Complexity of limit-cycles in conjunctive Boolean networks

Julio Aracena[1]

Joint work with
Florian Bridoux[2], Luis Gómez[3] and Lilian Salinas[1]
[1]Universidad de Concepción, Chile
[2] Université Aix-Marseille, France
[3] Universidad del Bío-Bío, Chile

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Conjunctive Boolean network

Definition

A Boolean network (BN) with n components is a discrete dynamical system usually defined by a global transition function:

$$f : \{0,1\}^n \to \{0,1\}^n, x \to f(x) = (f_1(x), \ldots, f_n(x)),$$

where each function $f_v : \{0,1\}^n \to \{0,1\}$ associated to the component v is called local activation function. We will say a Boolean network is conjunctive if $f_v(x) = \bigwedge_i x_i$.

The interaction graph $G(f) = (V, A)$ is defined by:
$V = \{1, \ldots, n\}$ and $A = \{(i,j) \in V \times V : \ f_j \text{ depends on } x_i\}$.

A limit cycle of f (with synchronous update schedule) is a sequence of configurations in $\{0,1\}^n$ $[x^0, \ldots, x^p]$, $p \geq 2$, such that $\forall i \in \{0, \ldots, p-1\}, x^{i+1} = f(x^i) \wedge x^0 = x^p$.

Block-sequential schedules

Definition

A block-sequential schedule is an ordered partition of the components of a Boolean network which defines the order in which the states of the network are updated in one unit of time.

Examples

$$s_1 = \{3,4\}\{1\}\{2\},$$
$$s_2 = \{1,2,3,4\},$$
$$s_3 = \{2\}\{3\}\{4\}\{1\}.$$

Dynamics of f with s

Definition (Robert 86)

Let f be a Boolean network and $s = B_1, B_2, \ldots, B_m$ a block-sequential update schedule. The dynamical behavior of f updated according s is given by:

$$\forall v \in B_1, \qquad x_v^{t+1} = f_v(x^t). \tag{1}$$

$$\forall v \in B_i, i > 1, \qquad x_v^{t+1} = f_v(x_u^{t+1} : u \in \bigcup_{j=1}^{i-1} B_j; x_u^t : u \in \bigcup_{j=i}^{m} B_j) \tag{2}$$

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This is equivalent to applying a function f^s to x:

$$x^{t+1} = f^s(x^t)$$

Where we define f^s as the composition of updating f block by block:

$$f^s = f^{B_m} \circ f^{B_{m-1}} \circ \cdots \circ f^{B_2} \circ f^{B_1}$$

where:

$$\forall x \in \{0,1\}^n, \quad f_v^{B_i}(x) = \begin{cases} x_v & \text{if } v \notin B_i \\ f_v(x) & \text{if } v \in B_i. \end{cases}$$

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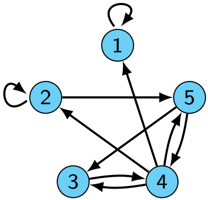
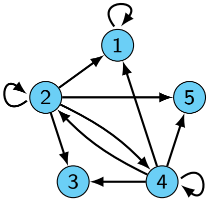
Remark: If f is a conjunctive network, then f^s too.

f^s



$f_1 = x_1 \wedge x_4$
$f_2 = x_2 \wedge x_4$
$f_3 = x_4 \wedge x_5$
$f_4 = x_3 \wedge x_5$
$f_5 = x_2 \wedge x_4$
$s = \{2\}\,\{5\}\,\{3\}\,\{4\}\,\{1\}$

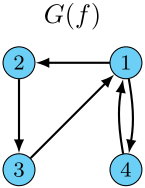
(a) $G(f) = G$



$f_1^s = x_1 \wedge x_4 \wedge x_2$
$f_2^s = x_2 \wedge x_4$
$f_3^s = x_4 \wedge x_2 \wedge x_4$
$f_4^s = x_4 \wedge x_2 \wedge x_4$
$f_5^s = x_2 \wedge x_4$

(b) $G(f^s) = \mathcal{P}(G, s)$

$G(f^s)$ can be calculated in polynomial time (Goles and Noual, 2012).

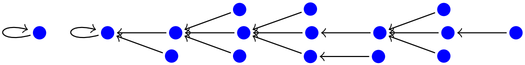


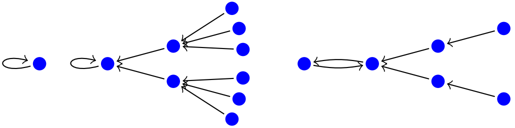
s

$s = \{1,2,3,4\}$

$s = \{1,4\}\{2,3\}$

Dynamics





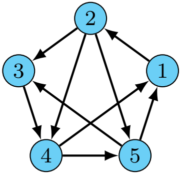
(Aracena, J., Goles, E., Moreira, A., Salinas, L., 2009; Demongeot J., Elena, A., Sené, S., 2008; Macauley, M., Mortveit, H.S., 2009).

Proposition (Goles and Noual, 2012)

Every conjunctive network f has a block-sequential update schedule s such that f^s has no limit cycle.

Example: Conjunctive network without limit cycles for every update schedule.

$$
\begin{aligned}
f_1(x) &= x_4 \wedge x_5 \\
f_2(x) &= x_1 \\
f_3(x) &= x_2 \wedge x_5 \\
f_4(x) &= x_2 \wedge x_3 \\
f_5(x) &= x_2 \wedge x_4
\end{aligned}
$$



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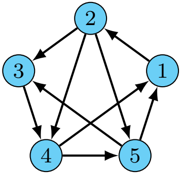


Limit Cycle Existence problem (LCE): Given f a conjunctive network, does there exist a block-sequential update schedule s such that f^s has a limit cycle?

Parallel update schedule and loop number

The existence of limit cycles in a conjunctive network f (with parallel update schedule) is related to the loop number of $G(f)$.

Definition

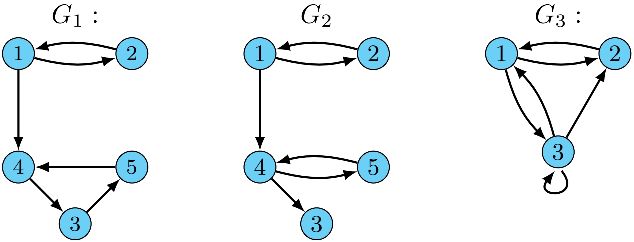
Given $G = (V, A)$ a non-trivial digraph with $V = \{1, \dots, n\}$. The loop number (or index of cyclicity) of G, $i(G)$, is defined by:

1. *If G is a non trivial strongly connected digraph,* $i(G) := gcd\{l(c) : \ c$ *is a cycle of G and $l(c)$ is its length*$\}$.
2. *If G is not strongly connected with at least a cycle,* $i(G) := mcm\{i(G_k) : G_k$ *is a non-trivial strongly connected component of G*$\}$.
3. $i(G) = 0$ *otherwise.*

If $i(G) = 1$, then G is primitive.

Remark: $i(G)$ can be calculated in polynomial time.

Examples. Given the following digraphs:



Then the loop numbers are:

Parallel update schedule and loop number

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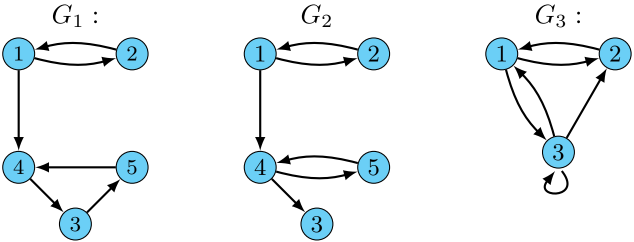
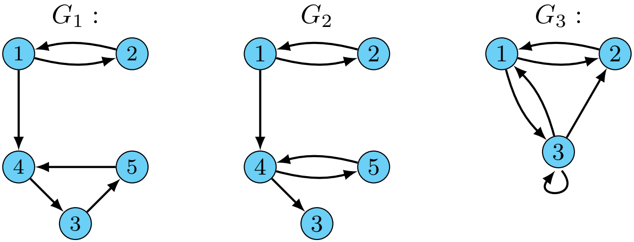


Then the loop numbers are: $i(G_1) = 6$,

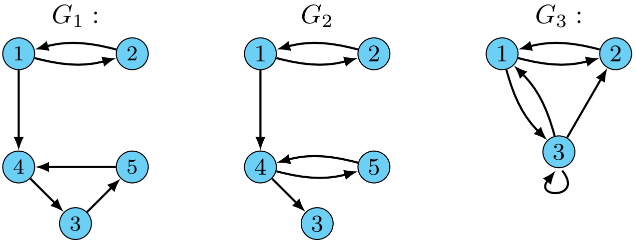
Parallel update schedule and loop number

Examples. Given the following digraphs:



Then the loop numbers are: $i(G_1) = 6$, $i(G_2) = 2$

Examples. Given the following digraphs:



Then the loop numbers are: $i(G_1) = 6$, $i(G_2) = 2$ y $i(G_3) = 1$.

Remark: if G is strongly connected and has a loop, then G is primitive.

LCE with synchronous update schedule

Theorem (Jarrah et al., 2010)

Let f be a conjunctive network. Then, f has no limit cycle with parallel update schedule if and only if either $G(f)$ is primitive or $G(f)$ has no cycles.

Corollary

LCE problem can be solved in polynomial time when s is the parallel update schedule.

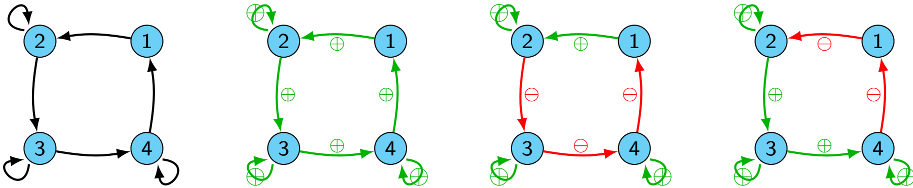
- LCE is NP-hard where f is an AND-OR network (Gómez, 2015)
- What happens if s is any block-sequential update schedule?

Given a interaction graph G and a block-sequential schedule s, the *update digraph* (G, s) is a digraph with a labeling function lab_s:

$$\text{lab}_s : A(G) \to \{\oplus, \ominus\}$$
$$\text{lab}_s(u, v) = \oplus \iff u \in B_i \wedge v \in B_j \wedge i \geq j$$

G $s_1 = \{1, 2, 3, 4\}$ $s_2 = \{2\}\{3\}\{4\}\{1\}$ $s_3 = \{3, 4\}\{1\}\{2\}$

$s_4 = \{4\}\{1\}\{3, 2\}$



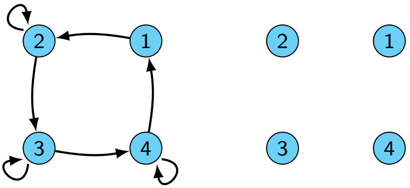
Aracena et al., 2009, 2011.

Parallel digraph

The *parallel digraph* is a digraph that represent the real dependence of the components of the Boolean network, according with the block-sequential schedule s.

$s = \{2\}\,\{3\}\,\{4\}\,\{1\}$

$G(f)$ $\qquad\qquad$ $\mathcal{P}(G(f), s) = G(f^s)$



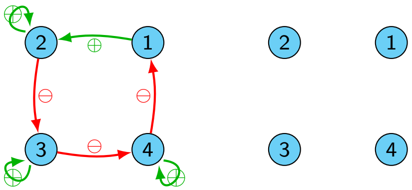
Parallel digraph

Can be obtained from the labeled digraph.
$\forall (u,v) \in V(G) \times V(G), (u,v) \in A(\mathcal{P}(G,s))$ if and only if:

- either (u,v) is labeled $\oplus$ or
- $\exists w \in V(G), (u,w)$ is labeled $\oplus$ and there exists a path from w to v labeled $\ominus$.

$s = \{2\}\,\{3\}\,\{4\}\,\{1\}$

$(G(f), s)$ $\qquad$ $\mathcal{P}(G(f), s) = G(f^s)$



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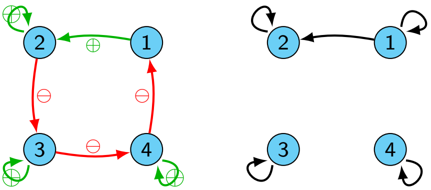

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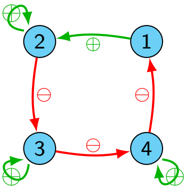
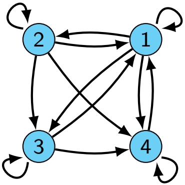
$(G(f), s)$



$\mathcal{P}(G(f), s) = G(f^s)$

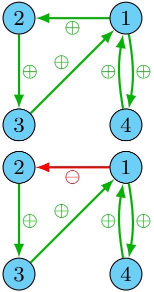


Primitivisation

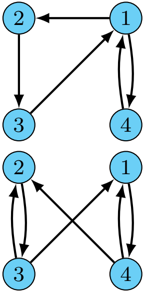
Lema

Let f be a conjunctive network with $G(f)$ strongly connected and s a block-sequential schedule. Then, $i(G(f^s)) = k > 1$ if and only if each cycle of $(G(f), s)$ has a multiple of k $\oplus-$labeled arcs.

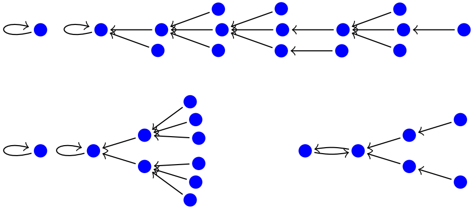
$(G(f), s)$



$G(f^s) = \mathcal{P}(G(f), s)$



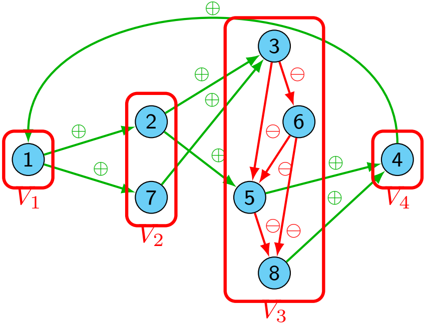
Dynamics



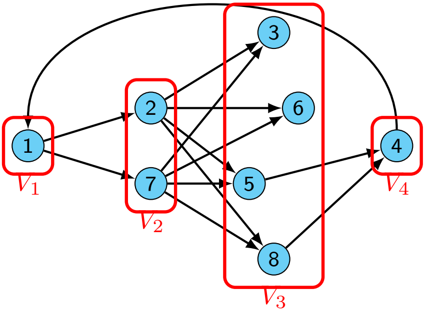
$\mathcal{P}(G,s)$ and (G,s) re-ordered.

Lema

Let f be a conjunctive network with $G(f)$ strongly connected. Then, there exists a block-sequential s such that $i(G(f^s))$ is no primitive if and only if each cycle of $(G(f),s)$ has an even number of $\oplus$−labeled arcs.

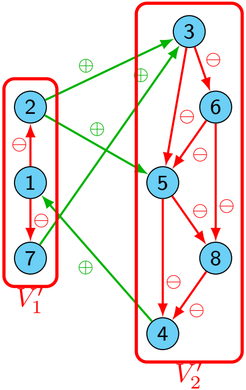


(G,s)

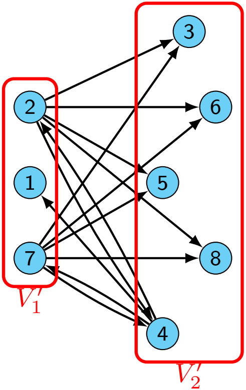


$\mathcal{P}(G,s)$

$\mathcal{P}(G, s)$ and (G, s) ordered according to V_1' and V_2'.



(G, s)

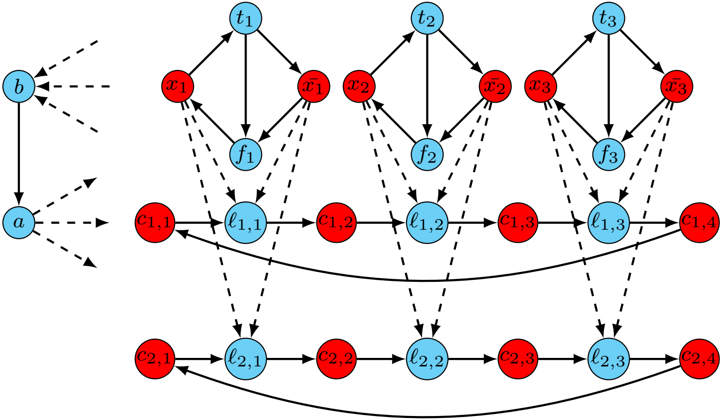


$\mathcal{P}(G, s)$

Theorem

LCE problem is NP-hard.

Proof (Idea)



LCE is NP-hard

Corollary

LCE is NP-hard with sequential update schedules.

Corollary

LCE is NP-hard even considering only limit cycles of constant length.

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Thank you!