Boolean Networks

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Brief History

"There is an urgent need for theories about the ways in which integrated genetic control systems might function."

– Stuart Kauffman (1969)

"The mere description of a situation as it is seen at a given state of research has often become heavy and tedious, requiring long sentences which are easily ambiguous or misleading. I have felt for some years an increasing necessity for a formalization of the concepts in the field."

– René Thomas (1973)

Boolean Abstraction

In the simplicity of the formalism, the modelled real system is necessarily abstracted.

Boolean network modelling constitutes a “top-down” abstraction, which allows us to generate hypotheses about the concrete system.

What kind of systems can be modelled by BNs

1. Made up of interacting entities.
2. Each entity is characterised by a variable quantity.
3. The events (and their mechanisms) are not directly observable, only their complete consequences.

“The base” model of complex interacting systems.

Definition - Syntax

$\mathbb{B} = \{0, 1\}$

A Boolean network of dimension $n \in \mathbb{N}$ is a function $f : \mathbb{B}^n \to \mathbb{B}^n$.

$x : \{1, \ldots, n\} \to \mathbb{B}$ is a configuration.

equivalently $x \in \mathbb{B}^n$

local function : $f_i : \mathbb{B}^n \to \mathbb{B}$

Influence Graph

Directed graph with signed edges.

$G = (V, E)$

$E \subseteq V \times \{+, -\} \times V$

In-neighbours of a node are known as **activators** or **inhibitors**.

i is an activator of j $\Leftrightarrow$ $(i, +, j) \in E$

i is an inhibitor of j $\Leftrightarrow$ $(i, -, j) \in E$

An influence graph is compatible with a Boolean network, if the edges "explain" the network.

difference

$\exists\, x, y \in \mathbb{B}^n$ with $\Delta(x, y) = \{i\} \wedge x_i = 0$ such that

$$\begin{cases} f_j(x) = 0 \wedge f_j(y) = 1 & \Rightarrow \quad (i, +, j) \in E \\ f_j(x) = 1 \wedge f_j(y) = 0 & \Rightarrow \quad (i, -, j) \in E \end{cases}$$

$f_1(x) = \neg x_3$

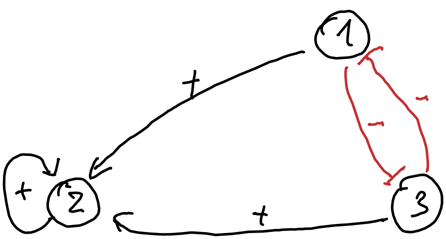
$f_2(x) = x_2 \wedge (x_1 \vee x_3)$

$f_3(x) = \neg x_1$

$x = (0, 0, 0)$

$y = (0, 0, 1)$

$j = 1$ $\quad$ $i = 3$



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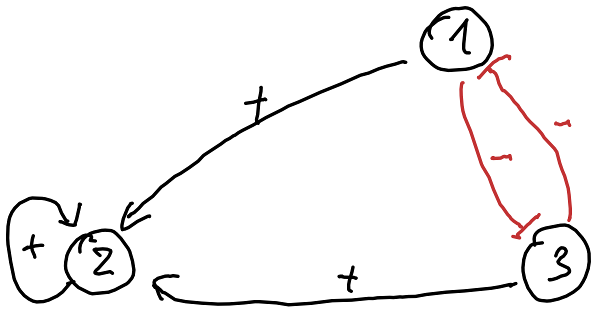


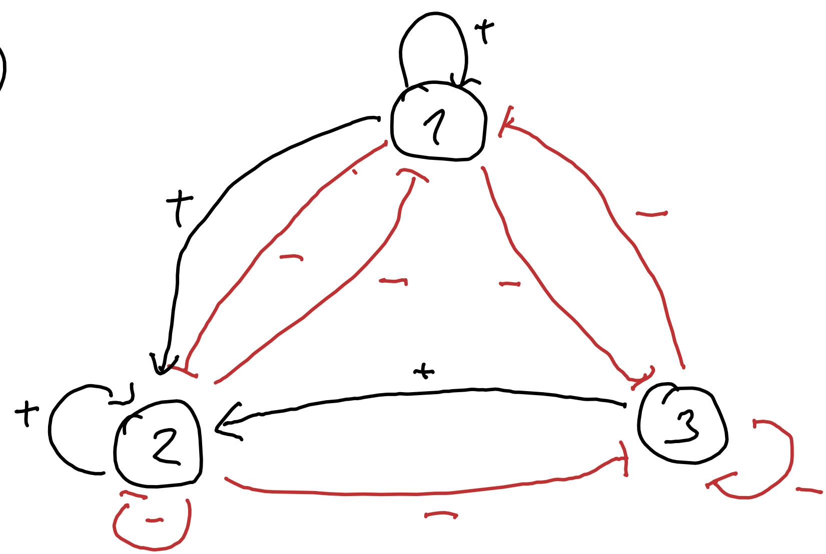
$g_1(x) = x_1 \wedge \neg x_2 \vee \neg x_3$

$g_2(x) = x_3 \wedge (x_1 \veebar x_2)$

$g_3(x) = \neg x_1 \vee \neg x_2 \vee \neg x_3$

$\veebar$ exclusive or (XOR)

$x \veebar y \approx (x \wedge \neg y) \vee (\neg x \wedge y)$



Discrete Regulatory Networks

Extension to a finite discrete domain
$\mathbb{M} = \{0, \dots, k_1\} \times \dots \times \{0, \dots, k_n\}$, $k_1, \dots, k_n \in \mathbb{N}$.

$f : \mathbb{M} \longrightarrow \mathbb{M}$

$x \in \mathbb{M}$

A special case are "Thomas networks", which retain the Boolean function.

D. Thieffry and R. Thomas. Dynamical behaviour of biological regulatory networks—ii. immunity control in bacteriophage lambda. *

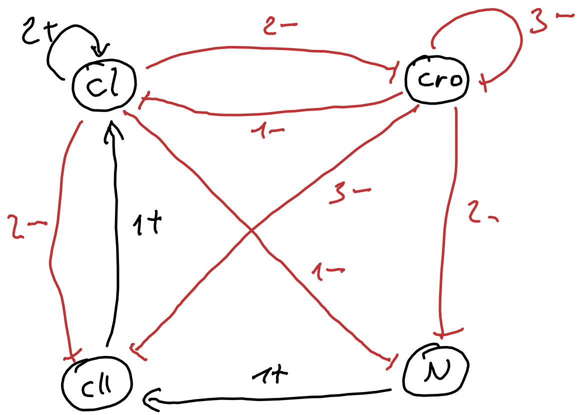
Bulletin of Mathematical Biology, 57(2):277–297, Mar 1995

$f : \mathbb{B}^n \longrightarrow \mathbb{B}^n$

$x \in \mathbb{M}$

edges have a threshold

step-wise updates



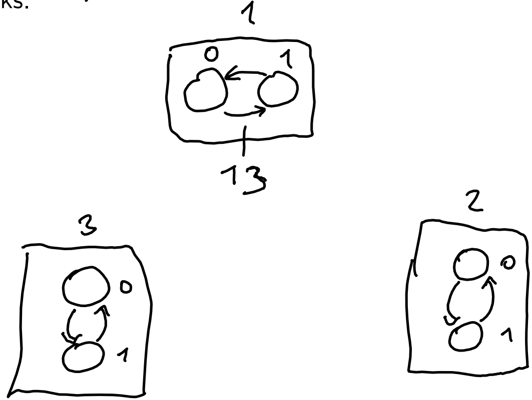
$\mathbb{M} = \{0, 1, 2\} \times \{0, 1, 2, 3\} \times$
$\times \mathbb{B} \times \mathbb{B}$

Automata Networks

Networks of communicating automata.

Cellular automata. von Neumann, 1966

Artificial neutral networks. McCulloch & Pitts, 1943



Dynamics

Updating function modifies configurations according to f.

$$\phi_i : \mathbb{B}^n \longrightarrow \mathbb{B}^n$$

$$\phi_i : x \longmapsto (x_1, \dots, x_{i-1}, f_i(x), x_{i+1}, \dots, x_n)$$

$$W \in \{1, \dots, n\}$$

$$\phi_W : x \longmapsto y \quad \text{such that}$$

$$\forall i \in \{1, \dots, n\} \quad y_i = \begin{cases} f_i(x) & \text{if } i \in W \\ x_i & \text{otherwise} \end{cases}$$

Transitions

An **elementary** transition exists for each application of an updating function.

$$x \xrightarrow{w}_f y \quad \Leftrightarrow \quad \phi_w(x) = y$$

A **non-elementary** transition exists for each predefined sequence of updating function applications.

$$x \xrightarrow{w_1,\ldots,w_k}_f y \quad \Leftrightarrow \quad \phi_{w_k} \circ \ldots \circ \phi_{w_1}(x) = y$$

A **trajectory** is a sequence of consecutive transitions.

$$x_0 \longrightarrow x_1 \longrightarrow \ldots \longrightarrow x_k \approx x_0 \longrightarrow^* x_k$$

An **updating mode** specifies a subset of elementary and non-elementary transitions.

$$(\mathbb{B}^n, \longrightarrow_{(f,\mu)}) \quad \mu\text{-updating mode}$$

↳ subset of elementary and non-elementary transitions

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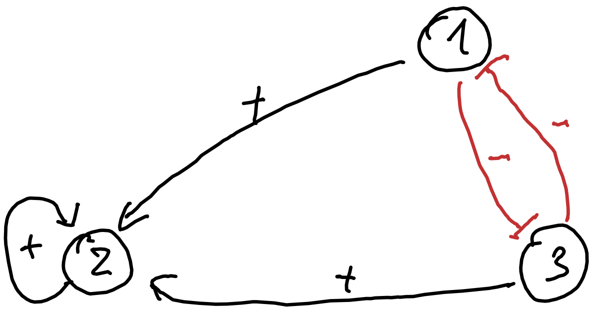
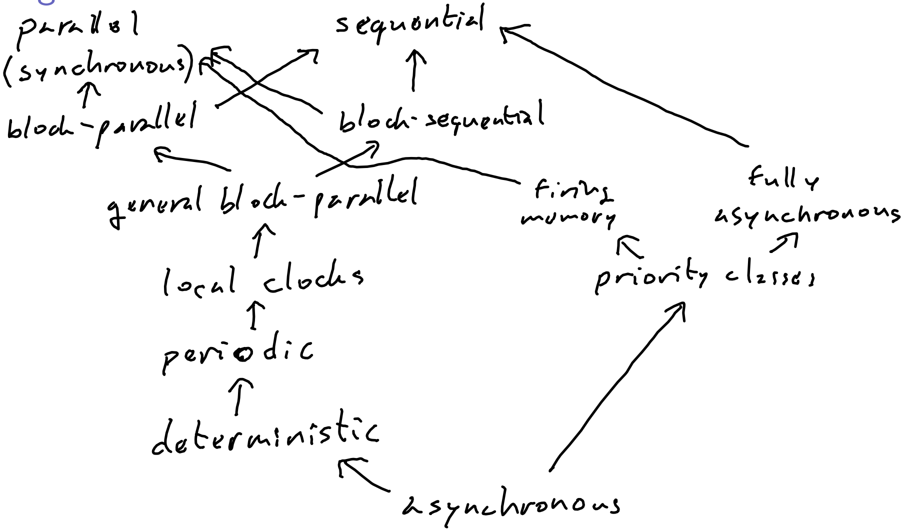
$x \in \mathbb{B}^3$

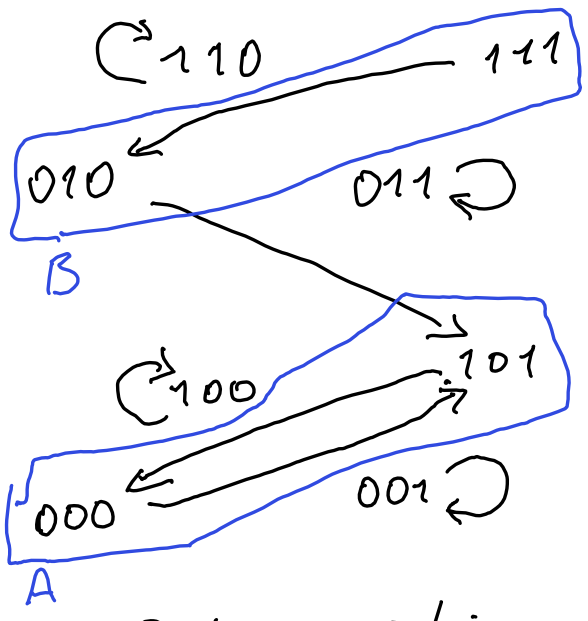


x	$f_1(x)$	$f_2(x)$	$f_3(x)$	ϕ_1	$\phi_{\{2,3\}}$	$\phi_{\{1,2,3\}}$
$(0,0,0)$	1	0	1	$(1,0,0)$	$(0,0,1)$	$(1,0,1)$
$(0,0,1)$	0	0	1	$(0,0,1)$	$(0,0,1)$	$(0,0,1)$
$(0,1,0)$	1	0	1	$(1,1,0)$	$(0,0,1)$	$(1,0,1)$

Updating Modes



Synchronous μ_s only transitions $x \xrightarrow{W}_f y$ such that $W = \{1, \dots, n\}$



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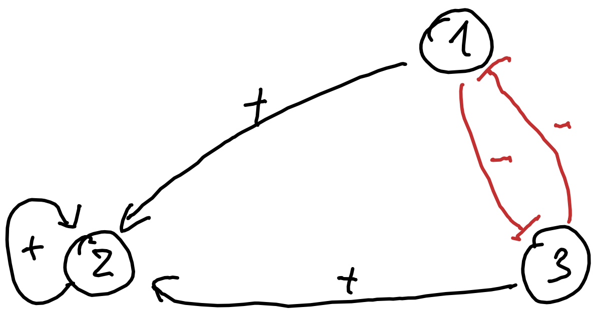
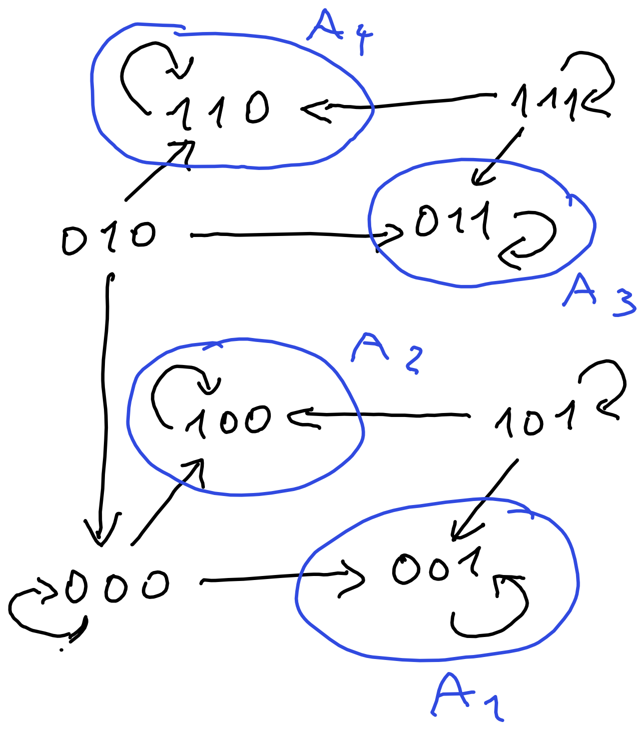


→ Deterministic

A → cyclic attractor (reachable bottom strongly connected component)

B → strong basin of attraction of A
" A is the only reachable attractor
(weak = A is reachable, but there are other reachable attractors.)

Fully asynchronous μ_F - only transitions $x \xrightarrow{W}_f y$ such that $W = \{i\}$ for $i \in \{1, \dots, n\}$



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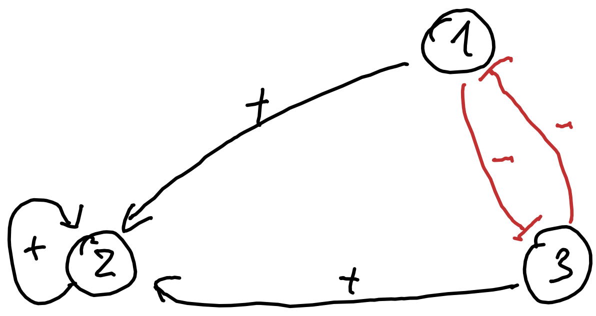


→ Non-deterministic

$A_1, \dots, A_4$ → attractors (simple)

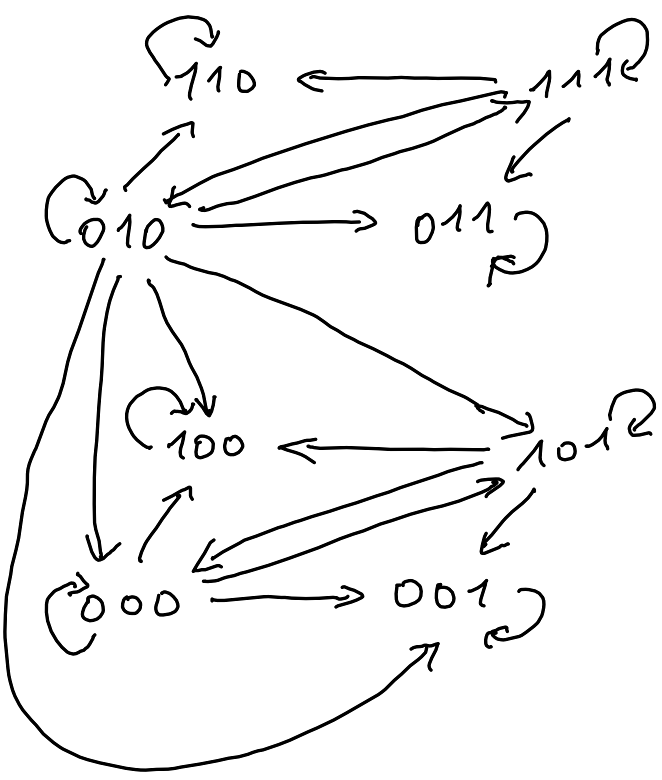
weak basins of attraction:

A_1 ... $\{101, 000, 010\}$ A_3 ... $\{111, 010\}$

A_2 ... $\{101, 000, 010\}$ A_4 ... $\{111, 010\}$

No strong basins!

Asynchronous μ_a - all elementary transitions $x \xrightarrow{W}_f y$, $W \subseteq \{1, \dots, n\}$



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