Pint, a static analyzer for dynamics of Automata Networks
Loïc Paulevé

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Input Model

- Asynchronous Automata Networks [1]
  - a [0, 1, 2]
  - b [0, 1]
  - c [0, 1, 2]
  - a 0 -> 1 when b=0
  - a 0 -> 2 when c=0
  - a 2 -> 1
  - b 1 -> 0 when a=0
  - b 0 -> 1 when a=2 and c=1
  - c 0 -> 1 when b=0
  - c 1 -> 2 when a=1 and b=0
  - c 2 -> 0 when b=1

  initial state a=0, b=1, c=0

- Encoding of Boolean networks and multi-valued.
- Import from SBML-qual/GINsim using LogicalModel
  https://github.com/colomoto/logicalmodel

  $logicalmodel sbml:an model.sbml model.an

- Other formats: SGBN-PD [2], Biocham, CellNetAnalyzer

Main Features

- Static analysis of transient reachability
  Combines over- and under-approximation [3]

  $pint-reach -i model.an g=1
  True/false/Incon

- Identification of cut sets: mutations for breaking goal
  Static analysis for under-approximation [4]

  $pint-reach --cutsets -i TCell-d.an BCL6=1
  "GR130"=1
  "STAT5"=0
  "C228"=1,"IL6R"=1

- Identification of bifurcation transitions for goal
  Static analysis for under-approximation [5]

  $pint-reach --bifurcation -i TCell-d.an BCL6=1
  "STAT5" 0 -> 1 when "IL6R"=1

- Model reduction preserving goal reachability [1]

  $pint-export --reduce-for-goal g=1 -i model.an
  - o reduced.an

- Other features: fixed points (SAT); transition graph analysis (attractors); stochastic simulation; embedded Boolean/Thomas networks (contribute M. Folschette); C bindings; interface with model-checkers (NuSMV, ITS, mole)

Technologies

- Abstract interpretation: traces abstraction causality analysis (Local Causality Graphs)
  formal over-/under-approximations of reachability
- Answer-Set Programming (ASP)
  logic programming for enumeration problems (NP)
- Implemented with OCaml programming language
- Free software: CeCILL licence

Applications to Biological Networks

- Gene regulatory networks; signalling pathways; etc.
- Tractable on very large networks (100-10,000 comp.)

  - Complexity of causality analysis: poly(nb automata,trs), exp(nb levels)

  - Identification of cut sets for goal (mutations)

<table>
<thead>
<tr>
<th>Model</th>
<th>local ts</th>
<th>nb states</th>
<th>%MM</th>
<th>fPE</th>
<th>iPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCell-d (101)</td>
<td>384</td>
<td>175,947,684</td>
<td>76</td>
<td>266</td>
<td></td>
</tr>
<tr>
<td>MPK (309)</td>
<td>161</td>
<td>60,194,500</td>
<td>11</td>
<td>260</td>
<td></td>
</tr>
<tr>
<td>P/D (21,000)</td>
<td>69</td>
<td>2,350,494</td>
<td>55</td>
<td>127</td>
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</tr>
</tbody>
</table>

  - Identification of bifurcations for goal

<table>
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<tr>
<th>Model</th>
<th>local ts</th>
<th>nb states</th>
<th>goal</th>
<th>iPE</th>
<th>oPE</th>
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<tr>
<td>MPK (309)</td>
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<tr>
<td>P/D (21,000)</td>
<td>0.76% (334)</td>
<td>4</td>
<td>266</td>
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</tr>
</tbody>
</table>

  - Goal-oriented reduction: make life easier for model-checking

<table>
<thead>
<tr>
<th>Model</th>
<th>local ts</th>
<th>nb states</th>
<th>Verification of goal reachability</th>
<th>Verification of cut set</th>
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  - In all cases, reduction took less than 0.1s.
  - Properties are equivalent in the reduced models.

For more information:

1. Paulevé, Goal-oriented Reduction of Automata Networks at CMSB 2016

For more information:

- Loic Paulevé <loic.pauleve@lri.fr>
  CNRS/LRI, Univ. Paris-Sud, Paris-Saclay, France