UNIVERSIDAD DE CONCEPCIÓN

Centro de Investigación en Ingeniería Matemática (CI^{2}MA)

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Julio Aracena, Laurence Calzone,
Jean - Paul Comet, Jacques Demongeot,
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Denis Thieffry

PREPRINT 2012-10

SERIE DE PRE-PUBLICACIONES

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Jean-Paul Comet [1] Adrien Richard [1] Julio Aracena [2]

Laurence Calzone [3] Jacques Demongeot [4,5]

Marcelle Kaufman [6] Aurélien Naldi [7]

El Houssine Snoussi [8] Denis Thieffry [9]

March 9, 2012

[1] Université Nice-Sophia Antipolis, Lab. I3S UMR CNRS 7271, 2000 Route des Lucioles, 06903 Sophia Antipolis, France

[2] Universidad de Concepción, CI2MA and Departamento de Ingeniería Matemática, Concepción, Chile

[3] Institut Curie, U900 INSERM, Mines ParisTech

[4] Université Joseph Fourier-Grenoble 1, AGIM CNRS FRE 3405, 38706 La Tronche, France

[5] IXXI, Institut Rhône-Alpin des systèmes complexes, 69007 Lyon, France

[6] Université Libre de Bruxelles, Unit of Theoretical and Computational Biology, C.P. 231, 1050 Bruxelles, Belgique

[7] Centre Intégratif de Génomique, UNIL-Université de Lausanne, CH-1015 Lausanne, Switzerland

[8] Université Mohammed V, Rabat, Maroco

[9] École Normale Supérieure, Institut de Biology de l'ENS (IBENS) INSERM U1024 & CNRS UMR 8197, Paris, France

Abstract

It has been proved, for several classes of continuous and discrete dynamical systems, that the presence of a positive (resp. negative) circuit in the interaction graph of a system is a necessary condition for the presence of multiple stable states (resp. a cyclic attractor). A positive (resp. negative) circuit is then said to be functional when it "generates" several stable states (resp. a cyclic attractor). However, there are no mathematical frameworks translating the underlying meaning of "generates". Focusing on Boolean networks, we recall and propose some definitions around the notion of functionality and state associated mathematical results.

Keywords: Boolean network, Interaction graph, Feedback circuit, Fixed point.

1 Introduction

Interactions between components of a dynamical system are often very roughly described by an interaction graph: Vertices represent components, and arcs are signed in order to denote positive or negative influences between components. It becomes natural to study what kind of information on the dynamics of a system can be deduced from its interaction graph. Thomas' conjectures [1], stated in the context of gene networks, provide a partial answer to this question: The presence of a positive (resp. negative) circuit is a necessary condition for the presence of multiple stable states (resp. a cyclic attractor); the sign of a circuit being defined as the product of the signs of its arcs. These conjectures have been proved for differential systems [2, 3, 4, 5, 6, 7] and discrete ones

[8, 9, 10, 11, 12, 13]. They lead to think that the essential role of circuits is to ensure the presence of multiple stable states (if positive) or cyclic attractors (if negative). Thomas and coworkers then said that a circuit is functional (or effective, operative) if it actually "fulfills this role" [14, 15]). Moreover, Snoussi and Thomas [16] connected this notion of functionality with conditions on the functioning of the interactions of circuits (stationarity of a singular characteristic state of a circuit).

In this paper we propose different notions of functionality in terms of *necessary conditions* - on the functioning of the interactions of circuits - for the presence of multiple stable states or cyclic attractors. The class of dynamical systems we choose for these definitions is the class of asynchronous Boolean networks which has been introduced by Thomas [17] as a model for the dynamics of gene networks: On the one hand, these systems are elementary instances of complex systems and are largely used, and on the other hand, for these systems, there exists a large number of results about Thomas' ideas.

This paper is organized as follows: Section 2 recalls classical notions associated with Boolean networks. In Sections 3, 4, 5 and 6, we define different kinds of functionality depending on the localization, in the phase space, of states where interactions are functioning. Section 7 summarizes the results associated with these definitions and the relationships between them. Section 8 is devoted to discussion.

Remark This paper results from a collective discussion that took place during the workshop *Logical formalism, gains and challenges for the modeling of regulatory networks, held at Rabat, Maroc, from 12th to 15th of April 2011*.

2 Preliminaries

Let $\mathbb{B} = \{0, 1\}$, and let I be a finite set. We denote by $\mathbb{B}^I$ the set of functions from I to $\mathbb{B}$, seen as points of the $|I|$-dimensional Boolean hypercube. For $i \in I$ and $x \in \mathbb{B}^I$, we denote by x_i the image of i by x, and we denote by $\overline{x}^i$ the point of $\mathbb{B}^I$ such that $\overline{x}^i_i = 1 - x_i$ and $\overline{x}^i_j = x_j$ for all $j \neq i$. The Hamming distance d between points of $\mathbb{B}^I$ is defined by: For all $x, y \in \mathbb{B}^I$, $d(x, y) = \sum_{i \in I} |x_i - y_i|$.

A **Boolean network** is a function $f : \mathbb{B}^I \to \mathbb{B}^I$. Set I is the set of network components and $\mathbb{B}^I$ is the set of possible states (or configurations). Hence, at a given state each component is either present or absent. For all $i \in I$, we denote by f_i the function from $\mathbb{B}^I$ to $\mathbb{B}$ defined by $f_i(x) = f(x)_i$. We say that f is **non-expansive** if $d(f(x), f(y)) \leq d(x, y)$ for all $x, y \in \mathbb{B}^I$. For $i, j \in I$, the partial **discrete derivative** of f_i with respect to x_j is the function $f_{ij} : \mathbb{B}^I \to \{-1, 0, 1\}$ defined by

$$f_{ij}(x) = \frac{f_i(\overline{x}^j) - f_i(x)}{\overline{x}^j_j - x_j}.$$

The matrix of these partial derivatives at a given point may be seen as the Jacobian matrix of the system at this point. In the following, we use graphs instead of matrices to handle these partial derivatives.

An **interaction graph** G consists in a set of vertices V and a set of signed arcs $A \subseteq V \times \{+, -\} \times V$. In such a graph, a **positive (resp. negative) circuit** is an elementary directed cycle with an even (resp. odd) number of negative arcs. If G and H are two interaction graphs, we write $G \subseteq H$ to mean that G is a subgraph of H (*i.e.* each vertex of G is a vertex of H and each arc of G is an arc of H).

Let $f : \mathbb{B}^I \to \mathbb{B}^I$ and $X \subseteq \mathbb{B}^I$. We denote by $Gf(X)$ the interaction graph whose the vertex set is I and that contains a positive (resp. negative) arc from j to i if there exists $x \in X$ such that $f_{ij}(x) > 0$ (resp. $f_{ij}(x) < 0$). Clearly if $X \subseteq Y$ then $Gf(X) \subseteq Gf(Y)$. For each $x \in \mathbb{B}^I$, we write $Gf(x)$ instead of $Gf(\{x\})$; this graph $Gf(x)$ is usually called the **local interaction graph** of f evaluated at point x, and it contains the same information as the Jacobian matrix of f at point x. We use $G(f)$ as an abbreviation of $Gf(\mathbb{B}^I)$; this graph $G(f)$ is usually called the **global interaction graph** of f.

The **asynchronous state graph** of f is the directed graph $\Gamma(f)$ defined by: The vertex set is $\mathbb{B}^I$, and for all $x, y \in \mathbb{B}^I$, there exists an arc from x to y if there exists $i \in I$ such that $y = \overline{x}^i$ and $f_i(x) \neq x_i$. The graph $\Gamma(f)$ can be seen as a (undeterministic) dynamical system in which each transition of a trajectory changes a unique component. The **attractors** of $\Gamma(f)$ are defined as its terminal strongly connected components (*i.e.* strongly connected components without out-going arc). The attractors of size 1 correspond to the fixed points of f: $\{x\}$ is an attractor of $\Gamma(f)$ if and only if $f(x) = x$. Attractors of size at least 2 are said **cyclic**.

3 Functionality of type 1

If $G(f)$ has an arc from j to i then $f_{ij} \neq \text{cst}$, *i.e.* the function f_i depends on variable x_j. This dependency is visible only at points x where $f_{ij}(x) \neq 0$. Then, a positive (resp. negative) arc from j to i is said **functional at point $\boldsymbol{x}$** if $f_{ij}(x) > 0$ (resp. $f_{ij}(x) < 0$). The first type of functionality we consider requires that all the arcs of a circuit C of $G(f)$ are functional at the same point.

Definition 1 *Let C be a circuit of $G(f)$ and $x \in \mathbb{B}^I$. C is* **functional of type 1 at $\boldsymbol{x}$** *if $C \subseteq Gf(x)$. C is* **functional of type 1** *if it is functional of type 1 for at least one $x \in \mathbb{B}^I$.*

Theorem 1 (Shih-Dong' theorem [18]) *If f has no functional circuits of type 1, then f has a unique fixed point x. Furthermore, $\Gamma(f)$ describes a weak convergence toward x: For all $y \in \mathbb{B}^I$, $\Gamma(f)$ has a path from y to x of length $d(x, y)$.*

The converge is said weak since, under the conditions of the statement, $\Gamma(f)$ may have cycles. Note that the following theorem gives the uniqueness part of Theorem 1 under weaker conditions.

Theorem 2 (Thomas' rule - type-1-functional positive circuits [10, 12]) *If f has no functional positive circuits of type 1, then $\Gamma(f)$ has a unique attractor, in particular f has at most one fixed point.*

We don't know if Thomas' rule holds for functional negative circuits of type 1:

Question 1 (Thomas' rule - type-1-functional negative circuits) *Is it true that if f has no functional negative circuits of type 1 then $\Gamma(f)$ has no cyclic attractors?*

This question has a positive answer in the non-expansive case (see Proposition 1 and Theorem 3 below). Moreover, since the absence of cyclic attractor implies the existence of at least one fixed point, the question has a weak form of interest: Is it true that if f has no functional negative circuits of type 1 then f has at least one fixed point? A positive answer to this weak form would provide the existence part of Theorem 1 under weaker conditions.

4 Functionality of type 2

For this type of functionality, we need additional definitions about functions resulting from f by fixing some coordinates. Let $J \subseteq I$ and $z \in \mathbb{B}^{I \setminus J}$. For all $x \in \mathbb{B}^J$, we denote by $x \cup z$ the point $y \in \mathbb{B}^I$ defined by: $y_i = x_i$ if $i \in J$ and $y_i = z_i$ if $i \in I \setminus J$. The **sub-function** of f induced by z is the function $h : \mathbb{B}^J \to \mathbb{B}^J$ defined by:

$$\forall x \in \mathbb{B}^J,\ \forall i \in J, \qquad h_i(x) = f_i(x \cup z).$$

Hence, h is the function that we obtain from f by fixing to z_i the value of each component $i \in I \setminus J$. Note that $\Gamma(h)$ has an arc from x to $\overline{x}^i$ if and only if $\Gamma(f)$ has an arc from $x \cup z$ to $\overline{x \cup z}^i$. Hence, $\Gamma(h)$ is isomorphic to the subgraph of $\Gamma(f)$ induced by the vertex set $\{x \cup z \,|\, x \in \mathbb{B}^J\}$ (the isomorphism is $x \mapsto x \cup z$). Furthermore, $Gh(x)$ has a positive (resp. negative) arc from j to i if and only if this arc is in $Gf(x \cup z)$, that is: For all $x \in \mathbb{B}^J$ and $i, j \in J$, we have $h_{ij}(x) = f_{ij}(x \cup z)$. Hence, $Gh(x)$ is the subgraph of $Gf(x \cup z)$ induced by J.

Definition 2 *Let C be a circuit of $G(f)$, let J be the vertices of C, let $z \in \mathbb{B}^{I \setminus J}$ and let h be the sub-function of f induced by z. C is* **functional of type 2 at z** *if $C = G(h)$. C is* **functional of type 2** *if it is functional of type 2 for at least one $z \in \mathbb{B}^{I \setminus J}$.*

Note that functions h whose the global interaction graph $G(h)$ is a cycle C have been deeply study (see [19, 20] for example); in particular, it is well known that if C is positive then h has exactly two fixed points and that if C is negative then h has no fixed points (so $\Gamma(f)$ has a cyclic attractor). Hence, an isolated circuit C effectively generates two fixed points in the positive case and a cyclic attractor in the negative case, and functionality of type 2 allows C to behave locally in the same way, in a sub-cube $\mathbb{B}^J$ of $\mathbb{B}^I$.

The following proposition shows that type-2-functionality can be defined in terms of type-1-functionality:

Proposition 1 *C is functional of type 2 at z if and only if C is functional of type 1 at $x \cup z$ for all $x \in \mathbb{B}^J$.*

Proof Suppose that $C = G(h)$ and that C has a positive (resp. negative) arc from j to i. Then for all $x \in \mathbb{B}^J$, we have $h_i(x) = x_j$ (resp. $h_i(x) = 1 - x_j$) so $h_{ij}(x) > 0$ (resp. $h_{ij}(x) < 0$). Hence, for all $x \in \mathbb{B}^J$, we have $C = G(h) =$

$Gh(x)$. We deduce that $C = Gh(x) \subseteq Gf(x \cup z)$ for all $x \in \mathbb{B}^J$. This proves one direction. For the other one, suppose that $C \subseteq Gf(x \cup z)$ for all $x \in \mathbb{B}^J$. If C has a positive arc from j to i then, for all $x \in \mathbb{B}^J$, we have $f_{ij}(x \cup z) > 0$ so $f_i(x \cup z) = x_j$ and so $h_i(x) = x_j$. So in $G(h)$, i has a unique predecessor j, and the arc from j to i is positive. Similarly, if C has a negative arc from j to i then, for all $x \in \mathbb{B}^J$, we have $f_{ij}(x \cup z) < 0$ so $f_i(x \cup z) = 1 - x_j$ and so $h_i(x) = 1 - x_j$. So in $G(h)$, i has a unique predecessor j, and the arc from j to i is negative. We deduce that $G(h) = C$. □

Another relationship between type-1- and type-2-functionalities has been established by Remy and Ruet [21]: If a cycle C is type-1-functional and if C has no chord in $G(f)$ then C is type-2-functional (a chord of C is an arc that is not in C and whose initial and terminal vertices are in C).

Theorem 3 (Thomas' rules - type-2-functional circuits - non-expansive case) *Suppose that f is non-expansive. If f has no functional positive circuits of type 2, then $\Gamma(f)$ has a unique attractor, and if f has no functional negative circuits of type 2, then $\Gamma(f)$ has no cyclic attractors.*

Proof (sketch) Suppose that f is non-expansive and that $G(f)$ has a circuit C with vertex set J. Let $x \in \mathbb{B}^J$ and $z \in \mathbb{B}^{I \setminus J}$. Assume that $Gf(x \cup z)$ contains C. Let h be the sub-function of f induced by z. Then C is an Hamiltonian circuit of $Gh(x)$ and since h is non-expansive too, it can be proved that $Gh(x) = C$ for all $x \in \mathbb{B}^J$, so that C is functional of type 2 at z. Hence we have the following property $\mathcal{P}$: *If C is functional of type 1 at $x \cup z$ then it is functional of type 2* *at* z. If $\Gamma(f)$ has multiple attractors, then by Theorem 2, f has a functional positive circuit of type 1, and by $\mathcal{P}$ it has a functional positive circuit of type 2. If $\Gamma(f)$ has a cyclic attractor, it has been proved in [22] (see also [23]) that f has a functional negative circuit of type 1, so by $\mathcal{P}$ it has a functional negative circuit of type 2. $\square$

The two following examples shows that Theorem 3 is false in the expansive case. It also shows that functionality of type 1 does not imply the one of type 2.

Remark In all examples, I is an interval $\{1, 2, \ldots, n\}$, and each point $x \in \mathbb{B}^I$ is seen as a string $x = x_1 x_2 \ldots x_n$. Also, interaction graphs are represented with T-end arrows for negative arcs and normal arrows for positive ones.

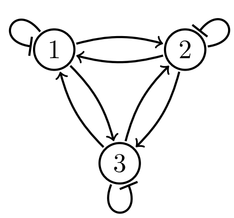
Example 1 *$I = \{1, 2, 3\}$ and $f : \mathbb{B}^I \to \mathbb{B}^I$ is defined by:*

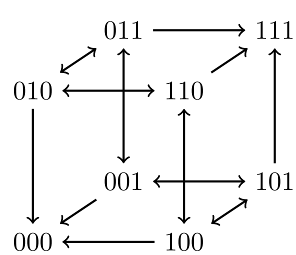
$$f_1(x) = (\overline{x_1} \wedge (x_2 \vee x_3)) \vee (x_2 \wedge x_3)$$

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

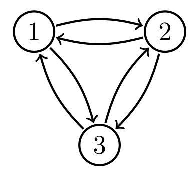
$$f_3(x) = (\overline{x_3} \wedge (x_1 \vee x_2)) \vee (x_1 \wedge x_2)$$

The global interaction graph of f and the asynchronous state graph of f are:

$G(f) =$ 

$\Gamma(f) =$ 

f has two fixed points, 000 *and* 111*, but one can check that it has no functional positive circuits of type 2. According to Theorem 2, f has at least one functional positive circuit of type 1 (so, for positive circuits, functionality of type 1 does not imply functionality of type 2). The only points for which the local interaction graph has a positive circuit are* 000 *and* 111*; for these two points the local interaction graph of f has actually 5 positive circuits:*

$Gf(000) = Gf(111) =$ 

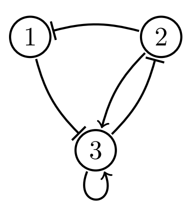
Example 2 *$I = \{1, 2, 3\}$ and $f : \mathbb{B}^I \to \mathbb{B}^I$ is defined by:*

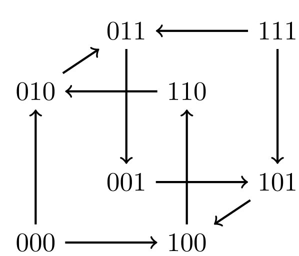
$$f_1(x) = \overline{x_2}$$

$$f_2(x) = \overline{x_3}$$

$$f_3(x) = (x_3 \wedge (\overline{x_1} \vee x_2)) \vee (\overline{x_1} \wedge x_2)$$

The global interaction graph of f and the asynchronous state graph of f are:

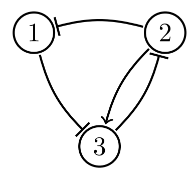
$G(f) =$ 

$\Gamma(f) =$ 

$\Gamma(f)$ has a unique attractor, $\{010, 011, 001, 101, 100, 110\}$, which is cyclic, but

one can check that f has no functional negative circuits of type 2. At each point excepted 011 *and* 100*, the local interaction graph contains at least one negative circuit (so, for negative circuits, functionality of type 1 does not imply functionality of type 2). For instance, at* 010 *and* 101 *the local interaction graph has two negative circuits:*

$$Gf(010) = Gf(101) =$$



5 Functionality of type 3

Recall that an arc from j to i is functional at point x if $f_{ij}(x) \neq 0$, that is, when $f_i(x) \neq f_i(\bar{x}^j)$. We then say that the arc is "visible" between the adjacent points x and $\bar{x}^j$. We now associate to each $X \subseteq \mathbb{B}^I$ an interaction graph $Gf[X]$ (slightly different from $Gf(X)$) which contains all visible arcs between adjacent points that belong both to X.

Formally, for all $X \subseteq \mathbb{B}^I$, we denote by $Gf[X]$ the interaction graph defined by: The vertex set is I, and there exists a positive (resp. negative) arc from j to i if there exists $x \in X$ such that $f_{ij}(x)$ is positive (resp. negative) *and* $\overline{x}^j \in X$. Clearly, $G(f) = Gf[\mathbb{B}^I]$, and if $Y \subseteq X$ then $Gf[Y] \subseteq Gf[X]$. Furthermore, because of the condition "*and* $\overline{x}^j \in X$", $Gf[X] \subseteq Gf(X)$, and for all $x \in \mathbb{B}^I$, $Gf[x]$ has no arcs.

For all $x \in \mathbb{B}^I$, we denote by $\Gamma(f)[x]$ the reachability set of x, that is, the set of points $y \in \mathbb{B}^I$ such that $\Gamma(f)$ has a path from x to y (by convention,

$x \in \Gamma(f)[x]$). Note that if X is an attractor of $\Gamma(f)$, then $\Gamma(f)[x] = X$ for all $x \in X$ (since X is strongly connected and has no out-going arcs).

Definition 3 *Let C be a circuit of $G(f)$ and $x \in \mathbb{B}^I$. C is* **functional of type 3 at x** *if $C \subseteq Gf[\Gamma(f)[x]]$. C is* **functional of type 3** *if it is functional of type 3 for at least one $x \in \mathbb{B}^I$.*

The following theorem shows that type-3-functional negative circuits are necessary for the presence of cyclic attractors.

Theorem 4 (Thomas' rule - type-3-functional negative circuits [10, 13]) *If X is a cyclic attractor of $\Gamma(f)$, then $Gf[X]$ has a negative circuit C, which is thus functional of type 3 at each point $x \in X$ (since $X = \Gamma(f)[x]$).*

Proposition 2 *Let C be a negative circuit of $G(f)$ with vertex set J, and let $z \in \mathbb{B}^{I \setminus J}$. If C is functional of type 2 at z, then it is functional of type 3 at $x \cup z$ for all for all $x \in \mathbb{B}^J$.*

Proof Suppose that C is functional of type 2 at z, and let h be the subfunction of f induced by z. Let $x \in \mathbb{B}^J$. As showed in [19], for every $x \in \mathbb{B}^J$, $\Gamma(h)[x]$ contains a cyclic attractor, and we deduce from Theorem 4 that $G(h)[\Gamma(h)[x]] = C$. Since $\Gamma(h)[x]$ is isomorphic to the subgraph of $\Gamma(f)$ induced by $X = \{y \cup z \,|\, y \in \Gamma(h)[x]\}$, we have $X \subseteq \Gamma(f)[x \cup z]$, and since $Gh(y)$ is a subgraph of $Gf(y \cup z)$ for all $y \in \mathbb{B}^J$, we deduce that $C = Gh[\Gamma(h)[x]] \subseteq Gf[X] \subseteq Gf[\Gamma(f)[x \cup z]]$. So C is functional of type 3. $\square$

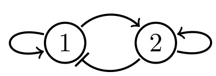
Theorem 4 shows that functionality of type 3 of a negative circuit is necessary for the presence of a cyclic attractor. However, the following example shows that functionality of type 3 of a positive circuit is not necessary for the presence of multiple attractors. It also shows that functionality of type 1 does not imply functionality of type 3, and that Proposition 2 does not hold for positive circuits.

Example 3 *$I = \{1, 2\}$ and $f : \mathbb{B}^I \to \mathbb{B}^I$ is defined by:*

$$f_1(x) = x_1 \wedge \overline{x_2}$$

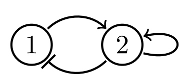
$$f_2(x) = x_1 \wedge x_2$$

The global interaction graph of f and the asynchronous state graph of f are:

$G(f) =$ 

$$\Gamma(f) = \begin{tikzcd} 01 \arrow[d] & 11 \arrow[l] \\ 00 & 10 \end{tikzcd}$$

Note that f has two fixed points. The local interaction graph of f at 11 is:

$Gf(11) =$ 

So f has positive and negative functional positive circuits of type 1. Furthermore, the sub-function of f induced by $x_1 = 1$ or by $x_2 = 0$ is the identity on $\mathbb{B}$. Since the global interaction graph of the identity on $\mathbb{B}$ is a positive circuit of length one, we deduce that f has functional positive circuits of type 2. However, f has no functional circuits of type 3. Indeed, there are no arcs in the following three graphs: $Gf[\Gamma(f)[00]] = Gf[00]$, $Gf[\Gamma(f)[10]] = Gf[10]$ and $Gf[\Gamma(f)[01]] = Gf[\{01, 00\}]$. Then, $Gf[\Gamma(f)[11]] = Gf[\{11, 01, 00\}]$ contains only an arc from vertex 1 to vertex 2. So for positive and negative circuits, *functionality of type 1 does not imply functionality of type 3. For positive circuits, functionality of type 2 does not imply functionality of type 3. Finally, type-3-functionality of a positive circuit is not necessary for the presence of multiple fixed points.*

The following example shows that, in the positive case, functionality of type 3 does not imply functionality of type 1 (thus it does not imply functionality of type 2).

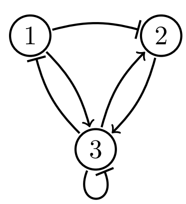
Example 4 *$I = \{1, 2, 3\}$ and $f : \mathbb{B}^I \to \mathbb{B}^I$ is defined by:*

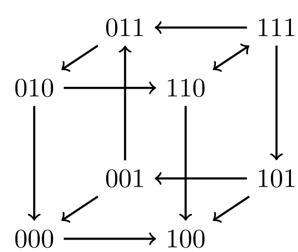
$$f_1(x) = \overline{x_3}$$

$$f_2(x) = \overline{x_1} \wedge x_3$$

$$f_3(x) = x_1 \wedge x_2 \wedge \overline{x_3}$$

The global interaction graph of f and the asynchronous state graph of f are:

$G(f) =$ 

$\Gamma(f) =$ 

$G(f)$ has a positive circuit of length 2 and a positive circuit of length 3. If $x = 111$ or 110 then $\Gamma(f)[x] = \mathbb{B}^I$ so $Gf[\Gamma(f)[x]] = G(f)$ and we deduce that both positive circuits are functional of type 3. However, f has no type-1-functional positive circuits. Indeed, for all $x \in \mathbb{B}^I$, if $Gf(x)$ contains the arc

from 2 *to* 3 *(resp. from* 3 *to* 2*) then* $x_1 = 1$ *(resp.* $x_1 = 0$*), so* $Gf(x)$ *cannot contain these two arcs. Thus the positive circuit of length 2 is not functional of type 1. Similarly, for all* $x \in \mathbb{B}^I$*, if* $Gf(x)$ *contains the arc from* 1 *to* 2 *(resp. from* 2 *to* 3*) then* $x_3 = 1$ *(resp.* $x_3 = 0$*), so* $Gf(x)$ *cannot contain these two arcs. Thus the positive circuit of length 3 is not functional of type 1.*

The following example gives the same conclusion for negative circuits.

Example 5 $I = \{1, 2, 3\}$ *and* $f : \mathbb{B}^I \to \mathbb{B}^I$ *is defined by:*

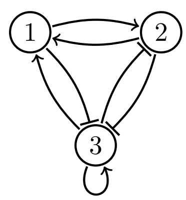
$$f_1(x) = x_2 \wedge x_3$$

$$f_2(x) = x_1 \wedge \overline{x_3}$$

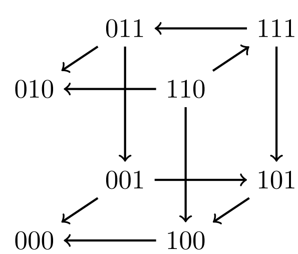
$$f_3(x) = \overline{x_1} \wedge \overline{x_2} \wedge x_3$$

The global interaction graph of f *and the asynchronous state graph of* f *are:*

$G(f) =$



$\Gamma(f) =$



$G(f)$ *has a negative circuit of length 2 and a negative circuit of length 3. If* $x = 110$ *then* $\Gamma(f)[x] = \mathbb{B}^I$ *so* $Gf[\Gamma(f)[x]] = G(f)$ *and we deduce that both negative circuits are functional of type 3. However,* f *has no type-1-functional negative circuits. Indeed, for all* $x \in \mathbb{B}^I$*, if* $Gf(x)$ *contains the arc from* 1 *to* 3 *(resp. from* 3 *to* 1*) then* $x_2 = 0$ *(resp.* $x_2 = 1$*), so* $Gf(x)$ *cannot contain these* *two arcs. Thus the negative circuit of length 2 cannot be functional of type 1. Similarly, for all $x \in \mathbb{B}^I$, if $Gf(x)$ contains the arc from 1 to 2 (resp. from 2 to 3) then $x_3 = 0$ (resp. $x_3 = 1$), so $Gf(x)$ cannot contain these two arcs. Thus the positive circuit of length 3 cannot be functional of type 1.*

6 Functionality of type 4

Functionality of type 4, the last considered here, is a relaxation of type-1- and type-3-functionalities.

Definition 4 *Let C be a circuit of $G(f)$ and $x \in \mathbb{B}^I$. C is* **functional of type 4 at x** *if $C \subseteq G(f)(\Gamma(f)[x])$. C is* **functional of type 4** *if it is functional of type 4 for at least one $x \in \mathbb{B}^I$.*

Proposition 3 *If C is functional of type 1 or 3 at x, then C is functional of type 4 at x.*

Proof Let $X = \Gamma(f)[x]$. Since $x \in X$ we have $Gf(x) \subseteq Gf(X)$, so if C is functional of type 1 at x then it is functional of type 4 at x. Then, since $Gf[X] \subseteq Gf(X)$, if C is functional of type 3 at x then it is functional of type 4 at x. $\square$

From this proposition, Theorem 2 and Theorem 4 we obtain:

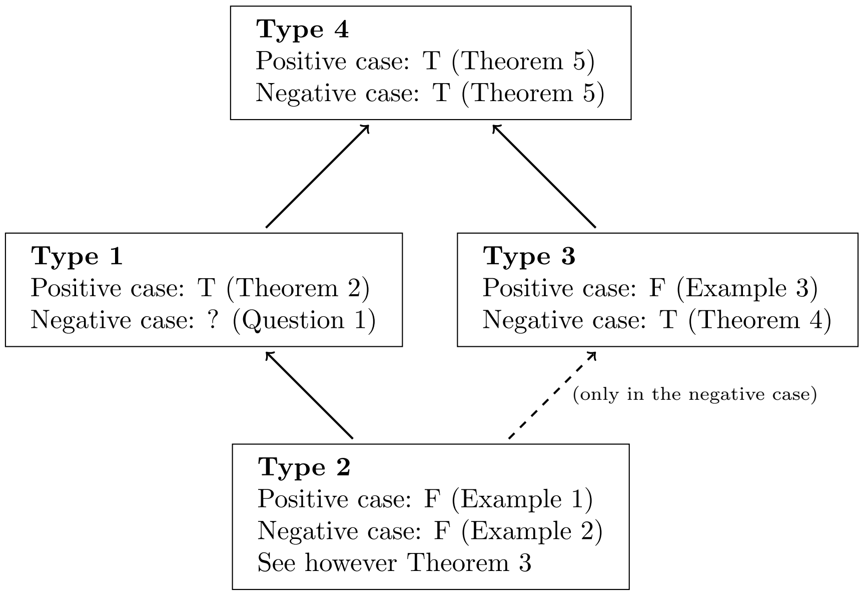
Theorem 5 (Thomas' rules - type-4-functional circuits) *If f has no functional positive circuits of type 4 then $\Gamma(f)$ has a unique attractor, and if*

f has no functional negative circuits of type 4 then $\Gamma(f)$ has no cyclic attractors.

Note that a positive answer to Question 1 would provide a strong generalization of the second assertion of this theorem. Note also that Example 3 shows that, in the positive and negative cases, functionality of type 4 does not imply functionality of type 3: In this example f has type-1-functional positive and negative circuits, thus it has type-4-functional positive and negative circuits, but no type-3-functional circuits. Finally note that Examples 4 and 5 shows that, in the positive and negative cases, functionality of type 4 does not imply functionality of type 1 (and thus it does not imply functionality of type 2): In Example 4 (resp. Example 5), f has type-3-functional positive (resp. negative) circuits, thus it has type-4-functional positive (resp. negative) circuits, but no type-1-functional positive (resp. negative) circuits.

7 Summary

In the following diagram, there is an arrow from a "box type k" to a "box type l" if and only if functionality of type k of a circuit C implies functionality of C of type l; there is a dashed arrow if and only if this implication holds only for negative circuits. In each "box type k", the mention "Positive case: T (resp. F)" means that functionality of type k of a positive circuit is necessary (resp. not necessary) for the presence of multiple attractors. The mention "Negative case: T (resp. F)" means that functionality of type k of a negative circuit is necessary (resp. not necessary) for the presence of a cyclic attractor.



8 Discussion

Recall the starting point: A positive (resp. negative) circuit is said functional when it "generates" multiple attractors (resp. a cyclic attractor), but it is rather difficult to formalize the underlying meaning of "generate". The approach presented here consists in exhibiting necessary conditions − on the functioning of the interactions of a circuit − for the presence of multiple attractors (positive case) or cyclic attractors (negative case). Then we obtain weak notions of functionality. For instance, Theorem 2 states that in the absence of type-1-functional positive circuit, there are no multiple attractors. The set of all type-1-functional positive circuits can then be seen as "responsible" for the presence of multiple attractors, but this "responsibility" cannot be assigned to one particular circuit.

All the proposed notions of functionality are based on functionality of an arc: A positive (resp. negative) arc from j to i is said functional at point x if $f_{ij}(x)$ is positive (resp. negative); this functionality is then "visible" between the adjacent points x and $\overline{x}^j$. A circuit is functional of type 1 when all its arcs are functional at the same point (this functionality may be called local or punctual), and it is functional of type 2 if all its arcs are functional in all points of a sub-cube of $\mathbb{B}^I$ (Proposition 1). A circuit is said functional of type 4, if each arc is functional somewhere in the set of states reachable from a given point. If in addition, the adjacent points revealing the functionality of each arc belong to this set, then the circuit is functional of type 3.

An "ideal" notion of functionality should correspond to conditions, as strong as possible, that work in both positive and negative cases (*i.e.* that are necessary for multiple attractors in the positive case, and for cyclic attractors in the negative case). As shown by the previous diagram, the only functionality working in both cases is of type 4. Unfortunately, it is the weakest type of functionality proposed here. Type 3 is stronger but it works only in the negative case, and the type 1, which is stronger too, is proved to work only in the positive case (the negative case remains an open question). Type 2, which is the strongest one, works in both cases only under very strong conditions on f.

Type 1 is the strongest working in the positive case, and a positive answer to Question 1, showing that this type works also in the negative case, would lead to a satisfactory notion of functionality. However, while all the theorems have natural extensions in the non Boolean discrete case, Question 1 has a negative answer in the non Boolean discrete case [13]. A positive answer to the question would also lead to a nice proof of Theorem 1: The uniqueness of the fixed point would be given by the positive case, and the existence by the negative case.

We addressed the functionality of circuits in a particular way by focusing on asynchronous Boolean networks with the associations positive circuit / multiple attractors and negative circuit / cyclic attractor. We choose this setting because it led to a large number of results about Thomas' ideas. Another way to address the functionality of a circuit would consist in looking for consequences of suppression of this circuit. Several non-straightforward questions arise: How to suppress a circuit? By removing an arc? But which arc? And what would be the dynamical system resulting from the suppression of an arc?

Acknowledgment We are grateful to Mohamed Hedi Ben Amor, Claudine Chaouiya, Madalena Chaves, Eric Fanchon, Pedro Monteiro, Mathilde Noual, Elisabeth Remy, Paul Ruet, Sylvain Sené, Christophe Soulé, Laurent Tournier and Laurent Trilling for fruitful discussions and comments on this paper. Moreover, the work of J. Aracena was partially supported by FONDECYT project 1090549 and by BASAL project CMM, Universidad de Chile.

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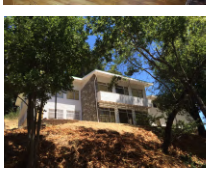

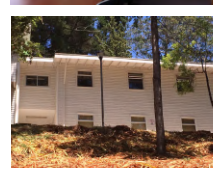

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