On the convergence of Boolean automata networks without negative cycles

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Boolean networks

$=$

Finite and heterogeneous CAs on $\{0, 1\}$

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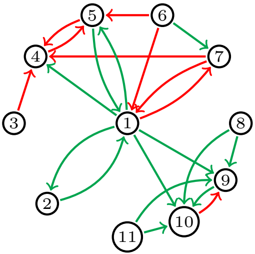
Classical models for

- **Neural networks** [McCulloch & Pitts 1943]
- **Gene regulatory networks** [Kauffman 1969, Tomas 1973]

Focus on **interaction graphs**



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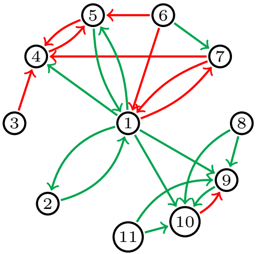
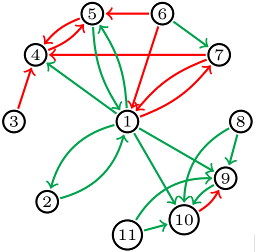


Question

What can be said on the dynamics of a Boolean network according to its interaction graph ?

Focus on **interaction graphs**



[Arabidopsis Thaliana]

Question

What can be said on the dynamics of a Boolean network according to its interaction graph ?

Application to **gene networks**: reliable information on the interaction graph only.

Definitions

Setting

There are $\boldsymbol{n}$ **components** (cells) denoted from 1 to n

The set of possible **states** (configurations) is $\{0,1\}^n$

The **local transition function** of component $i \in [n]$ is **any map**

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

The resulting **global transition function** is

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

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We consider the **fully-asynchronous** updating
$\hookrightarrow$ very usual in the context of **gene networks** [Thomas 73]

Given a map $v : \mathbb{N} \to [n]$, the **fully-asynchronous** dynamics is

$$x_{v(t)}^{t+1} = f_{v(t)}(x^t), \qquad x_i^{t+1} = x_i^t \quad \forall i \neq v(t)$$

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Definition

The **asynchronous state graph** of f, denoted by $\boldsymbol{ASG(f)}$, is the directed graph on $\{0,1\}^n$ with the following set of arcs:

$$\{\ x \to \bar{x}^i \mid x \in \{0,1\}^n,\ i \in [n],\ x_i \neq f_i(x)\ \}$$

Example

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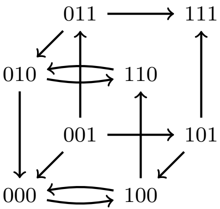
$ASG(f)$



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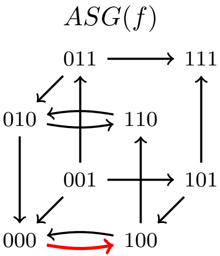

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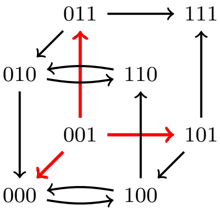

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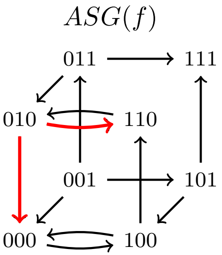

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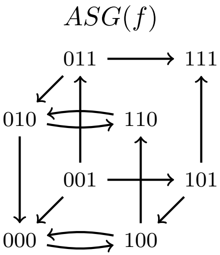

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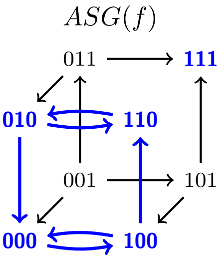

The **attractors** of $ASG(f)$ are its **terminal strong components**

- Attractor of size one = **fixed point**
- Attractor of size at least two = **cyclic attractor**

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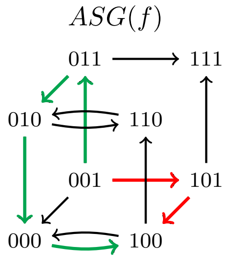

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A path from a state x to a state y is a **direct path** if its length ℓ is equal to the Hamming distance between x and y (so $\ell \leq n$).

Definition

The **interaction graph** of f, denoted $G(f)$, is the signed directed graph on $\{1, \ldots, n\}$ with the following arcs:

- There is a **positive arc** $j \to i$ iff there is a state x such that

$$f_i(x_1, \ldots, x_{j-1}, \mathbf{0}, x_{j+1}, \ldots, x_n) = \mathbf{0}$$
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$j \to i \in G(f) \iff f_i(x)$ depends on x_j

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Asynchronous State Graph

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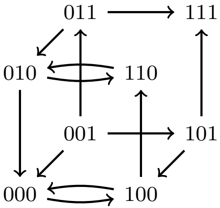

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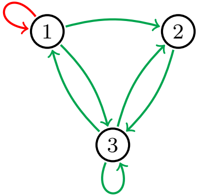

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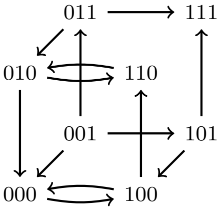

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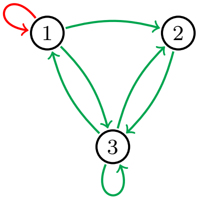

Question

What can be said on $ASG(f)$ according to $G(f)$?

Results

Theorem [Robert 1980]

If $G(f)$ has **no cycles** then

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$\Rightarrow$ **complexity comes from cycles of the interaction graph**

Two kinds of cycles have to be considered:

- **Positive cycles**: **even** number of negative arcs
- **Negative cycles**: **odd** number of negative arcs

Theorem on positive cycles [Aracena 2004]

If all the positive cycles of $G(f)$ can be destroyed by removing k vertices, then $ASG(f)$ has at most 2^k attractors.

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Theorem on negative cycles [Richard 2010]

If $G(f)$ has **no negative cycles** then $ASG(f)$ has a path from every state x to a fixed point

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Our contribution

If $G(f)$ has **no negative cycles** then $ASG(f)$ has a **direct path** from every state x to a fixed point

Sketch of proof

Theorem If $G(f)$ has no negative cycles then $ASG(f)$ has a direct path from any state x to a fixed point

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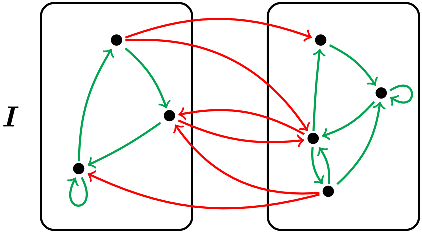

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Conclusion: We can suppose that **$G(f)$ has only positive arcs**
This is equivalent to say that **f is monotonous**:

$$\forall x, y \in \{0,1\}^n \qquad x \leq y \Rightarrow f(x) \leq f(y)$$

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Lemma 1 $f(\mathbf{0}) = \mathbf{0}$ and $f(\mathbf{1}) = \mathbf{1}$

Suppose $f(\mathbf{0}) \neq \mathbf{0}$, that is, $f_i(\mathbf{0}) = 1$ for some i

Then since f is monotonous, $f_i(x) = 1$ for all $x \in \{0, 1\}^n$

Thus $f_i = cst$, so i has no in-neighbor in $G(f)$

Thus $G(f)$ is not strong, a contradiction

We prove similarly $f(\mathbf{1}) = \mathbf{1}$.

Theorem If $G(f)$ is **strong** and f is **monotonous** then $ASG(f)$ has a direct path from any state x to a fixed point

Lemma 2 The set of states reachable from x, denoted by $R(x)$, has a unique maximal element, reachable from x by a direct path

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If not there is a path $x \rightsquigarrow z \rightarrow \bar{z}^i$ with $z \leq y$ and $\bar{z}^i \not\leq y$.

Thus $\bar{z}^i_i = 1$ and $y_i = 0$, so $z \rightarrow \bar{z}^i$ increases component i.

Thus $f_i(z) = 1$ and since $z \leq y$ and f_i is monotonous, $f_i(y) = 1$.

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If $x = \mathbf{0}$ the theorem is true since $f(\mathbf{0}) = \mathbf{0}$. Suppose that $x > \mathbf{0}$

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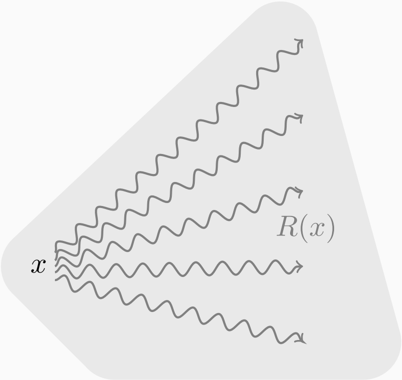

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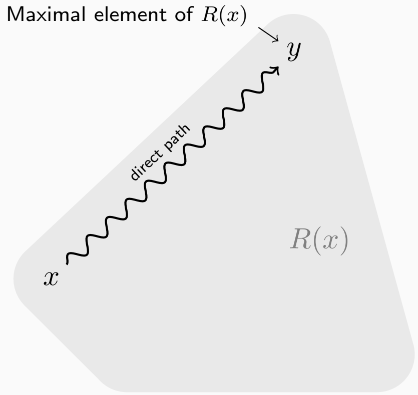

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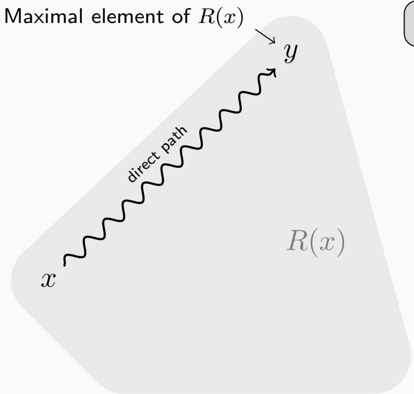

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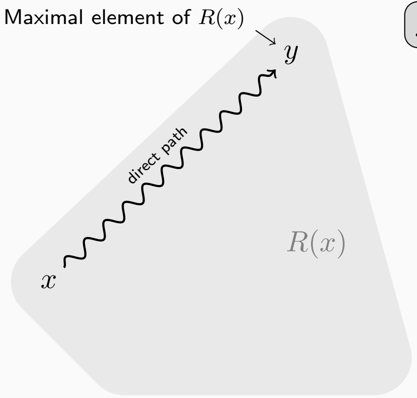

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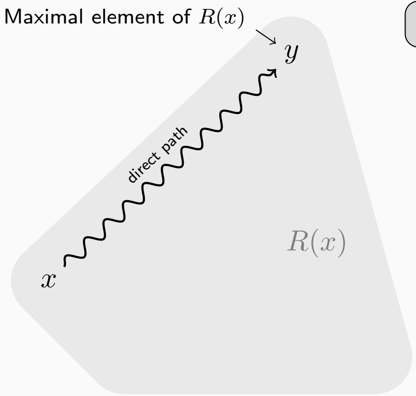

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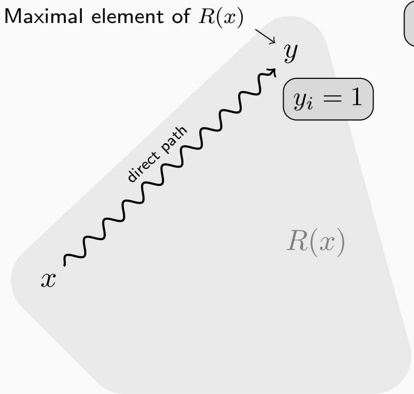

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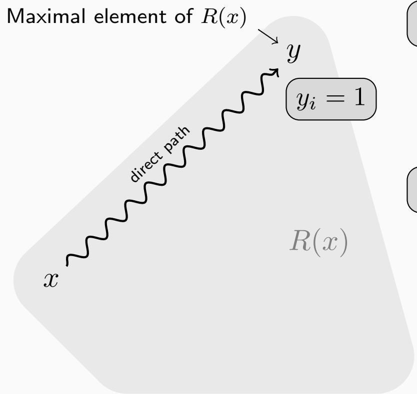

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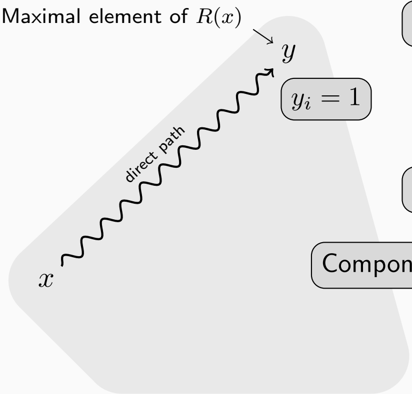

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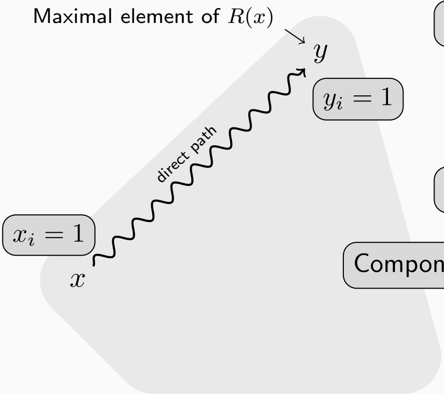

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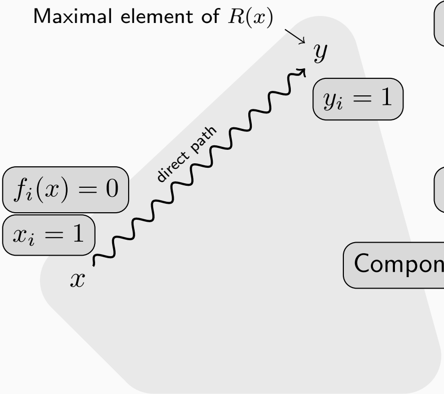

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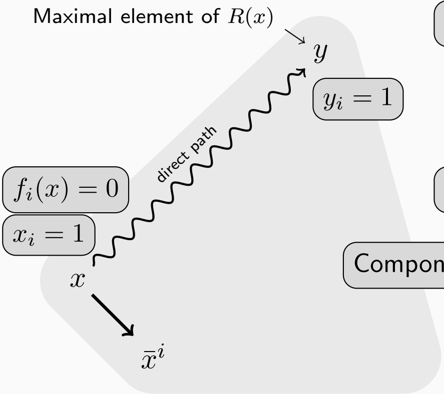

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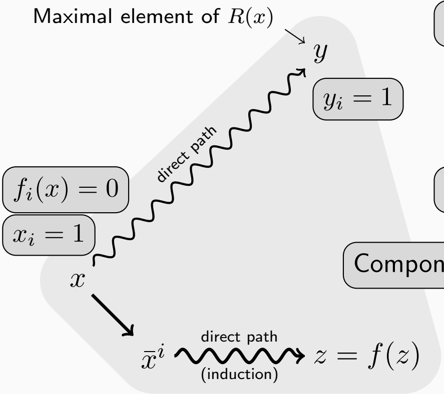

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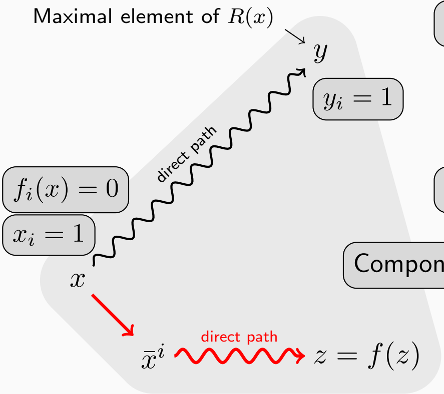

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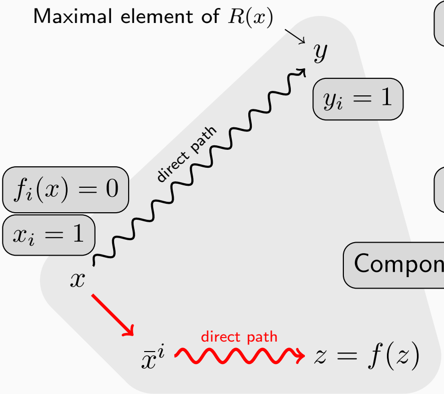

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Algorithm in $\mathcal{O}(n^2)$

Further results & perspectives

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Suppose that $G(f)$ has no negative cycles.

The set of fixed points reachable from x has a *unique* maximal element x^+ and a *unique* minimal element x^-, which are reachable in at most $2n - 4$ transitions (thigh bound).

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Thank you!