A Framework for Modular Modeling and Analysis of Signaling Networks

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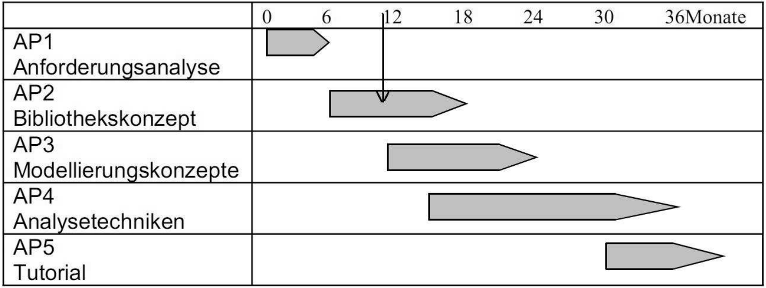
MOPS meeting, Magdeburg
January 18, 2010

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


0
6
12
18
24
30
36Monate
AP1
Anforderungsanalyse
AP2
Bibliothekskonzept
AP3
Modellierungskonzepte
AP4
Analysetechniken
AP5
Tutorial

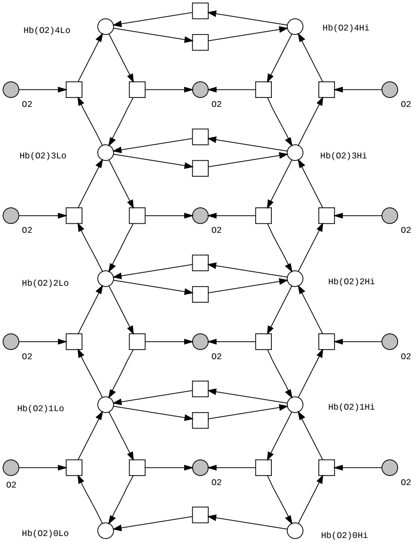
Project Results

August 2009 – January 2010

Overview of main results

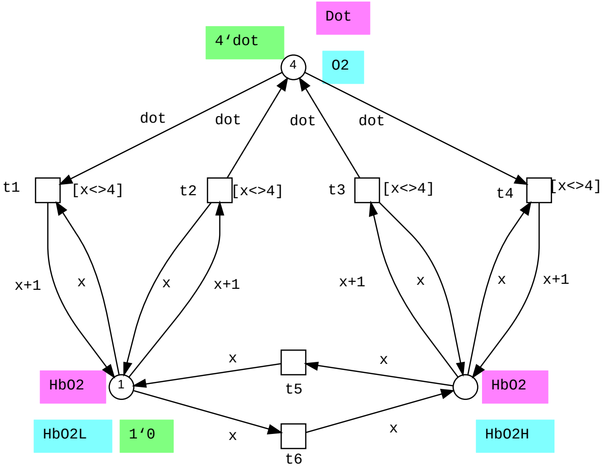
- prototype colored qualitative Petri nets (QPN^C)
- prototype colored stochastic Petri nets (SPN^C)
- prototype animation of QPN^C and SPN^C
- prototype simulation of SPN^C

Cooperative ligand binding - the *QPN* model

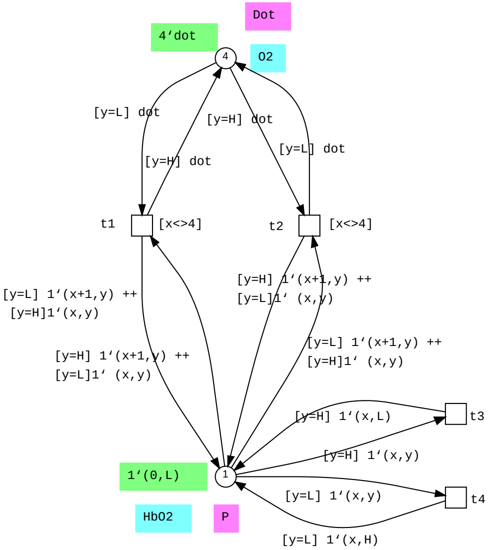


Reference:
Wolfgang Marwan, Annegret Wagler, Robert Weismantel. Petri Nets as a Framework for the Reconstruction and Analysis of Signal Transduction Pathways and Regulatory Networks. Natural Computing, 8(3).

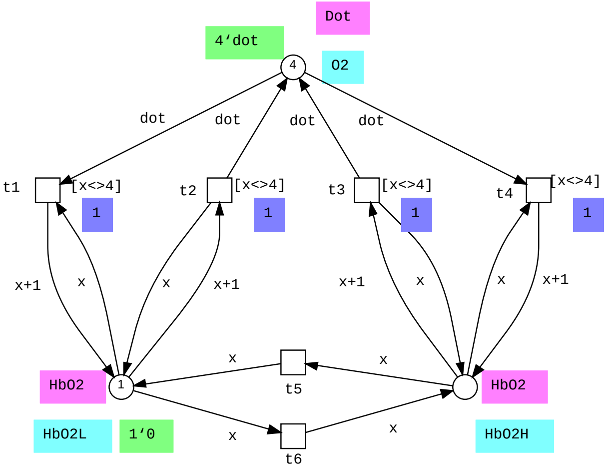
Cooperative ligand binding - the QPN^C model



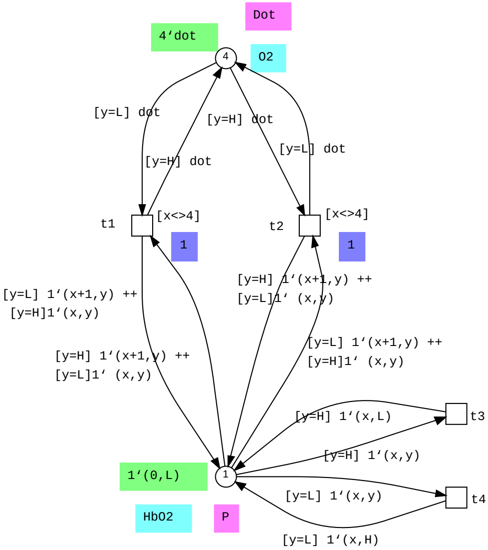
Cooperative ligand binding - the QPN^C model



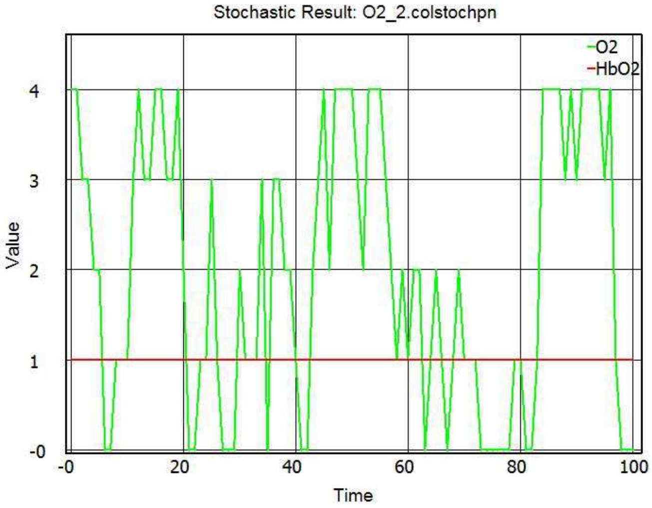
Cooperative ligand binding - the SPN^C model



Cooperative ligand binding - the SPN^C model



Cooperative ligand binding - simulation results



QPN^C/SPN^C - Notation

Multi-set:

- A multi-set m over a non-empty set S is a mapping $m : S \rightarrow N$, where N denotes the set of all non-negative integers.
- Intuitively, a multi-set is a set that can contain several occurrences of the same element.
- It can be represented as a formal sum: $m = \sum_{s \in S} m(s)s$.
- The coefficient $m(s)$ is called multiplicity of s in m.
- In the followings, we use the notation $Bag(S)$ to denote the set of multisets over S.

QPN^C/SPN^C - Notation

Denotations:

- $Type(v)$: the type of a variable, v
- $Type(expr)$: the type of an expression,$expr$
- $Var(expr)$: the set of variables in an expression,$expr$
- $Boolean$: the boolean type, containing the elements false, true
- $Type(A) = Type(v)|v \in A$, where A is a set of variables

QPN^C - Definition

A QPN^C is an eight-tuple $QPN^C = < \sum, P, T, F, c, g, f, m_0 >$, where:

- $\sum$ is a finite set of non-empty types, also called color sets.
- P is a finite, nonempty, and disjoint set of places.
- T is a finite, nonempty, and disjoint set of transitions.
- F is a finite set of arcs, such that $F \subseteq (P \times T) \cup (T \times P)$.

QPN^C - Definition

- $c : P \cup T \rightarrow \sum$ is a color function, which maps each place p or each transition t to a type or color set $c(p)$ or $c(t)$.
- g is a guard function. It is defined from T into expressions such that: $\forall t \in T : [Type(g(t)) = Boolean \wedge Type(Var(g(t))) \subseteq \sum]$.
- f is an arc expression function. It is defined from F into expressions such that: $\forall a \in F : [Type(f(a)) = c(p) \wedge Type(Var(f(a))) \subseteq \sum]$, where p is the place that connects the arc a.
- m_0 is an initialization function. It is defined from P into expressions such that: $\forall p \in P : [Type(m_0(p)) = c(p) \wedge m_0(p) \in Bag(c(p))]$.

SPN^C - Definition

A SPN^C is a ten-tuple $SPN^C = QPN^C + < v, l >$, where:

- T is the union of three disjoint transition sets, i.e. $T := T_{stoch} \cup T_{im} \cup T_{timed}$ with:
  - T_{stoch}, the set of stochastic transitions with exponentially distributed waiting time,
  - T_{im}, the set of immediate transitions with waiting time zero, and
  - T_{timed}, the set of transitions with deterministic waiting time.
- $v : T_{stoch} \rightarrow H$ is a function, which assigns a stochastic hazard function $h_{t(c)}$ to each transition instance $t(c)$ of $t \in T_{stoch}$, whereby $H := \bigcup_{t \in T_{stoch}} \{h_{t(c)} | h_{t(c)} : IN_0^{|^\bullet t|} \rightarrow IR^+\}$ is the set of all stochastic hazard functions, and $v(t(c)) = h_{t(c)}$ for all transitions $t \in T_{stoch}$. $t(c)$ is an instance of t, $c \in c(t)$.
- $l : T_{timed} \rightarrow IR^+$ assigns to each deterministic transition instance $t(c)$ of $t \in T_{timed}$ a non-negative deterministic waiting time.

QPN^C/SPN^C - Modeling

Features:

- drawing of the Petri net graph as usual
- rich data types for color set definition
  - basic types: int, string, bool, enum, index
  - structured types: product, union
- user-defined functions
- type and syntax checking

QPN^C/SPN^C - Modeling

Procedure:

- define color sets, variables, constants, and functions
- assign color sets to places and define initial markings
- define arc expressions
- define guards for transitions
- define rate functions for transitions (**only** SPN^C)
- syntax checking (manually or automatically)

QPN^C/SPN^C - Animation

- automatic animation
- single-step animation by manually choosing a binding

SPN^C - Simulation

- simulation is done on an automatically unfolded Petri net
- simulation results for colored or uncolored places/transitions

SPN^C - Analysis

- Numerical probabilistic model checking
  - higher accuracy, but subject to state explosion
  - specific models, such as DTMCs, CTMCs, MDPs
- Approximate probabilistic model checking
  - low accuracy, but not subject to state explosion
  - handle state spaces beyond current limits of exact analysis
  - systems with complex dynamics as semi-Markov processes or generalized semi-Markov processes
  - systems with an infinite state space

Next Steps

Next steps

- Apply colored stochastic Petri nets to MOPS project
- Develop analysis techniques for colored stochastic Petri nets
- Continue to analyze the capabilities and equivalence of Cell Illustrator and Snoopy
- Coupling with the database developed by M2,
  needs to be discussed

Thank You !

Begin to demonstrate QPN^C/SPN^C