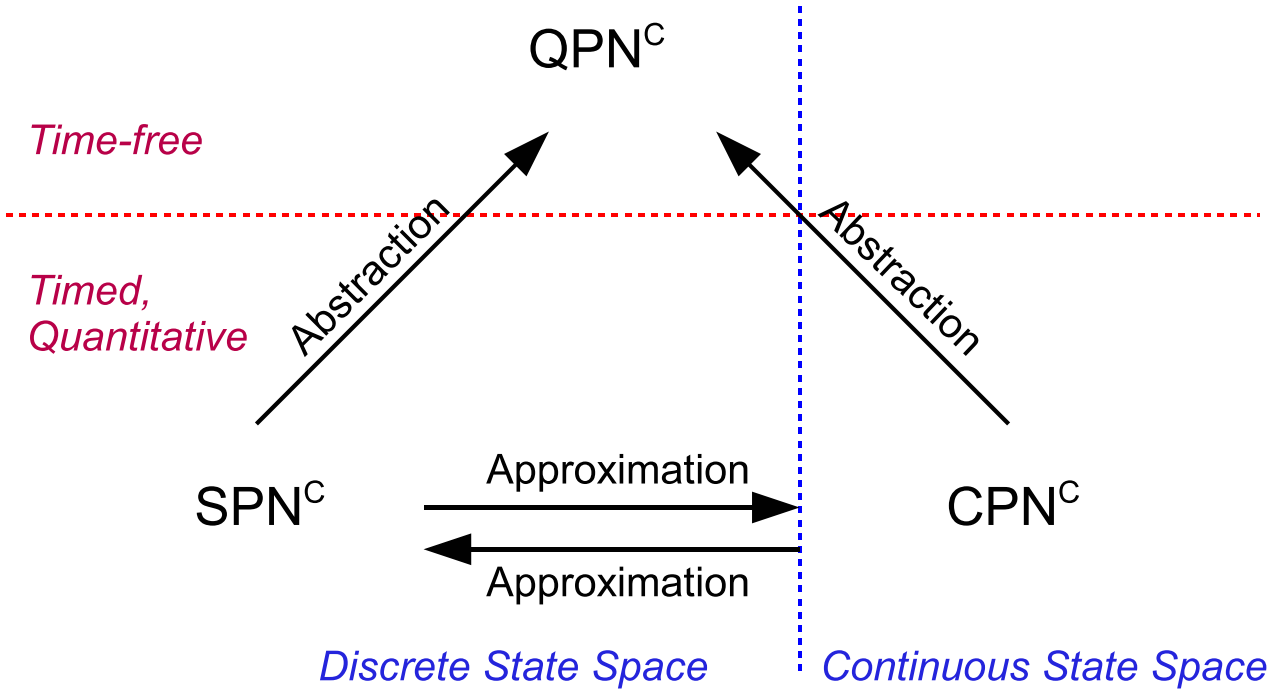
- Low-level Petri nets do not scale,
- Mainly restricted to relatively small models,
- Difficult to manage and understand large-scale nets,
- Increasing risk of modeling errors for large-scale nets.

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



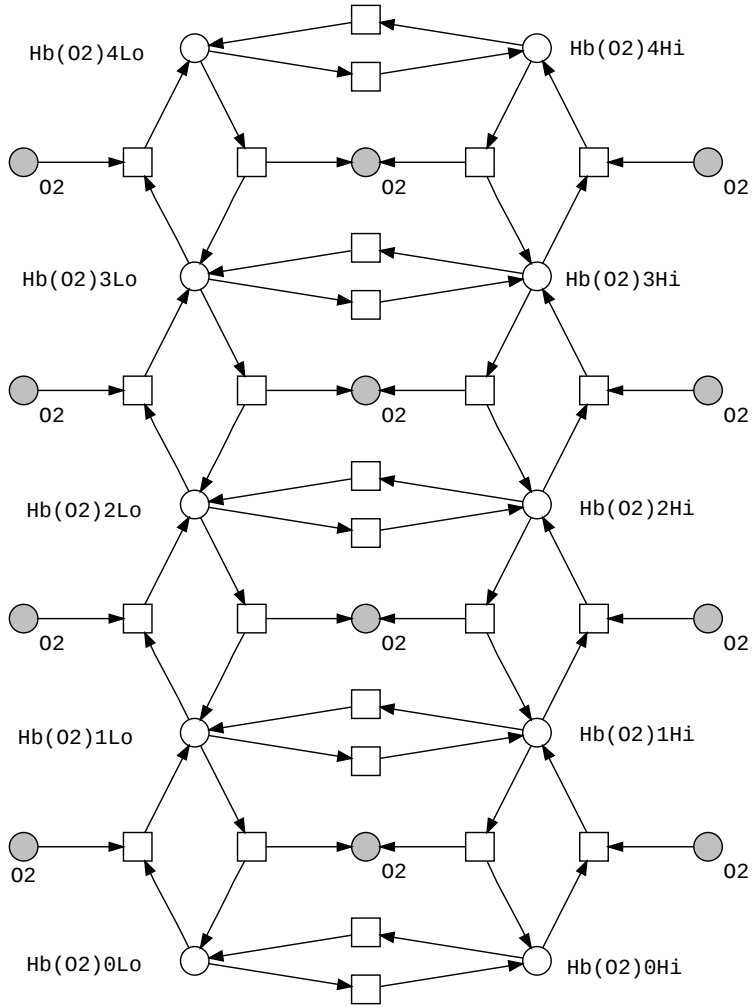
Colored qualitative Petri net (QPN^C)

- A colored extension of extended P/T net,

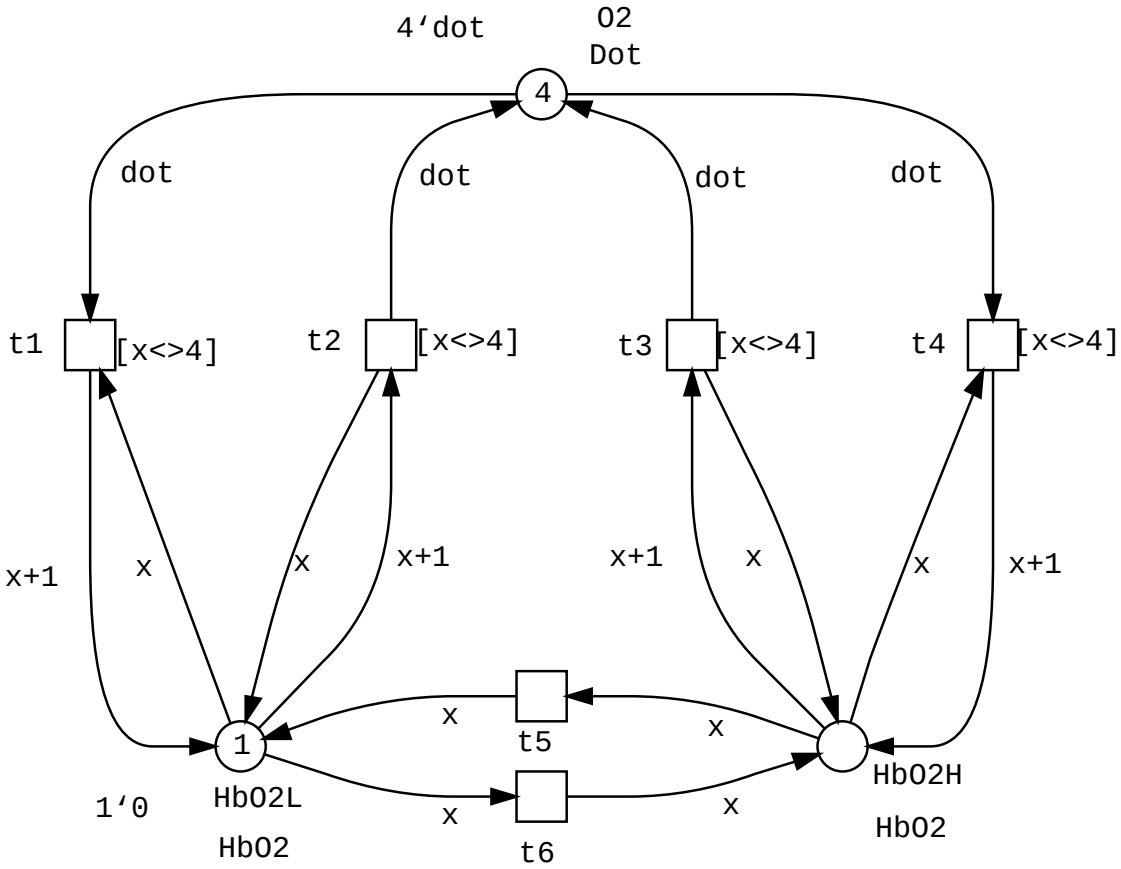
  e.g., inhibitor arc and read arc,

- Predefined data types for color set definition:
  - Basic types: integer, string, Boolean, enumeration, index,
  - Structured types: product, union.

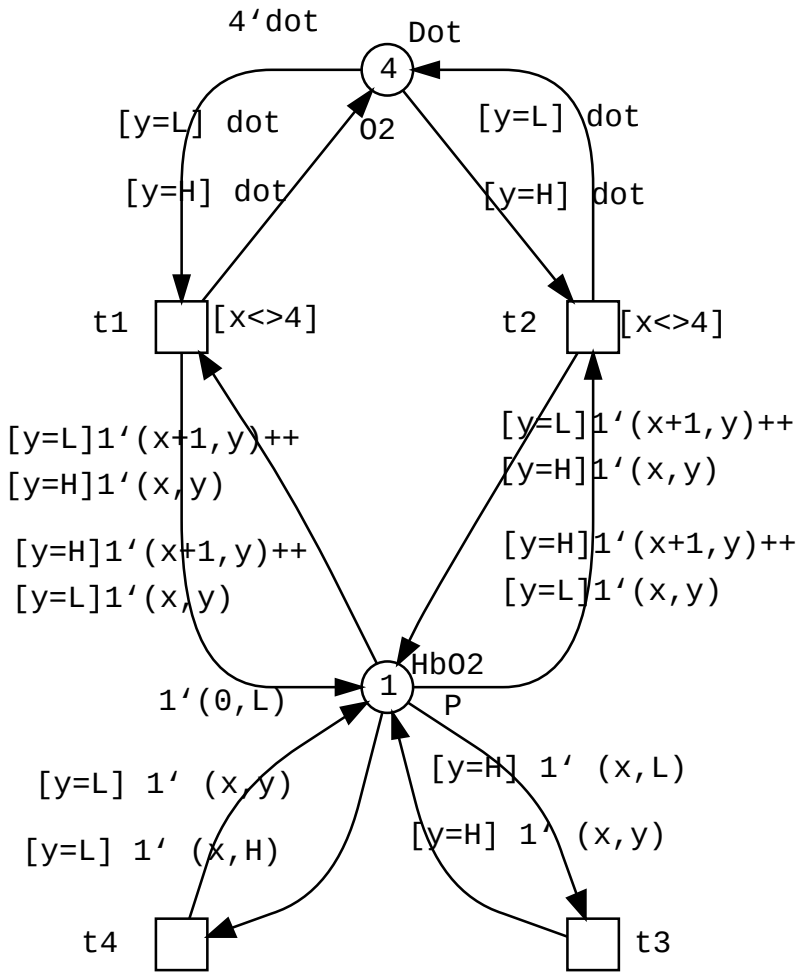
An example: Cooperative binding of oxygen to hemoglobin



An example: Cooperative binding of oxygen to hemoglobin



An example: Cooperative binding of oxygen to hemoglobin



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 Gilespie 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.

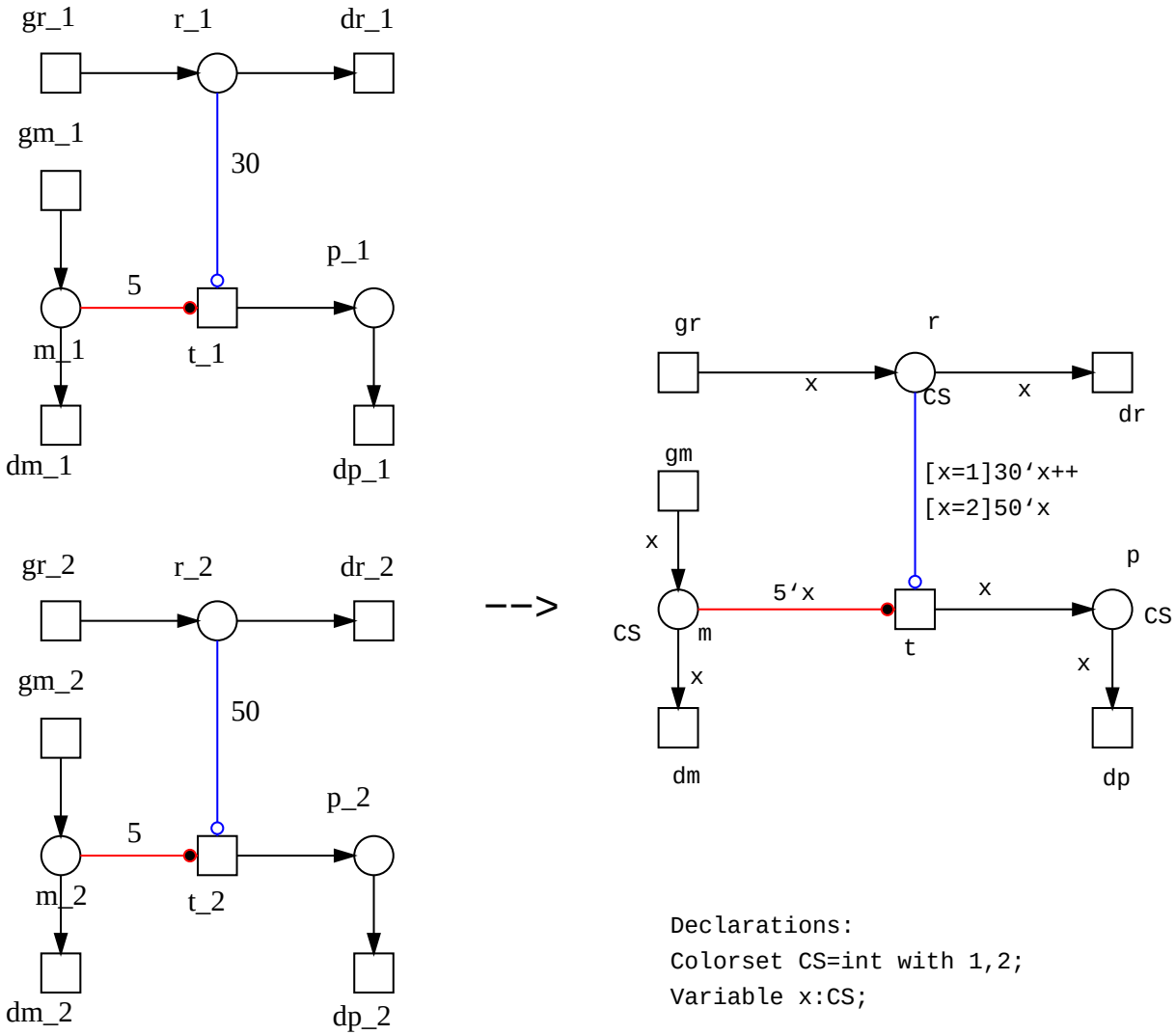
Specification of initial markings

- 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.

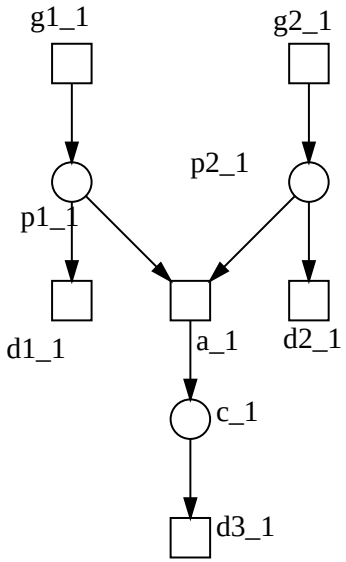
Color/Predicate/Function	marking
all()	2
1	2
4,5,7	2
$x > 10$	2

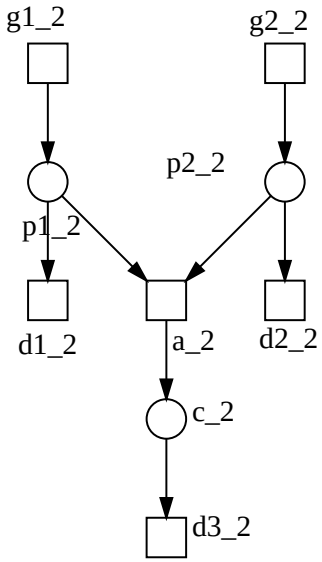
Colorset CS = int with 1-100;

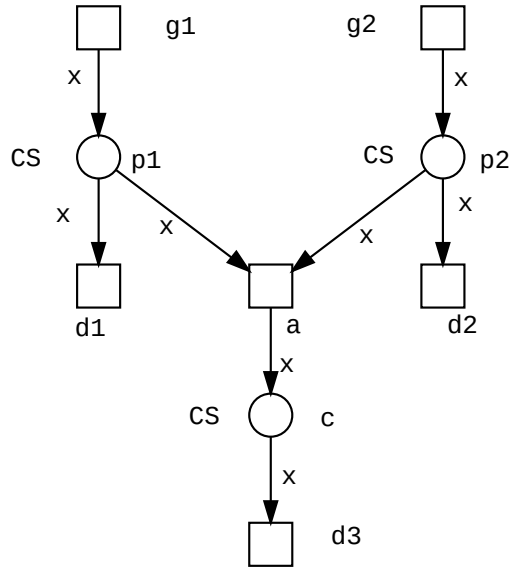
Supporting special arc types



Specifying a rate function for each instance of a colored transition





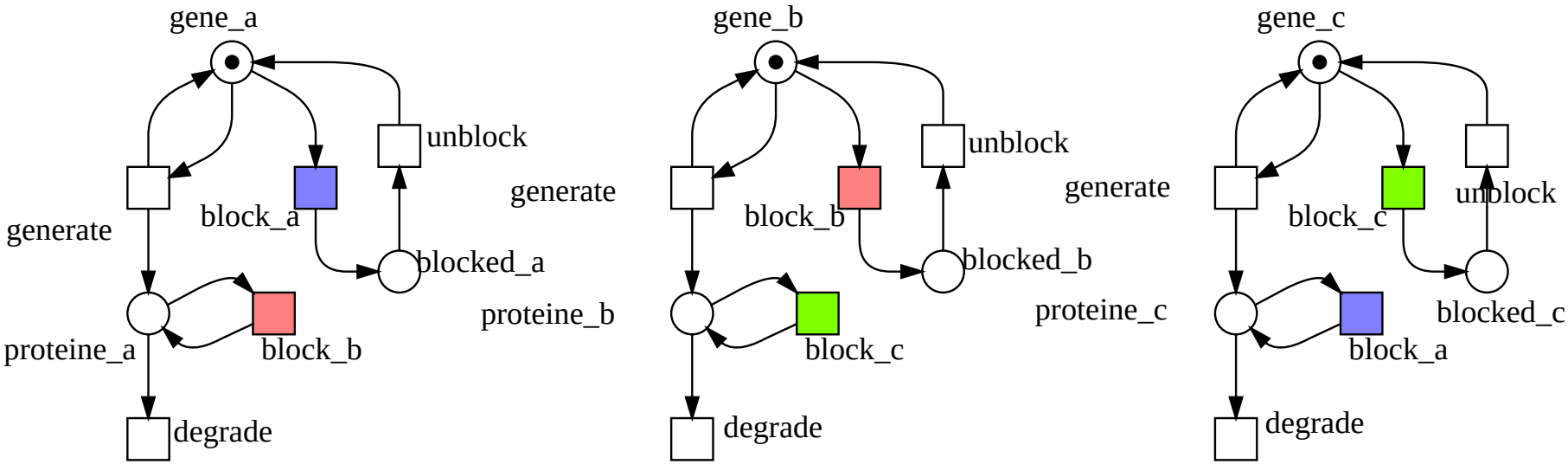



```
Declarations:
Colorset CS = int with 1-2;
Variable x : CS;
```

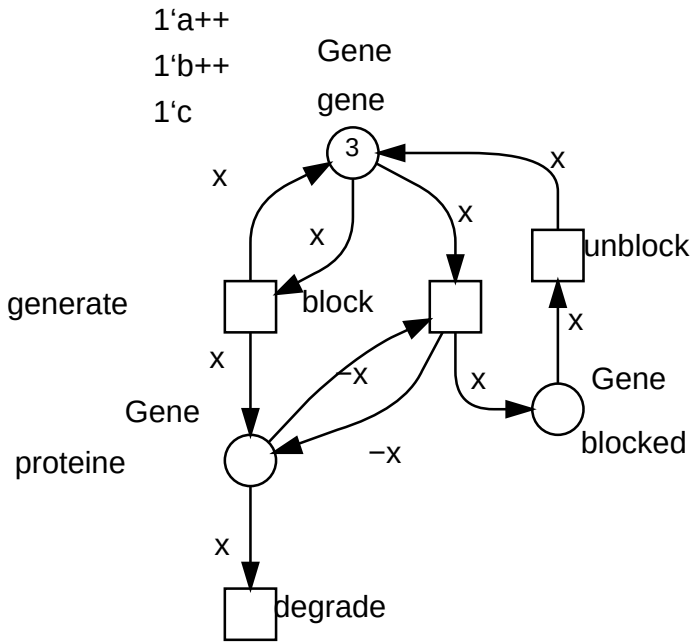
```
[x=1] MassAction( 0.01 )
[x=2] LevelInterpretation(0.1,16)
```

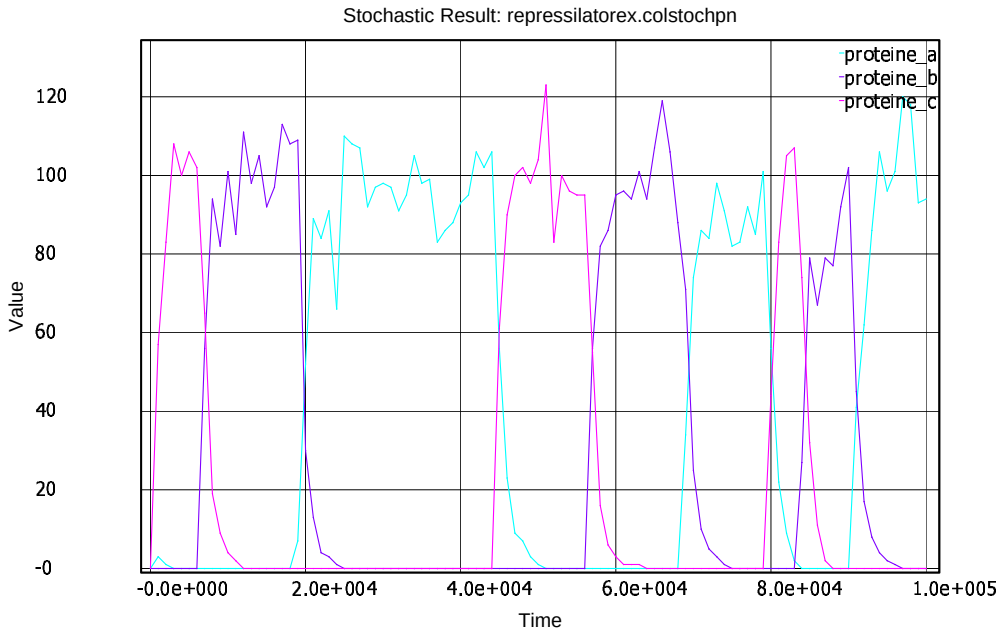
Example

Stochastic Petri net model for the repressilator



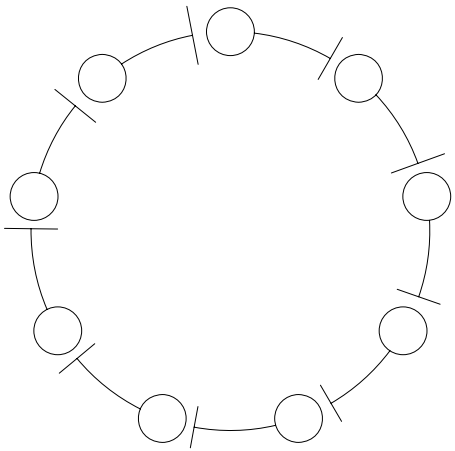
Colored stochastic Petri net model for the repressilator

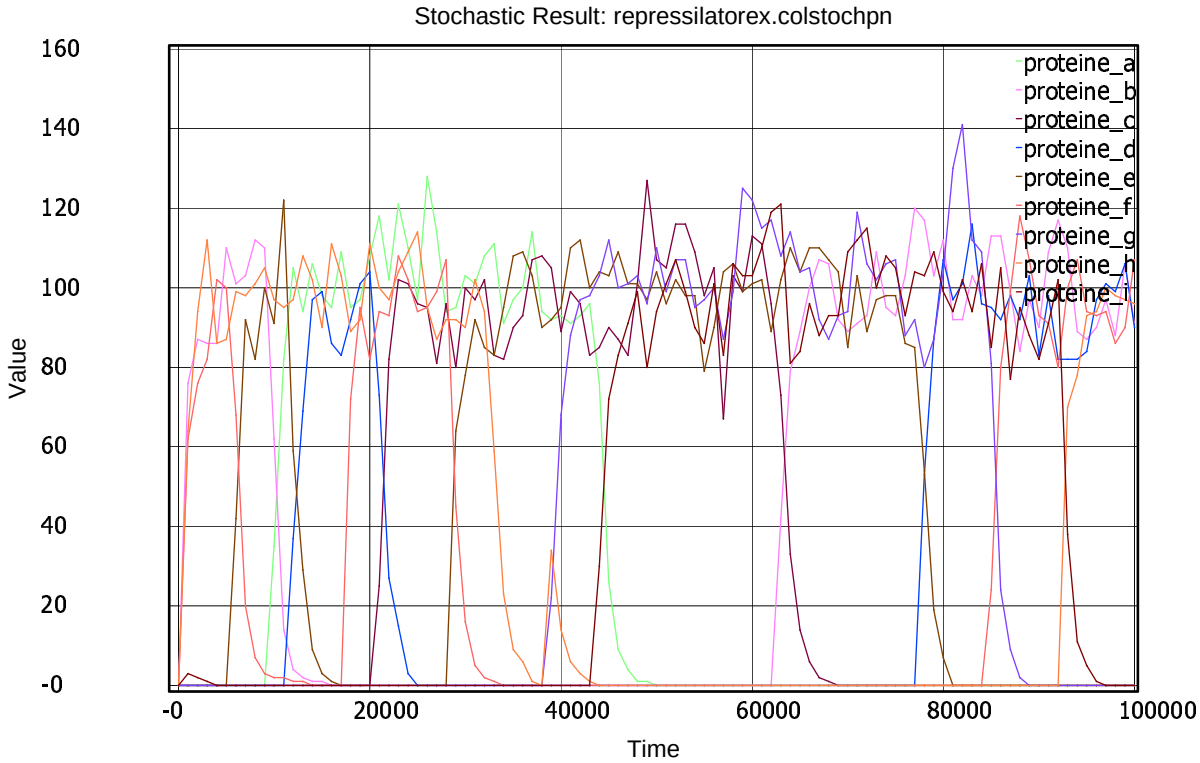




Transition	Rate function
generate	$0.1 * gene$
block	$1.0 * proteine$
unblock	$0.0001 * blocked$
degrade	$0.001 * proteine$

Colored stochastic Petri net model for the repressilator





Increasing net size = increasing color set.

Thank You !

Begin to demonstrate QPN^C / SPN^C