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

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BioModels.Net
Repository of chemical reaction systems for systems biology

Example: Michaelis–Menten enzymatic reactions

Structural model: Reaction graph
Petri-net = reaction graph + discrete dynamics

Siphons in Petri nets
Dynamic Characterization: a subset $S$ of places such that
once $S$ is empty, it remains empty
$$\forall p \in S, m_p = 0 \land m \rightarrow m' \Rightarrow \forall p \in S, m_p' = 0$$

Structural Characterization: $S$ siphon iff
$S \subseteq S$ (*$S$ set of predecessors $S^*$ set of successors)
e.g. in Michaelis–Menten: $\{S, SE\} = \{t_1, t_2\} \subseteq S$ ($S$, $SE$)

Related work: P-invariant, conservation law ODE invariant


Useful for liveness analyses in biology
Characterize dead-locks. e.g. starch production and accumulation in the potato tubers during growth


Finding Siphons: a Combinatorial Problem
NP-complete Problems:
- Finding a siphon of cardinality $k$
- Finding minimal siphons in general petri nets S. Tanimoto, M. Yamauchi, and T. Watanabe. IEICE.
- Finding a minimal siphon containing a place $p$

1999 Time complexity analysis of the minimal siphon extraction problem of petri nets. S. Tanimoto, M. Yamauchi, and T. Watanabe. IEICE.

Nevertheless, our Goal: Enumerating all minimal siphons!
State-of-the-art algorithms:
1986 Generating siphons and traps by petri net representation of logic equations. M. Kinuyama and T. Murata. SIG-IECE.
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.

Resolution with SAT and CLP($\mathcal{E}$)

<table>
<thead>
<tr>
<th>database</th>
<th># models</th>
<th>total time (in ms.)</th>
<th>state-of-the-art algorithm</th>
<th>miniSAT</th>
<th>GNU Prolog</th>
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Kohn’s map of cell cycle 81 28 1 221
Biomodel #175 3042 $\infty$ 137000 $\infty$
Biomodel #205 32 21 1 34
Biomodel #239 64 2980 1 22

CP in GNU Prolog as good as miniSAT.
Amazingly fast resolution on some large instances!

Bounded tree-widths (extension of the paper)
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 propositional width.

Theorem. The following problems
- finding siphon of cardinality $k$
- finding minimal siphon containing a place $p$
- are polynomial for Petri-nets of fixed tree-width.


Biomodels generally have small tree-width.

Modeling leads to understanding
- Boolean model outperforms state-of-the-art algorithms.
- “Real life” instances may have characteristics that NP-complete proofs ignore: bounded tree-width, regularity...