Pint, a static analyzer for dynamics of Automata Networks
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Pint • Static Analyzer for Dynamics of Automata Networks

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Input Model
- Asynchronous Automata Networks [1]
  
  - a 0 ➔ 1 when b=0
  - a 0 ➔ 2 when c=0
  - 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: SBGN-PD [2], Biocham, CellNetAnalyzer

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

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 4 -i TCell-d.an BCL6=1
  "GP130"=1
  "STAT5"=0
  "C22B"=1, "IL6R"=1

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

  $ pint-reach --bifurcations -i TCell-d.an BCL6=1
  "STAT5" 0 ➔ 1 when "IL2B"=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 (contrib M. Folschette); C bindings; interface with model-checkers
  (NuSMV, ITS, mole)

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)
  
  - | Cutsets | TCell-d (101) | RBE2F (370) | MAPK (308) | PâD (21,000) |
  - | ≤4-cuts | 0.03s (27) | 0.06s (51) | 0.1s (34) | 3% (37) |
  - | ≤9-cuts | 0.03s (27) | 0.76s (334) | 0.5s (43) | 2.6h (1257) |

- Identification of bifurcations for goal
  
  - | Model | local trs | nb states | goal | 10s | 100s | 100s |
  - | TCell-d (101) | 384 | 4 ≥10² | RORGT=1 | 10s | 20s | 20s |
  - | ∥TGF | 7 | 25s | 4.2s |
  - | TGF (101) | 384 | KO | BCL6=1 | 10s | 20s | 20s |
  - | ∥MAPK | 10s | 25s | 20s |

- Goal-oriented reduction: make life easier for model-checking
  
<table>
<thead>
<tr>
<th>Model</th>
<th>local trs</th>
<th>nb states</th>
<th>Verification of reachable &amp; unreachable states</th>
<th>Verification of cut set</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCell-d (101)</td>
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<td>4 ≥10²</td>
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In all cases, reduction took less than 0.1s.
Properties are equivalent in the reduced models.

For more information...