A Boolean Model for Enumerating Minimal Siphons and Traps in Petri nets

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Chemical Reaction Systems for Systems Biology

BioModels.Net
Repository of chemical reaction systems for systems biology
403 curated models
biggest model: 194 species, 313 reactions
average: ~ 50 species, ~ 90 reactions
Example: Michaelis–Menten enzymatic reactions
Reaction model:
1996 Finding minimal siphons in general petri nets.
S. Tanimoto, M. Yamauchi, and T. Watanabe. IEICE.
1962 Finding siphons is reduced to finding Boolean assignments satisfying these formulas.

Siphons in Petri nets
Dynamic Characterization: a subset \( S \) of places such that once \( S \) is empty, it remains empty
\[ \forall p \in S, m_p = 0 \quad \Rightarrow \quad \forall p \in S, m_p' = 0 \]
Structural Characterization: \( S \) siphon iff \( S \subseteq S^* \)
\((S \) set of predecessors, \( S^* \) set of successors\)
e.g. in Michaelis–Menten: \( S(\text{SE}) = \{t_1, t_{-1}\} \subseteq S(\text{SE})^* = \{t_1, t_{-1}, t_2\}\)

Finding minimal siphons

Booleans Model of Siphons
variables \( \forall \ p \ X_p = 1 \Leftrightarrow p \in S \)
constraints \( \forall \ p \ X_p = 1 \Rightarrow \bigwedge_{t \in T} \bigvee_{p \in B(t)} X_p = 1 \)
Finding siphons is reduced to finding Boolean assignments satisfying these formulas.

Search strategy
Find \textit{minimal siphons} first
All \textit{siphons} Branch & Bound
Value selection strategy: \textit{first 0 then 1}
1. add the constraint \( \bigwedge_{p \in S} X_p = 0 \)
2. \textit{restart} the search efficiently
In theory: \( S \ni \text{S}_0 \)
Siphons in search tree \( \Rightarrow \text{S}_1 \ni \text{S}_0 \)
In practice: \textit{replay} search procedure

Resolution with SAT and CLP(\( E \))

<table>
<thead>
<tr>
<th>database</th>
<th>#models</th>
<th>total time (in ms.)</th>
<th>miniSAT algorithm</th>
<th>GNU Prolog</th>
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<tbody>
<tr>
<td>Biomodels.net</td>
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<td>19734</td>
<td>411</td>
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<td>Petriweb</td>
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<td>2325</td>
<td>156</td>
<td>6</td>
</tr>
</tbody>
</table>

Kohn’s map of cell cycle
Biomodel #175
3042
\( \infty \)
137000
\( \infty \)
Biomodel #205
32
1
21
Biomodel #239
64
2980
1
22

Bounded tree-widths

Lemma. If a Petri-net has a tree-width \( w \), then the associated Boolean model has tree-width \( O(w) \).
Proof. The tree decomposition of the Petri-net maps to a tree decomposition of the associated Boolean model of proportional width.

Theorem. The following problems
Finding siphon of cardinality \( k \)
Finding minimal siphon containing a place \( p \)
are \textit{polynomial} for Petri-nets of \textit{fixed} tree-width.

Biomodels generally have \textit{small} tree-width.

Finding Siphons: a Combinatorial Problem

NP-complete Problems:
Finding a siphon of cardinality \( k \)
Finding smallest siphon containing a place \( p \)
Finding minimal siphons in \( p \) petri net representation of logic equations.
M. Kinuyama and T. Murata. SIG-IEICE.
2003 Some results on the computation of minimal siphons in petri nets.
R. Cordone, L. Ferrarini, and L. Piroddi. IEEE DC.
2005 Enumeration algorithms for minimal siphons in petri nets based on place constraints. R. Cordone, L. Ferrarini, and L. Piroddi. IEEE TSC.