Complexity of maximum and minimum fixed point problems in Boolean networks

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joint work with

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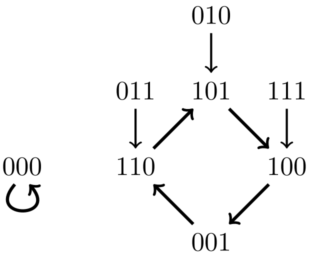
Boolean Network (BN)

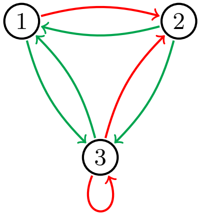
The local functions of $f : \{0,1\}^3 \to \{0,1\}^3$ are defined by

$$\begin{cases} f_1(x) &= x_2 \vee x_3 \\ f_2(x) &= \overline{x_1} \wedge \overline{x_3} \\ f_3(x) &= \overline{x_3} \wedge (x_1 \vee x_2) \end{cases}$$

Synchronous dynamics



Interaction graph



BNs are classical models for **gene networks**. When biologists study a gene network, the **interaction graph** is often the first reliable data.

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INTERACTION GRAPH CONSISTENCY PROBLEM

Input: An interaction graph G and a dynamical property P.

Question: Is there a BN **on** G with a dynamics satisfying P?

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Interaction Graph Consistency Problem

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Question: Is there a BN **on** G with a dynamics satisfying P?

$\hookrightarrow$ Talk of Stéphanie Chevalier

$\hookrightarrow$ Dynamical properties often concern the **number of fixed points**.

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$\hookrightarrow$ Talks of Guilhem Gamard, Julio Aracena, Kévin Perrot.

$\hookrightarrow$ It is **NP-complete** to decide if a BN has a fixed point [Kosub 2008].

Definitions

$$\max(G) := \textbf{maximum number of fixed points} \text{ in a BN on } G$$
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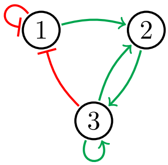

$\max(G) = 1$
$\min(G) = 0$

x	$f^1(x)$	$f^2(x)$	$f^3(x)$	$f^4(x)$	$f^5(x)$	$f^6(x)$	$f^7(x)$	$f^8(x)$
000	100	100	100	100	100	100	100	100
001	000	**001**	010	011	100	101	110	111
010	100	101	100	101	100	101	100	101
011	001	001	**011**	**011**	101	101	111	111
100	000	000	010	010	**100**	**100**	110	110
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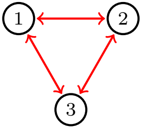

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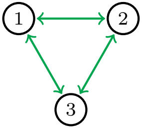
(8 BNs)



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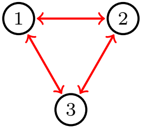

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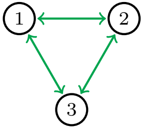

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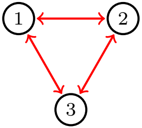

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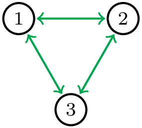

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k-MaxProblem: Given G, do we have $\max(G) \geq k$?

k-MinProblem: Given G, do we have $\min(G) < k$?

$\max(G) \geq 1$?

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Recall that it is **NP-complete** to decide if a BN has a fixed point.

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It is **NP-complete** to decide if $\max(G) \geq 2$.

It is **NP-complete** to decide if $\max(G) \geq k$ for every fixed $k \geq 2$.

$\max(G) \geq k$? is in NP

Theorem [Perrot, R. 2021]

There is an algorithm with the following specifications:

Input: G and k pairs of states $(x^1, y^1) \dots (x^k, y^k)$.

Output: Decide if there is a BN f on G with $f(x^\ell) = y^\ell$ for $1 \leq \ell \leq k$.

Running time: $n^{O(k^2)}$.

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$\hookrightarrow$ There is an excepting branch if and only if $\max(G) \geq k$.

$\hookrightarrow$ The running time is $n^{O(k^2)}$ thus polynomial since k is fixed.

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Given a CNF formula ϕ, we can built in polytime G_ϕ such that

$$\max(G_\phi) \geq 2 \iff \phi \text{ is satisfiable}$$

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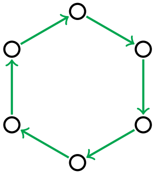
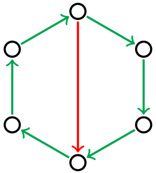


2 fixed points



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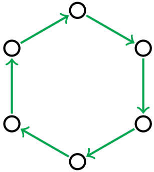

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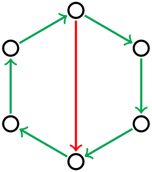

1 fixed point

The idea is to "control" with ϕ the "effectiveness" of the negative chord, so that the chord can be "ineffective" if and only if ϕ is satisfiable.

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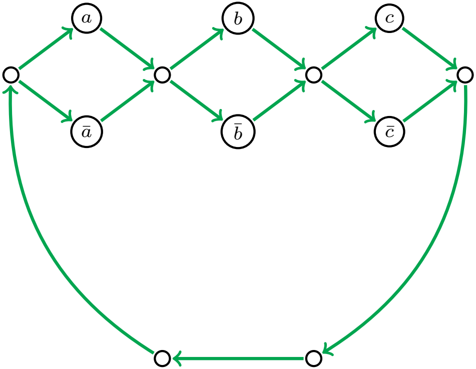
Example with $\phi = (a \vee \bar{b} \vee c) \wedge (\bar{a} \vee \bar{c})$.



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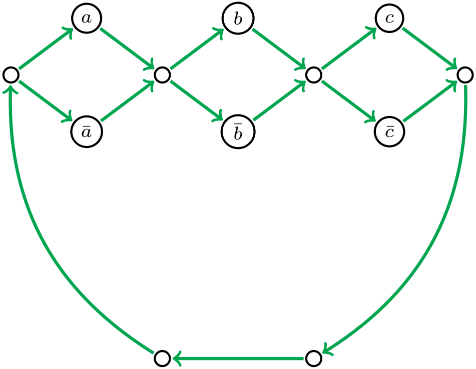

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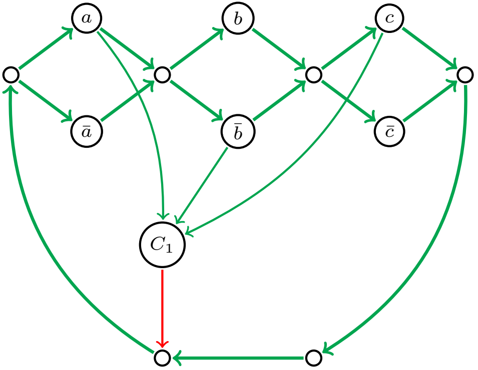

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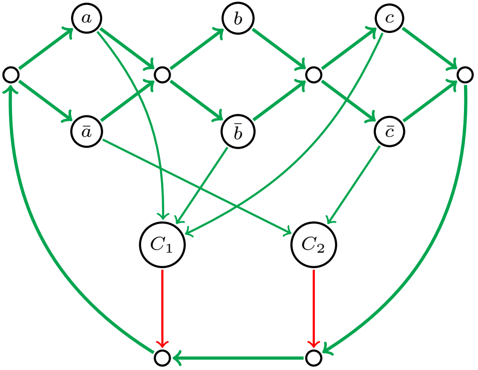

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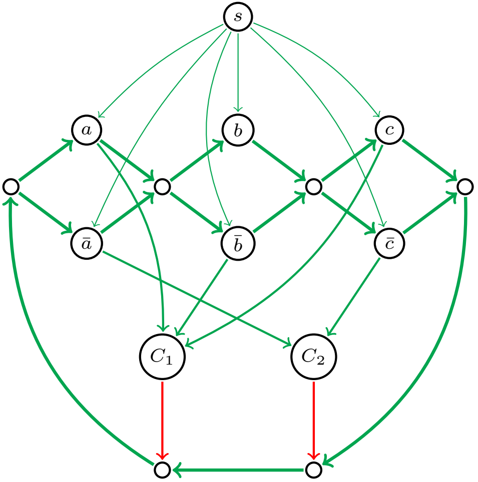

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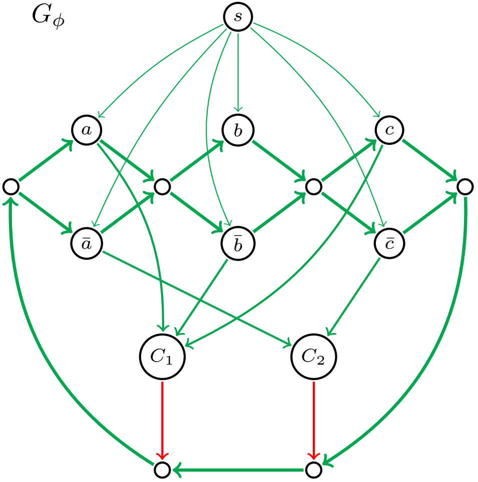

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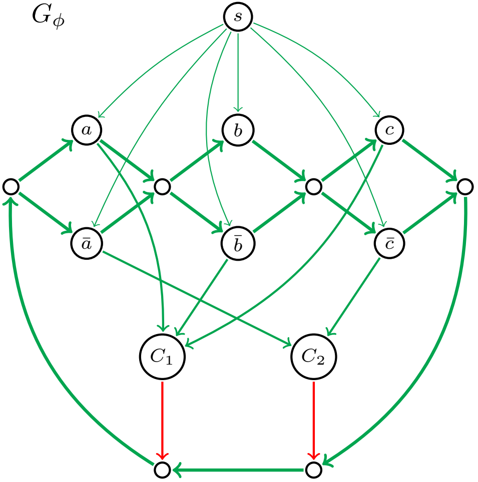

ϕ is sat. $\Rightarrow \max(G) \geq 2$

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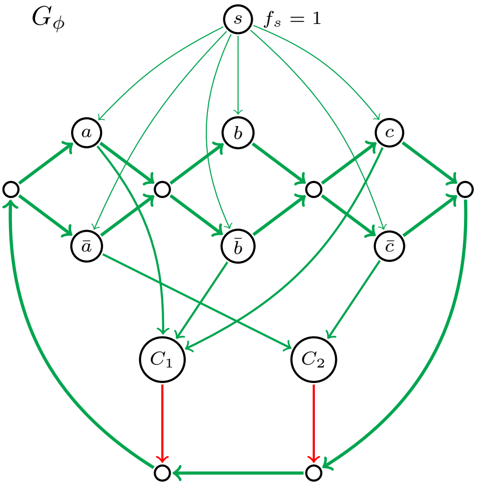

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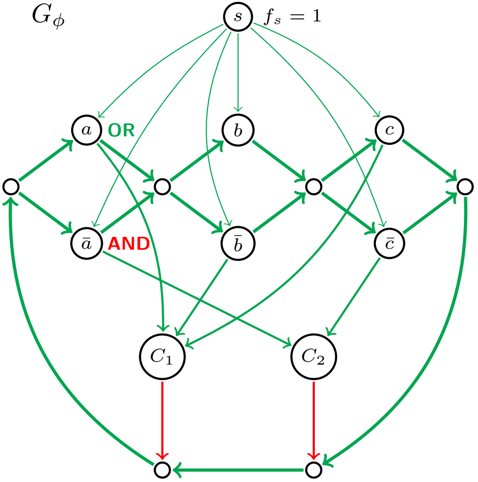

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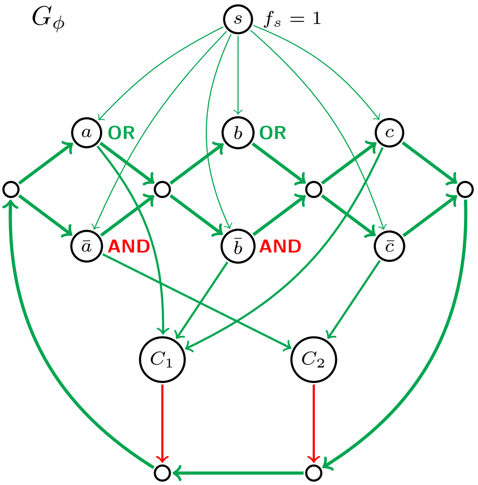

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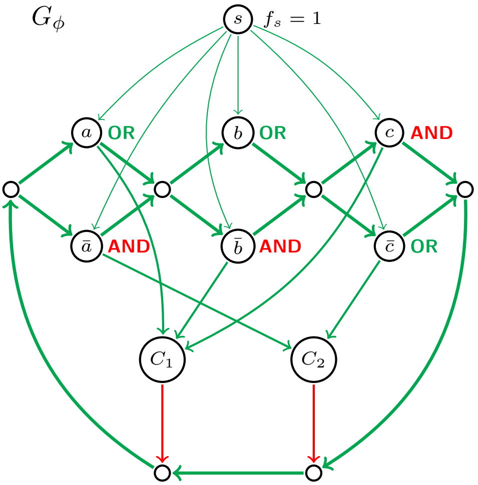

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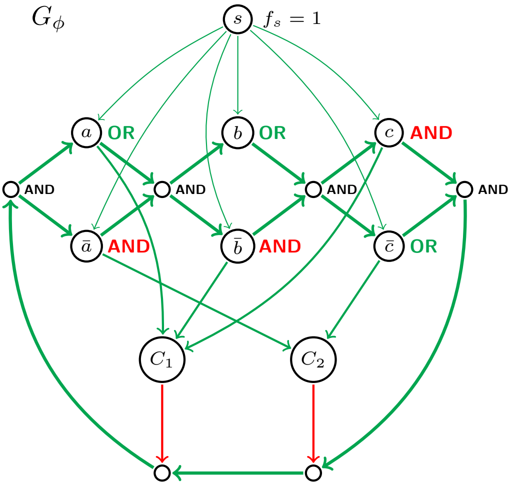

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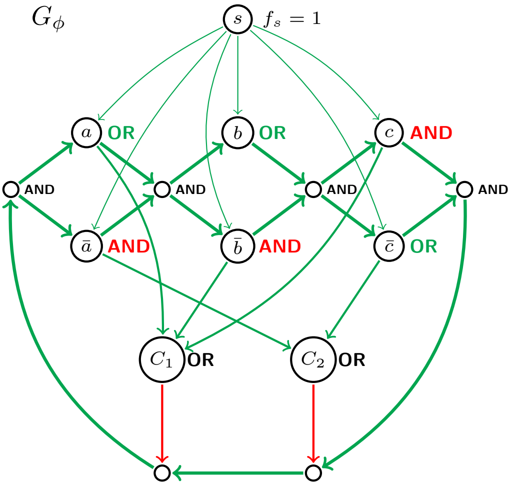

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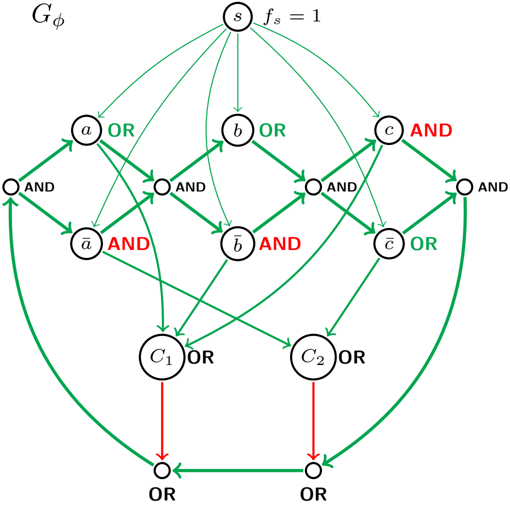

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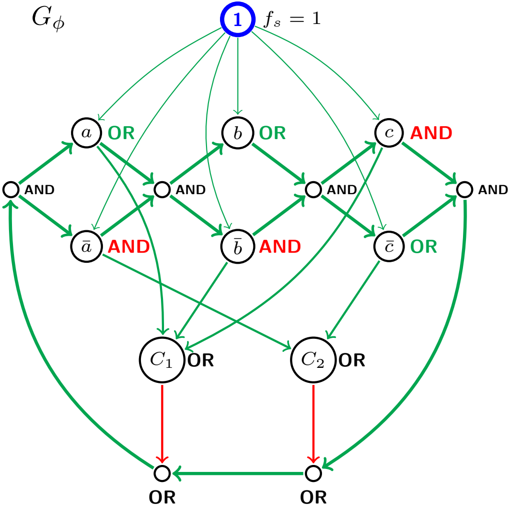

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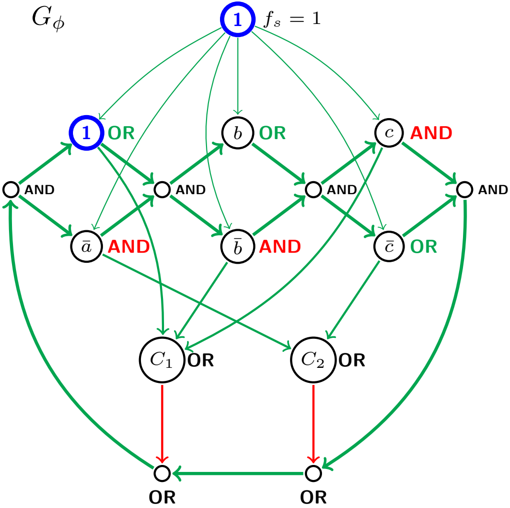

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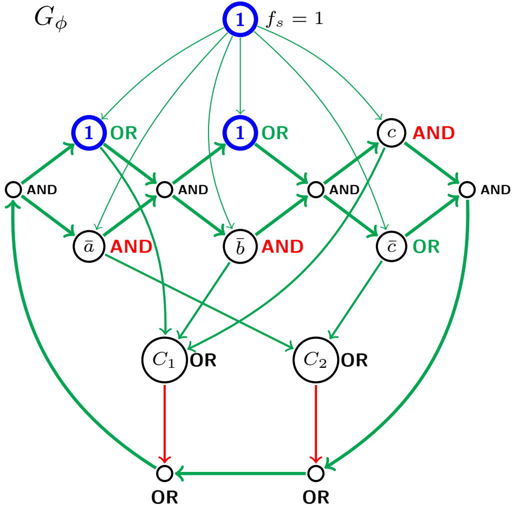

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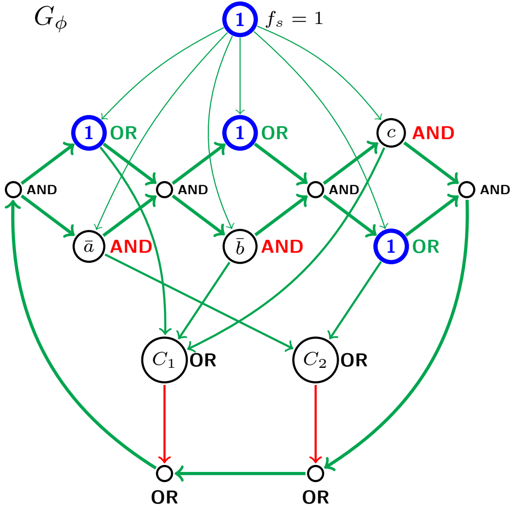

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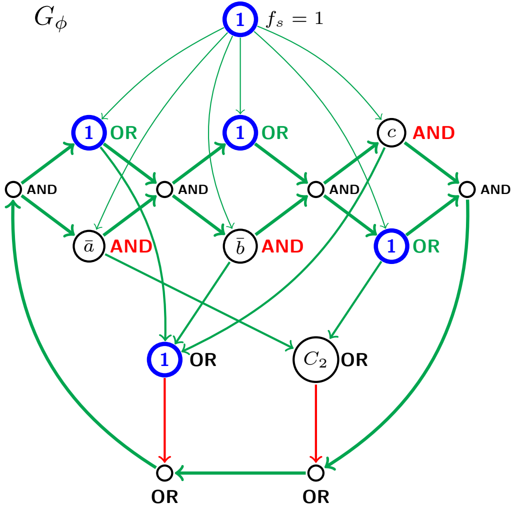

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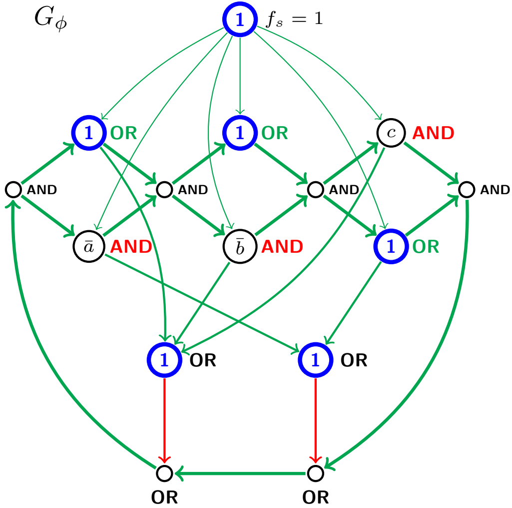

ϕ is sat. $\Rightarrow \max(G) \geq 2$

Consider a true assignment:
$a = 1,\ b = 1,\ c = 0$

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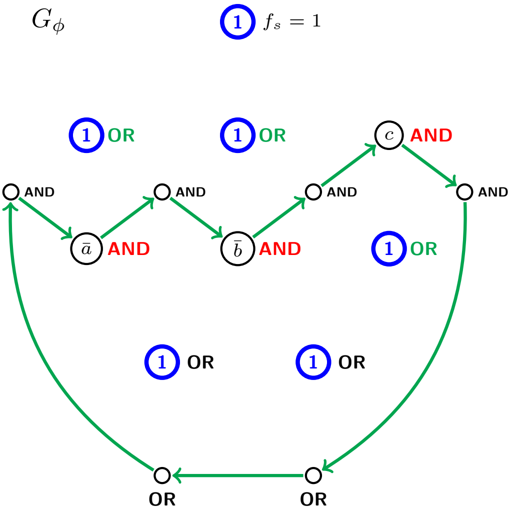

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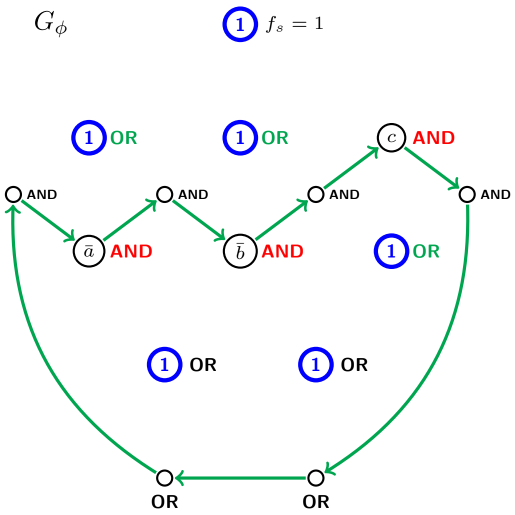

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Isolated positive cycle
$\Downarrow$
2 fixed points

$\max(G) \geq 2?$ is NP-hard

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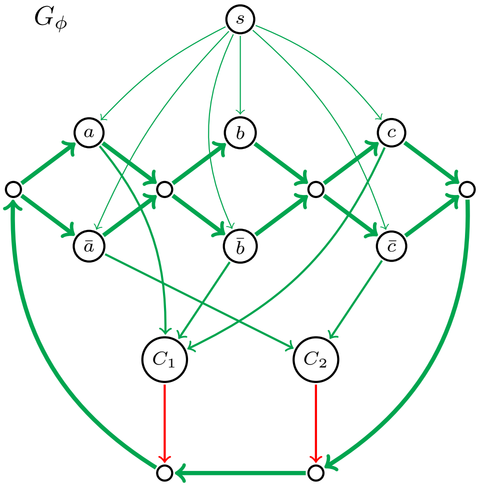

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Let f be a BN on G with two fixed points: x and y

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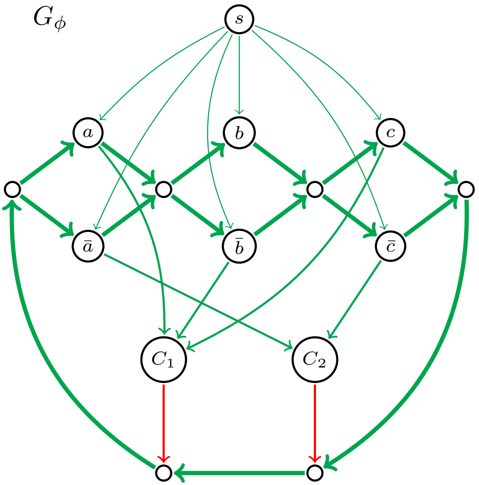

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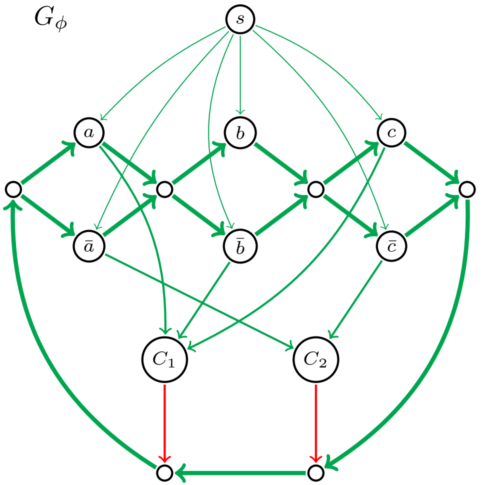

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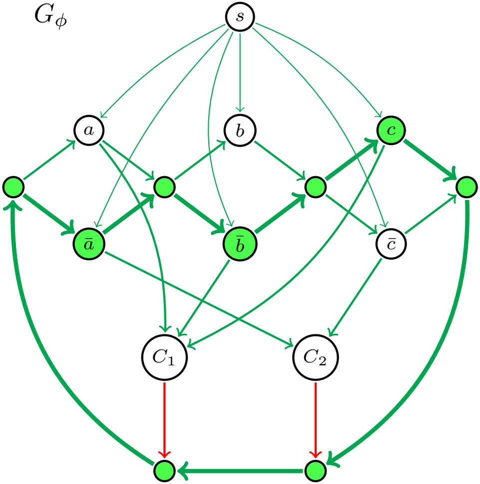

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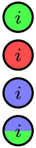

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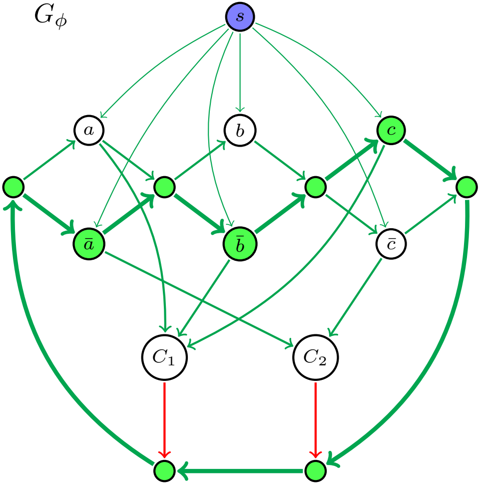

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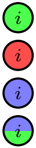

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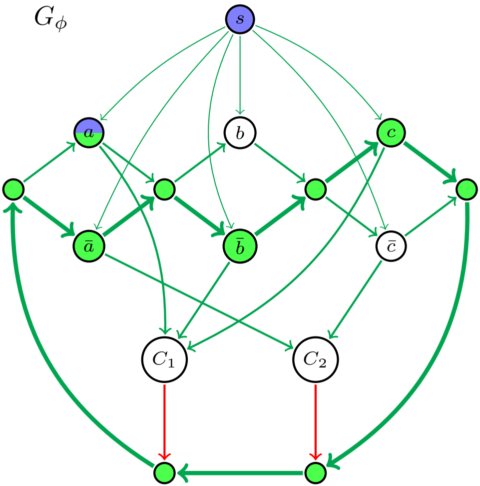

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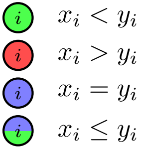

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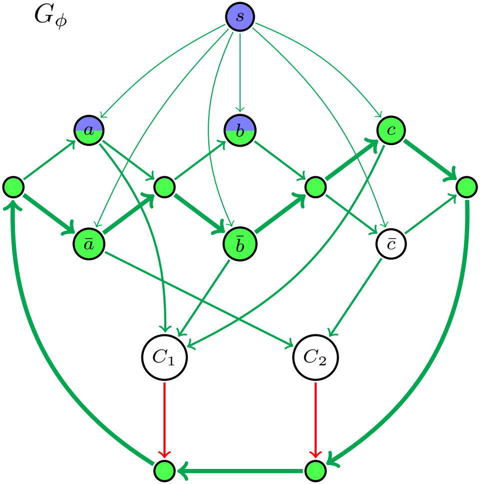

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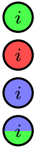

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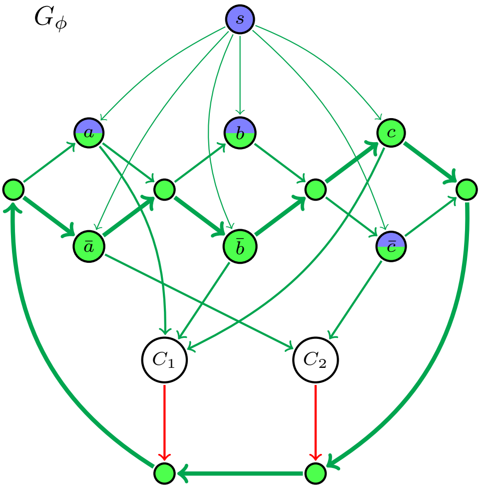

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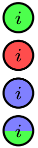

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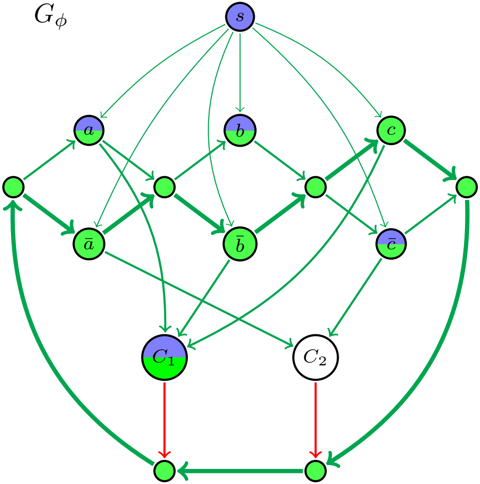

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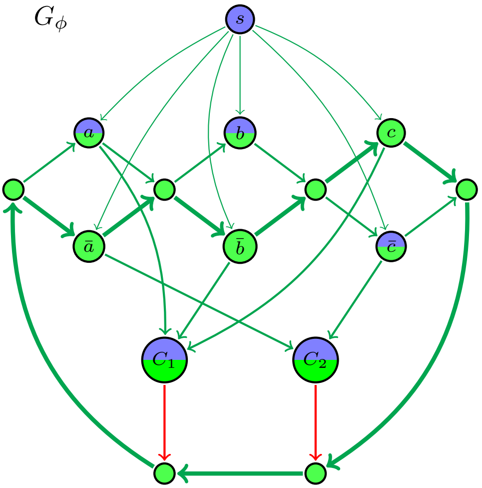

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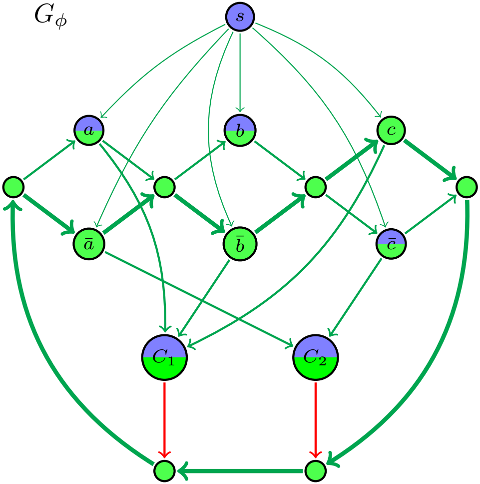

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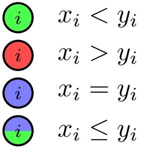

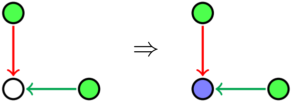

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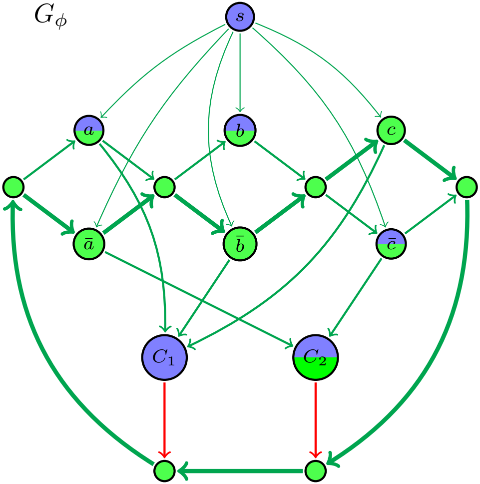

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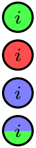

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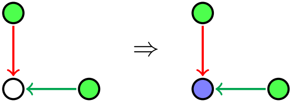

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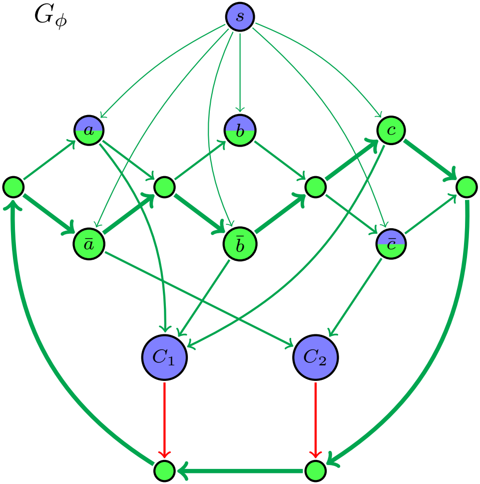
G_ϕ



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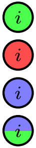

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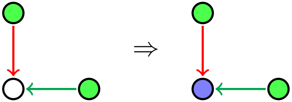

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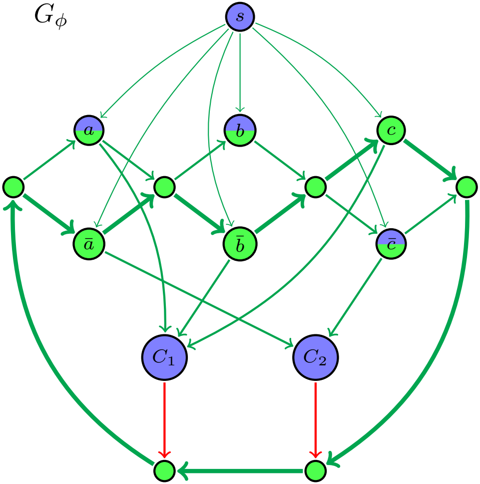

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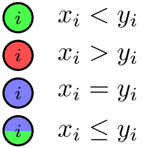

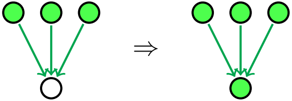

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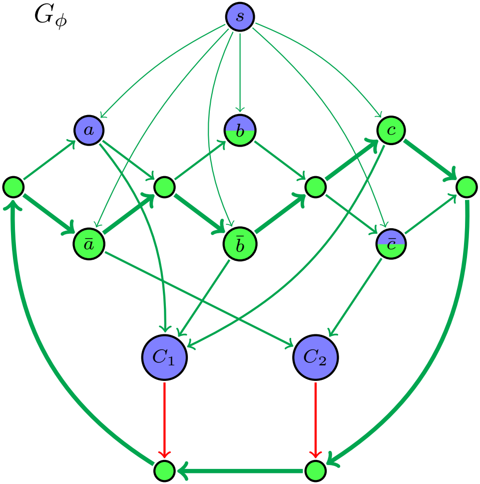

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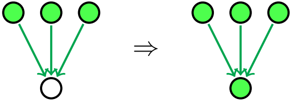

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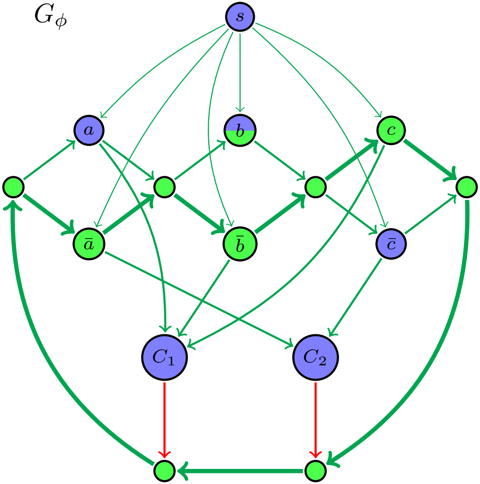

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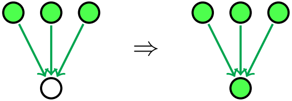

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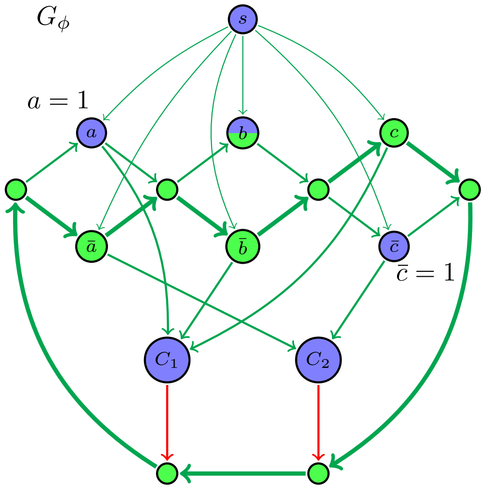

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$a = 1,\ b = 0,\ c = 0$
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are true assignments of ϕ

Summary

k-MaxProblem: Given G, do we have $\max(G) \geq k$?

Theorem

k-MaxProblem is in **P** if $k \leq 1$ and **NP-complete** if $k \geq 2$.

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It is **NEXPTIME-complete** to decide if $\min(G) = 0$.

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The reduction is from SuccinctSAT and (much more) technical.

Free k

$\textsc{MaxProblem}$: Given G **and k**, do we have $\max(G) \geq k$?

$\textsc{MinProblem}$: Given G **and k**, do we have $\min(G) < k$?

Free k

MaxProblem: Given G **and k**, do we have $\max(G) \geq k$?

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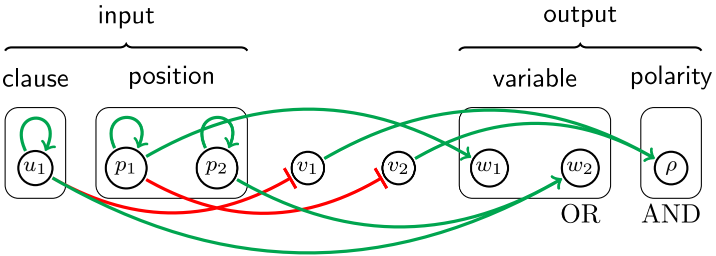
Theorem

MaxProblem and MinProblem are **NEXPTIME-complete**.

Reduction to SuccinctSat

A succinct representation of $\phi = (a \vee \bar{b} \vee \bar{c}) \wedge (\bar{a} \vee \bar{c})$:



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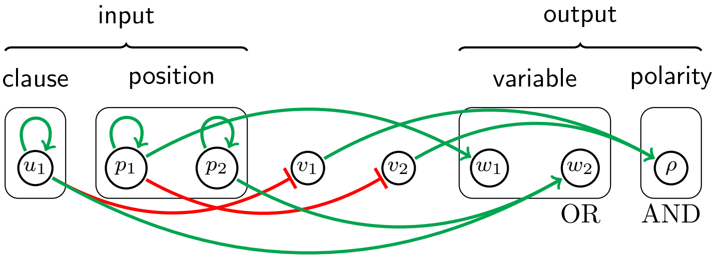


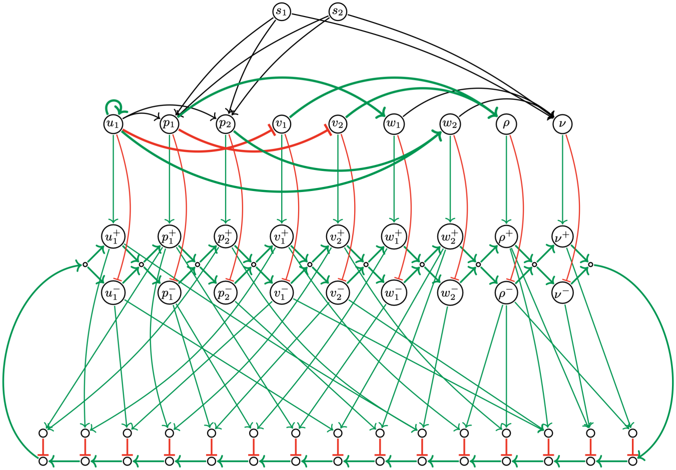
Theorem

Given a succinct CNF formula ϕ with m clauses we can built in polytime H_ϕ such that

$$\max(H_\phi) \geq 2^{m+1} \iff \phi \text{ is satisfiable}$$

Reduction to SUCCINCTSAT

The interaction graph H_ϕ for $\phi = (a \vee \bar{b} \vee \bar{c}) \wedge (\bar{a} \vee \bar{c})$.



Overview

Problem	$k = 1$	$k \geq 2$ fixed	k part of the input
$\max(G) \geq k$	**P**	**NP-complete**	**NEXPTIME-complete**
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When the maximum in-degree of G is bound by a constant $d \geq 2$:

Problem	$k=1$	$k \geq 2$ fixed	k part of the input
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$\min(G) < k$	**NP^{NP}-complete**		**$NP^{\#P}$-complete**

Positive Feedback Bound

Let $\tau^+(G)$ be the min nb of vertices delete to make G positive cycle-free.

An important result concerning fixed points in BNs is:

Positive Feedback Bound [Aracena 2008]

$$\max(G) \leq 2^{\tau^+(G)}.$$

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$$\max(G) \leq 2^{\tau^+(G)}.$$

Theorem

It is **NEXPTIME-complete** to decide if $\max(G) = 2^{\tau^+(G)}$.

Conclusion

We study, from a complexity point of view, a natural class of problems.

INTERACTION GRAPH CONSISTENCY PROBLEM

Input: An interaction graph G and a dynamical property P.

Question: Is there a BN **on** G with a dynamics satisfying P?

We obtain exact classes of complexity for this problem when

- P is "to have at least/most k fixed points",
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- the maximum in-degree of G is bounded or not.

Perspectives

1. **Other dynamical properties.**

   $\hookrightarrow$ number/size of cyclic attractors in the (a)synchronous case.

2. **Non-Boolean case** and **unsigned case**.