# Synchronism vs asynchronism in Boolean automata networks

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#### Outline

- 1 Introduction
- 2 Main definitions
- 3 Deterministic periodic updates
- 4 Non-deterministic updates

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## Introduction BANs, non formally

- A discrete computational model of interaction systems.
- From a theoretical standpoint:
  - Simple setting and representation.
  - Able to capture dynamically a lot of behavioural intricacies and heterogeneities.
- From a more practical/applied standpoint:
  - · Originate from neural theoretical modelling (McCulloch, Pitts, 1943).
  - Developed in the context of genetics (Kauffman, 1969; Thomas, 1973).
  - The most used mathematical objects for genetic regulation qualitative modelling.

### Introduction The (a-)synchronicity problematic(s)

- The causality of events along time depends on the relation between automata updates and "time" but...
  - How to define this relation?
  - How to study the causal perturbations due to changes of this relation?
- Mathematical pertinence:
  - Neat problematic at the frontier of dynamical systems, combinatorics, complexity and computability.
- Biological pertinence:
  - · Genetic expression and chromatin dynamics.
- A remaining question: does model synchronicity stand for modelled system simultaneity?

#### Main definitions Outline

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#### Main definitions

#### BANs and interaction graphs

A Boolean automata network (BAN) of size n is a function

$$f: \mathbb{B}^n \to \mathbb{B}^n$$
  
 $x = (x_0, x_1, \dots, x_{n-1}) \mapsto f(x) = (f_0(x), f_1(x), \dots, f_{n-1}(x))$ 

where  $\forall i \in \{0, ..., n-1\}$ ,  $x_i \in \mathbb{B}$  is the state of automaton i, and  $\mathbb{B}^n$  is the set of configurations.

The interaction graph of f is the signed digraph G(f):  $(V, E \subseteq V \times V)$  where:

- $V = \{0, \dots, n-1\};$
- $(i,j) \in E$  is positive if  $\exists x \in \mathbb{B}^n$  s.t.

$$f_j(x_0,\ldots,x_{i-1},\mathbf{0},x_{i+1},\ldots,x_{n-1})=0$$
 and  $f_j(x_0,\ldots,x_{i-1},\mathbf{1},x_{i+1},\ldots,x_{n-1})=1$ ;

•  $(i,j) \in E$  is negative if  $\exists x \in \mathbb{B}^n$  s.t.

$$f_i(x_0,\ldots,x_{i-1},\mathbf{0},x_{i+1},\ldots,x_{n-1})=1$$
 and  $f_i(x_0,\ldots,x_{i-1},\mathbf{1},x_{i+1},\ldots,x_{n-1})=0$ .

#### Main definitions

#### BANs and interaction graphs

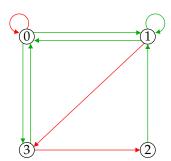
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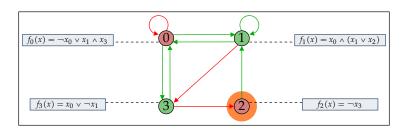
where  $\forall i \in \{0, ..., n-1\}$ ,  $x_i \in \mathbb{B}$  is the state of automaton i, and  $\mathbb{B}^n$  is the set of configurations.

$$f : \mathbb{B}^{4} \to \mathbb{B}^{4}$$

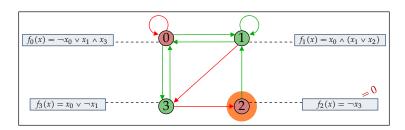
$$f = \begin{cases} f_{0}(x) = \neg x_{0} \lor x_{1} \land x_{3} \\ f_{1}(x) = x_{0} \land (x_{1} \lor x_{2}) \\ f_{2}(x) = \neg x_{3} \\ f_{3}(x) = x_{0} \lor \neg x_{1} \end{cases}$$

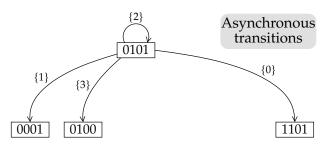


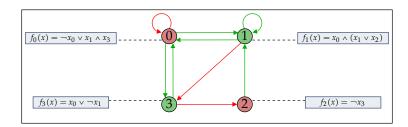
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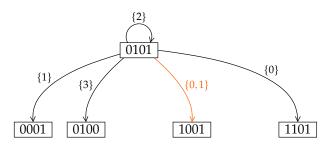


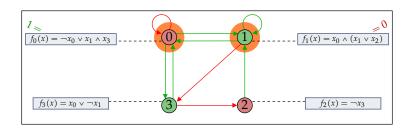


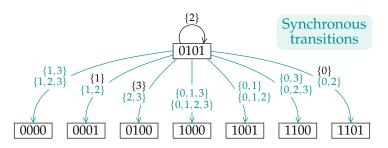


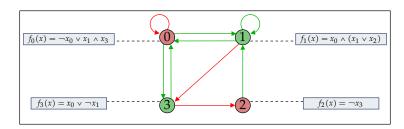












### Main definitions Update modes and BAN behaviours

- ► An update mode is a way of organising the automata updates along time.
- It can be deterministic (periodic or not) or non-deterministic (stochastic or not).
- There exists an infinite number of update modes.

### Main definitions Update modes and BAN behaviours

- An update mode is a way of organising the automata updates along time.
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- ▶ The update mode defines the network behaviour.
- ► The behaviour of a BAN *f* is described by a transition graph

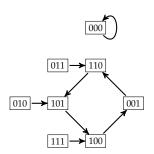
$$\mathscr{G}_{\bullet}(f) = (\mathbb{B}^n, T \subseteq \mathbb{B}^n \times (\mathscr{P}(V) \setminus \varnothing) \times \{0,1\}^n),$$

where • represents a given "fair" update mode.

$$f : \mathbb{B}^3 \to \mathbb{B}^3$$

$$f = \begin{cases} f_0(x) = x_1 \lor x_2 \\ f_1(x) = \neg x_0 \land x_2 \\ f_2(x) = \neg x_2 \land (x_0 \lor x_1) \end{cases}$$

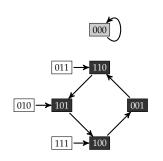
#### Parallel evolution



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#### Parallel evolution

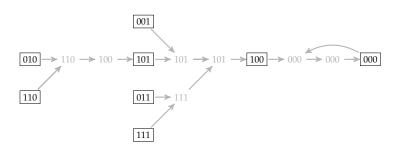


- An attractor of  $(f, \bullet)$  is a terminal SCC of  $\mathscr{G}_{\bullet}(f)$ .
- A fixed point (stable configuration) is a trivial attractor.
- A limit cycle (stable oscillation) is a non-trivial attractor.

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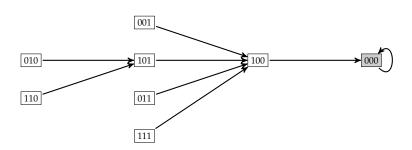
#### $(\{0\},\{1\},\{2\})$ -sequential evolution



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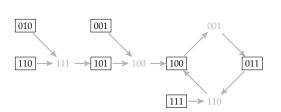
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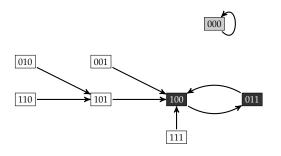
#### $(\{0,2\},\{1\})$ -block-sequential evolution



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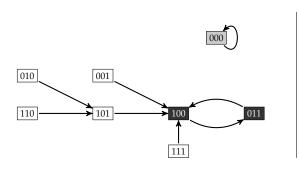
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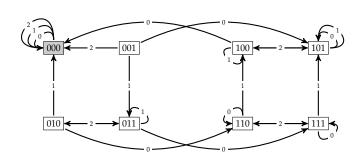
Number of ordered partitions:

$$\mathcal{B}_{n}^{\text{ord}} = \sum_{k=0}^{n-1} \binom{n}{k} \mathcal{B}_{k}^{\text{ord}},$$
with  $\mathcal{B}_{0}^{\text{ord}} = 1$ .

$$f : \mathbb{B}^3 \to \mathbb{B}^3$$

$$f = \begin{cases} f_0(x) = x_1 \lor x_2 \\ f_1(x) = \neg x_0 \land x_2 \\ f_2(x) = \neg x_2 \land (x_0 \lor x_1) \end{cases}$$

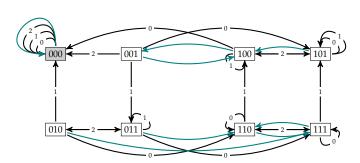
#### Asynchronous evolution



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#### Asynchronous evolution $+ \{0,2\}$ -synchronous transitions



#### Deterministic periodic updates Outline

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- 2 Main definitions

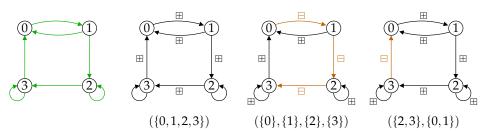
- 3 Deterministic periodic updates
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### Deterministic periodic updates Update graphs

Given an interaction graph G = (V, E), a labelled graph is a graph (G, lab), with lab :  $E \to \{ \boxminus, \boxminus \}$ .

A labelled graph (G, lab) is an update graph if there exist  $s : V \to \{1, ..., n\}$  s.t.

$$\forall (i,j) \in E, \ \mathsf{lab}(i,j) = \begin{cases} \exists & \text{if } s(i) \geqslant s(j) \\ \exists & \text{if } s(i) < s(j) \end{cases}.$$



# Deterministic periodic updates Update graphs and dynamics

Let f be a BAN and G(f) = (V, E) its interaction graph, let  $\pi$  be the parallel update mode, and let  $s \neq s'$  be two distinct block-sequential modes different from  $\pi$ .

Theorem 1 (Aracena et al., 2009)

If 
$$G(f, lab_s) = G(f, lab_{s'})$$
 then  $\mathscr{G}_s(f) = \mathscr{G}_{s'}(f)$ .

Theorem 2 (Tchuente, 1988; Aracena et al., 2009)

If *s* is defined as 
$$\forall j \in \{0, \dots, n-1\}, \forall i \text{ s.t. } (i,j) \in E, s(i) \geqslant s(j) \text{ then } \mathscr{G}_s(f) = \mathscr{G}_\pi(f).$$

Theorem 3 (Aracena et al., 2009)

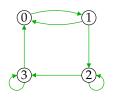
Consider s and f s.t. all the loops in G(f) are positive. Then there exists s' such that  $\mathscr{G}_s(f)$  and  $\mathscr{G}_{s'}(f)$  do not have any common limit cycle.

### Deterministic periodic updates Update graphs and dynamics

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$$s_1 \equiv (\{1\}, \{0\}, \{2\}, \{3\})$$

$$s_2 \equiv (\{1\}, \{2\}, \{0\}, \{3\})$$

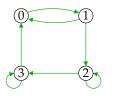
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### Deterministic periodic updates Update graphs and dynamics

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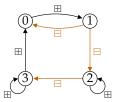
$$f = \begin{cases} f_0(x) = x_1 \land x_3 \\ f_1(x) = x_0 \\ f_2(x) = x_1 \lor x_2 \\ f_3(x) = x_2 \land x_3 \end{cases}$$



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$$s_2 \equiv (\{1\}, \{2\}, \{0\}, \{3\})$$

$$s_3 \equiv (\{1\}, \{2\}, \{0, 3\})$$











### Deterministic periodic updates Interaction cycles

2 types of interaction cycles, the positive and the negative ones:

an even number of negative arcs  $C_6^+$   $C_6^ C_6^ C_6^$ 

#### Seminal results:

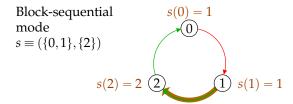
Theorem 4 (Robert, 1986)

If G(f) is acyclic, then f admits a unique attractor which is a fixed point.

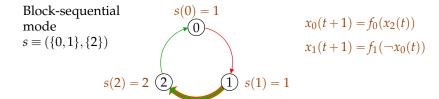
Theorem 5 (Thomas, 1981; Richard, Comet, 2007)

If there are no positive cycles in G(f), f admits no more than one fixed point.

## Deterministic periodic updates Impact of update modes on cycles

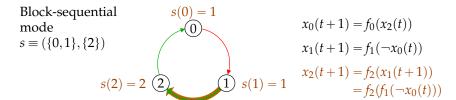


### Deterministic periodic updates Impact of update modes on cycles



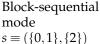
#### Deterministic periodic updates

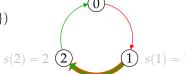
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#### Deterministic periodic updates

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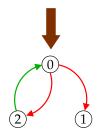


$$x_0(t+1) = f_0(x_2(t))$$

$$x_1(t+1) = f_1(\neg x_0(t))$$

$$x_2(t+1) = f_2(x_1(t+1))$$

$$= f_2(f_1(\neg x_0(t)))$$



Interaction graph G(f,s) = (V, E(s))

Each arc  $(i,j) \in E(s)$  represents the dependence of  $x_i(t+1)$  on  $x_i(t)$ .

# Deterministic periodic updates Impact of update modes on cycles

$$inv(s)$$
= {(i,i+1) | s(i) < s(i+1)}

# Deterministic periodic updates Impact of update modes on cycles

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# Deterministic periodic updates Impact of update modes on cycles

$$= \{(i, i+1) \mid s(i) < s(i+1)\}$$

Theorems (Goles, Noual, 2010)

- ▶ The dynamics induced by two update modes s and s' are equal iff inv(s) = inv(s').
  - Given a cycle of size n, the total number of distinct dynamics induced by blocksequential update modes is:

$$\sum_{k=0}^{n-1} \binom{n}{k} = 2^n - 1.$$

- $\triangleright$  inv(s)  $\neq$  inv(s')  $\Longrightarrow$  no common limit cycles.
- ▷ Iterating a cycle of size n with an update mode s with |inv(s)| = k corresponds to iterating a cycle of same sign and of size n k in parallel.

### Deterministic periodic updates

# Impact of update modes on cycles

Theorem 6 (Goles, Noual, 2010)

 $inv(s) \neq inv(s') \implies no common limit cycles.$ 

Proof

First, let us note that 
$$\forall i, j \in V, f[j, i] : \begin{cases} f_j \circ f_{j-1} \circ \cdots \circ f_i & \text{if } i \leq j \\ f_j \circ f_{j-1} \circ \cdots \circ f_0 \circ f_{n-1} \circ \cdots \circ f_i & \text{if } i > j \end{cases}$$

Suppose that  $(i, i+1) \in \text{inv}(s) \setminus \text{inv}(s')$  and that  $\exists x = x^s(t) = x^{s'}(t)$  s.t.

$$x^{s}(t+1) = x^{s'}(t+1)$$
. Then:

$$x_{i+1}^s(t+2) = f_{i+1}(x_i^s(t+2)) = f[i+1, i^*+1](x_{i^*}^s(t+1)),$$

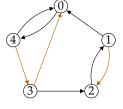
and 
$$x_{i+1}^{s'}(t+2) = f_{i+1}(x_i^{s'}(t+1)) = f_{i+1}(x_i^{s}(t+1)) = f[i+1,i^*+1](x_{i^*}^{s}(t)),$$
 where  $i^* = \max(\{k < i \mid s(k) \ge s(k+1)\}).$ 

By the injectivity of  $f[i+1,i^*+1]$ , if  $x^s(t+2) = x^{s'}(t+2)$  then  $x_{i^*}(t+1) = x_{i^*}(t)$ . Now, if x belongs to an attractor that is induced identically by both s and s', then  $x^{s}(t) = x^{s'}(t)$  $\forall t$ . As result, in this case,  $\forall t$ ,  $x_{i\star}^s(t+1) = x_{i\star}^{s'}(t) = x_{i\star}^s(t)$ . In other terms, the state of node  $i^*$  is fixed in the attractor. Hence the states of all nodes are fixed in the attractor which therefore is a fixed point.

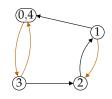
# Deterministic periodic updates Update graphs other related results

## 2: Is a labelled graph an update graph?

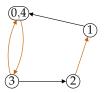
Labelled graph (*G*, lab)



Reduced labelled graph  $(G, lab)^{\boxplus}$ 



Reversed labelled graph  $(G, lab)_R^{\boxplus}$ 

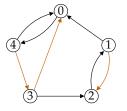


# Deterministic periodic updates

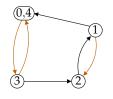
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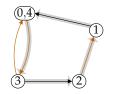




Reduced labelled graph  $(G, lab)^{\boxplus}$ 



Reversed labelled graph  $(G, lab)_{\mathbb{P}}^{\boxplus}$ 

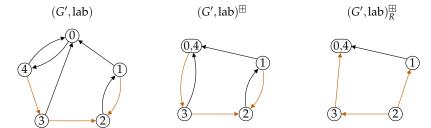


Theorem 7 (Aracena et al., 2011)

A labelled digraph (G, lab) is an update graph iff  $(G, lab)_R^{\boxplus}$  does not contain any forbidden cycle.

# Deterministic periodic updates Update graphs other related results

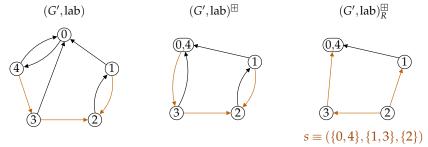
## $\mathcal{Q}$ : How to find the most compact update mode on (G, lab)?



# Deterministic periodic updates

# Update graphs other related results

## $\mathcal{Q}$ : How to find the most compact update mode on (G, lab)?



Algorithm Init. Take  $G' := (G, lab)_R^{\bigoplus}$  and t := 1.

- (1) Compute the paths  $P_{\boxminus} = \{P \mid \#(\boxminus \in P) \text{ is max.}\}\ \text{on } G'.$  If  $P_{\boxminus} = \emptyset$ , goto (4).
- (2) The targets T of the last negative arc of each P of  $P_{\square}$ , and their successors S(T) are scheduled at time step t. t := t + 1.
- (3) Remove T, S(T) and all their incoming arcs from G', and go back to (1).
- (4) All the remaining nodes are scheduled all at once, at time step t.

# Non-deterministic updates Outline

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- 2 Main definitions

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# Non-deterministic updates Basic definitions and notations

$$\forall x = (x_0, \dots, x_{n-1}) \in \mathbb{B}^n, \forall i \in V, \ \overline{x}^i = (x_0, \dots, x_{i-1}, \neg x_i, x_{i+1}, \dots, x_{n-1})$$
$$\forall x \in \mathbb{B}^n, \forall W = W' \uplus \{i\} \subseteq V, \ \overline{x}^W = \overline{(\overline{x}^i)}^{W'} = \overline{(\overline{x}^{W'})}^i$$

The sign of an influence of i on j in x is

$$\operatorname{sign}_{x}(i,j) = \frac{f_{j}(x) - f_{j}(\overline{x}^{i})}{x_{i} - \overline{x}_{i}^{i}} = \operatorname{s}(x_{i}) \cdot (f_{j}(x) - f_{j}(\overline{x}^{i})),$$

where  $s : b \in \mathbb{B} \mapsto b - \neg b \in \{-1, 1\}.$ 

Given 
$$x, y \in \mathbb{B}^n$$
,  $D(x, y) = \{i \in V \mid x_i \neq y_i\}$  and  $d(x, y) = |D(x, y)|$ .

 $E(x) = \{(i,j) \in V \times V \mid \text{sign}_x(i,j) \neq 0\}$  represents the set of effective influences of G(f) in x, which formally means that

$$\forall i, j \in V, \exists x \in \mathbb{B}^n, f_i(x) \neq f_i(\overline{x}^i) \iff (i, j) \in E.$$

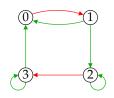
# Monotonicity, unstabilities and frustrations

A local function  $f_i$  is locally monotonic in j if either:

$$\forall x, f_i(x_0, \dots, x_{j-1}, 0, x_{j+1}, \dots, x_{n-1}) \leq f_i(x_0, \dots, x_{j-1}, 1, x_{j+1}, \dots, x_{n-1})$$
  
$$\forall x, f_i(x_0, \dots, x_{j-1}, 0, x_{j+1}, \dots, x_{n-1}) \geq f_i(x_0, \dots, x_{j-1}, 1, x_{j+1}, \dots, x_{n-1})$$

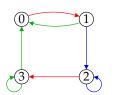
or: 
$$\forall x, f_i(x_0, \dots, x_{j-1}, 0, x_{j+1}, \dots, x_{n-1}) \ge f_i(x_0, \dots, x_{j-1}, 1, x_{j+1}, \dots, x_{n-1})$$

$$f = \begin{cases} f_0(x) = x_1 \land x_3 \\ f_1(x) = \neg x_0 \\ f_2(x) = x_1 \lor x_2 \\ f_3(x) = \neg x_2 \lor x_3 \end{cases}$$



is monotonic.

$$g = \begin{cases} g_0(x) = x_1 \wedge x_3 \\ g_1(x) = \neg x_0 \\ g_2(x) = x_1 \oplus x_2 \\ g_3(x) = \neg x_2 \vee x_3 \end{cases}$$



is not.

# Monotonicity, unstabilities and frustrations

A local function  $f_i$  is locally monotonic in j if either:

$$\forall x, f_i(x_0, \dots, x_{j-1}, 0, x_{j+1}, \dots, x_{n-1}) \le f_i(x_0, \dots, x_{j-1}, 1, x_{j+1}, \dots, x_{n-1})$$

or: 
$$\forall x, f_i(x_0, \dots, x_{j-1}, 0, x_{j+1}, \dots, x_{n-1}) \ge f_i(x_0, \dots, x_{j-1}, 1, x_{j+1}, \dots, x_{n-1})$$

An automaton  $i \in V$  is unstable (resp. stable) in  $x \in \mathbb{B}^n$  if it belongs to the set  $U(x) = \{i \in V \mid f_i(x) \neq x_i\}$  (resp.  $\overline{U}(x) = V \setminus U(x)$ ).

$$f = \begin{cases} f_0(x) = -x_1 \\ f_1(x) = x_0 \end{cases}$$



x	$f_0(x)$	$f_1(x)$	U(x)
(0,0)	1	0	{0}
(0,1)	0	0	{1}
(1,0)	1	1	{1}
(1.1)	0	1 1	{0}

# Monotonicity, unstabilities and frustrations

A local function  $f_i$  is locally monotonic in j if either:

$$\forall x, f_i(x_0, \dots, x_{j-1}, 0, x_{j+1}, \dots, x_{n-1}) \leq f_i(x_0, \dots, x_{j-1}, 1, x_{j+1}, \dots, x_{n-1})$$
  
$$\forall x, f_i(x_0, \dots, x_{j-1}, 0, x_{j+1}, \dots, x_{n-1}) \geq f_i(x_0, \dots, x_{j-1}, 1, x_{j+1}, \dots, x_{n-1})$$

An automaton  $i \in V$  is unstable (resp. stable) in  $x \in \mathbb{B}^n$  if it belongs to the set

$$U(x) = \{i \in V \mid f_i(x) \neq x_i\} \quad \text{(resp. } \overline{U}(x) = V \setminus U(x)\text{)}.$$

An influence  $(i, j) \in E$  is frustrated in x iff it belongs to

$$FRUS(x) = \{(i,j) \in E \mid \mathbf{s}(x_i) \cdot \mathbf{s}(x_j) = -\operatorname{sign}(i,j)\}.$$

$$f = \begin{cases} f_0(x) = x_2 \\ f_1(x) = x_0 \lor \neg x_1 \\ f_2(x) = \neg x_0 \land x_1 \end{cases}$$



$$\begin{aligned} & \text{FRUS}(000) = \{(0,2)\} \\ & \text{FRUS}(001) = \{(1,2),(2,0)\} \\ & \text{FRUS}(010) = \{(0,1),(0,2),(1,2)\} \\ & \text{FRUS}(011) = \{(0,1),(2,0)\} \end{aligned}$$

or:

# Relations between unstabilities and frustrations

Remark (Noual, S., 2017)

If  $j \in U(x)$  then  $\exists i \in V^-(j), (i,j) \in FRUS(x)$ .

$$f = \begin{cases} f_0(x) = \neg x_0 \\ f_1(x) = x_0 \lor \neg x_2 \\ f_2(x) = x_1 \end{cases}$$



$$\begin{aligned} & \text{FRUS}(000) = \{ & (0,0) & , (2,1) \} \\ & \text{FRUS}(001) = \{ & (0,0) & , (1,2) \} \\ & \text{FRUS}(110) = \{ & (0,0) & , (1,2) \} \\ & \text{FRUS}(111) = \{ & (0,0) & , (2,1) \} \end{aligned}$$

N.B: The reciprocal does not hold.

$$f = \begin{cases} f_0(x) = x_2 \\ f_1(x) = x_0 \lor \neg x_1 \\ f_2(x) = \neg x_0 \land x_1 \end{cases}$$



$$FRUS(000) = \{ (0,2) \}$$

$$FRUS(001) = \{ (1,2), (2,0) \}$$

$$FRUS(010) = \{ (0,1), (0,2), (1,2) \}$$

$$FRUS(011) = \{ (0,1), (2,0) \}$$

# Relations between unstabilities and frustrations

Lemma 1 (Noual, S., 2017)

Adding frustrated influences incoming an unstable automaton cannot stabilise it. Formally, noting  $V^-_{FRUS(x)}(j) = V^-(j) \cap \{i \in V \mid (i,j) \in FRUS(x)\}$ , we have:

$$\forall x, y \in \mathbb{B}^n, j \in \mathrm{U}(x) \land \left(V_{\mathrm{FRUS}(x)}^-(j) \subseteq V_{\mathrm{FRUS}(y)}^-(j)\right) \implies j \in \mathrm{U}(y).$$

Proof

Input provided by i to j:  $b_i^j(x) = b(\text{sign}(i,j) \cdot \mathbf{s}(x_i)) = \begin{cases} x_j & \text{if } (i,j) \notin \text{FRUS}(x) \\ \neg x_i & \text{otherwise} \end{cases}$ . By local monotonicity,

$$f_{j}(x) = \bigwedge_{k \leq m} c_{k}(x) = \bigwedge_{k \leq m} \left( \bigvee_{i \in V_{k}^{j}} \mathsf{b}_{i}^{j}(x) = \bigvee_{\substack{i \in V_{k}^{j} \\ (i,j) \in \mathsf{FRUS}(x)}} \neg x_{j} \lor \bigvee_{\substack{i \in V_{k}^{j} \\ (i,j) \notin \mathsf{FRUS}(x)}} x_{j} \right),$$

where  $V_k^j$  is the set of in-neighbours of j involved in the kth clause.

Let *x* be unstable, admitting thus at least one frustrated incoming influence. Let *y* be such that it admits at least one more frustrated incoming influence than x. Since  $f_i$  can be written as a conjunction of disjunctive clauses, the values of these clauses for y are necessarily the same as for x.

# Non-deterministic updates Critical cycles

Let f be a BAN, G = (V, E) its interaction graph, and x a configuration in  $\mathbb{B}^n$ . A cycle  $C = (V_C, E_C)$  of G is x-critical if  $E_C \subseteq FRUS(x)$ .

A cycle *C* is critical if it is *x*-critical for some *x*.

Proposition 1 (Noual, S., 2017)

A critical cycle is a NOPE-cycle, *i.e.* <u>n</u>egative of <u>o</u>dd length or <u>p</u>ositive of <u>e</u>ven length.

#### Proof

Let 
$$x \in \mathbb{B}^n$$
. By definition of frustrated influences, if  $C = (V_C, E_C)$  is  $x$ -critical, has length  $\ell$  and sign  $s$  then: 
$$\prod_{(i,j)\in E_C} -\mathrm{sign}(i,j) = (-1)^\ell \times s = \prod_{(i,j)\in E_C} s(x_i) \cdot s(x_j) = 1.$$

$$f = \begin{cases} f_0(x) = x_0 \land \neg x_1 \\ f_1(x) = \neg x_0 \land x_1 \end{cases}$$



x	$f_0(x)$	$f_1(x)$	FRUS(x)
(0,0)	0	0	{(0,1),(1,0)}
(0,1)	0	1	Ø
(1,0)	1	0	Ø
(1,1)	0	0	$\{(0,1),(1,0)\}$

# Non-deterministic updates Transitions and trajectories

Name	Notation	Definition
Asynchronous	$x \longrightarrow y$	$d(x,y) \leq 1$
Synchronous	$x \longrightarrow y$	d(x,y) > 1
Elementary	$x \longrightarrow y$	$x \longrightarrow y \in \{x \longrightarrow y\} \cup \{x \longrightarrow y\}$
		$x \longrightarrow y$ not decomposable into smaller
Non-sequentialisable	$x \longrightarrow y$	elementary transitions

For all  $x, y \in \mathbb{B}^n$  s.t.  $x \neq y$ , x is willing (resp. unwilling) towards y if  $D(x,y) \subseteq U(x)$  (resp.  $D(x,y) \cap U(x) = \emptyset$ ).

A trajectory from x to y is a path  $x \longrightarrow \dots \longrightarrow y$  in the transition graph.

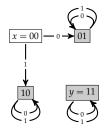
Let  $x = x(0) \implies x(1) \implies \dots \implies x(m-1) \implies y = x(m)$  be a trajectory from x to y. If  $\forall t < m$ ,  $D(x(t+1),y) \subsetneq D(x(t),y)$ , this trajectory is direct. It performs no reversed changes, *i.e.*  $\forall t < m$ ,  $x(t)_i = y_i \implies \forall t < t' \le m$ ,  $x(t')_i = y_i$ .

# Results relating trajectories and critical cycles

Proposition 2 (Noual, S., 2017)

Let *x* a willing configuration towards *y*.

- 1. If there are no asynchronous trajectories from x to y, then D(x,y) induces a NOPE-cycle that is x-critical.
- 2. If D(x,y) does not induce an x-critical cycle, then there is a *direct* asynchronous trajectory from x to y.



$$f = \begin{cases} f_0(x) = x_0 \lor \neg x_1 \\ f_1(x) = \neg x_0 \lor x_1 \end{cases}$$

x	$f_0(x)$	$f_1(x)$	U(x)
(0,0)	1	1	D(x,y)
(0,1)	0	1	Ø
(1,0)	1	0	Ø
(1,1)	1	1	Ø

# Results relating trajectories and critical cycles

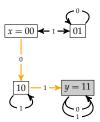
Proposition 2 (Noual, S., 2017)

Let *x* a willing configuration towards *y*.

- 1. If there are no asynchronous trajectories from x to y, then D(x,y) induces a NOPE-cycle that is x-critical.
- 2. If D(x,y) does not induce an x-critical cycle, then there is a *direct* asynchronous trajectory from x to y.

$$f = \begin{cases} f_0(x) = x_0 \lor \neg x_1 \\ f_1(x) = x_0 \lor \neg x_1 \end{cases}$$

X	$f_0(x)$	$f_1(x)$	U(x)
(0,0)	1	1	{0,1}
(0,1)	0	0	{1}
(1,0)	1	1	{1}
(1,1)	1	1	Ø



# Results relating trajectories and critical cycles

Proposition 2 (Noual, S., 2017)

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## Implication

When m local changes are possible in x, then, unless there is a NOPE-cycle of size m, these m changes can be made asynchronously without risking a deadlock, i.e. a situation in which some transitions would have transformed x into a configuration x(t) from which y is not reachable anymore.

# Results relating trajectories and critical cycles

Proposition 2 (Noual, S., 2017)

Let *x* a willing configuration towards *y*.

- 1. If there are no asynchronous trajectories from x to y, then D(x,y) induces a NOPE-cycle that is x-critical.
- 2. If D(x,y) does not induce an x-critical cycle, then there is a *direct* asynchronous trajectory from x to y.

Corollary 1 (Noual, S., 2017)

*If*  $x \rightarrow y$  *exists, then* D(x,y) *induces a* NOPE-cycle *which is x-critical.* 

## **Implication**

In a BAN with no NOPE-cycles of size smaller or equal than  $m \in \mathbb{N}$ , any synchronous change affecting no more than m automata states can be totally sequentialised.

# Non-deterministic updates Structural sensitivity: impact of synchronism

Class N	Class F
"null" sensitivity	"weak" sensitivity
Class G	Class D
"medium" sensitivity	"strong" sensitivity

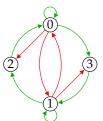
# Structural sensitivity: main result

### Theorem 8 (Noual, S., 2017)

- 1) Synchronism-sensitivity requires the existence of a NOPE-cycle.
- 2) Significant sensitivity requires the existence of a NOPE-cycle of length strictly smaller than the BAN size as well as of a negative cycle.
- 3) In the absence of a Hamiltonian NOPE-cycle and positive loops on all automata, little sensitivity also requires a NOPE-cycle of length strictly smaller than the BAN size.

## A monotonic BAN belonging to sensitivity class **D**:

$$f = \begin{cases} f_0(x) = x_2 \lor (x_0 \land \neg x_1) \\ f_1(x) = x_3 \lor (\neg x_0 \land x_1) \\ f_2(x) = \neg x_0 \land x_1 \\ f_3(x) = x_0 \land \neg x_1 \end{cases}$$

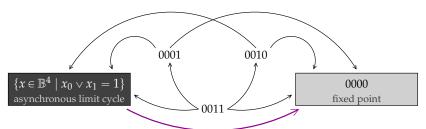


# Non-deterministic updates Structural sensitivity: main result

### Theorem 8 (Noual, S., 2017)

- 1) Synchronism-sensitivity requires the existence of a NOPE-cycle.
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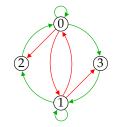
## A monotonic BAN belonging to sensitivity class **D**:



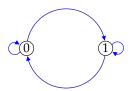
# Non-deterministic updates Class **D** and local (non-)monotonicity

#### 2: How are these two BANs related?

$$f = \begin{cases} f_0(x) = x_2 \lor (x_0 \land \neg x_1) \\ f_1(x) = x_3 \lor (\neg x_0 \land x_1) \\ f_2(x) = \neg x_0 \land x_1 \\ f_3(x) = x_0 \land \neg x_1 \end{cases}$$



$$g = \begin{cases} g_0(x) = x_0 \oplus x_1 \\ g_1(x) = x_0 \oplus x_1 \end{cases}$$



(S., 2012)

# References

- J. Aracena et al.. On the robustness of update schedules in Boolean networks. *BioSystems*, 97:1–8, 2009.
- J. Aracena et al.. Combinatorics on update digraphs in Boolean networks. *Discrete Applied Mathematics*, 159:401–409, 2011.
- E. Goles, M. Noual. Block-sequential update schedules and Boolean automata circuits. Proceedings of AUTOMATA'2010, DMTCS, 41–50, 2010.
- M. Noual, S.. Synchronism vs asynchronism in monotonic Boolean automata networks. *Natural Computing*, doi:10.1007/s11047-016-9608-8, 2017.
- S.. Sur la bio-informatique des réseaux d'automates, HDR, 2012.
- M. Tchuente. Cycles generated by sequential iterations. Discrete Applied Mathematics, 20:165–172, 1988.