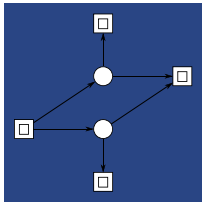

Brandenburg
University of Technology
Cottbus

A Framework for Modular Modeling and Analysis of Signaling Networks

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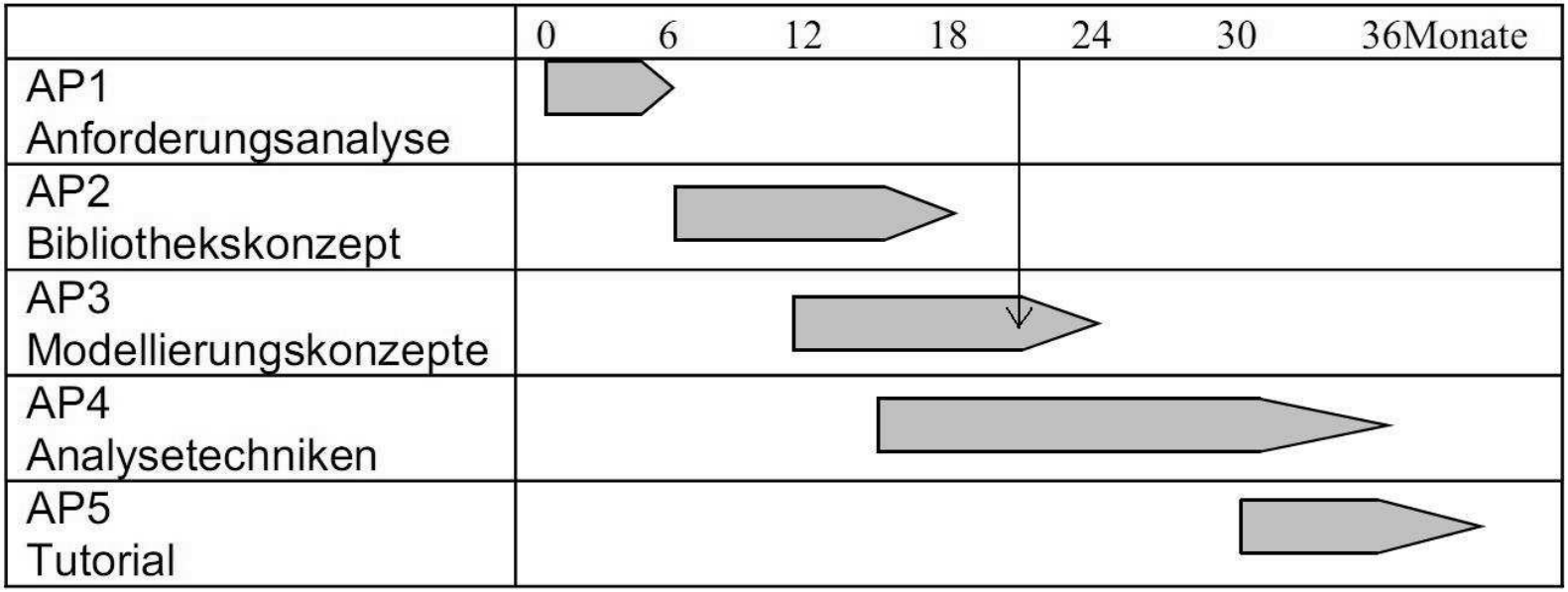
MOPS meeting, Berlin
March 4 2011

Project Milestones

Project milestones

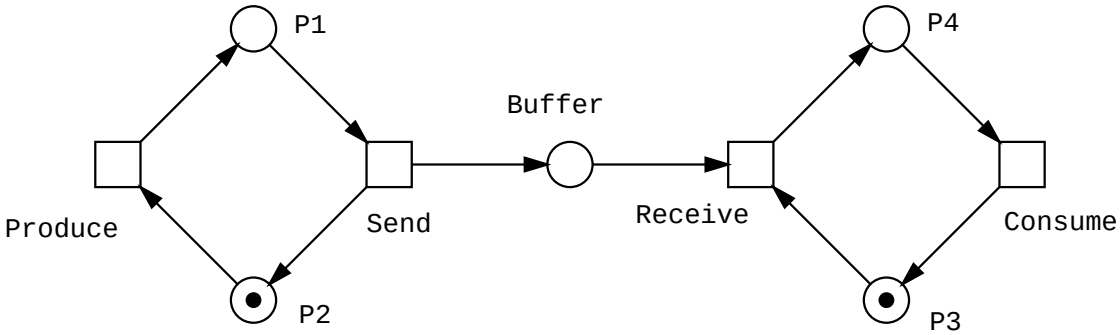
- WP1 - Requirements analysis
- WP2 - Library approach for generic model components
- WP3 - Modeling concepts for dealing with model alternatives
- WP4 - Analysis techniques for identification and behavior comparison of model components
- WP5 - Tutorial

Schedule

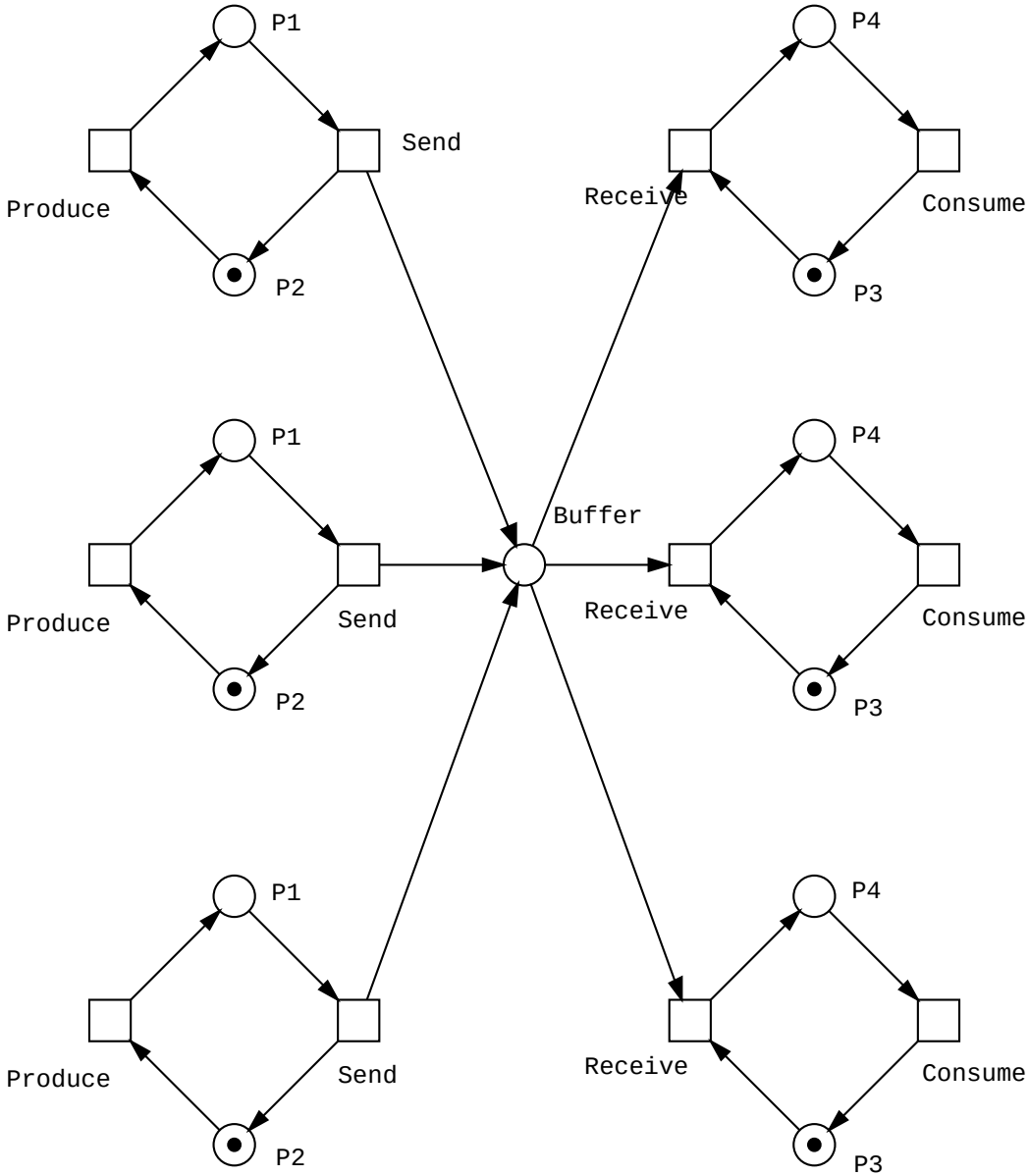

0
6
12
18
24
30
36Monate
AP1
Anforderungsanalyse
AP2
Bibliothekskonzept
AP3
Modellierungskonzepte
AP4
Analysetechniken
AP5
Tutorial

Introduction

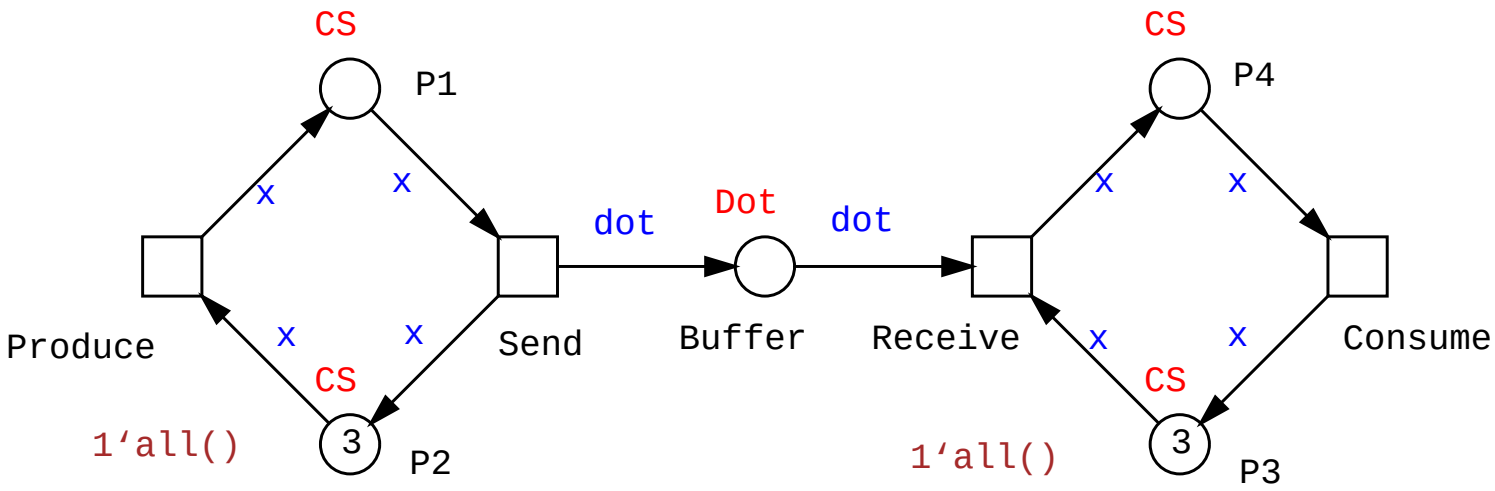
Producer-Consumer



Producer-Consumer



Producer-Consumer



Why use colored Petri nets

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

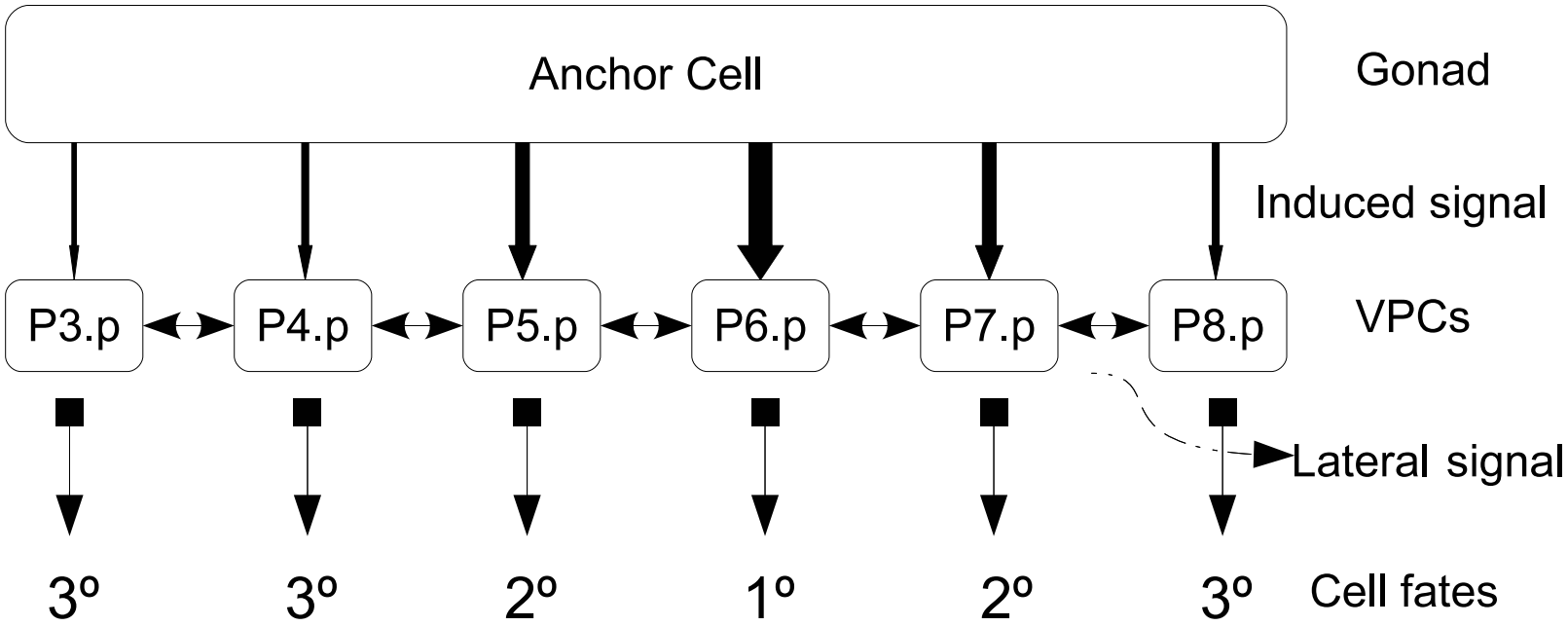
Project Results

November 2010 – March 2011

Overview of main results

- Scenarios to apply colored Petri nets in systems biology
- Analysis of colored Petri nets
- Case studies

Scenario 1: biological systems with similar objects (e.g. cells, genes, receptors, transducers)



- Colset CS = integer with 3-8;

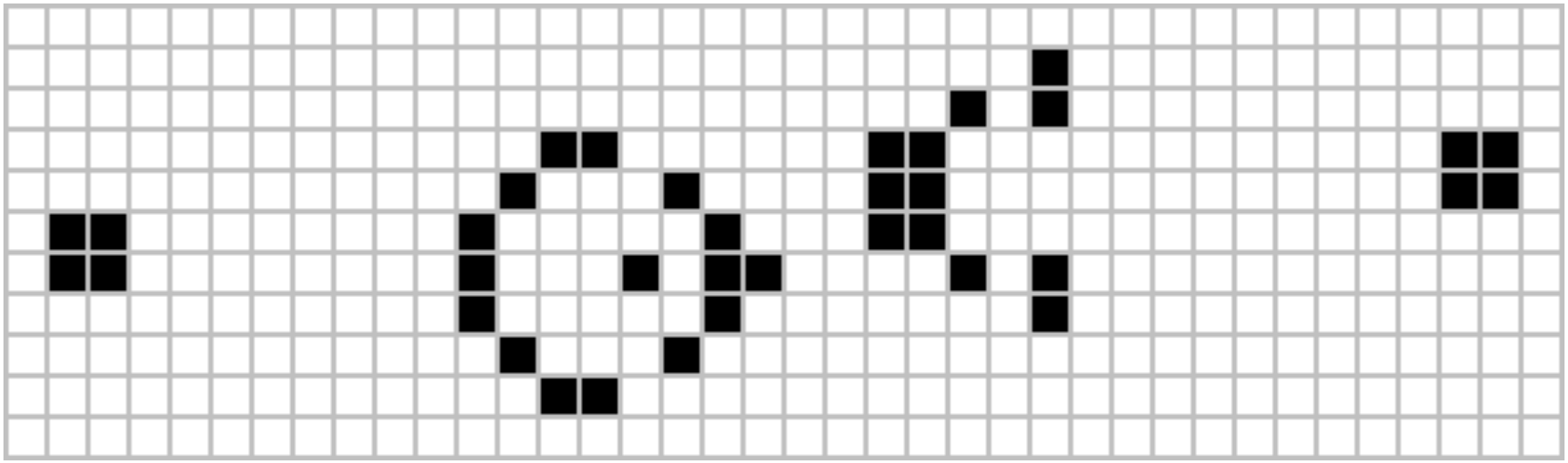
Scenario 2: agent-based models with a grid

Game of Life

- two-dimensional grid
- States: "populated" or "unpopulated" ("empty")
- Rules:
  - Rule 1. Survivals. Each cell with two or three neighbors survives for the next generation.
  - Rule 2. Deaths. Each cell with four or more neighbors dies from overpopulation. Every cell with one neighbor or none dies from loneliness.
  - Rule 3. Births. Each empty cell with exactly three neighbors becomes populated.

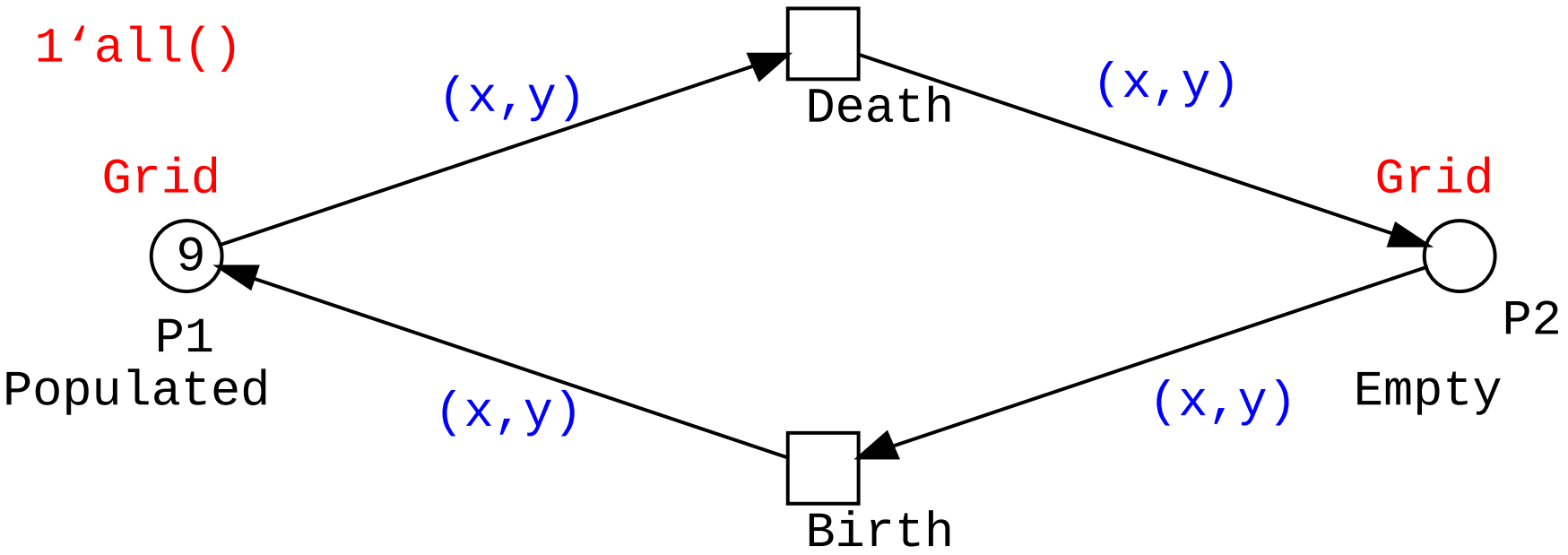
Ref: [Gardner70] Martin Gardner. The fantastic combinations of John Conway's new solitaire game "life". Scientific American. 223: 120-123. (1970)

Scenario 2: agent-based models with a grid



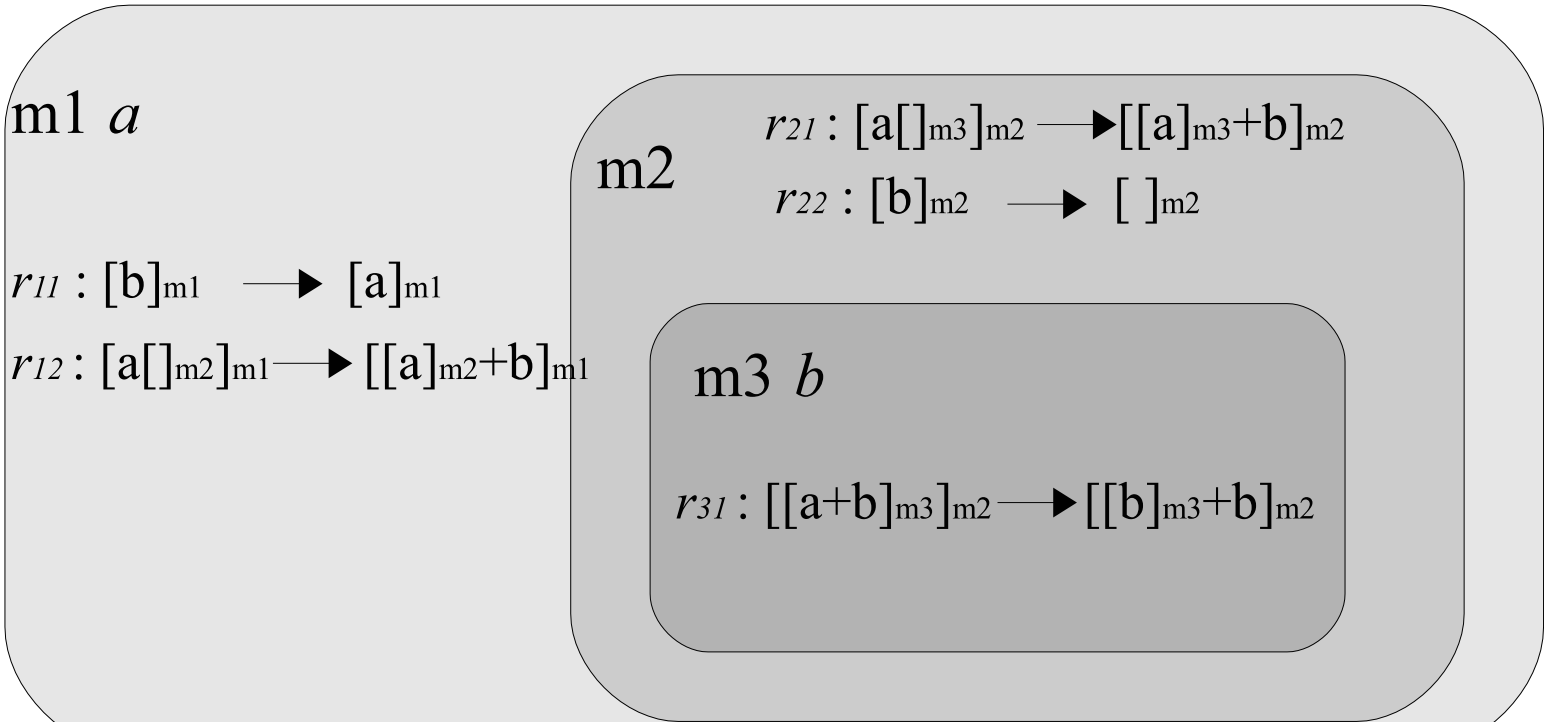
Ref: http://en.wikipedia.org/wiki/File:Game_of_life_glider_gun.svg

Scenario 2: agent-based models with a grid

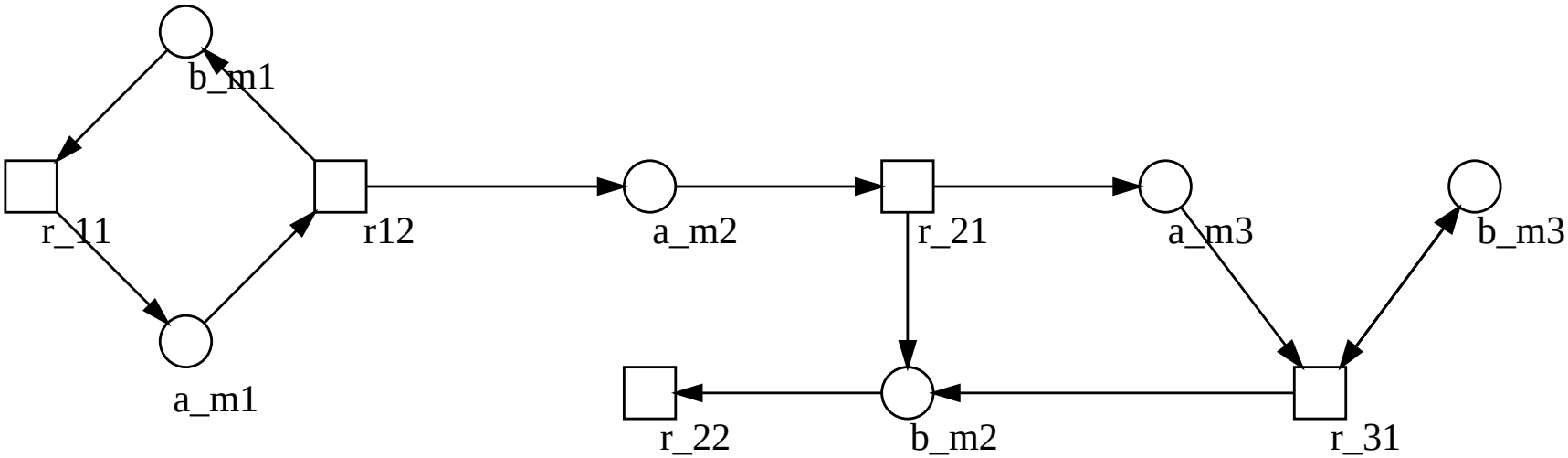


- Colset Row = integer with 1-m;
- Colset Column = integer with 1-n;
- Colset Grid = product Row × Column;

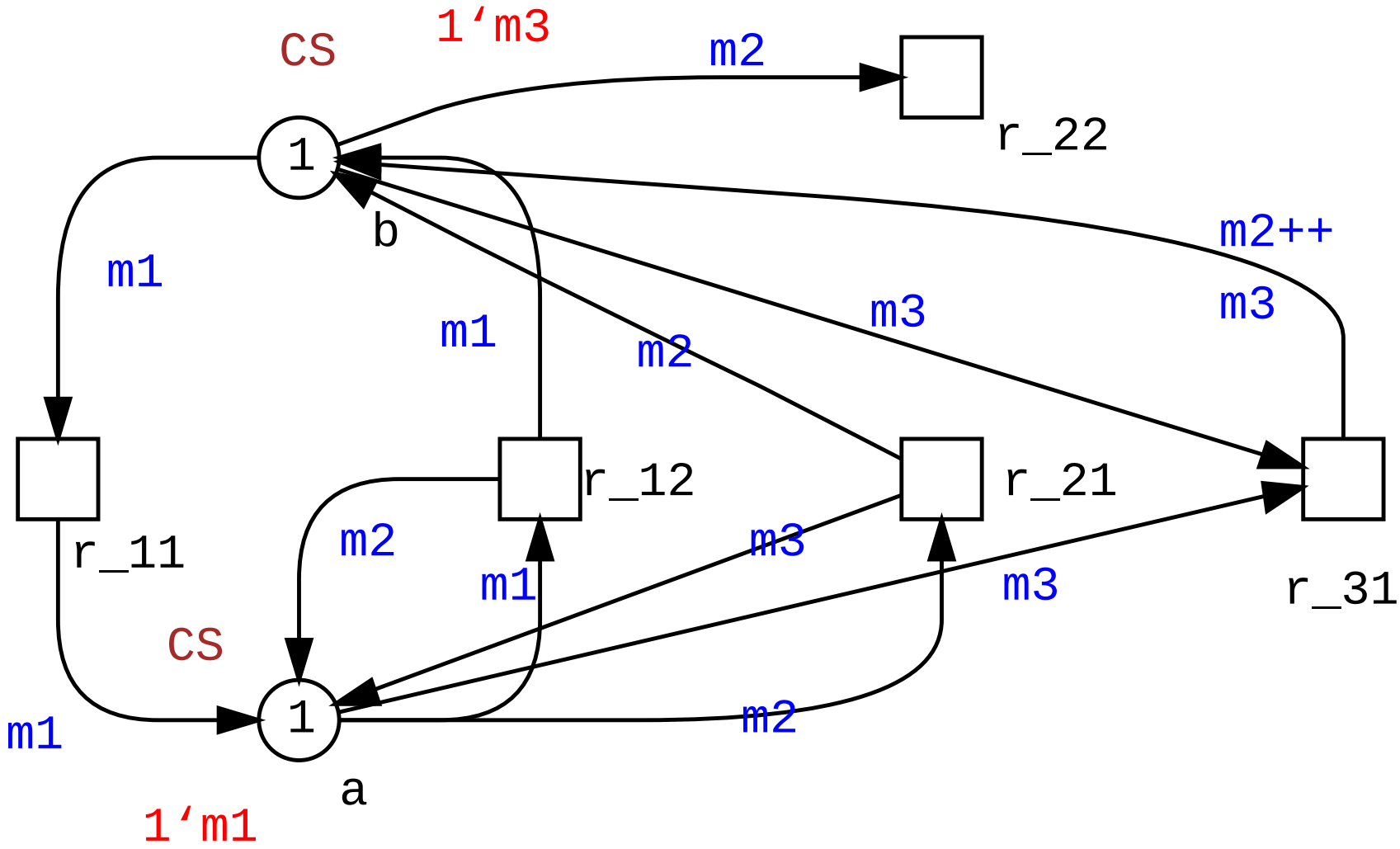
Scenario 3: membrane systems



Scenario 3: membrane systems

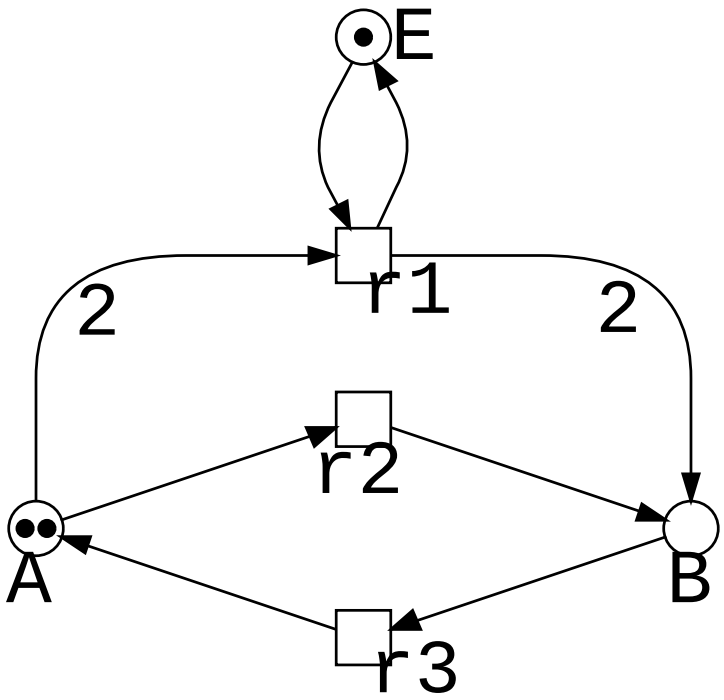


Scenario 3: membrane systems



- Colset CS = enum with m1,m2,m3;

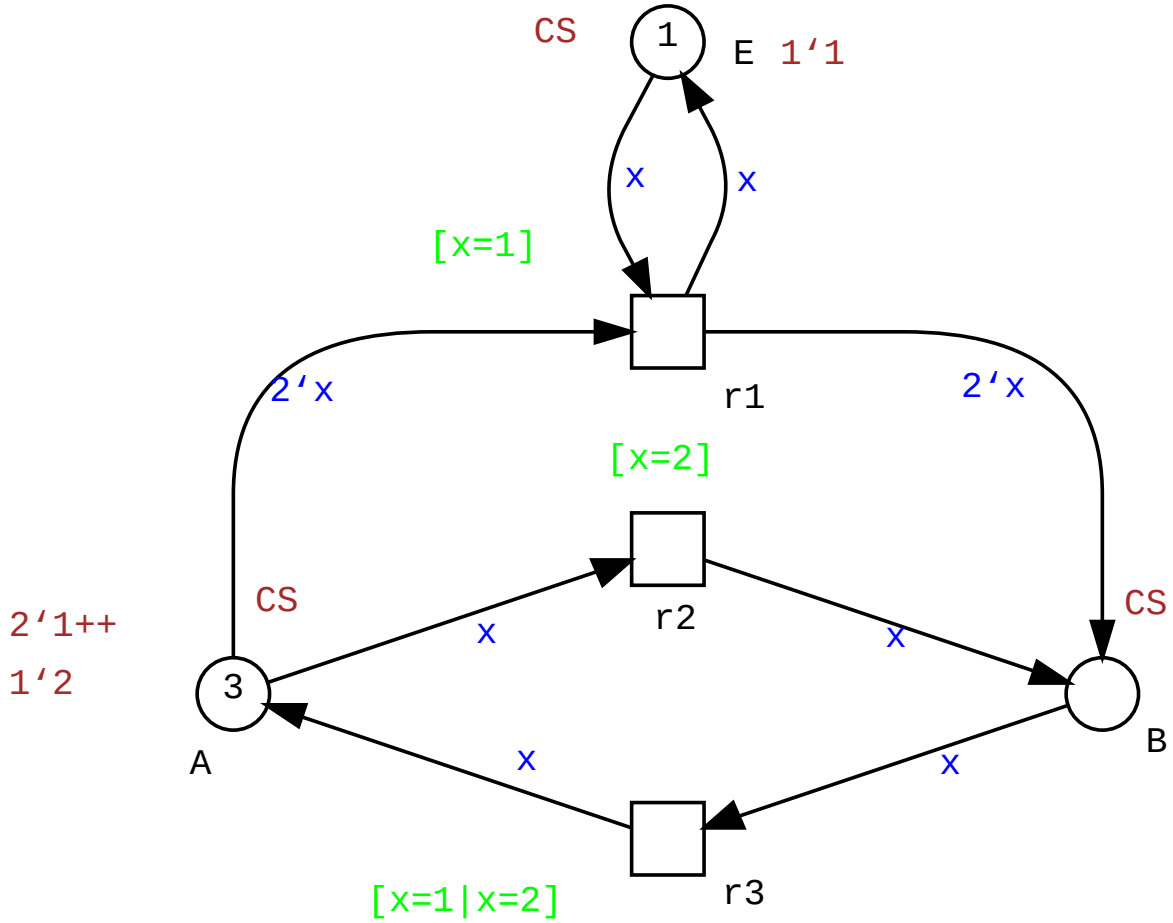
Scenario 4: T-invariants



The minimal T-invariants:

- $y_1 = (1, 0, 2) = (r1, 2 \cdot r3)$
- $y_2 = (0, 1, 1) = (r2, r3)$

Scenario 4: T-invariants



- Colset CS = integer with 1,2;

Structural analysis of colored Petri nets

Charlie: a tool to analyze qualitative Petri nets.

- structural properties,
- P- and T-invariants,
- reachability graph based analysis.

Procedure:

1. Export a colored Petri net to a APNN file,
2. Structural analysis of the APNN file using Charlie.

CSL model checking of colored Petri nets

Marcie: a tool for qualitative and quantitative analyis of generalized stochastic Petr nets with extended arcs.

- qualitative analysis based on interval decision diagrams,
- quantitative analysis based on symbolic exact numerical analysis,
- quantitative analysis based on explicit approximative numerical analysis .

Procedure:

1. Export a colored Petri net to a APNN file,
2. CSL model checking of the APNN file using Marcie.

PLTL checking of colored Petri nets

MC2: a model checker by Monte Carlo sampling, for simulative PLTL model checking

- reads sets of simulation traces,
- PLTL (a probabilistic linear-time temporal logic) model checking.

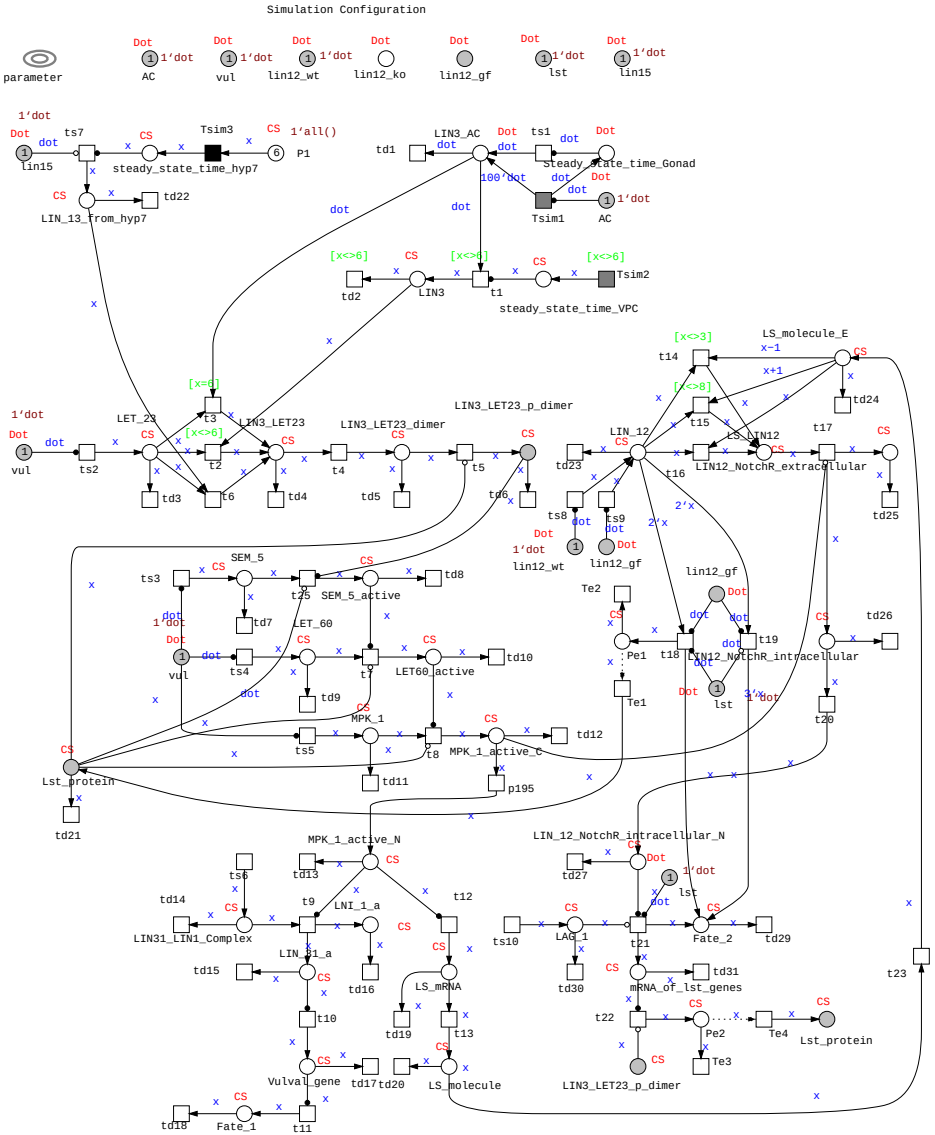
Procedure:

1. Run simualtion to get simulation traces,
2. PLTL model checking of these traces using MC2.

Case studies

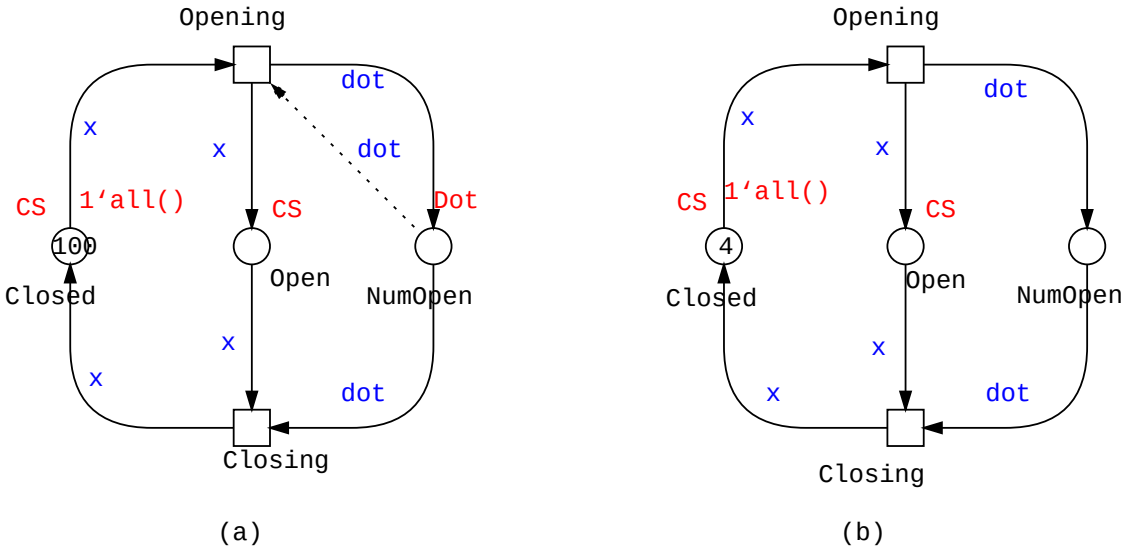
- the cooperative ligand binding,
- the C. elegans vulval development,
- the repressilator,
- the halobacterium phototaxis,
- the viral infection,
- Ca^{2+}-regulated intracellular Ca^{2+} channels,
- pain switch.

Case studies: C. elegans vulval development



Li C, Nagasaki M, Ueno K, Miyano S: Simulation-based model checking approach to cell fate specification during Caenorhabditis elegans vulval development by hybrid functional Petri net with extension. BMC Systems Biology 2009, 3:42.

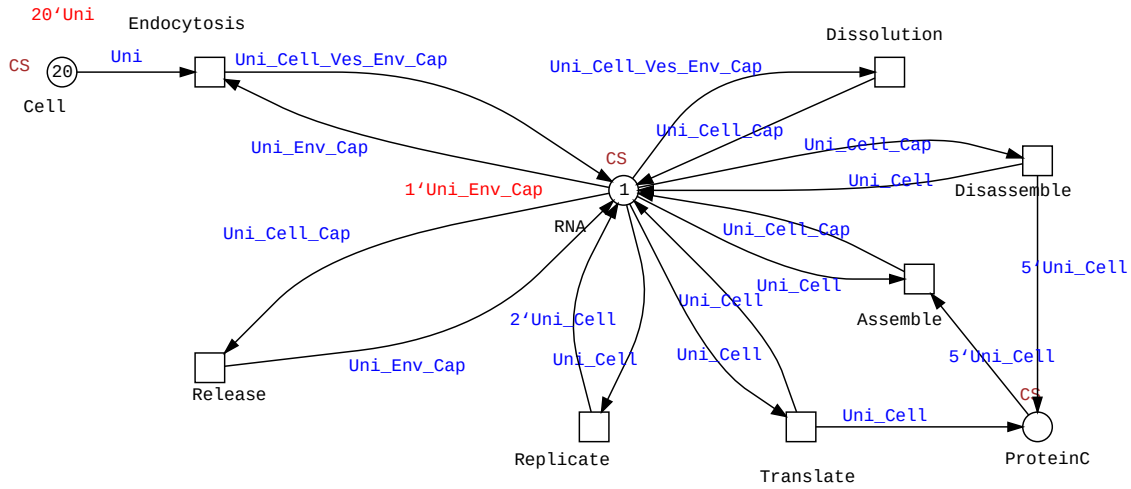
Ca^{2+}-regulated intracellular channels



- Colset CS = integer with 1-N;

Ruth Lamprecht, Gregory D. Smith, and Peter Kemper. Stochastic Petri net models of Ca2+ signaling complexes and their analysis. Natural Computing. Special Issue: Petri Nets and BioSystems. (2009)

the viral infection



- Colset CS = enum with *Uni*, *Uni_Cell_Ves_Env_Cap*, *Uni_Cell_Cap*, *Uni_Env_Cap* and *Uni_Cell*;

A. Spicher, O. Michel, M. Cieslak, J. Giavitto, P. Prusinkiewicz: Stochastic P systems and the simulation of biochemical processes with dynamic compartments. BioSystems. 91, 458-472 (2008)

Next Steps

Next steps

- Continue to color pain switch models,
- Improve the manual for colored Petri nets,
- Improve colored Petri nets,
- Investigate more analysis techniques for colored Petri nets,
- Coupling with the database developed by M2,
  needs to be discussed.

Thank You for your attention!

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