



Inverse problems on the blocksequential operator in Boolean networks

Julio Aracena[†], **Luis Cabrera-Crot***,
Adrien Richard^o and Lilian Salinas⁺

* PhD Student in Computer Science, U. of Concepción, Chile.¹

† Department of Mathematical Engineering, U. of Concepción, Chile.

+ Department of Computer Science, U. of Concepción, Chile.

o CRNS and Université Côte d'Azur, France

International Workshop on Boolean Networks
January 9th, 2020



Contents



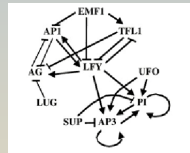
- 1 Motivation
- 2 Algorithm
- 3 Work in progress



Motivation



- Complex Systems



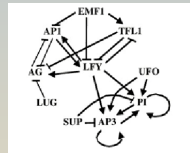
(L. Mendoza and E. Alvarez, 1998)



Motivation



- Complex Systems
- Boolean networks $f : \{0, 1\}^n \rightarrow \{0, 1\}^n$



(L. Mendoza and E. Alvarez, 1998)

$$f_1(x) = x_4$$

$$f_2(x) = x_1 \wedge x_2$$

$$f_3(x) = x_2 \vee x_3$$

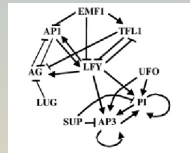
$$f_4(x) = x_3 \wedge x_4$$



Motivation



- Complex Systems
- Boolean networks $f : \{0, 1\}^n \rightarrow \{0, 1\}^n$
 - Interaction Graph



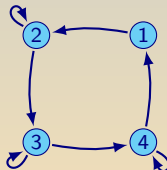
(L. Mendoza and E. Alvarez, 1998)

$$f_1(x) = x_4$$

$$f_2(x) = x_1 \wedge x_2$$

$$f_3(x) = x_2 \vee x_3$$

$$f_4(x) = x_3 \wedge x_4$$





Block-sequential schedule



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

$$s_1 = \{3, 4\}\{1\}\{2\},$$

$$s_2 = \{1, 2, 3, 4\},$$

$$s_3 = \{2\}\{3\}\{4\}\{1\}.$$



Labeled digraph



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

$$lab_s : A(G) \rightarrow \{\oplus, \ominus\}$$

$$lab_s(u, v) = \oplus \iff s(u) \geq s(v)$$

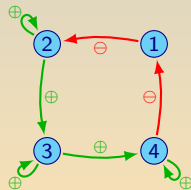
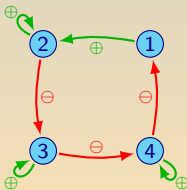
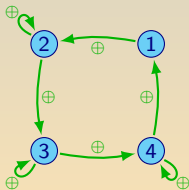
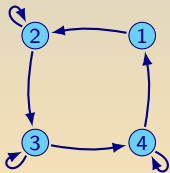
G

$$s_1 = \{1, 2, 3, 4\}$$

$$s_2 = \{2\} \{3\} \{4\} \{1\}$$

$$s_3 = \{3, 4\} \{1\} \{2\}$$

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





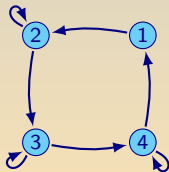
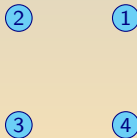
Parallel digraph



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

Also, is equivalent to the interaction graph of a Boolean network with equal dynamic behavior when is updated in parallel (one only block).

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

 G

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




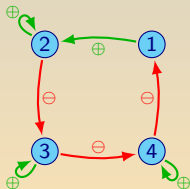
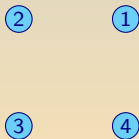
Parallel digraph



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

Also, is equivalent to the interaction graph of a Boolean network with equal dynamic behavior when is updated in parallel (one only block).

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

 (G, s)

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




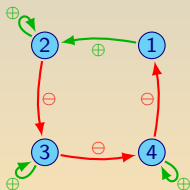
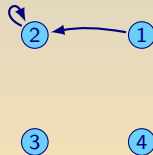
Parallel digraph



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

Also, is equivalent to the interaction graph of a Boolean network with equal dynamic behavior when is updated in parallel (one only block).

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

 (G, s)

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




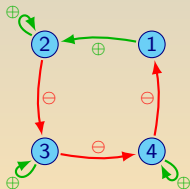
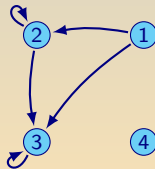
Parallel digraph



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

Also, is equivalent to the interaction graph of a Boolean network with equal dynamic behavior when is updated in parallel (one only block).

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

 (G, s)

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




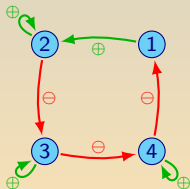
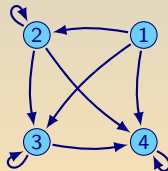
Parallel digraph



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

Also, is equivalent to the interaction graph of a Boolean network with equal dynamic behavior when is updated in parallel (one only block).

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

 (G, s)

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




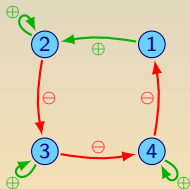
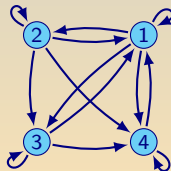
Parallel digraph



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

Also, is equivalent to the interaction graph of a Boolean network with equal dynamic behavior when is updated in parallel (one only block).

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

 (G, s)

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




Parallel digraph

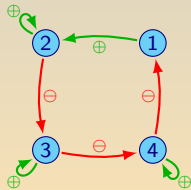


Can be obtained from the labeled digraph.

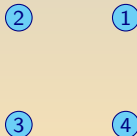
$\forall (u, v) \in V(G) \times V(G), (u, v) \in A(\mathcal{P}(G, s))$ if and only if:

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

(G, s)



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





Parallel digraph



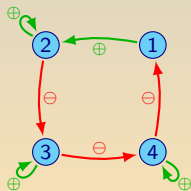
Can be obtained from the labeled digraph.

$\forall (u, v) \in V(G) \times V(G), (u, v) \in A(\mathcal{P}(G, s))$ if and only if:

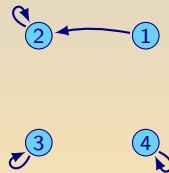
- (u, v) is labeled \oplus .

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

(G, s)



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





Parallel digraph



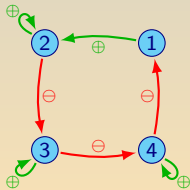
Can be obtained from the labeled digraph.

$\forall (u, v) \in V(G) \times V(G), (u, v) \in A(\mathcal{P}(G, s))$ if and only if:

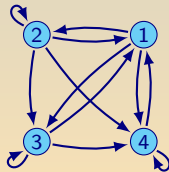
- (u, v) is labeled \oplus .
- $\exists w \in V(G), (u, w)$ is labeled \oplus and exists a path from w to v labeled \ominus .

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

(G, s)



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





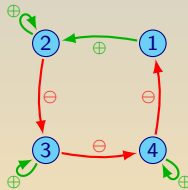
Parallel digraph



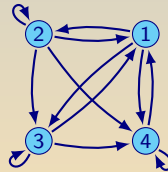
The function that associates (G, s) with the digraph $\mathcal{P}(G, s)$ is called **block-sequential operator** and can be constructed in polynomial time.

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

(G, s)



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





Inverse problem



Given a digraph P and a block-sequential schedule s , does there exist a digraph G such that $\mathcal{P}(G, s) = P$?

$$s = \{1\} \{2\}$$

P





Inverse problem



Given a digraph P and a block-sequential schedule s , does there exist a digraph G such that $\mathcal{P}(G, s) = P$?

$$s = \{1\} \{2\}$$

 (G, s)
 P


Unique solution



Inverse problem



Given a digraph P and a block-sequential schedule s , does there exist a digraph G such that $\mathcal{P}(G, s) = P$?

$$s = \{1\} \{2\}$$

P





Inverse problem



Given a digraph P and a block-sequential schedule s , does there exist a digraph G such that $\mathcal{P}(G, s) = P$?

$$s = \{1\} \{2\}$$

 (G, s)
 P


Multiple solutions



Inverse problem



Given a digraph P and a block-sequential schedule s , does there exist a digraph G such that $\mathcal{P}(G, s) = P$?

$$s = \{1\} \{2\}$$

 P 



Inverse problem



Given a digraph P and a block-sequential schedule s , does there exist a digraph G such that $\mathcal{P}(G, s) = P$?

$$s = \{1\} \{2\}$$

P



No solution



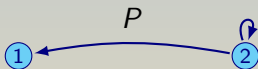
Contents



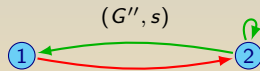
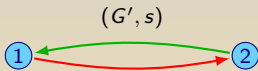
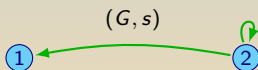
1 Motivation

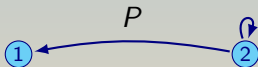
2 Algorithm

3 Work in progress

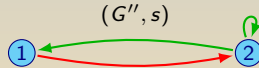
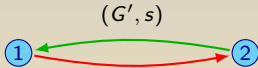
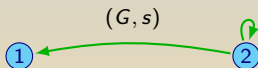


For example, for the schedule $\{1\} \{2\}$, there are three preimages:



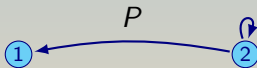


For example, for the schedule $\{1\} \{2\}$, there are three preimages:

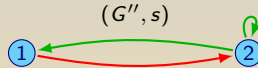
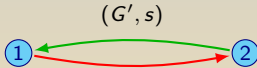
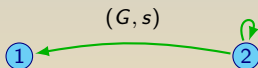


Theorem

Let s be a block-sequential schedule and G and G' two digraphs such that $\mathcal{P}(G, s) = \mathcal{P}(G', s)$. Then $\mathcal{P}(G \cup G', s) = \mathcal{P}(G, s)$.



For example, for the schedule $\{1\} \{2\}$, there are three preimages:

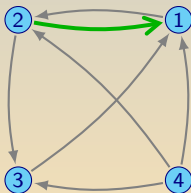
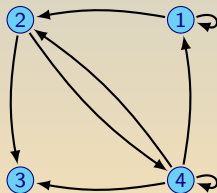


Theorem

For this reason, if for a digraph P and a block-sequential schedule s there exists at least one preimage G , then there exists a maximum preimage.

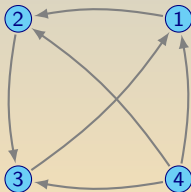
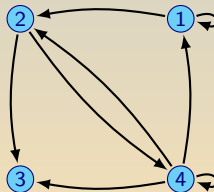

 \bar{P} Rule

$\forall (u, v)$ such that $lab(u, v) = \oplus$, if $(u, v) \notin P$, then $(u, v) \notin G$.

 (G, s)

 P



 \bar{P} Rule

$\forall (u, v)$ such that $lab(u, v) = \oplus$, if $(u, v) \notin P$, then $(u, v) \notin G$.

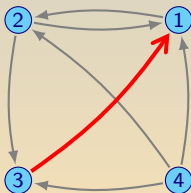
 (G, s)

 P




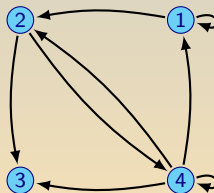
Transitive Rule

$\forall (u, v)$ such that $lab(u, v) = \ominus$, if $\exists w$ such that $(w, u) \in P$ and $(w, v) \notin P$, then $(u, v) \notin G$.

(G, s)



P

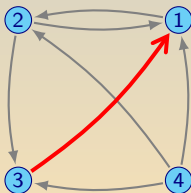




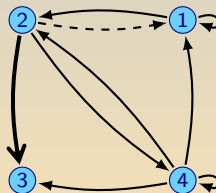
Transitive Rule

$\forall (u, v)$ such that $lab(u, v) = \ominus$, if $\exists w$ such that $(w, u) \in P$ and $(w, v) \notin P$, then $(u, v) \notin G$.

(G, s)



P

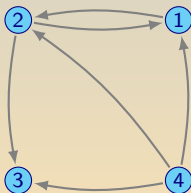




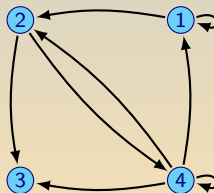
Transitive Rule

$\forall (u, v)$ such that $lab(u, v) = \ominus$, if $\exists w$ such that $(w, u) \in P$ and $(w, v) \notin P$, then $(u, v) \notin G$.

(G, s)



P



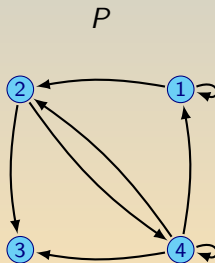


Algorithm MaxPI: Step 1 - Build and label



Input

Given a digraph P and a block-sequential schedule $s = \{3\} \{1\} \{2, 4\}$.





Algorithm MaxPI: Step 1 - Build and label

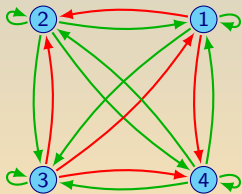


Input

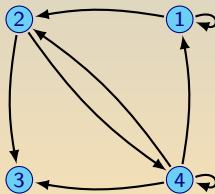
Given a digraph P and a block-sequential schedule $s = \{3\} \{1\} \{2, 4\}$.

Initially: $G \leftarrow K_n$, $n = |V(P)|$.

(G, s)



P





Algorithm MaxPI: Step 2a

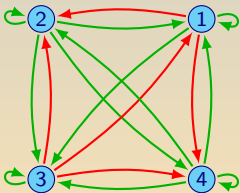
Removing green arcs



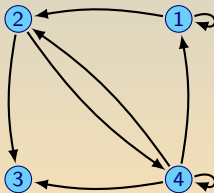
Rule

$\forall (u, v) \in A(G)$ that does not satisfy the " \bar{P} rule",
 (u, v) is removed from G .

(G, s)



P





Algorithm MaxPI: Step 2a

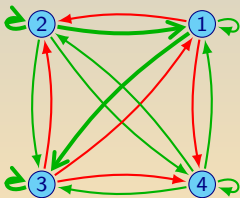
Removing green arcs



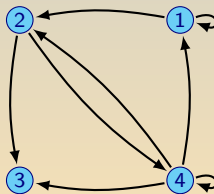
Rule

$\forall (u, v) \in A(G)$ that does not satisfy the " \bar{P} rule",
 (u, v) is removed from G .

(G, s)



P





Algorithm MaxPI: Step 2a

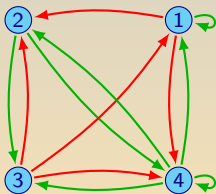
Removing green arcs



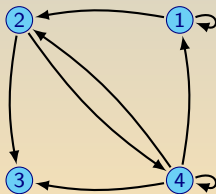
Rule

$\forall (u, v) \in A(G)$ that does not satisfy the " \bar{P} rule",
 (u, v) is removed from G .

(G, s)



P





Algorithm MaxPI: Step 2b

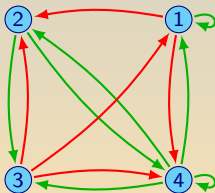
Removing red arcs



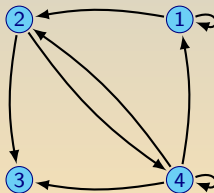
Rule

$\forall (u, v) \in A(G)$ that does not satisfy the “Transitive rule”,
 (u, v) is removed from G .

(G, s)



P





Algorithm MaxPI: Step 2b

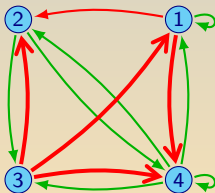
Removing red arcs



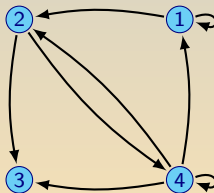
Rule

$\forall (u, v) \in A(G)$ that does not satisfy the “Transitive rule”,
 (u, v) is removed from G .

(G, s)



P





Algorithm MaxPI: Step 2b

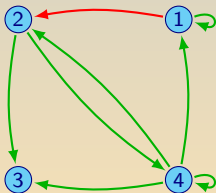
Removing red arcs



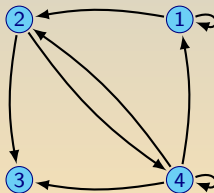
Rule

$\forall (u, v) \in A(G)$ that does not satisfy the “Transitive rule”,
 (u, v) is removed from G .

(G, s)



P

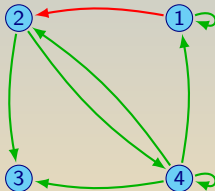




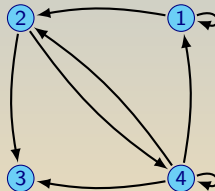
Algorithm MaxPI: Step 3 - Validation



(G, s)

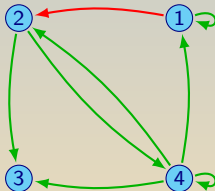
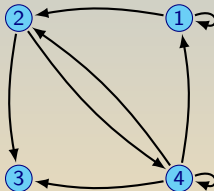
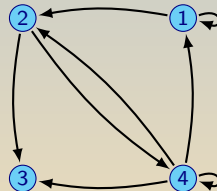


P



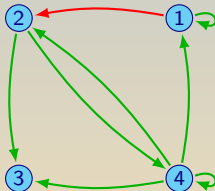
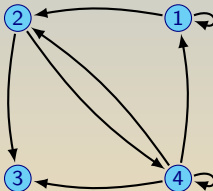
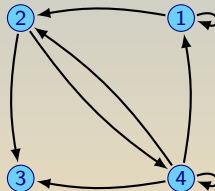


Algorithm MaxPI: Step 3 - Validation


 (G, s)

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

 P




Algorithm MaxPI: Step 3 - Validation


 (G, s)

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

 P


Output

Since $\mathcal{P}(G, s) = P$, the algorithm return (G, s) as maximum preimage of P with the schedule s .



Another example of MaxPI: Step 1



Input

Given a digraph P and a block-sequential schedule $s = \{1\} \{2\}$.





Another example of MaxPI: Step 1



Input

Given a digraph P and a block-sequential schedule $s = \{1\} \{2\}$.

Initially: $G \leftarrow K_n$, $n = |V(P)|$.





Another example of MaxPI: Step 2a



Removing green arcs, according " \overline{P} rule".





Another example of MaxPI: Step 2a



Removing green arcs, according " \overline{P} rule".





Another example of MaxPI: Step 2a



Removing green arcs, according " \overline{P} rule".





Another example of MaxPI: Step 2b



Removing red arcs, according “Transitive rule”.





Another example of MaxPI: Step 2b



Removing red arcs, according “Transitive rule”.





Another example of MaxPI: Step 2b



Removing red arcs, according “Transitive rule”.

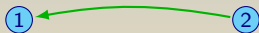




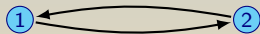
Another example of MaxPI: Step 3



(G, s)



P



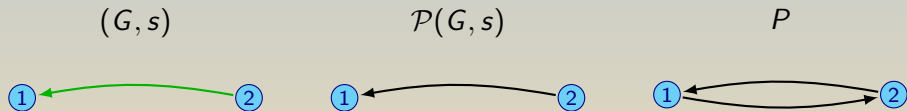


Another example of MaxPI: Step 3

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



Another example of MaxPI: Step 3

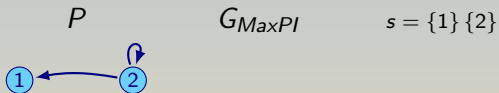


Output

Since $\mathcal{P}(G, s) \neq P$, P does not have preimage for the schedule s .

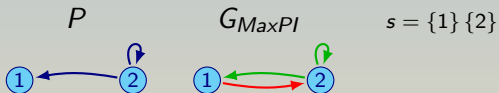


Algorithm for enumeration of preimages



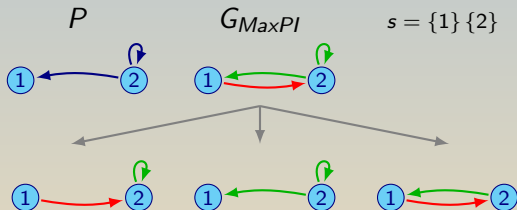


Algorithm for enumeration of preimages



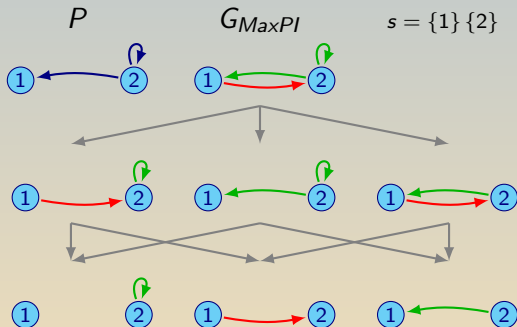


Algorithm for enumeration of preimages



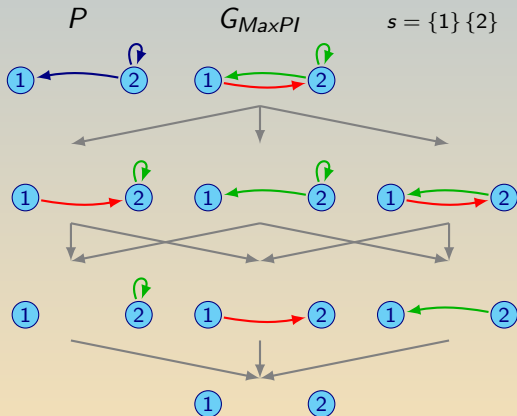


Algorithm for enumeration of preimages





Algorithm for enumeration of preimages





Algorithm for enumeration of preimages



Lemma

Let s be a block-sequential schedule and G and G' two digraphs such that $V(G) = V(G')$. If $G \subseteq G'$, then $\mathcal{P}(G, s) \subseteq \mathcal{P}(G', s)$.



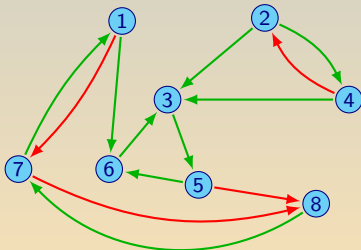
Algorithm for enumeration of preimages



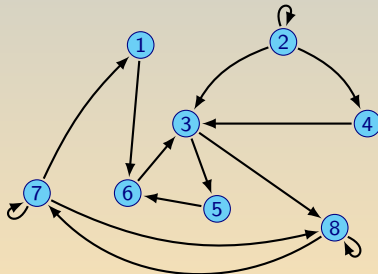
Lemma

Let s be a block-sequential schedule and G and G' two digraphs such that $V(G) = V(G')$. If $G \subseteq G'$, then $\mathcal{P}(G, s) \subseteq \mathcal{P}(G', s)$.

(G, s)



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





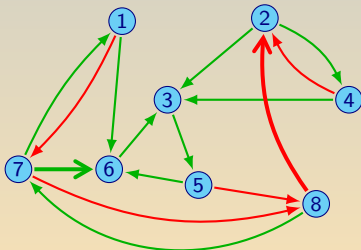
Algorithm for enumeration of preimages



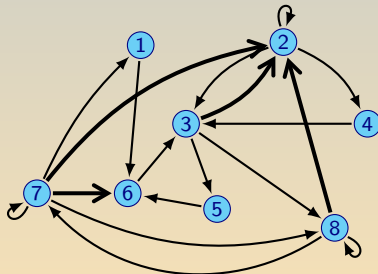
Lemma

Let s be a block-sequential schedule and G and G' two digraphs such that $V(G) = V(G')$. If $G \subseteq G'$, then $\mathcal{P}(G, s) \subseteq \mathcal{P}(G', s)$.

(G', s)



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





Algorithm for enumeration of preimages



Proposition

Let s be a block-sequential schedule and G and G'' two digraphs such that $G'' \subseteq G$. If $\mathcal{P}(G, s) = \mathcal{P}(G'', s)$, then

$$\forall G', G'' \subseteq G' \subseteq G, \mathcal{P}(G', s) = \mathcal{P}(G, s) = \mathcal{P}(G'', s).$$



Algorithm for enumeration of preimages



Proposition

Let s be a block-sequential schedule and G and G'' two digraphs such that $G'' \subseteq G$. If $\mathcal{P}(G, s) = \mathcal{P}(G'', s)$, then

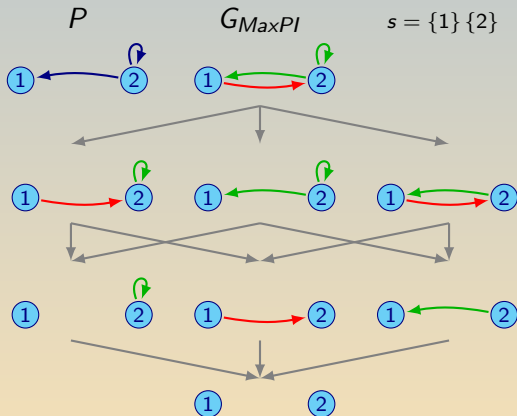
$$\forall G', G'' \subseteq G' \subseteq G, \mathcal{P}(G', s) = \mathcal{P}(G, s) = \mathcal{P}(G'', s).$$

Proof

Since $G'' \subseteq G' \subseteq G$, then $\mathcal{P}(G'', s) \subseteq \mathcal{P}(G', s) \subseteq \mathcal{P}(G, s)$. Since $\mathcal{P}(G'', s) = \mathcal{P}(G, s)$, then $\mathcal{P}(G'', s) = \mathcal{P}(G', s) = \mathcal{P}(G, s)$.

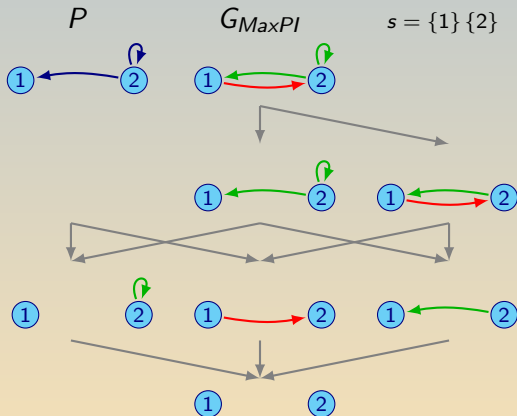


Algorithm for enumeration of preimages



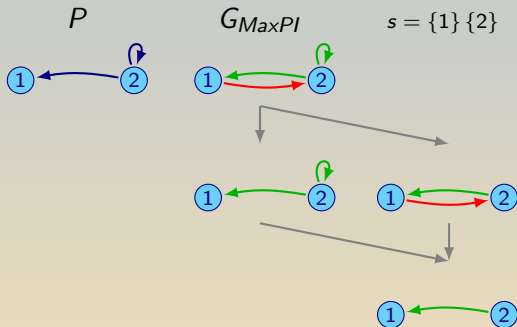


Algorithm for enumeration of preimages



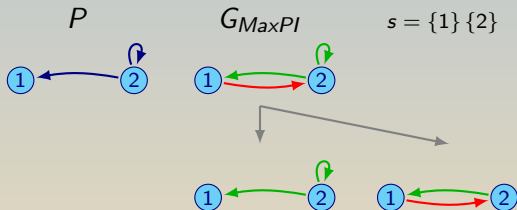


Algorithm for enumeration of preimages





Algorithm for enumeration of preimages





Algorithm for enumeration of preimages



Complexity

The complexity of this algorithm has a **polynomial delay**.



Algorithm for enumeration of preimages



Complexity

The complexity of this algorithm has a **polynomial delay**.

Since there are cases with an exponential number of pre-images, listing all the pre-images has an **exponential cost**



Algorithm for enumeration of preimages

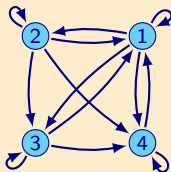


Complexity

The complexity of this algorithm has a **polynomial delay**.

Since there are cases with an exponential number of pre-images, listing all the pre-images has an **exponential cost**

For example, this digraph with the block-sequential schedule $\{2\} \{3\} \{4\} \{1\}$ has 8 preimages, corresponding to $2^{\frac{(n-2)(n-1)}{2}}$.





Contents

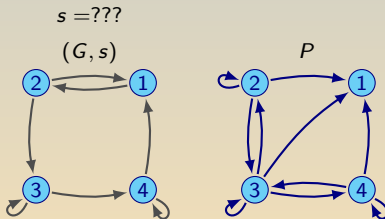


- 1 Motivation
- 2 Algorithm
- 3 Work in progress**



Problem

Given two digraphs G and P , does there exist a block-sequential schedule s such that $\mathcal{P}(G, s) = P$?





Work in progress...



Theorem

If G and P are acyclic digraphs, it is possible to decide if there is labeling function lab such that $\mathcal{P}(G, lab) = P$ in polynomial time.



Work in progress...



Theorem

If G and P are acyclic digraphs, it is possible to decide if there is labeling function lab such that $\mathcal{P}(G, lab) = P$ in polynomial time.

How?

With an algorithm that label the arcs of G , according the following rules:



Work in progress...



Theorem

If G and P are acyclic digraphs, it is possible to decide if there is labeling function lab such that $\mathcal{P}(G, lab) = P$ in polynomial time.

How?

With an algorithm that label the arcs of G , according the following rules:

- "Transitive rule": If $\exists u, v, w \in V(G)$, such that $(u, v) \in G$, $(w, u) \in P$ and $(w, v) \notin P$, then $lab(u, v) = \oplus$.



Work in progress...



Theorem

If G and P are acyclic digraphs, it is possible to decide if there is labeling function lab such that $\mathcal{P}(G, lab) = P$ in polynomial time.

How?

With an algorithm that label the arcs of G , according the following rules:

- “Transitive rule”: If $\exists u, v, w \in V(G)$, such that $(u, v) \in G$, $(w, u) \in P$ and $(w, v) \notin P$, then $lab(u, v) = \oplus$.
- “ \bar{P} rule”: If $\exists u, v \in V(G)$, such that $(u, v) \in G$ and $(u, v) \notin P$, then $lab(u, v) = \ominus$.



Work in progress...



Theorem

If G and P are acyclic digraphs, it is possible to decide if there is labeling function lab such that $\mathcal{P}(G, lab) = P$ in polynomial time.

How?

With an algorithm that label the arcs of G , according the following rules:

- “Transitive rule”: If $\exists u, v, w \in V(G)$, such that $(u, v) \in G$, $(w, u) \in P$ and $(w, v) \notin P$, then $lab(u, v) = \oplus$.
- “ \bar{P} rule”: If $\exists u, v \in V(G)$, such that $(u, v) \in G$ and $(u, v) \notin P$, then $lab(u, v) = \ominus$.
- If $\exists u, v \in V(G)$, such that if (u, v) is labeled \ominus , then an arc that is not in P is formed, then $lab(u, v) = \oplus$.



Work in progress...



Theorem

If G and P are acyclic digraphs, it is possible to decide if there is labeling function lab such that $\mathcal{P}(G, lab) = P$ in polynomial time.

How?

With an algorithm that label the arcs of G , according the following rules:

- “Transitive rule”: If $\exists u, v, w \in V(G)$, such that $(u, v) \in G$, $(w, u) \in P$ and $(w, v) \notin P$, then $lab(u, v) = \oplus$.
- “ \bar{P} rule”: If $\exists u, v \in V(G)$, such that $(u, v) \in G$ and $(u, v) \notin P$, then $lab(u, v) = \ominus$.
- If $\exists u, v \in V(G)$, such that if (u, v) is labeled \ominus , then an arc that is not in P is formed, then $lab(u, v) = \oplus$.
- If $\exists u, v \in V(G)$, such that if (u, v) is labeled \oplus , then an arc that is in P cannot be formed, then $lab(u, v) = \ominus$.



Work in progress...



Theorem

If G and P are acyclic digraphs, it is possible to decide if there is labeling function lab such that $\mathcal{P}(G, lab) = P$ in polynomial time.

How?

With an algorithm that label the arcs of G , according the following rules:

- “Transitive rule”: If $\exists u, v, w \in V(G)$, such that $(u, v) \in G$, $(w, u) \in P$ and $(w, v) \notin P$, then $lab(u, v) = \oplus$.
- “ \bar{P} rule”: If $\exists u, v \in V(G)$, such that $(u, v) \in G$ and $(u, v) \notin P$, then $lab(u, v) = \ominus$.
- If $\exists u, v \in V(G)$, such that if (u, v) is labeled \ominus , then an arc that is not in P is formed, then $lab(u, v) = \oplus$.
- If $\exists u, v \in V(G)$, such that if (u, v) is labeled \oplus , then an arc that is in P cannot be formed, then $lab(u, v) = \ominus$.
- If $\exists u, v \in V(G)$, such that if (u, v) is labeled \ominus , then an arc that is in P cannot be formed, then $lab(u, v) = \oplus$.



Work in progress...



If one arc is labeled \oplus and \ominus by different rules, then the decision problem answer is “There is no labeling function lab such that $\mathcal{P}(G, lab) = P$ ” ..



Work in progress...

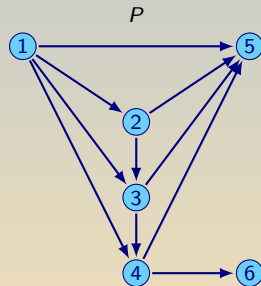
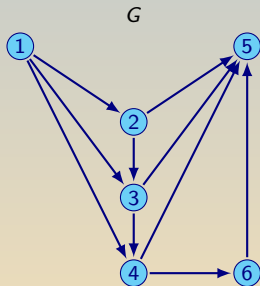


If one arc is labeled \oplus and \ominus by different rules, then the decision problem answer is “There is no labeling function lab such that $\mathcal{P}(G, lab) = P$ ” ..

Otherwise, the labeling function formed by all the arcs labeled by the algorithm plus negative arcs (replacing the arcs not labeled by the algorithm) is a labeling function such that $\mathcal{P}(G, lab) = P$.

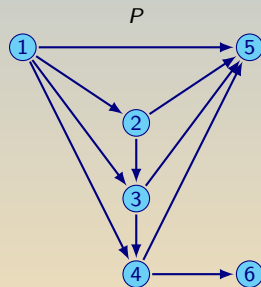
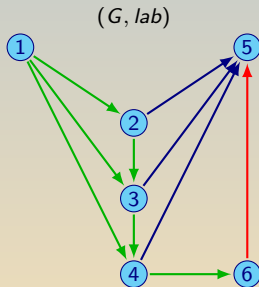
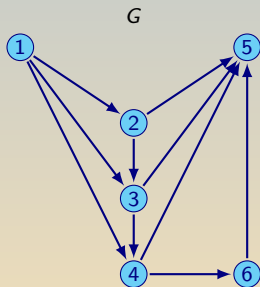


Work in progress...



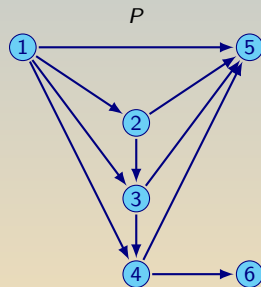
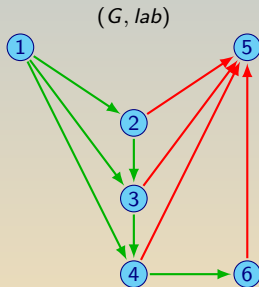
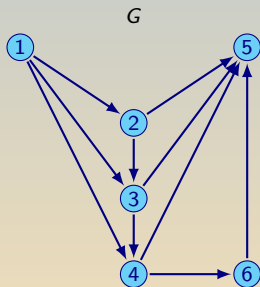


Work in progress...





Work in progress...



Work in progress...

- And for the acyclic case?

Work in progress...

- And for the acyclic case?

Still in progress

Work in progress...

- And for the acyclic case?

Still in progress

Thank You!