

Fixing Boolean networks asynchronously

Julio Aracena and Lilian Salinas

Universidad de Concepción, Chile

Maximilien Gadouleau

Durham University, UK

Adrien Richard

CNRS, Université Côte d'Azur, France

Séminaire "Dynamique, Arithmétique, Combinatoire"

Équipe I2M de l'IML

Marseille, le 13 mars 2018

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

$$f : \{0, 1\}^n \rightarrow \{0, 1\}^n$$

$$x = (x_1, \dots, x_n) \mapsto f(x) = (f_1(x), \dots, f_n(x)).$$

The **dynamics** is usually described by the successive iterations of f

$$x \rightarrow f(x) \rightarrow f^2(x) \rightarrow f^3(x) \rightarrow \dots$$

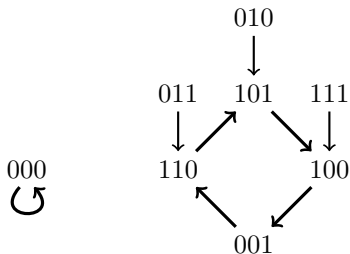
Fixed points correspond to stable states.

Example with $n = 3$

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

x	$f(x)$
000	000
001	110
010	101
011	110
100	001
101	100
110	101
111	100

Dynamics



The **interaction graph** of f is the digraph $G(f)$ on $[n] := \{1, \dots, n\}$ s.t.

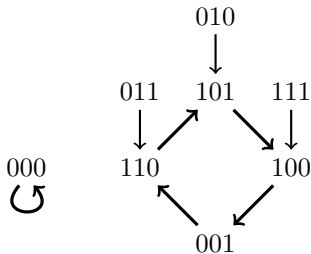
$$j \rightarrow i \text{ is an arc} \iff f_i \text{ depends on } x_j.$$

Example

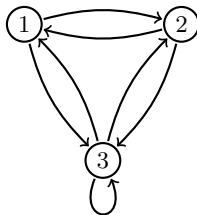
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001	110
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Dynamics



Interaction graph



Many applications, in particular:

- **Neural networks** [McCulloch & Pitts 1943]
- **Gene networks** [Kauffman 1969, Thomas 1973]
- **Network Coding** [Riis 2007]

Synchronous dynamics: all components are updated at each step:

$$x \rightarrow f(x) \rightarrow f^2(x) \rightarrow f^3(x) \rightarrow \dots$$

Asynchronous: one component is updated at each step.

↪ Update component i at state x means reach the state

$$x \xrightarrow{i} f^i(x) := (x_1, \dots, x_{i-1}, f_i(x), x_{i+1}, \dots, x_n).$$

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The **asynchronous graph** $\Gamma(f)$ describes all the possible trajectories:
the vertex set is $\{0, 1\}^n$ and $x \rightarrow f^i(x)$ for all $x \in \{0, 1\}^n$ and $i \in [n]$.

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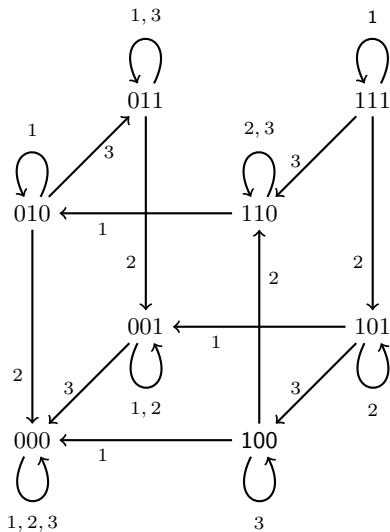
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It can be regarded as a **Finite Deterministic Automata** where

1. the alphabet is $\Sigma := [n]$;
2. the set of states is $Q := \{0, 1\}^n$;
3. the transition function $\delta : Q \times \Sigma \rightarrow Q$ is $\delta(x, i) := f^i(x)$.

Example

x	$f(x)$
000	000
001	000
010	001
011	001
100	010
101	000
110	010
111	100



Notation: If $w = i_1 i_2 \dots i_k \in [n]^*$ then $f^w(x)$ is the state obtained from x by updating successively the components i_1, i_2, \dots, i_k , that is,

$$f^w(x) := (f^{i_k} \circ f^{i_{k-1}} \circ \dots \circ f^{i_1})(x).$$

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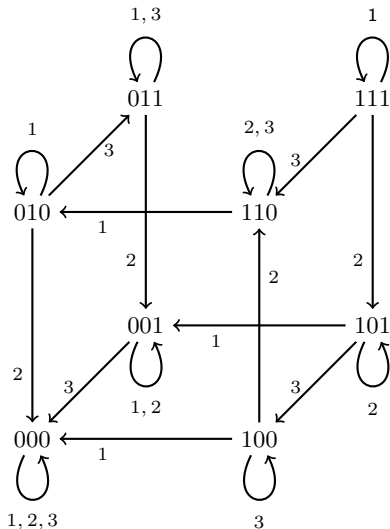
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Definition 2. A word w **fixes a family** \mathcal{F} of BNs if it fixes each $f \in \mathcal{F}$. The **fixing length** $\lambda(\mathcal{F})$ is the min length of a word fixing \mathcal{F} .

Example: 1231 is fixing (and no shorter word is fixing, thus $\lambda(f) = 4$).

x	$f(x)$
000	000
001	000
010	001
011	001
100	010
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111	100



Remarks

1. f is fixable only if f has a fixed point.
2. If f has a unique fixed point then:

$$w \text{ fixes } f \iff w \text{ is synchronizing.}$$

3. A family \mathcal{F} is fixable if and only if each $f \in \mathcal{F}$ is fixable.

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Theorem 1 [Bollobás, Gotsman and Shamir 1993]

There is a positive fraction $\phi(n)$ of fixable BNs with n components:

$$\lim_{n \rightarrow \infty} \phi(n) = 1 - \frac{1}{e} \geq 0.64.$$

Example of fixable families

1. $F_M(n)$: **Monotone BNs** ($2^{\Theta(\sqrt{n}2^n)}$):

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

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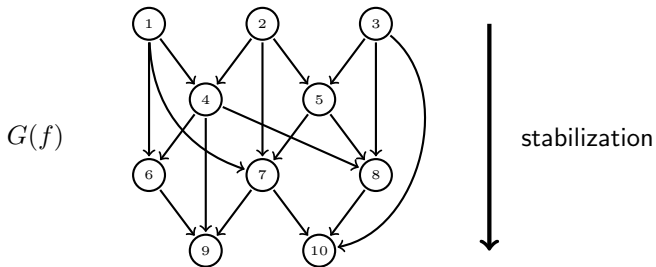
$$\forall x \in \{0, 1\}^n, \quad x \leq f(x).$$

4. $F_P(n)$: **Monotone BNs whose interaction graph is a Path** ($2n!$).

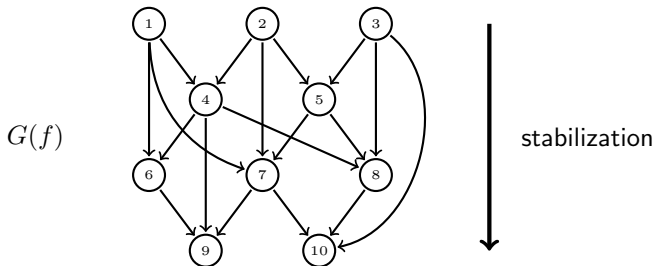
Theorem [Aracena, Gadouleau, R., Salinas 2018+]

Networks	\mathcal{F}	$\max_{f \in \mathcal{F}} \lambda(f)$	$\lambda(\mathcal{F})$
Acyclic	$F_A(n)$	n	$\Theta(n^2)$
Path	$F_P(n)$	n	$\Theta(n^2)$
Increasing	$F_I(n)$	$\Theta(n^2)$	$\Theta(n^2)$
Monotone	$F_M(n)$	$\Omega(n^2)$	$O(n^3)$

Acyclic networks



$w := 1, 2, 3, 4, 5, 6, 7, 8, 9, 10$ is a fixing word



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Proposition. Let $f \in F_A(n)$ and $w \in [n]^*$.

1. If w is a topological sort of $G(f)$, then w fixes f , thus $\lambda(f) = n$.
2. If w contains a topological sort of $G(f)$ then w fixes f .
3. If w contains all the permutations of $[n]$, then it fixes $F_A(n)$.

An **n -complete** word is a word $w \in [n]^*$ that contains (as subsequences) all the permutations of $[n]$.

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Corollary. Every n -complete word fixes $F_A(n)$, thus

$$\lambda(F_A(n)) \leq \lambda(n).$$

What is the magnitude order of $\lambda(n)$?

For an **upper-bound**, let

$$w := \underbrace{123 \dots n}_1 \underbrace{123 \dots n}_2 \cdots \underbrace{123 \dots n}_n$$

Let $\pi = i_1 i_2 \dots i_n$ be a permutation of $[n]$. Then

$$w := \underbrace{123 \dots n}_{\text{contains } i_1} \underbrace{123 \dots n}_{\text{contains } i_2} \cdots \underbrace{123 \dots n}_{\text{contains } i_n}$$

Hence w contains π . Thus w is n -complete: $\lambda(n) \leq |w| = n^2$.

What is the magnitude order of $\lambda(n)$?

For a **better upper-bound**, let

$$w := \underbrace{123 \dots n}_1 \underbrace{n(n-1) \dots 321}_2 \underbrace{123 \dots n}_3 \cdots \underbrace{123 \dots n}_n$$

Then w is n -complete, and

$$w' := \underbrace{123 \dots n}_1 \underbrace{(n-1) \dots 321}_2 \underbrace{23 \dots n}_3 \cdots \underbrace{23 \dots n}_n$$

is also n -complete, thus $\lambda(n) \leq |w'| = n^2 - n + 1$.

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Theorem

$$\lambda(n) \leq n^2 - 2n + 4 \quad \text{for all } n \geq 1 \quad [\text{Adleman 1974}]$$

$$\lambda(n) \leq n^2 - 2n + 3 \quad \text{for all } n \geq 10 \quad [\text{Zlinescu 2011}]$$

$$\lambda(n) \leq \left\lceil n^2 - \frac{7}{3}n + \frac{19}{3} \right\rceil \quad \text{for all } n \geq 7 \quad [\text{Radomirovic 2012}]$$

What is the magnitude order of $\lambda(n)$?

For a **lower-bound**, note that if w is n -complete then

$$n! \leq |\{\text{subsequences of length } n \text{ contained in } w\}| \leq \binom{|w|}{n} \leq \frac{|w|^n}{n!}$$

Hence,

$$|w|^n \geq (n!)^2 \geq \left(\frac{n}{e}\right)^{2n} \quad \text{thus} \quad |w| \geq \left(\frac{n}{e}\right)^2.$$

We deduce that

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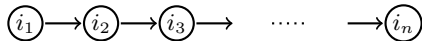
Theorem [Kleitman, Kwiatkowski 1976]

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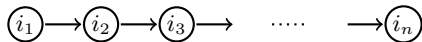
For a **lower-bound**, let $\pi = i_1 i_2 \dots i_n$ a permutation of $[n]$, and consider the monotone BN f whose interaction graph is



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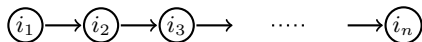
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Proposition 2. A word fixes $F_P(n)$ if and only if it is n -complete, thus

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Since $F_P(n) \subseteq F_A(n)$ we deduce that $\lambda(n) \leq \lambda(F_A(n))$ and thus

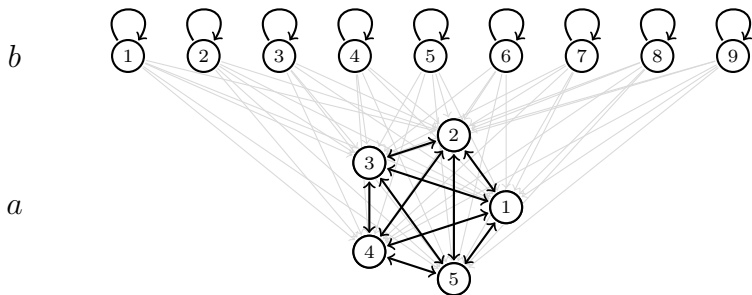
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Theorem [Aracena, Gadoudeau, R., Salinas 2018+]

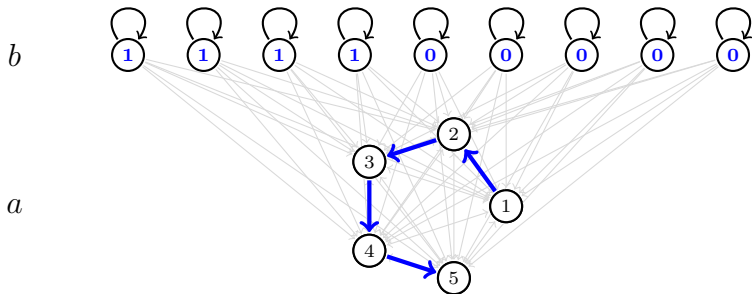
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A monotone network hard to fixe

A monotone BN f with $n = a + b$, which is hard to fix:

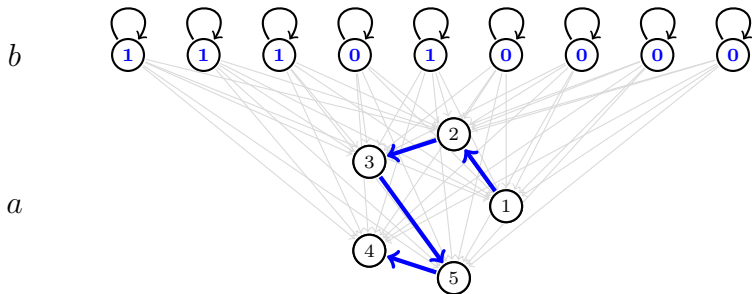


A monotone BN f with $n = a + b$, which is hard to fixe:



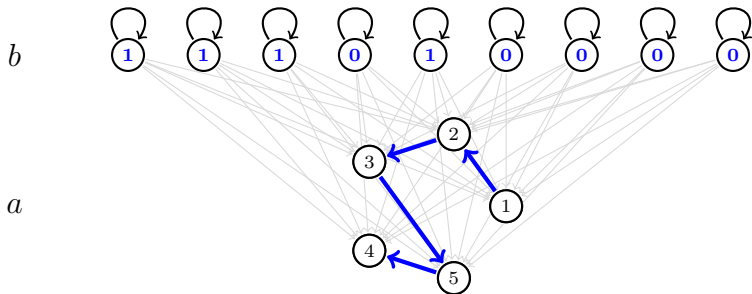
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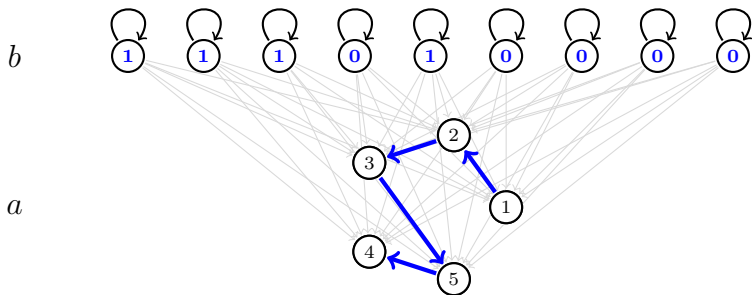
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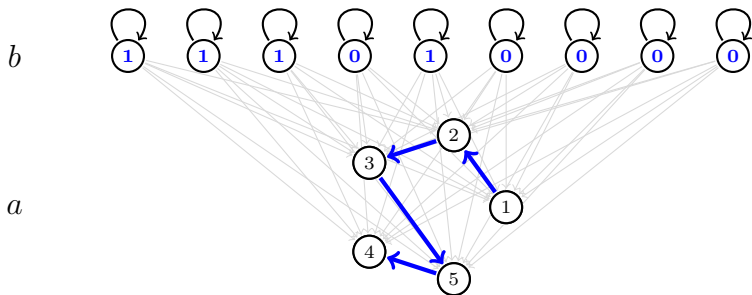
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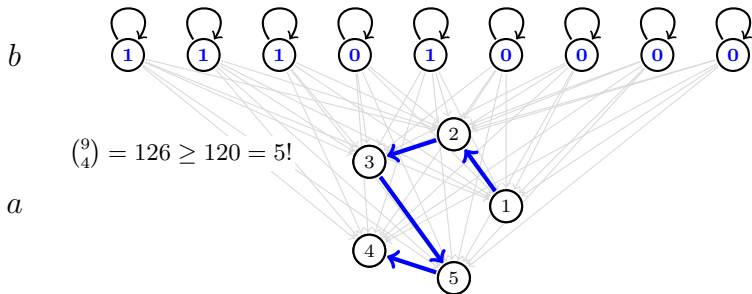
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The construction is based on the fact that a word containing the $n!$ permutations of S_n must be of quadratic length.

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Theorem. There exists $\Pi_n \subseteq S_n$ of size $2^{o(n)}$ such that any word containing all the permutations in Π_n is of length $\geq n^2/3$.

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In the construction f , we encode S_a with $b = O(a \log a)$ inputs.

But we can encode Π_a with $b = o(a)$ only, and get

$$\lambda(f) \geq \frac{a^2}{3} \sim \frac{n^2}{3}.$$

Theorem [Aracena, Gadouleau, R., Salinas 2018+]

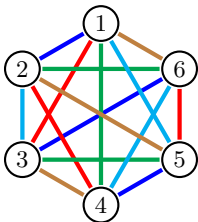
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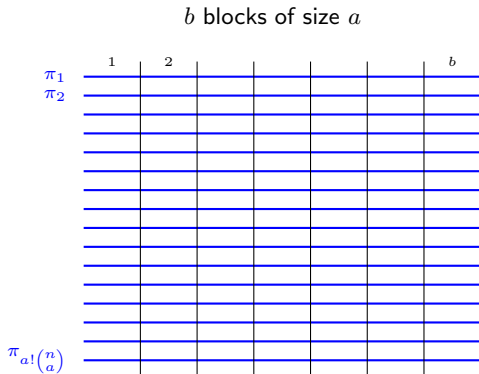
Baranyai' theorem [1975]

If $n = ab$, there exists a collection of $\frac{1}{b} \binom{n}{a}$ partitions of $[n]$ into a -sets, such that each a -subset of $[n]$ appears in exactly one partition.

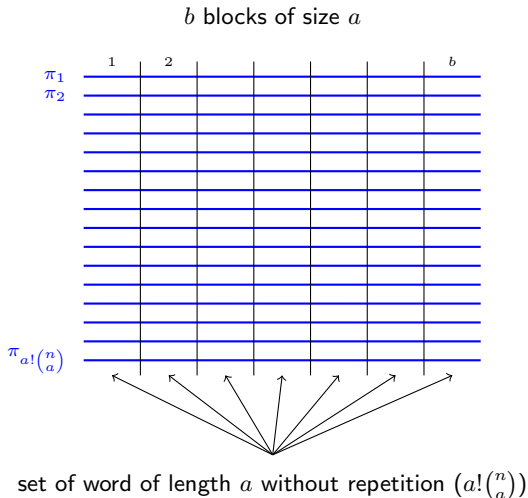
For $a = 2$ this is equivalent to that, for n even, there is a partition of the edges of K_n into perfect matchings.



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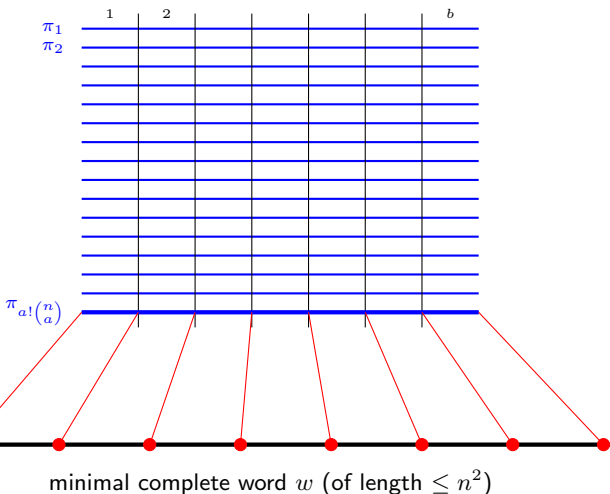


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b blocks of size a



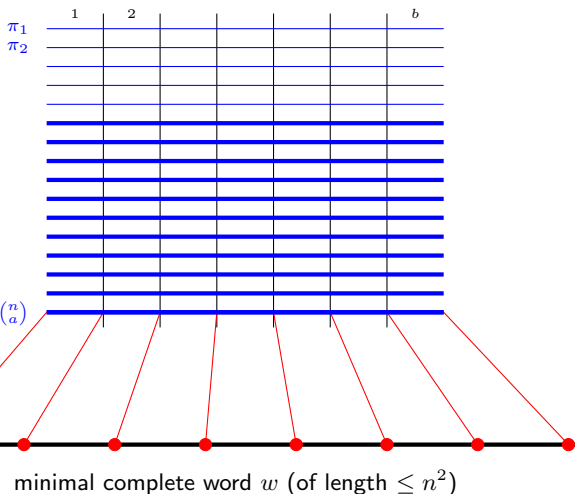
profile of the permutation

at most n^{2b} possible profiles

minimal complete word w (of length $\leq n^2$)

For $n = ab$, there exists a collection $\Pi_n \subseteq S_n$ of size $a! \binom{n}{a} \leq n^a$ with the following properties:

b blocks of size a



at least $\frac{a! \binom{n}{a}}{n^{2b}}$
permutations with
the same profil

profile of the
permutation

at most n^{2b}
possible profils

minimal complete word w (of length $\leq n^2$)

By a counting argument

$$|w| \geq \left(n^{-\frac{2b}{a}}\right) \frac{n(n-a)}{e}$$

Taking $a = n^{\frac{1}{2}+\epsilon}$ and $b = n^{\frac{1}{2}-\epsilon}$ we get

$$|w| \sim \frac{n^2}{e} \quad \text{and} \quad |\Pi_n| \leq n^{n^{\frac{1}{2}+\epsilon}} = 2^{o(n)}.$$

Theorem [Aracena, Gadouleau, R., Salinas 2018+]

Networks	\mathcal{F}	$\max_{f \in \mathcal{F}} \lambda(f)$	$\lambda(\mathcal{F})$
Acyclic	$F_A(n)$	n	$\Theta(n^2)$
Path	$F_P(n)$	n	$\Theta(n^2)$
Increasing	$F_I(n)$	$\Omega(n^2)$	$O(n^2)$
Monotone	$F_M(n)$	$\Omega(n^2)$	$O(n^3)$

Fixing all increasing networks

Let f be any BN with n components and $x \in \{0, 1\}^n$.

1. f is **increasing from** x if $f^u(x) \leq f^{uv}(x)$ for all $u, v \in [n]^*$.
2. f is **decreasing from** x if $f^u(x) \geq f^{uv}(x)$ for all $u, v \in [n]^*$.

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Proposition. $\lambda(F_I(n)) = \lambda(n) = n^2 - o(n^2)$.

Theorem [Aracena, Gadouleau, R., Salinas 2018+]

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A cubic word fixing all the monotone networks

Lemma. If f is monotone and w is n -complete, then

$x \leq f(x) \Rightarrow f$ is increasing from $x \Rightarrow f^w(x)$ if a fixed point of f

$x \geq f(x) \Rightarrow f$ is decreasing from $x \Rightarrow f^w(x)$ if a fixed point of f

Let ω^n be an n -complete word of length $\lambda(n)$ for each $n \geq 1$

Theorem. The word $W^n := \omega^1 \omega^2 \dots \omega^n$ fixes $F_M(n)$ and $|W^n| \leq n^3$.

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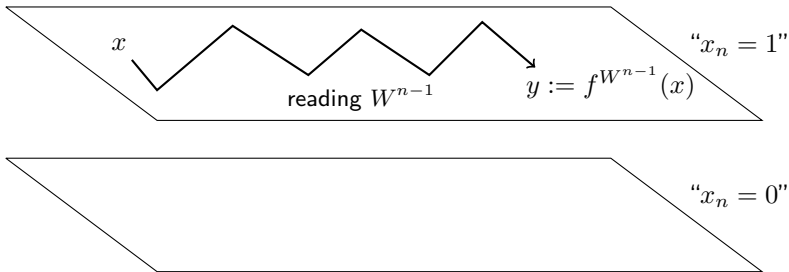
Suppose that W^{n-1} fixes $F_M(n-1)$ and let $f \in F_M(n)$.

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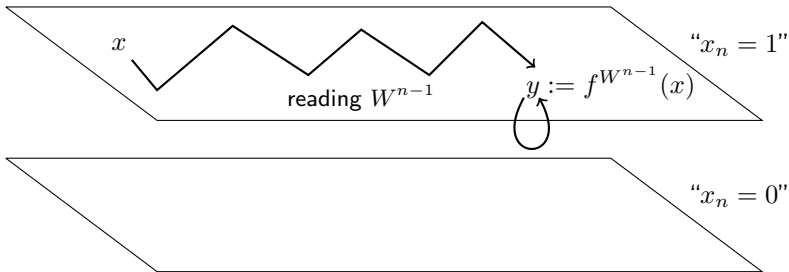


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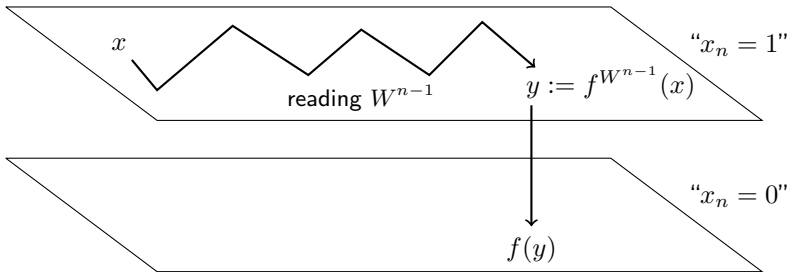
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We have $W^n = W^{n-1} \omega^n$.

Suppose that W^{n-1} fixes $F_M(n-1)$ and let $f \in F_M(n)$.



1. If y is a FP then $f^{\omega^n}(y)$ is a FP.
2. If not $f(y) = y + e_n$ thus $y \leq f(y)$ or $y \geq f(y)$, thus $f^{\omega^n}(y)$ is FP.

Theorem [Aracena, Gadouleau, R., Salinas 2018+]

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Conclusion

It is interesting to regard the asynchronous dynamics as a DFA.

Emphasis on the notion of **fixing words**.

↔ Some results in the monotone case, with various technics

↔ n -complete words, Baranyai's theorem etc.

Question. Is it as hard to fixe one $f \in F_M(n)$ as $F_M(n)$?

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What about classical notions in DFA?

A word w is a **synchronizing word** of a BN f if f^w is constant.

Černý's conjecture for Boolean networks

If a BN f has a synchronizing word, then it has one of length $\leq 2^{2n}$.