GINsim overview and new features

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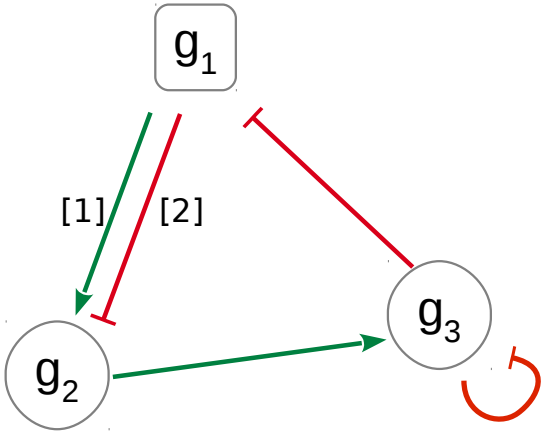
CoLoMoTo meeting
April 17-18, 2014

Logical modeling



- Nodes: genes, proteins...

  Activity level (Boolean, MV)

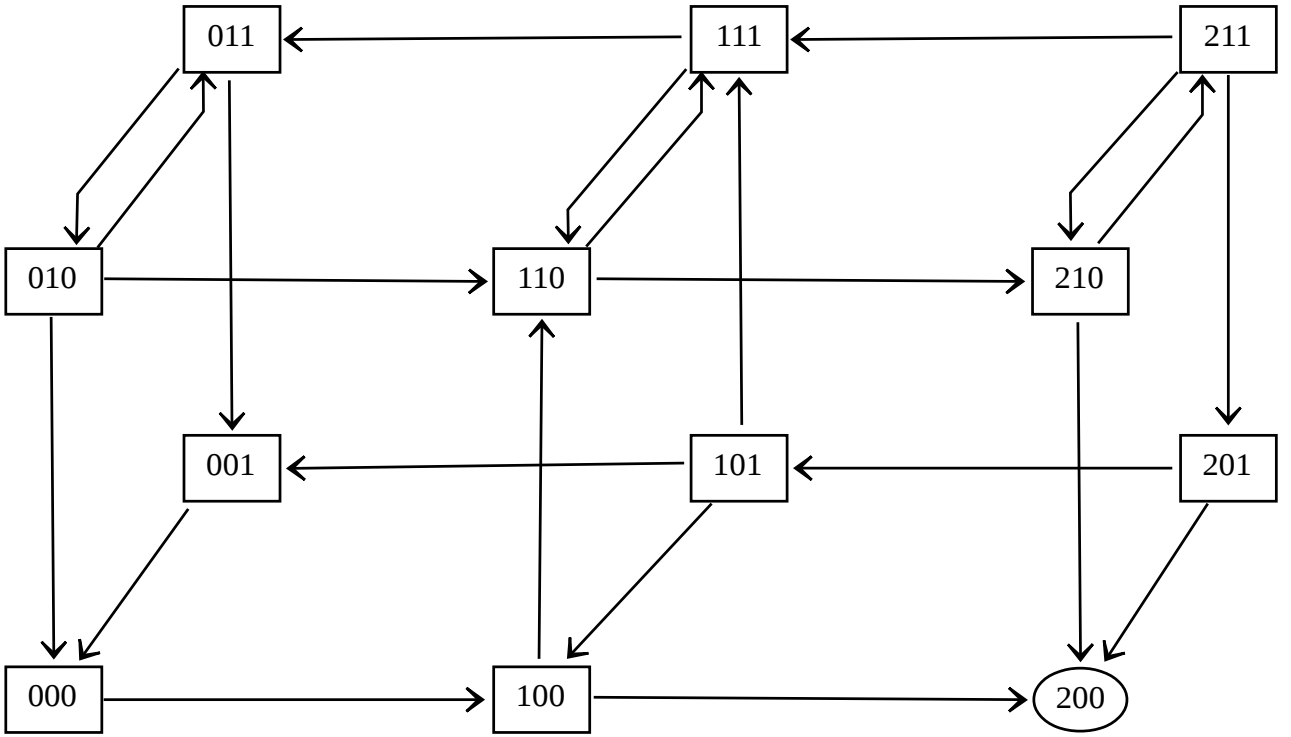
- Edges: interactions

  Threshold for MV source

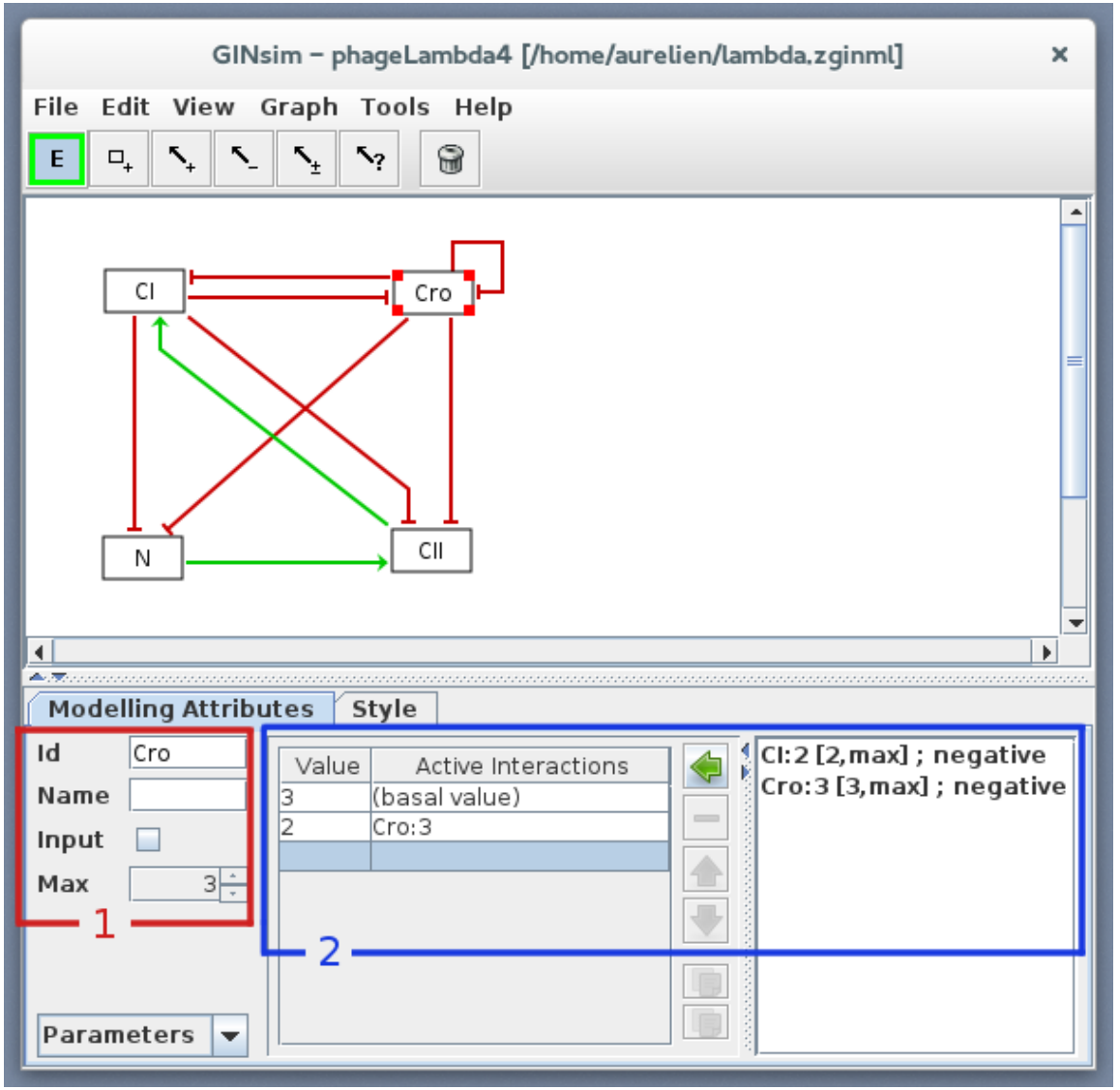
- Logical rules

  next(G3) = G2 and not G3

State Transition Graph



GINsim



Logical parameters or functions
State transition graphs: (a)synchronous, with priorities

A Naldi et al. Bio Systems (2009)

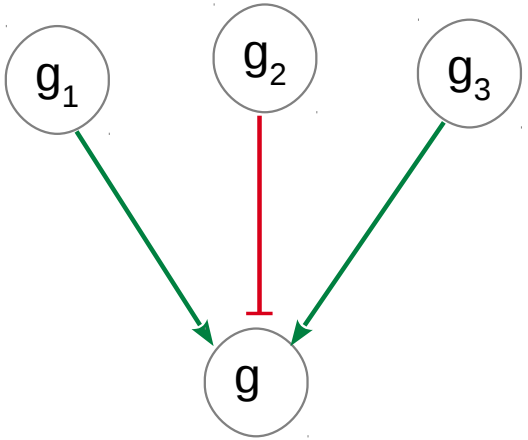
Features overview

- Graphical User Interface
- Edit the Regulatory Graph
- Simulation: compute the State Transition Graph
- Analysis tools
- Exports

Construct a Regulatory Graph

- Add Components and Interactions
  - Manual layout and visual settings
- Annotations
  - Needs improvements, rely more on SBML standards
- Real model: logical parameters
- Perturbations

Reminder on Logical Parameters



g1	g2	g3	g
0	0	0	0
0	0	1	1
0	1	0	0
0	1	1	0
1	0	0	1
1	0	1	1
1	1	0	0
1	1	1	0

Logical parameters
∅ (basal value)
g3
g2
g2,g3
g1
g1,g3
g1,g2
g1,g2,g3

logical parameter = List of active interactions

1 parameter = 1 line in the truth table

Simulation

- Updating mode
  - (a)synchronous
  - Priority classes
- Selected Initial State(s)
- Apply perturbation
- Regular or “compact” result (Hierarchical graph)

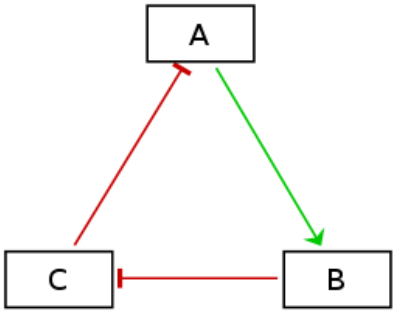
Perturbations

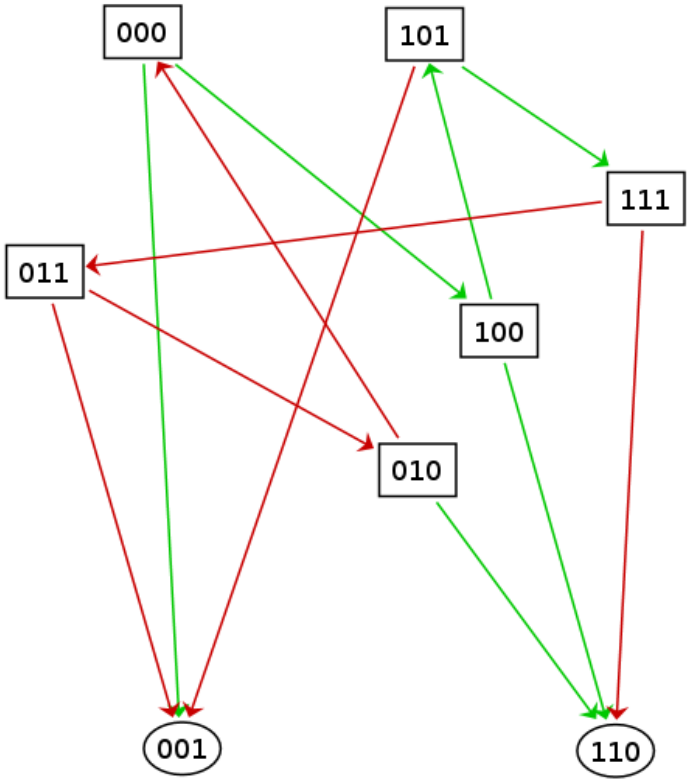
Anything which changes the model :)

- Fix the value of a component (KO, ectopic expression)
- Restrict a component in a range (multivalued case)
- Remove an interaction
  (block a component only for one of its targets)
- Multiple perturbations

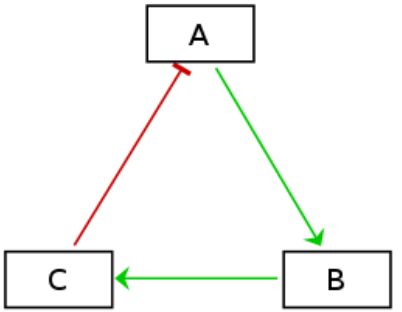
Circuit Analysis

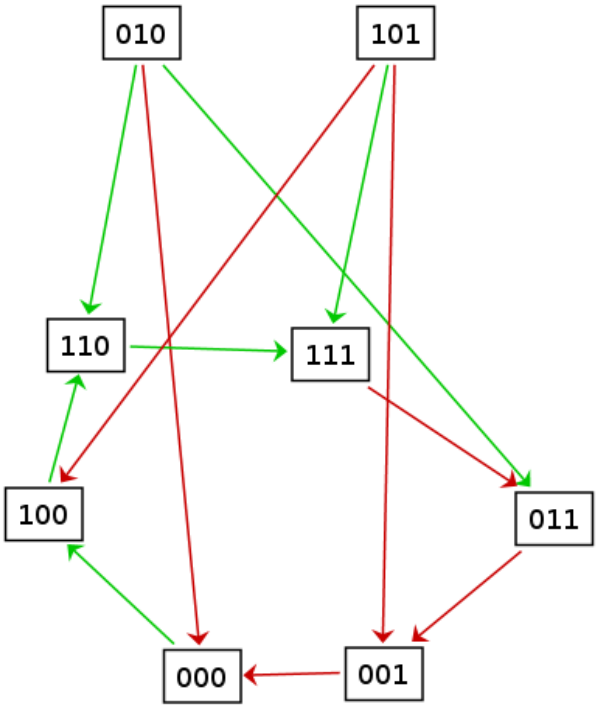
Positive: multiple attractors





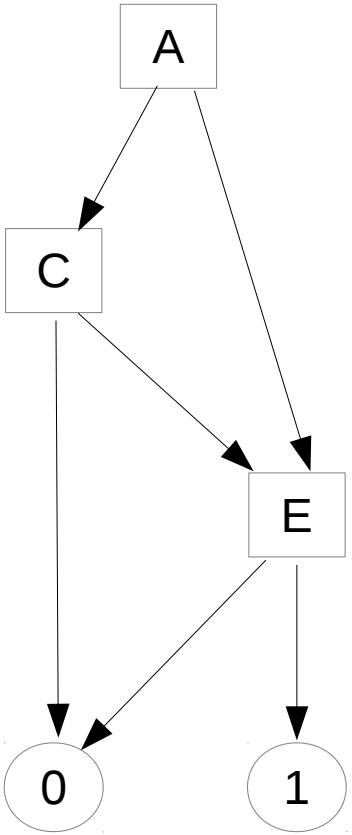
Negative: oscillations





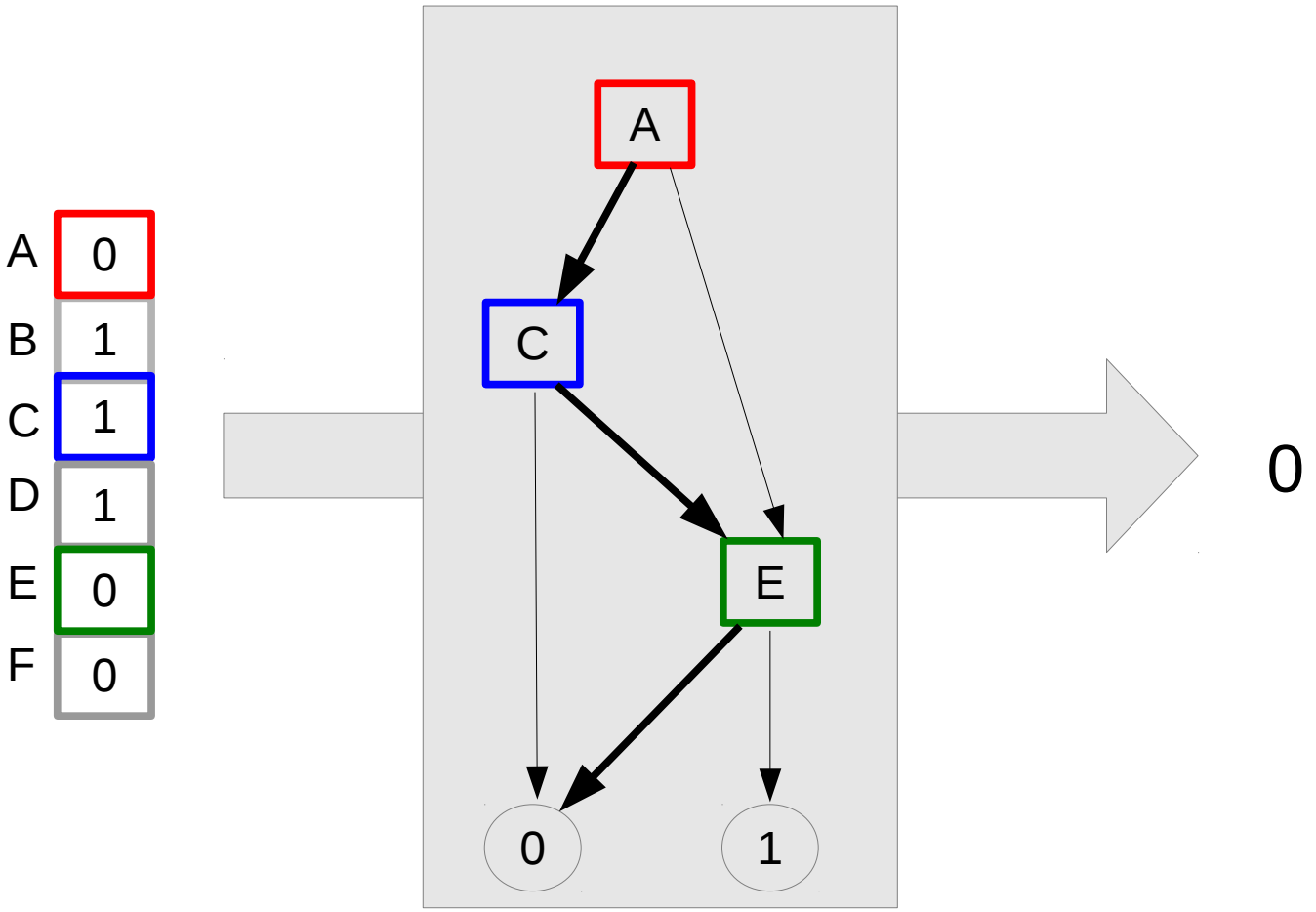
Decision Diagrams (MDD)

(A or C) and E



- A,B,C,D,E,F: ordered
- Fast (at most 6 tests, here 3)
- Predictable
- Picking order is hard

MDD query



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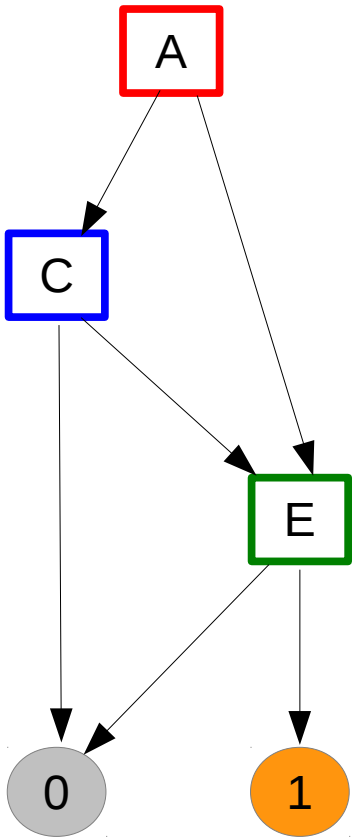
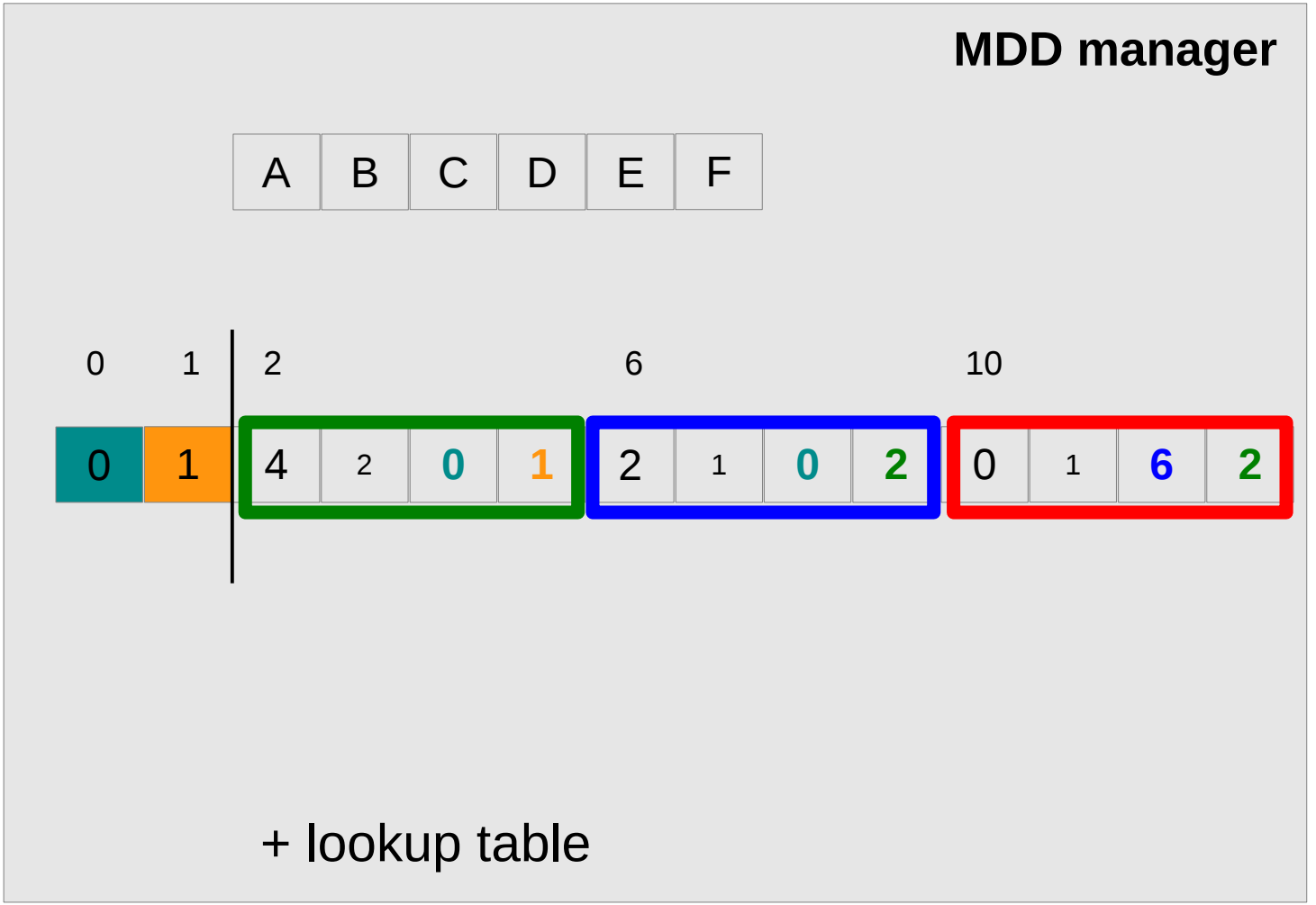
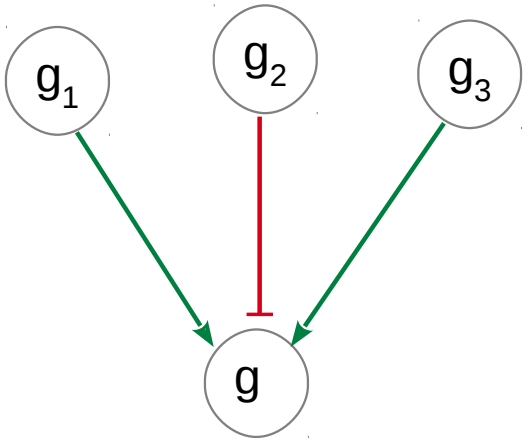




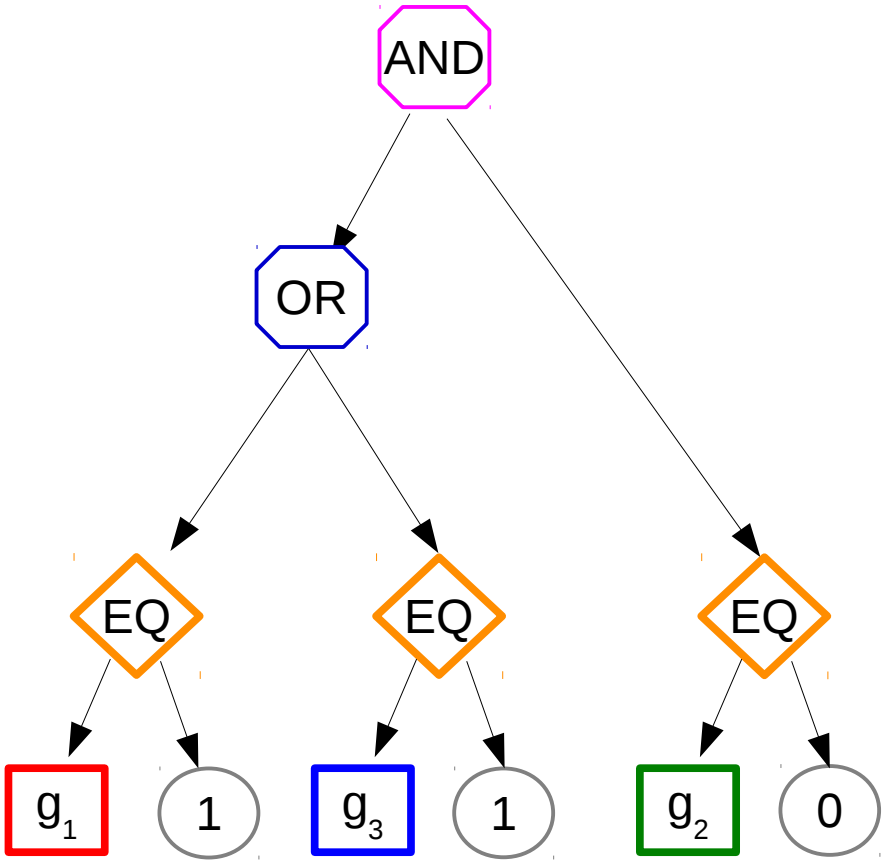
Multi-valued: some variables have more than two children

Functions in SBML-qual (and other)



$(g_1 \mid g_3) \,\&\, !\, g_2$

$(g_1{=}1 \mid g_3{=}1) \,\&\, g_2{=}0$



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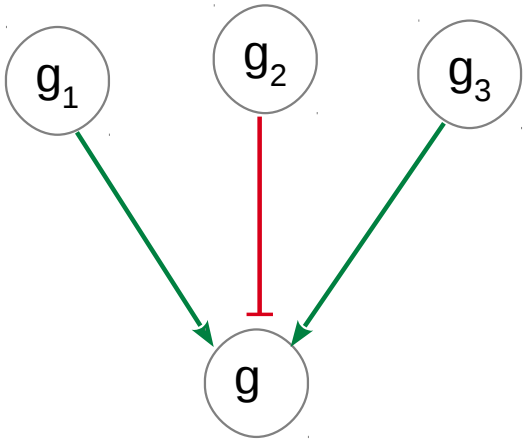

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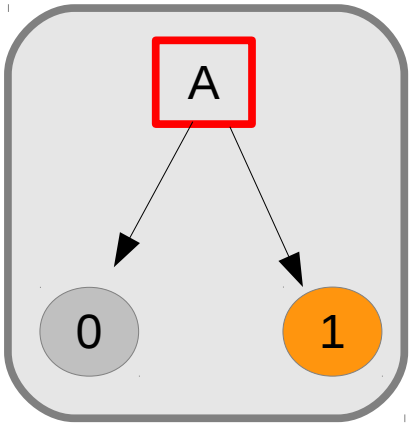
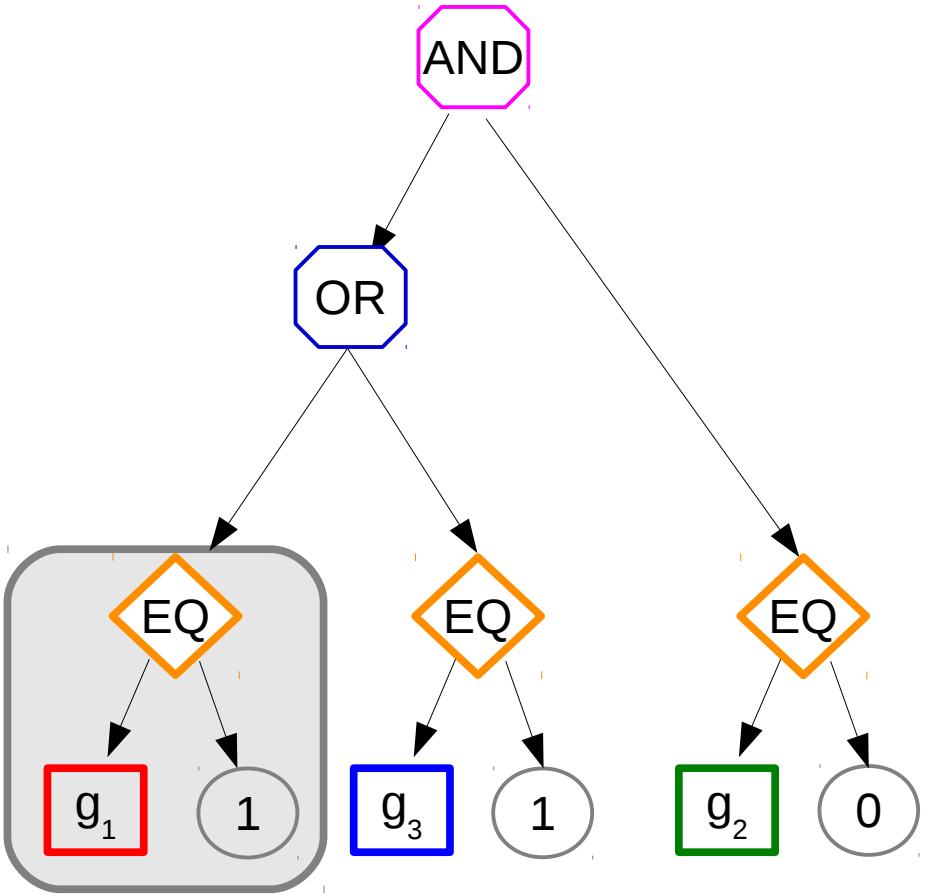
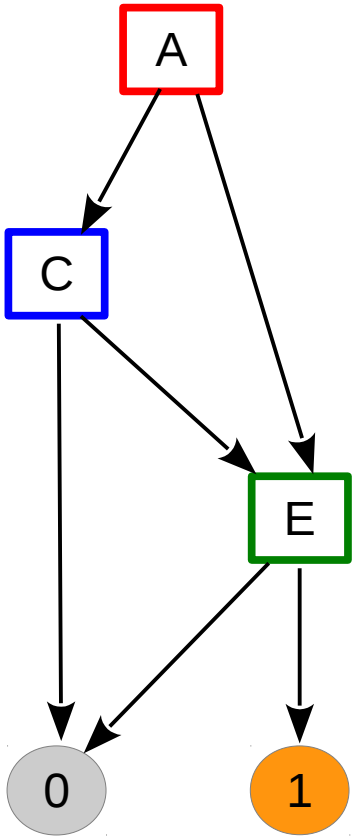


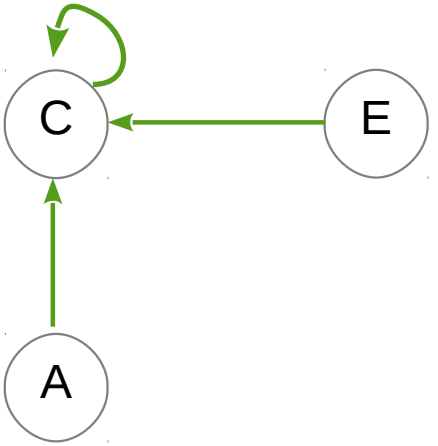


MDD manipulation for “OR”, “AND” operators

Identification of stable states

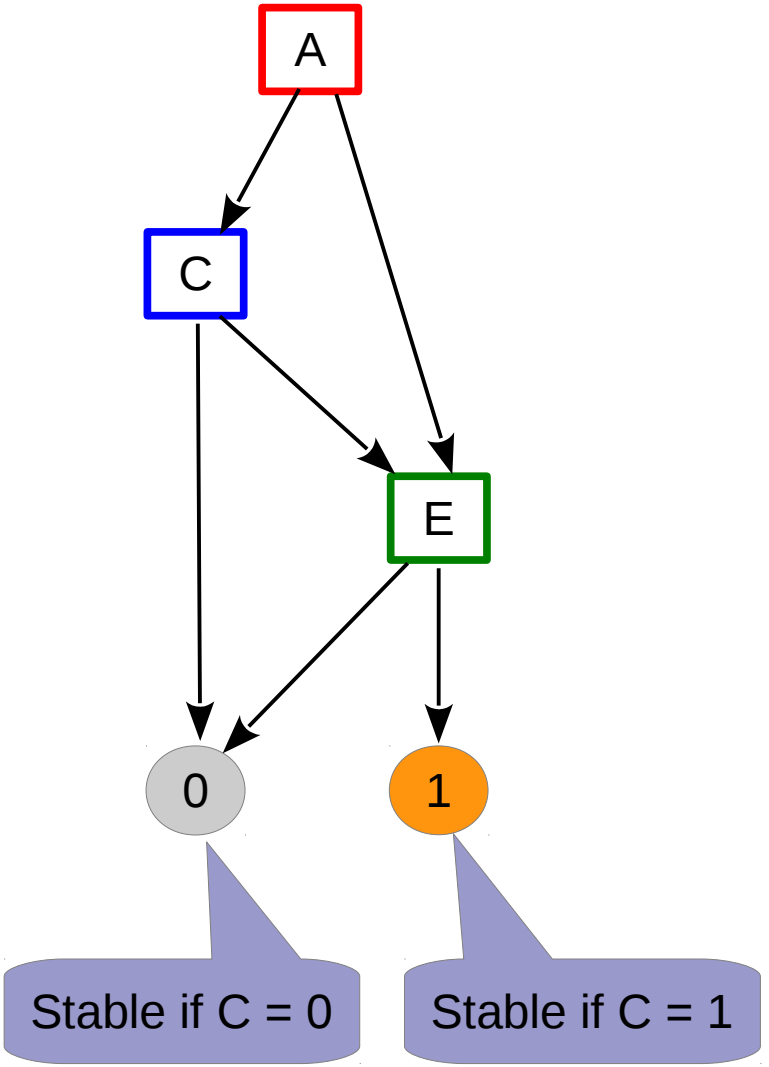


Function for C



(A | C) & E

Identification of stable states



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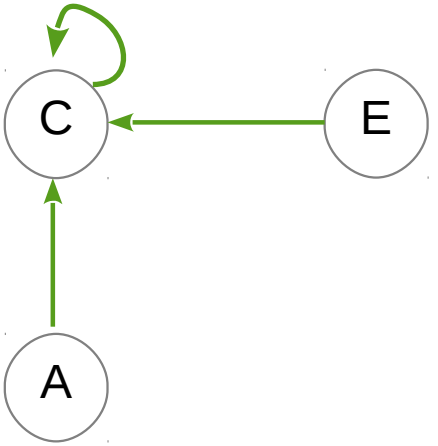

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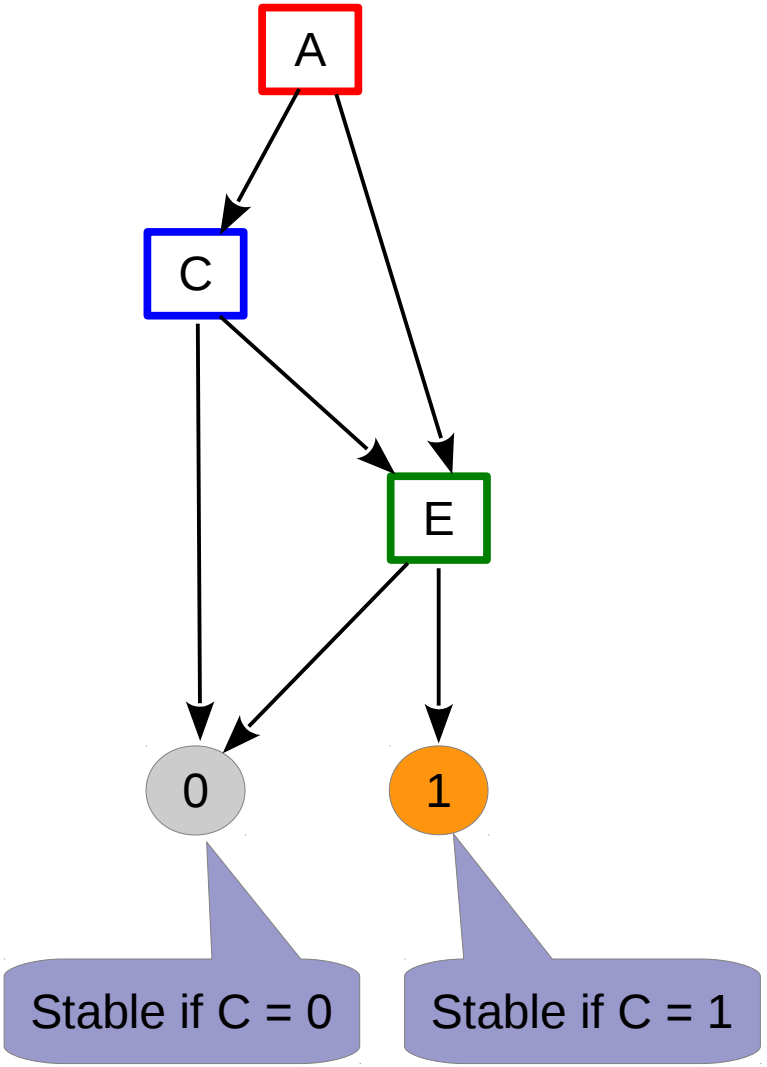
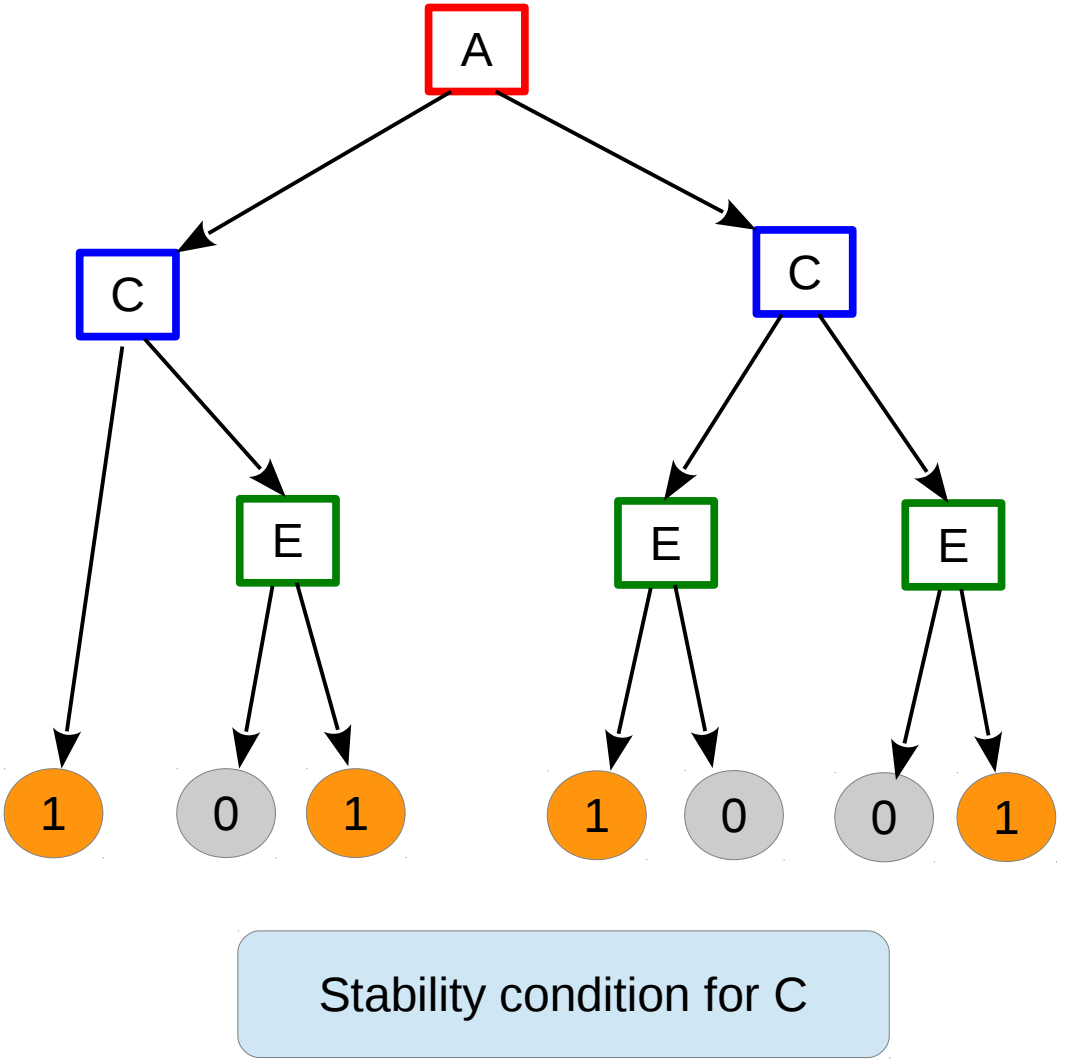
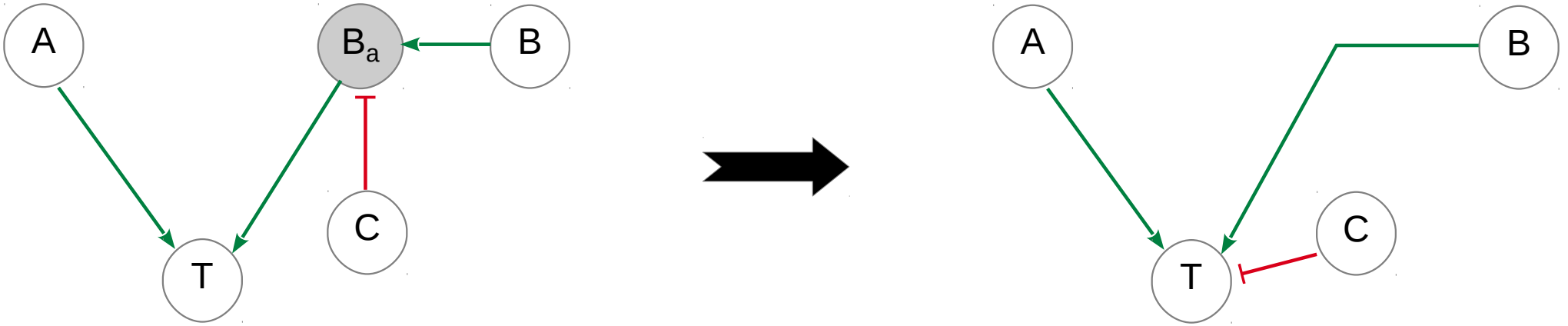




(A | C) & E

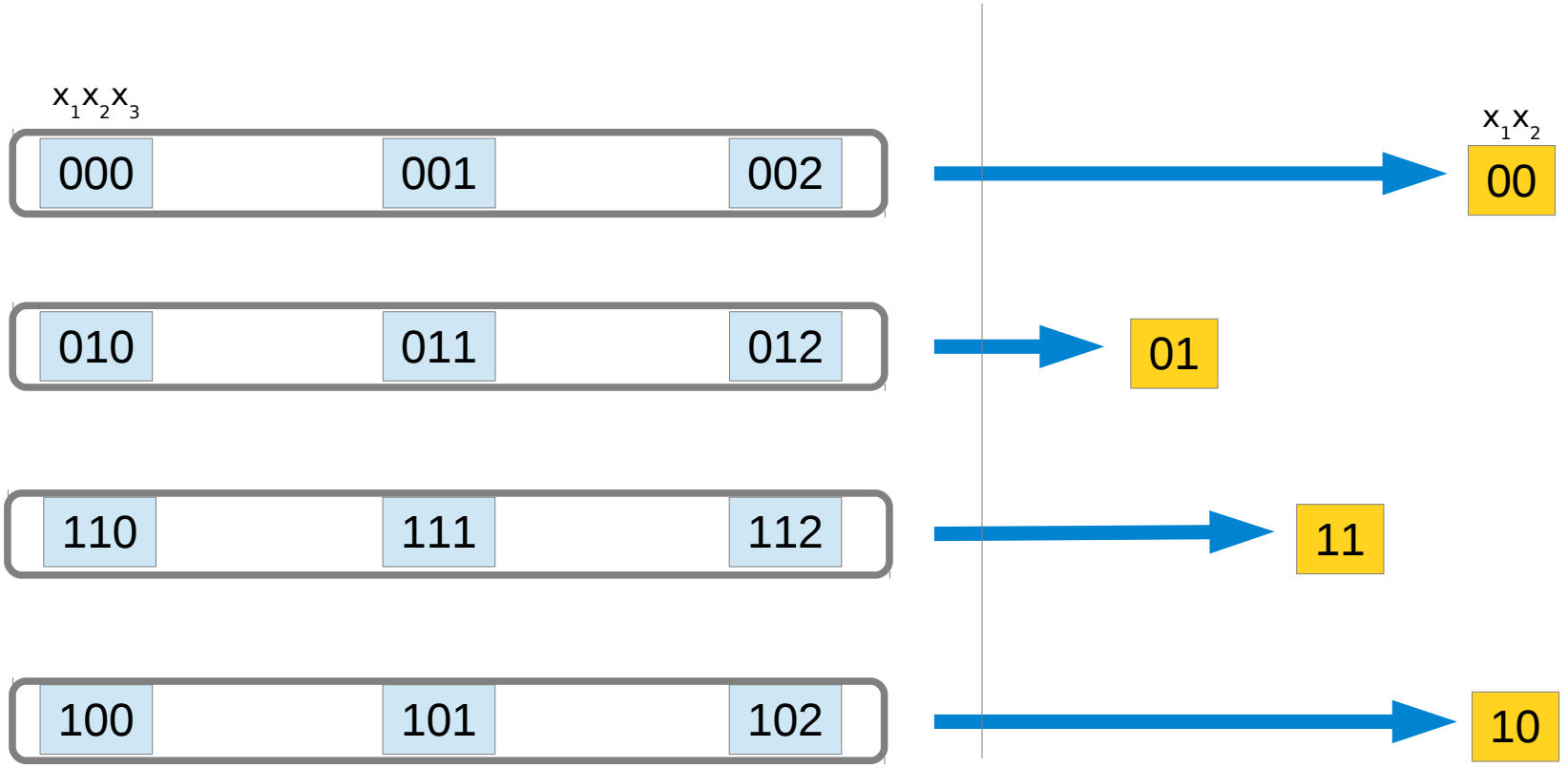
(!C & !(A & E)) | (C & E)

Model reduction



- Construct an explicit model
- Algorithm to “hide” some components
  - Transfer the role of regulators into targets
  - Preserve dynamical properties
    Self-regulated components are protected

Impact on dynamics



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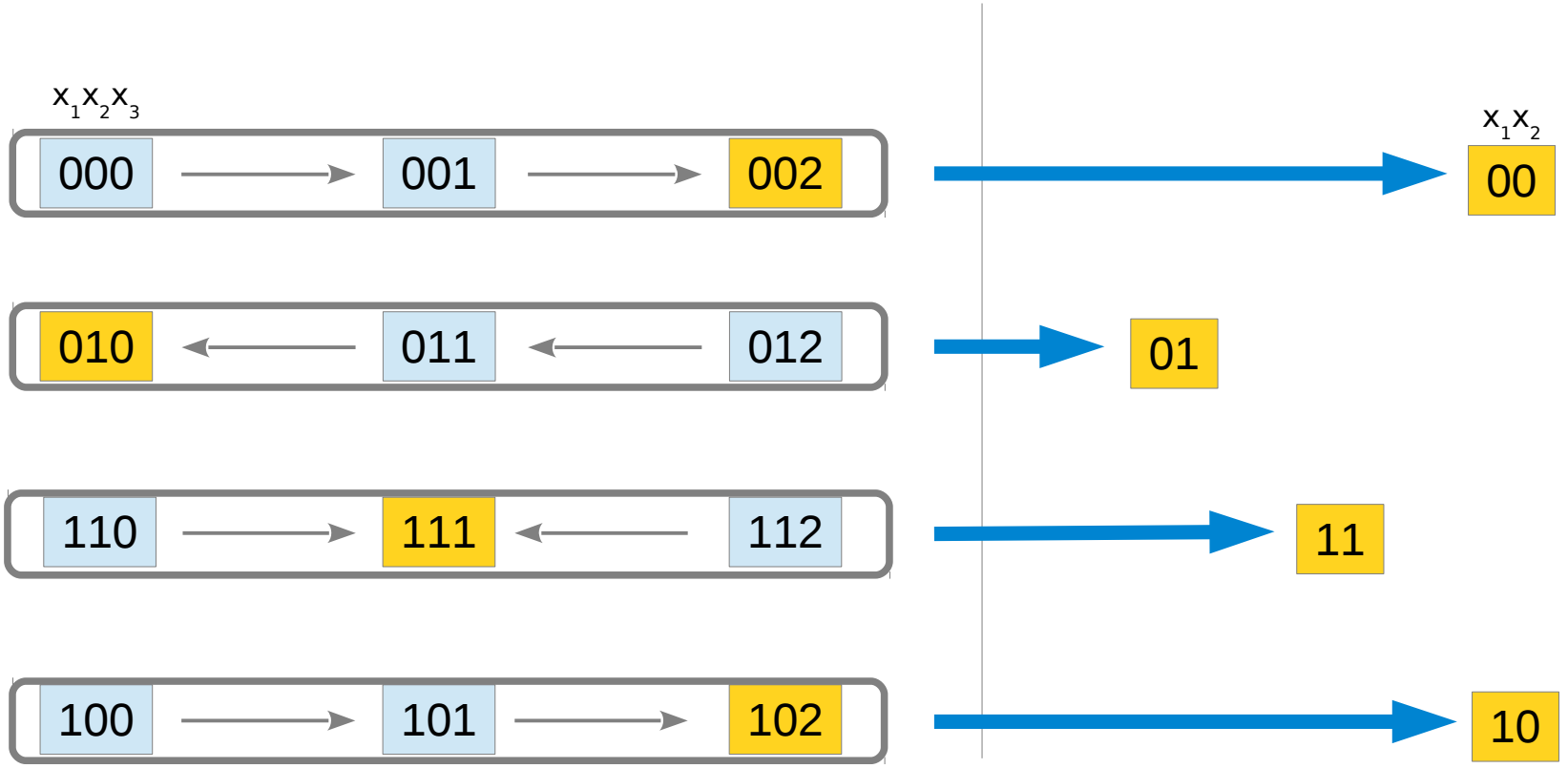
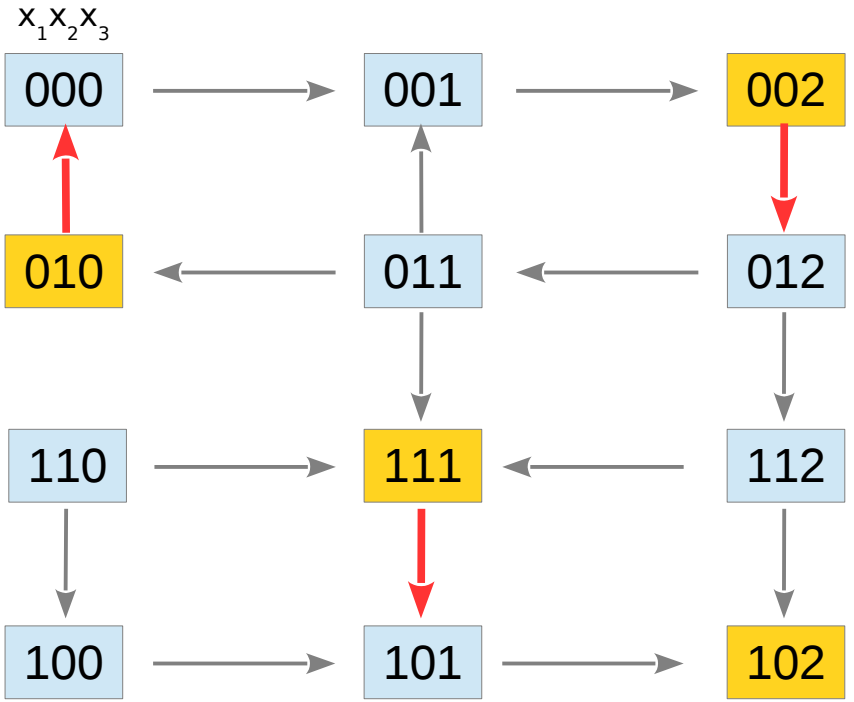
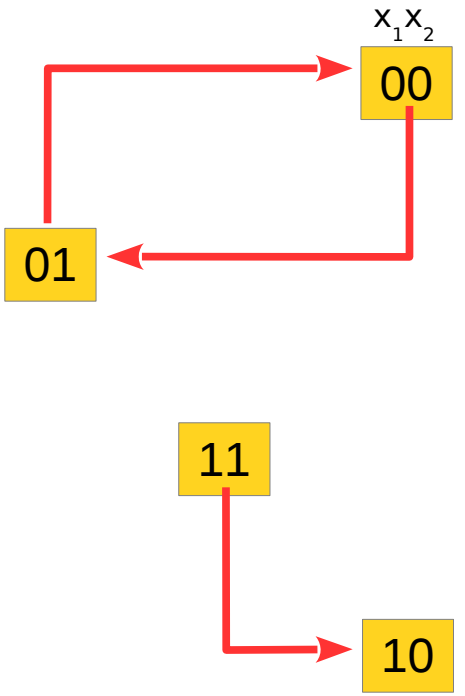


Impact on dynamics



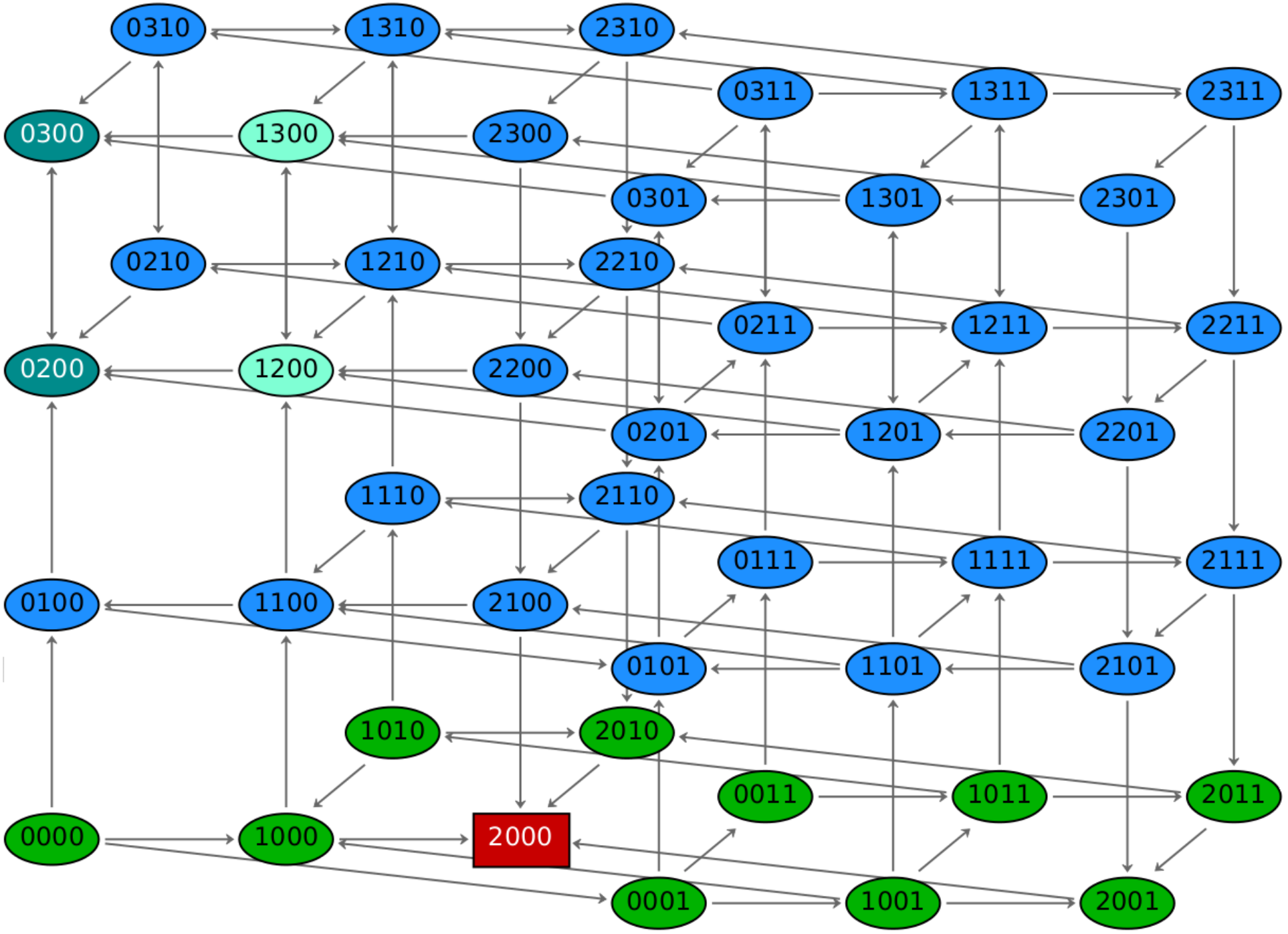


Properties of the reduction

- Dynamics similar to priority classes (hidden = fast)
- Representative states
- Stable states are identical
- Reachability can be lost, not made-up
- Complex attractors are “preserved”
  - Can be split, transient cycles can become terminal
- Some “safe” reductions: no transition lost

A Naldi et al. Theor. Comp. Sc. (2011)

Hierarchical Graph



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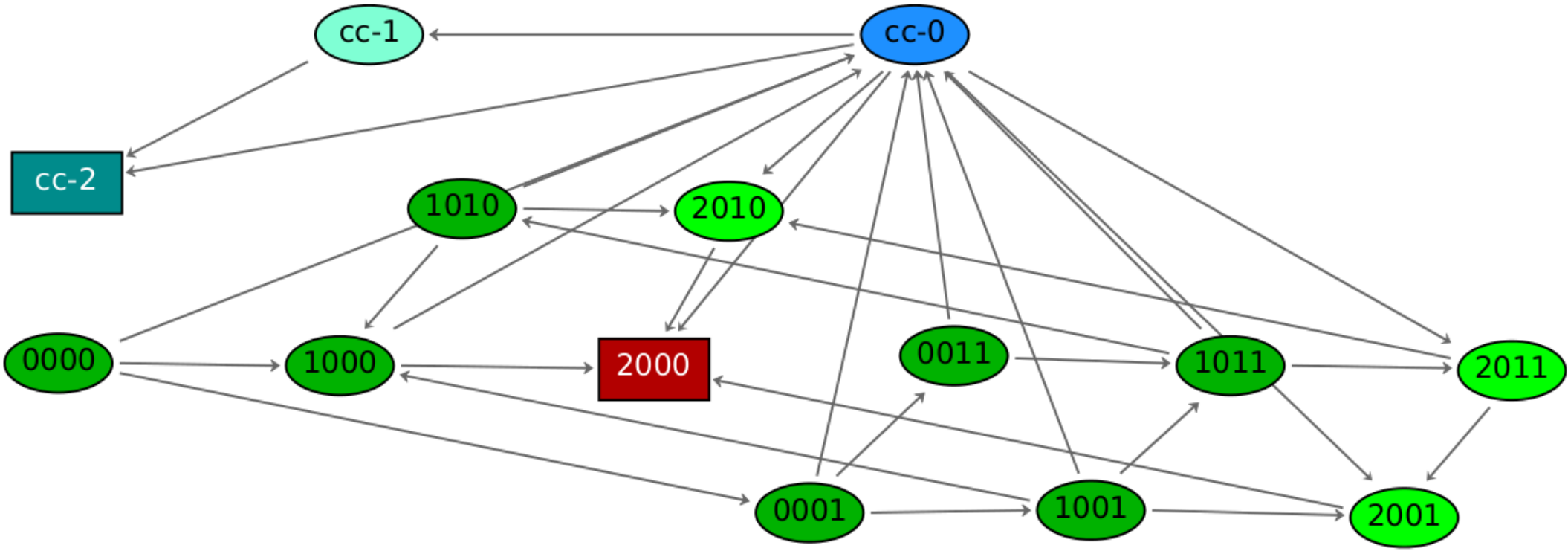

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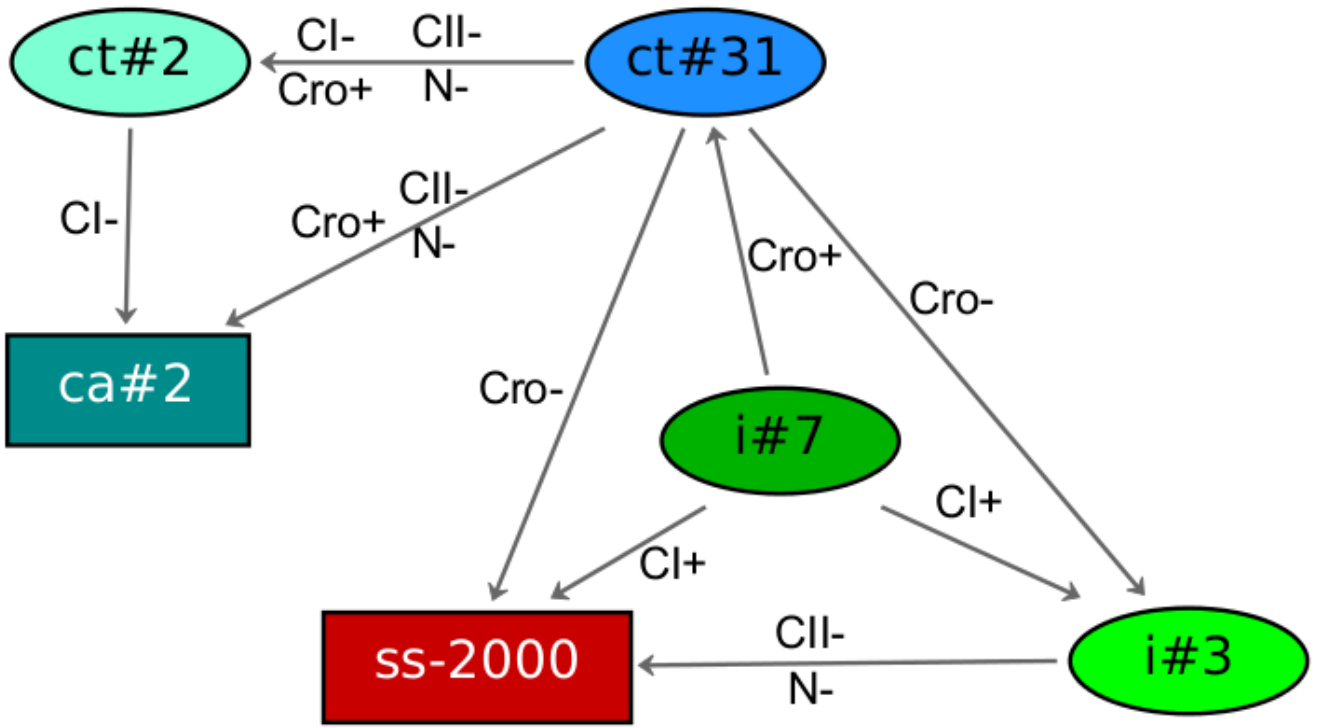
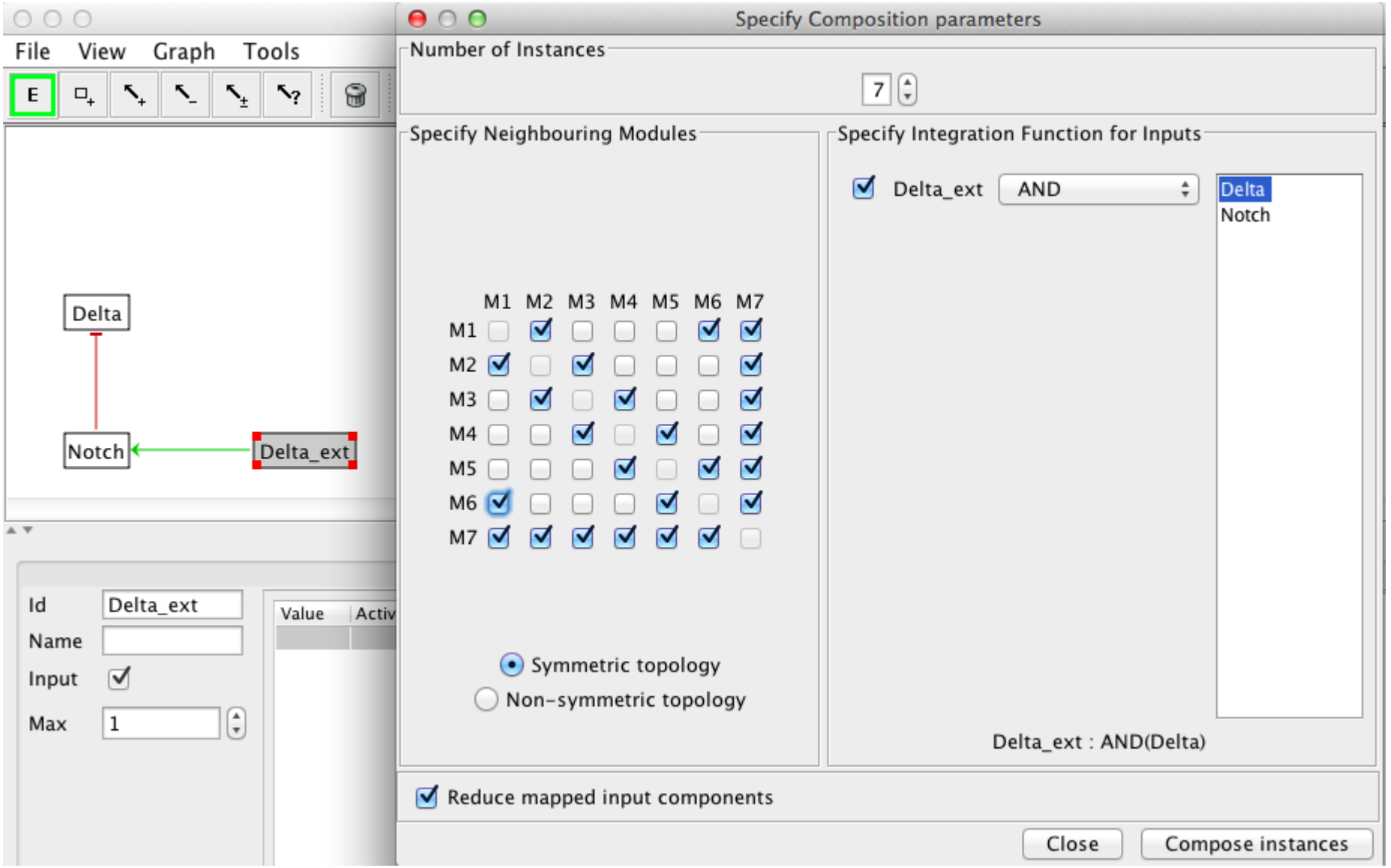


Model Composition



N Mendes et al. Bioinformatics (2013)

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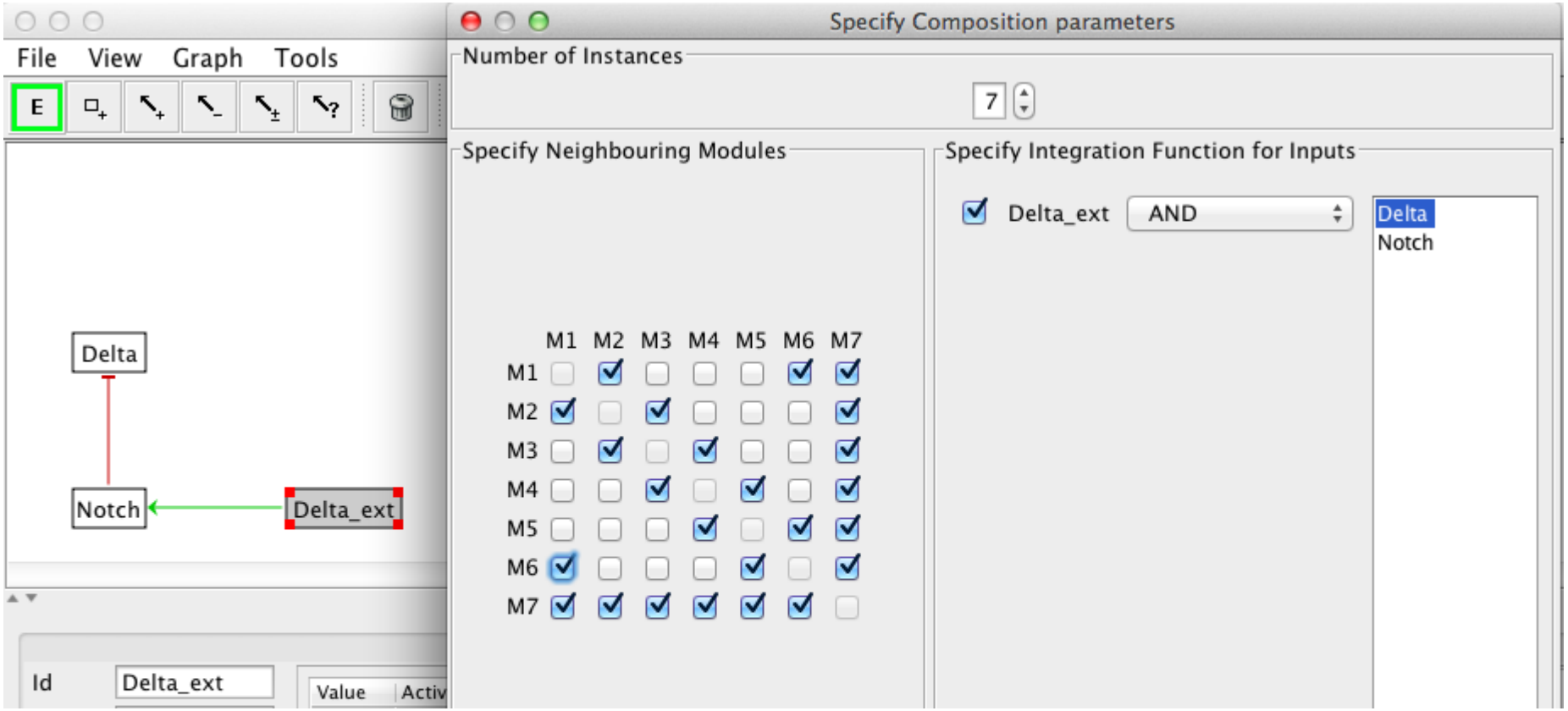

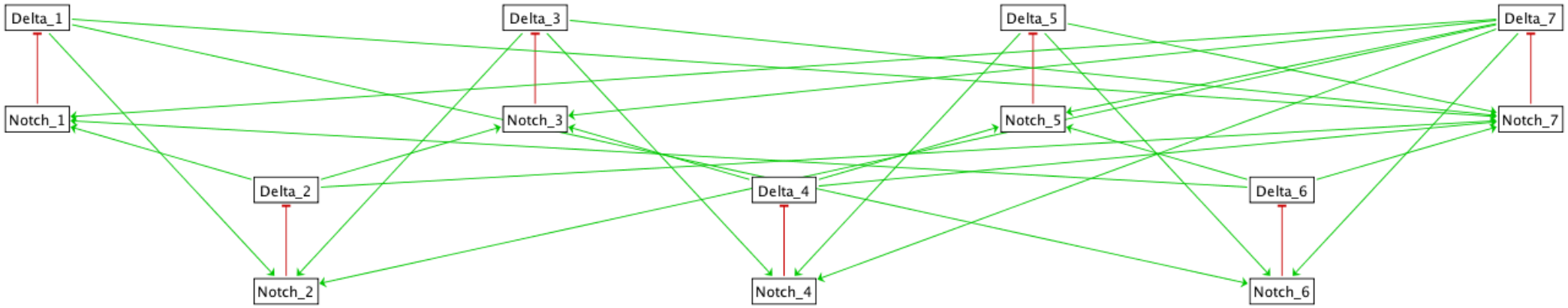

N Mendes et al. Bioinformatics (2013)

Exports

- Image of the graph (SVG, PNG)
- Documentation
- Petri net
- Model checker
- SBML qual
- Others: GNA, boolsim

Upcoming in GINsim 3.0

- Large architecture change
  - Backend: Core,Services
  - GUI (core and services)
  - Much improved scripting (using Jython)
- Backend relies on LogicalModel lib
  - Better MDD implementation
- New view canvas and styles
- Imports
  - SBML qual, Truth table, boolsim

Future plans

- Improve annotation support
- Function editor
  - Automatic functions
  - Improve hand-crafted functions
- Allow external extensions

People

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Marseille, France

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