Complexity of maximum and minimum fixed point problem in Boolean networks

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joint work with

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A **Boolean network (BN)** with n components is a function

$$f : \{0,1\}^n \to \{0,1\}^n$$
$$x = (x_1, \dots, x_n) \mapsto f(x) = (f_1(x), \dots, f_n(x))$$

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Global transition function

Locale transition functions

$f_i : \{0,1\}^n \to \{0,1\}$

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The synchronous dynamics is given by

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

The asynchronous dynamics is more realistic in many cases.

Fixed points of f are **stable states** for **both** dynamics.

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The **interaction graph (IG)** of f is the **signed digraph** defined by

- the vertex set is $\{1, \dots, n\}$,
- there is a positive edge $j \to i$ if there is $x \in \{0,1\}^n$ such that

$$f_i(x_1, \dots, x_{j-1}, \mathbf{0}, x_{j+1}, \dots, x_n) = \mathbf{0}$$
$$f_i(x_1, \dots, x_{j-1}, \mathbf{1}, x_{j+1}, \dots, x_n) = \mathbf{1}$$

- there is a negative edge $j \to i$ if there is $x \in \{0,1\}^n$ such that

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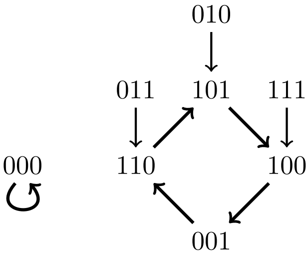
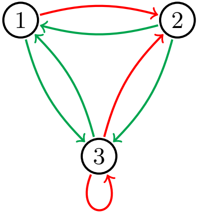
Example with $n = 3$

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

Synchronous dynamics



Interaction graph



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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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Theorem [Kosub 2008]

It is **NP-complete** to decide if a BN has a fixed point.

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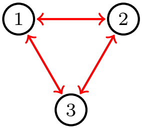

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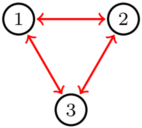

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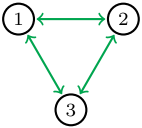

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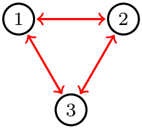

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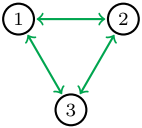

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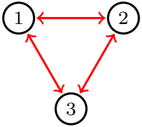

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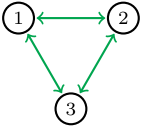

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k-MaxProblem: Given G, do we have $\max(G) \geq k$?

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

$\max(G) \geq 1$?

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

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Theorem [Aracena 2008]

1. If $\max(G) \geq 2$, then G has a positive cycle. [Thomas' 1st rule]

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Theorem [Aracena 2008]

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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

There is an algorithm with the following specifications:

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

Output: A BN f on G with $f(x^\ell) = y^\ell$ for $1 \leq \ell \leq k$, if it exists.

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

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If $\max(G) \geq k$, there is a BN f on G with k fixed points $x^1, \dots, x^k$.

Then $(x^1, \dots, x^k)$ is a certificat of size $O(kn)$ which can be checked in $O(k^2 n^2)$-time by giving as input G and the couples $(x^1, x^1), \dots, (x^k, x^k)$.

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

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Theorem

Given a SAT formula ϕ with n variables and m clauses, we can built in $O(n+m)$-time an interaction graph G_ϕ with $O(n+m)$ vertices s.t.

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

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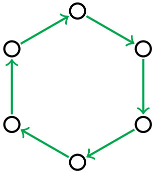
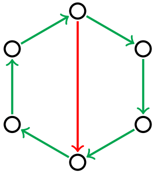


2 fixed points



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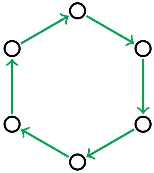

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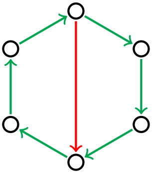

1 fixed point

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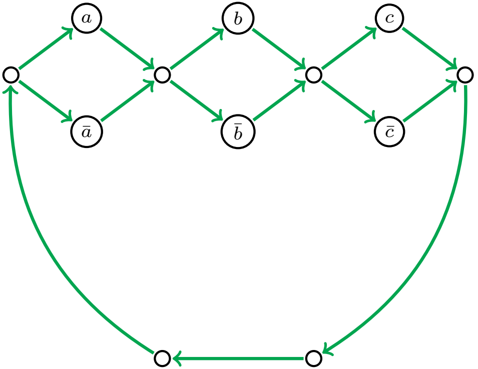
Example with $\phi = (a \vee \bar{b} \vee c) \wedge (\bar{a} \vee \bar{c})$.



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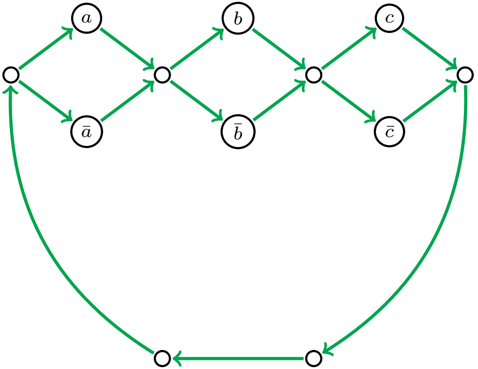

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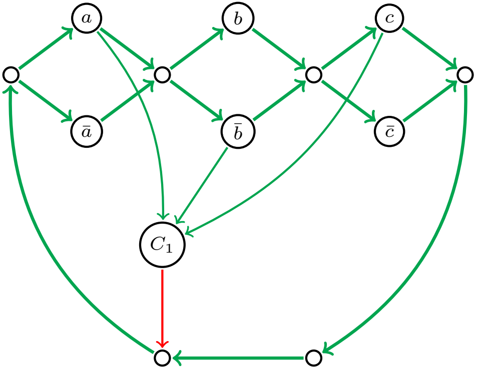

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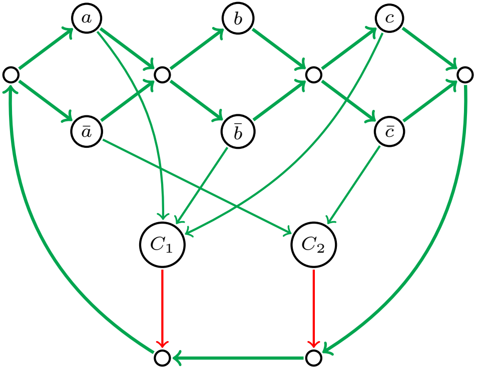

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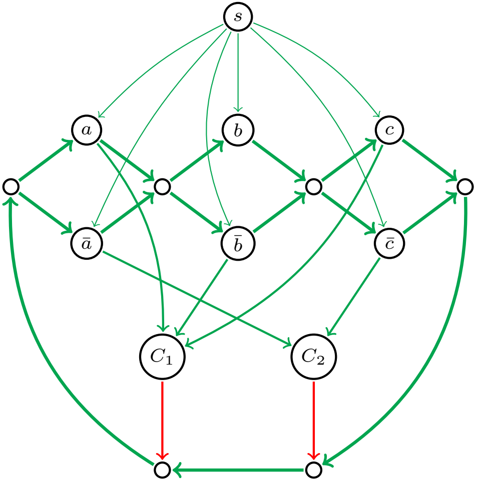

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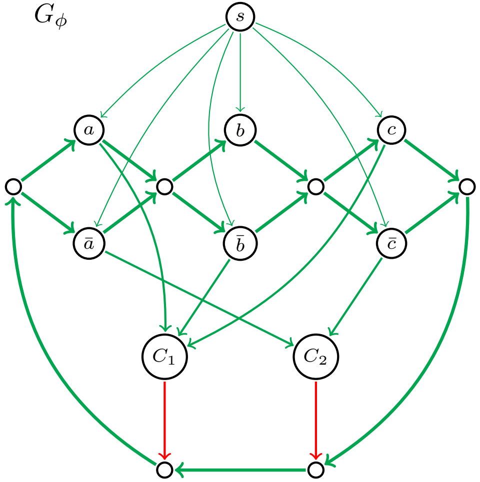

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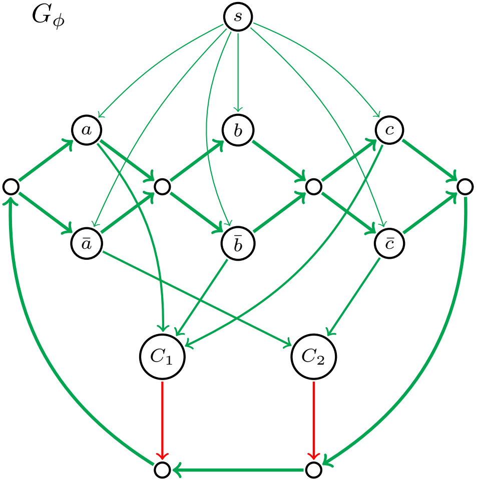

ϕ is sat. $\Rightarrow \max(G) \geq 2$

Consider a true assignment:
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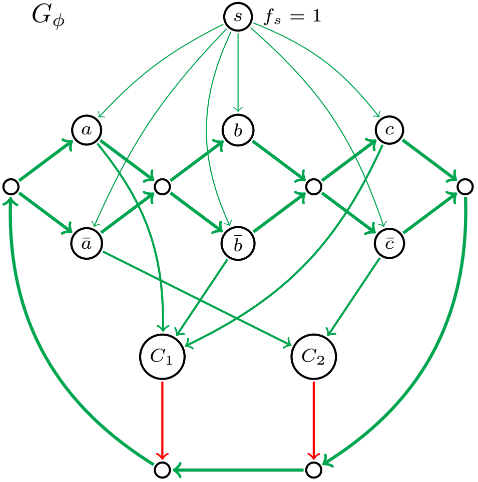

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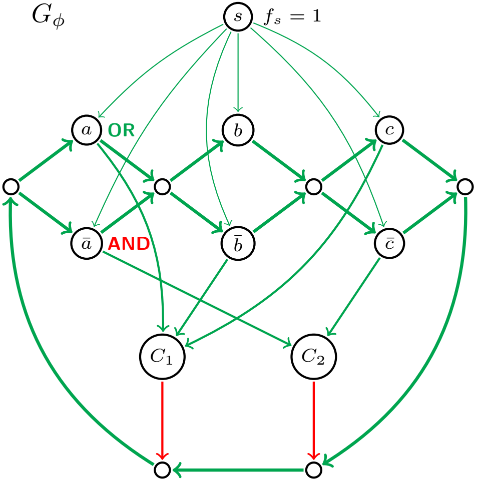

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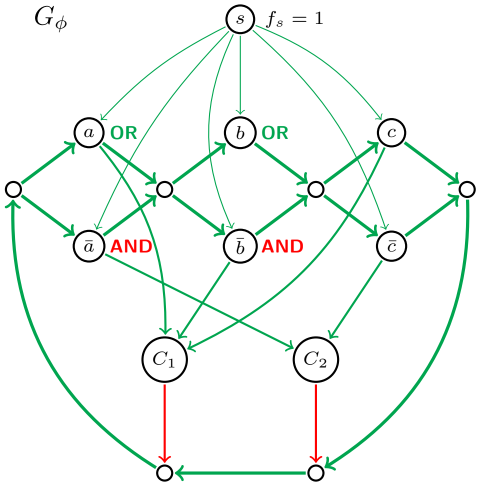

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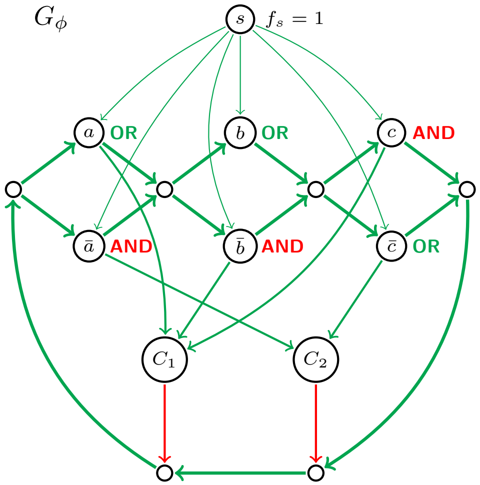

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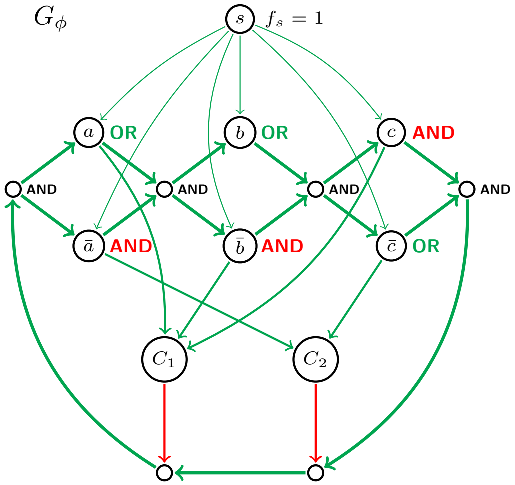

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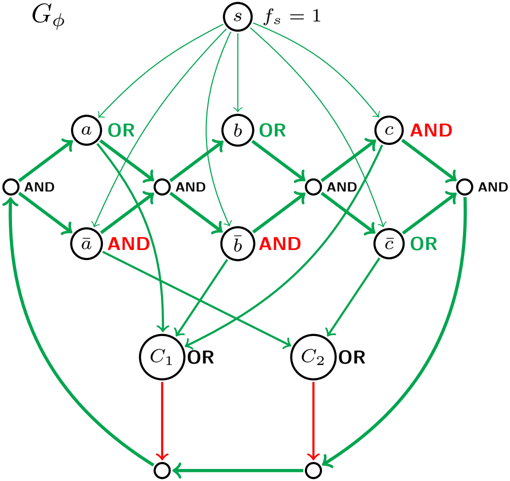

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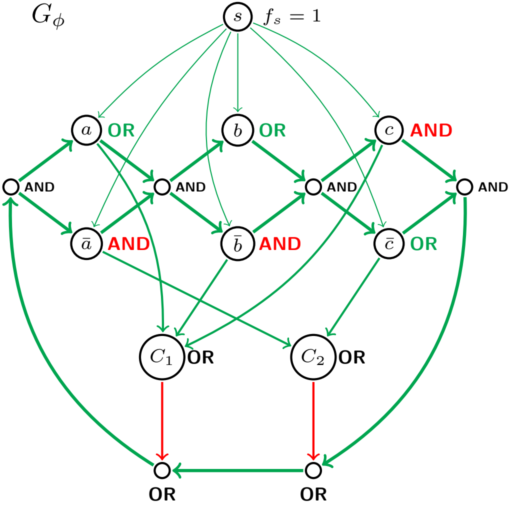

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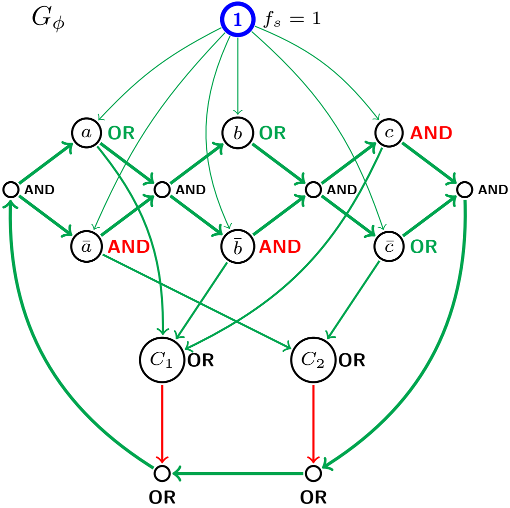

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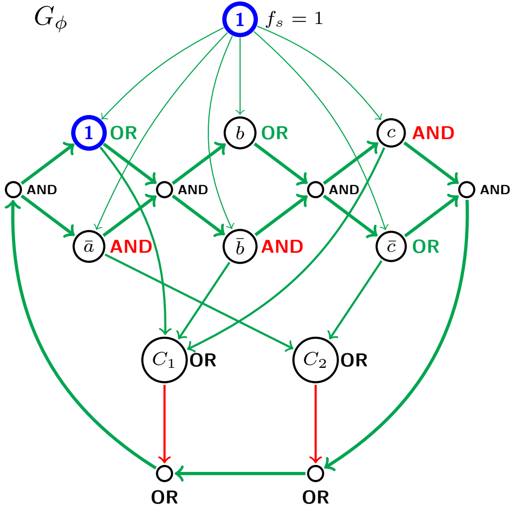

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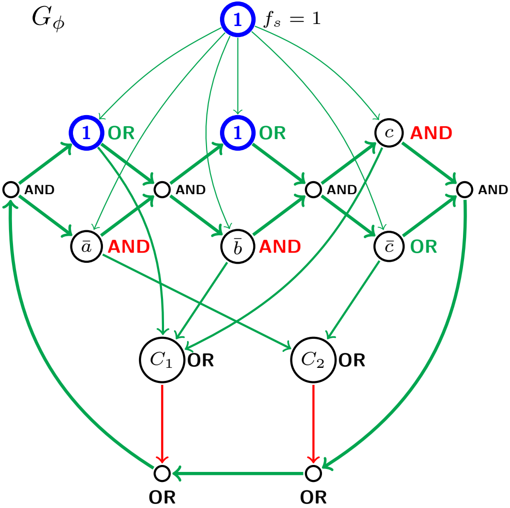

ϕ is sat. $\Rightarrow \max(G) \geq 2$

Consider a true assignment:
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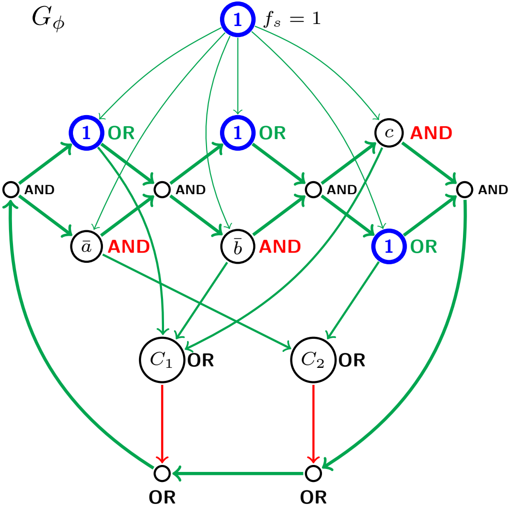

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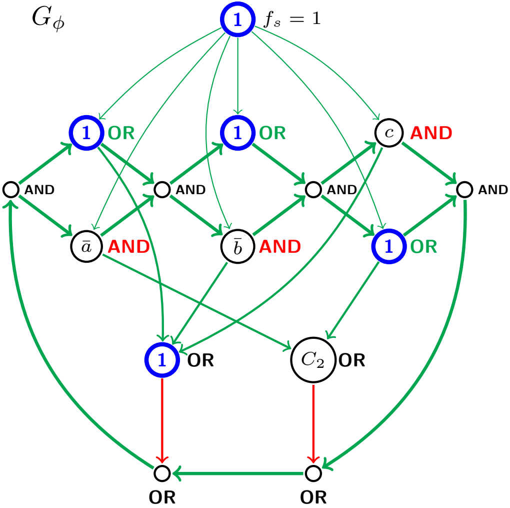

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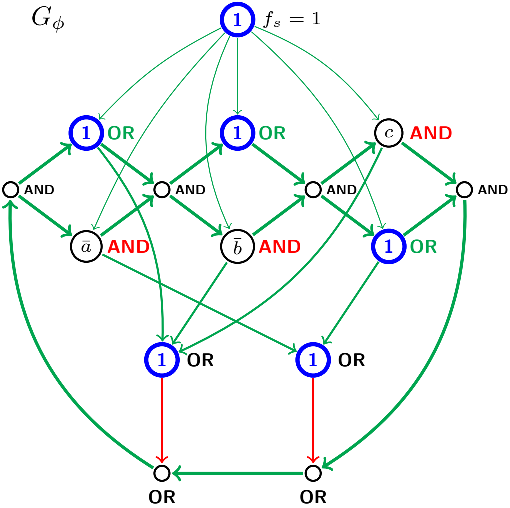

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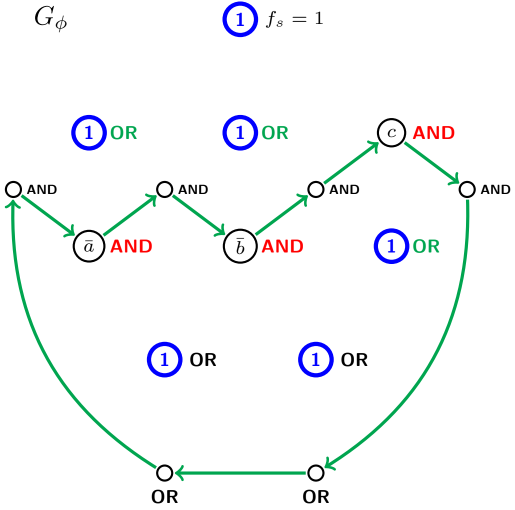

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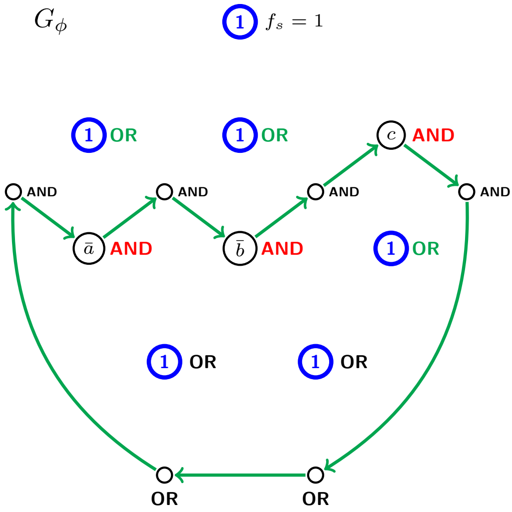

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Isolated positive cycle
$\Downarrow$
2 fixed points

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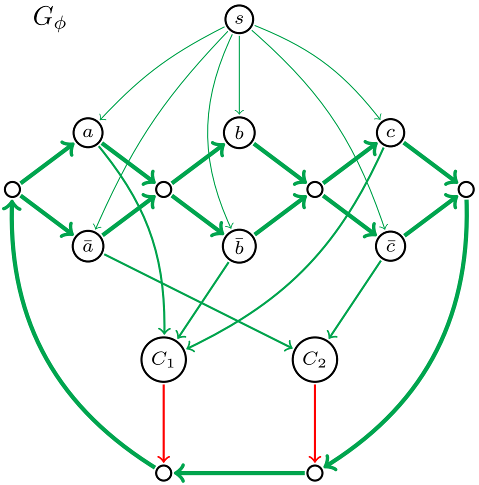

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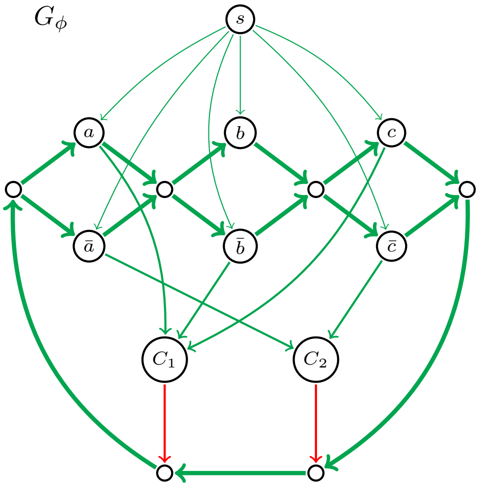

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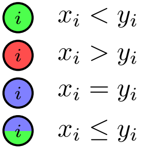

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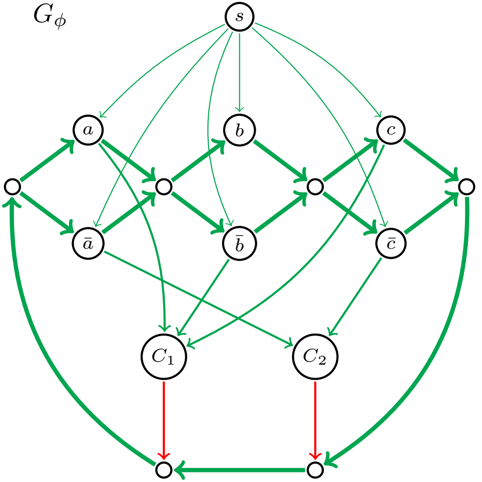

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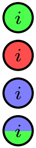

$x_i < y_i$

$x_i > y_i$

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Since all the positive cycles are full-positive, by a thm of Aracena there is a positive cycle where vertices are all ● or all ●

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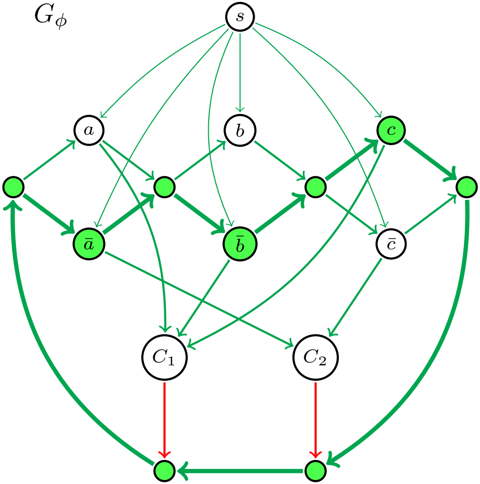

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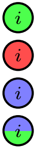

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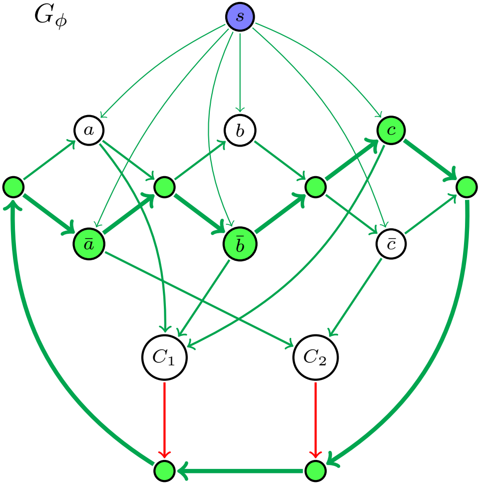

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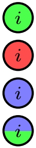

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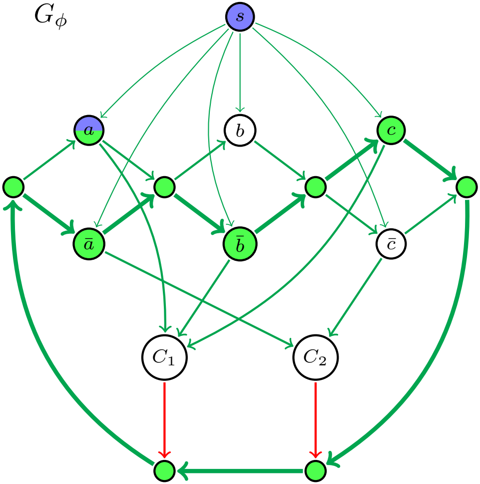

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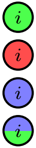

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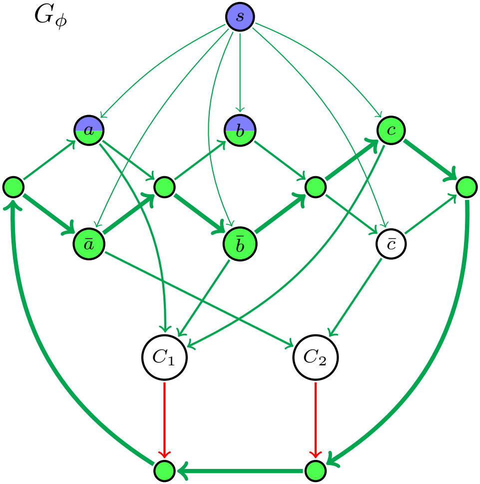

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Let f be a BN on G with two fixed points: x and y

- (green) $x_i < y_i$
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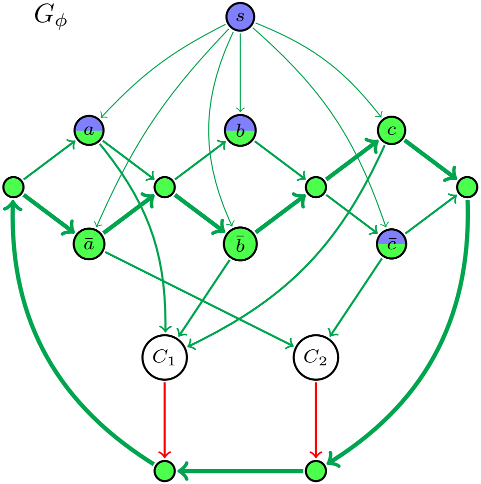

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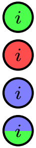

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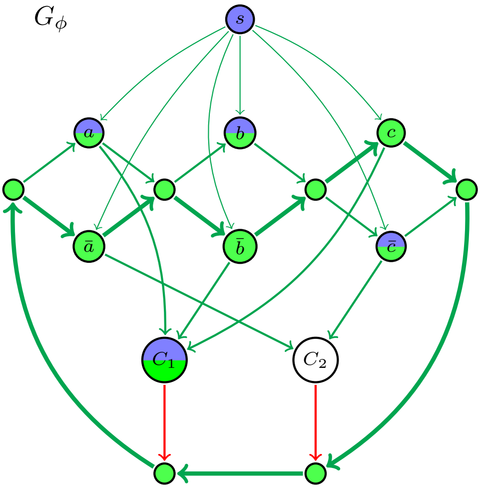

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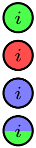

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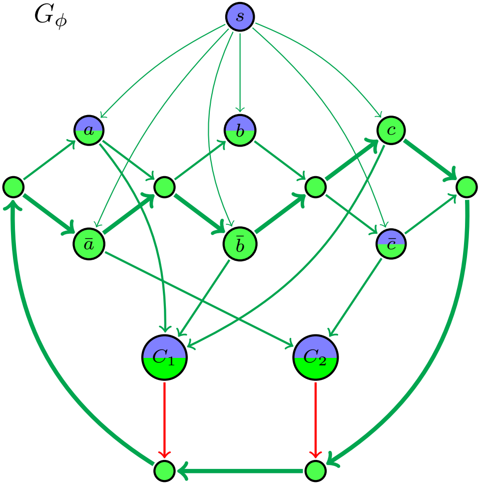

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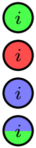

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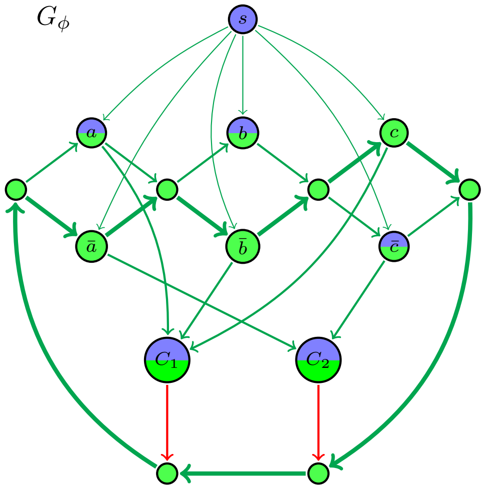

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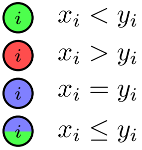

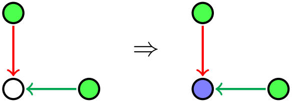

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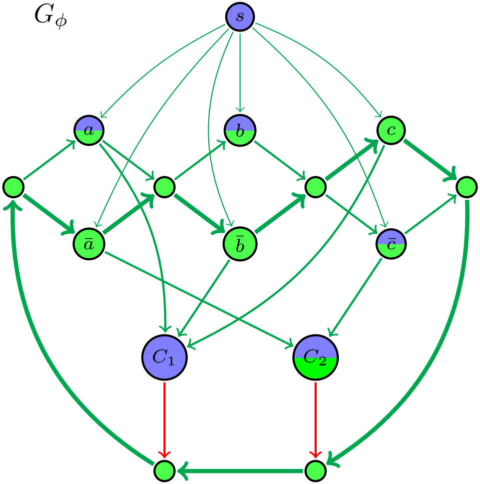

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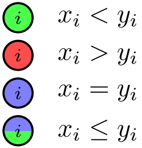

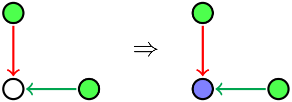

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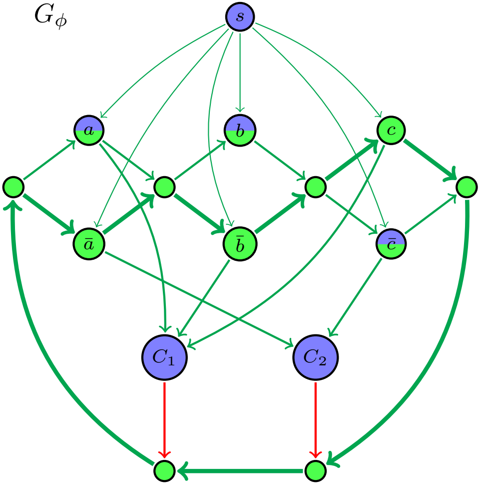

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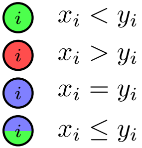

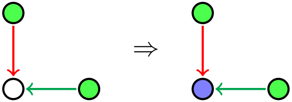

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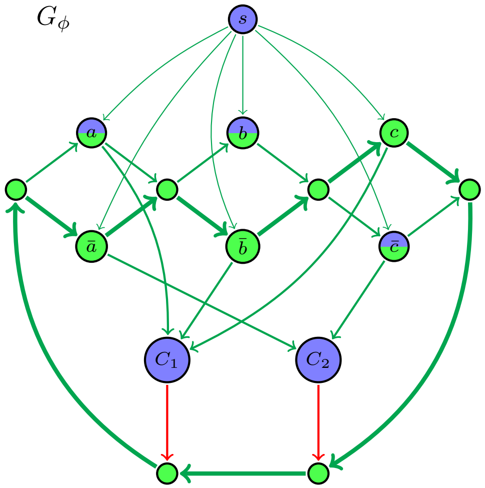

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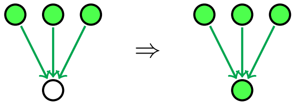

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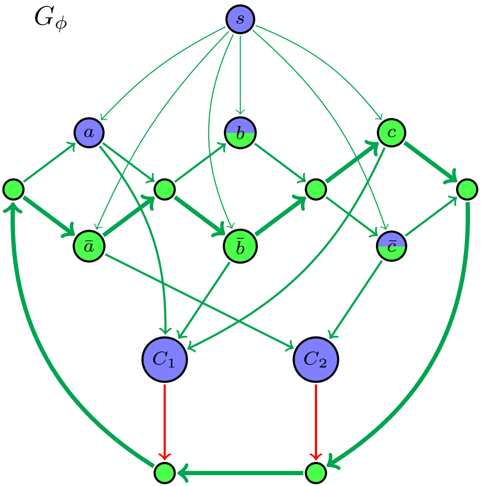

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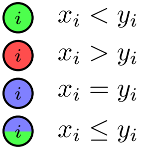

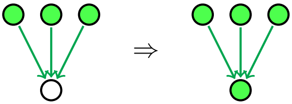

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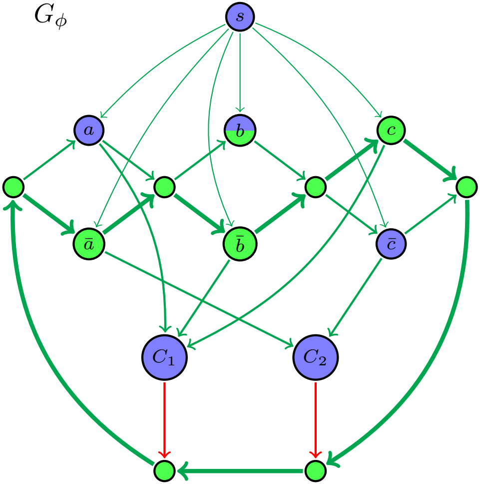

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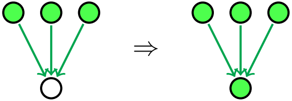

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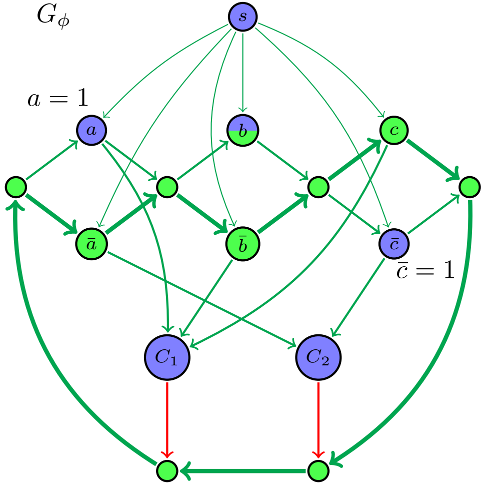

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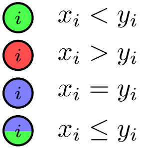

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are true assignments of ϕ

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

This problem is much more difficult:

Theorem

k-MinProblem is **NEXPTIME-complete** for every k.

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

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Theorem

k-MinProblem is **NEXPTIME-complete** for every k.

With a construction very similar to G_ϕ, we can prove that $\min(G) \leq k$? is **NP-hard**. But to prove the **NEXPTIME-hardness**, we use a much more technical reduction from SuccintSAT.

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

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

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

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

Theorem

$\textsc{MaxProblem}$ and $\textsc{MinProblem}$ are **NEXPTIME-complete**.

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

$$P = \text{"to have at least/most } k \text{ fixed points"}$$

Our main result is about bistability:

It is **NP-complete** to decide if there is a BN on G with two fixed points.

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Perspectives

1. **Other dynamical properties.**

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

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