Elsevier Editorial System(tm) for Discrete Applied Mathematics
Manuscript Draft

Manuscript Number: DA45

Title: Relations between gene regulatory networks and cell dynamics in Boolean models

Article Type: Contribution

Keywords: Dynamical systems, Boolean networks, Gene regulatory graphs, Genetic regulation, Thomas' rules

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Abstract:
An asynchronous Boolean dynamics somehow represents the
joint evolution of a system of Boolean-discretized variables. In a biological context, this kind of objects is notably used to model the evolution of the expression levels of genes. From such a dynamics one can associated a (genetic) regulatory graph which summarizes the influence of each variable on another. It has been predicted by Thomas' rules, which were formally proved in particular in the Boolean framework, that some behaviors of a dynamics, in particular the presence of several stationary points, are possible only if the corresponding regulatory graph contains some specific features, notably feedback loops. In this work, we first give a necessary condition to the presence of a single stationary point in a dynamics and next derive a necessary condition for multi-stationarity, which is slightly stronger than the one required in the first Thomas' rule. Next we reverse the approach and study the properties of dynamics corresponding to particular kinds of regulatory graphs. Such types of results was already known for regulatory graphs reduced to simple circuits. We consider here regulatory graphs combining several circuits which all share a common component. We show the corresponding dynamics contains at most two stationary points and give more precise results in the case there are less than two positive circuits or less than two negative circuits in the regulatory graphs considered.

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Relations between gene regulatory networks and cell dynamics in Boolean models

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1. Introduction

The main motivation of this work arises from the study of biological regulatory networks. At a certain level of abstraction, the state of a living cell is modelized as a system of variables containing the quantitative levels of its components (let say essentially the genes/proteins). Biological knowledge indicates that the evolution of the expression level of a gene is regulated by the expression levels of some genes (its activators or repressors which can include itself)[1]. The whole set of regulations for all the genes is generally summarized by graph-type objects which can take into account more or less complex types of regulation like for instance joint influence. Here we focus on the simplest representation: the regulatory graph contains an edge from a gene to another if the first gene regulates the expression of the other in some condition (the levels of other genes being fixed, a modification of the level of the regulator, induces a change in the level of the second one). This edge is signed following the "sense" of this influence (activation or repression).

By assuming the system isolated, the joint dynamics of the set of variables is seen as just resulting of these regulations between genes. Relying regulatory graph properties with the whole dynamics of the system is a challenging problem which has been studied in different kinds of representations of the dynamics. Two great types of modelizations can be distinguished depending whether the variables are considered continuous or discrete [2, 3]. In the first case, the dynamics of the system obeys a differential equation of the form $\dot{x} = F(x)$ where x is a real-valued vector reporting the expression levels of the genes (see for instance [4]). The discrete case is quite different: since the number of the variables of the system is finite, considering a classic dynamical system always leads to trivial dynamics (ultimately periodic) which cannot capture all the diversity of living cells. The object we work with can be seen as a state space discretization of a continuous model defined as in [4]. This discretized dynamics is summarized by the so-called asynchronous dynamical graph [5] in which there is an edge between two discretized states if the trajectory of a point x in the continuous dynamics passes from the subset corresponding to the first discretized state to the subset corresponding to the second one. Since the system still evolves continuously in time, we neglect the case where two events occur simultaneously. Therefore, in an asynchronous dynamical graph, only edges connecting two configurations differing in a single variable are considered.

For all types of modelization there are generic ways, derived from biological points of view, to associate a regulatory graph to a given dynamics. Famous examples of connection from the dynamical behavior of the system to some regulatory graph properties are the Thomas' rules [6] which can be stated as follows:

1. a necessary condition for multistability (*i.e.* the existence of several stationary points in the dynamics) is the presence of a positive circuit in the regulatory graph,
2. a necessary condition for the existence of an attractive cycle in the dynamics is the existence of a negative circuit.

From a biological point of view, the first rule corresponds to a basic case of cell differentiation and the second one to homeostasis or periodic behavior. These rules have been proved true in several frameworks: in piecewise linear [7], continuous [8, 9, 4] and discrete (Boolean and multivalued) [10, 11, 5] dynamical systems.

In the present work we deal with the same Boolean formalism as in [5]. We first give a necessary condition for the presence of a single stationary point from which we derive a necessary condition for the existence of several stationary points in the dynamics, slightly stronger than the one stated in the first Thomas' rule. Next we study what the knowledge of the regulatory graph can say about the number of stationary points in a corresponding dynamics. It was shown the stationary points of a dynamics are completely determined in the case where its regulatory graph is a simple circuit. To put it explicitly, if the regulatory graph is a positive circuit, there are two stationary points in the corresponding dynamics while there is no stationary point in dynamics having just negative feedback loops as regulatory graphs [12]. We consider here regulatory graphs which combine several circuits with the property all these circuits share a common component. Though the first graphs studied, called flower-graphs, have a very simple structure, we show, by using two transformations we introduce, they can be seen as backbones of the general class of regulatory graphs combining several circuits through a particular component (we call hub-graphs). A first result is that the corresponding dynamics contain at most two stationary points. We give more precise results when the number of positive or negative circuits of the regulatory graph is smaller than two. Nevertheless the behavior of a dynamics corresponding to a regulatory graph with both more than two positive circuits and more than two negative circuits, cannot be predicted. In particular it can contained zero, one or two stationary points.

The paper is organized as follows. In Section 2 we introduce the basic definitions and notations used in the paper and present formally how regulatory graphs or networks are associated to dynamics. Section 3 is devoted to the stationarity phenomena. In particular we study the conditions in which a unique stationary point can arise and give a stronger necessary condition for multistationarity. In Section 4, we start by studying the behavior of a component influenced by several regulators and apply these results to dynamics associated to very simple regulatory graphs, flower-graphs, while containing several circuits. Then we introduce two transformations over asynchronous dynamics which conserve both the number of stationary points and the essential features of the corresponding regulatory graphs, notably the number and the signs of the circuits. These transformations are next used to transpose the results about flower-graphs onto hub-graphs. We give a short conclusion in the last section.

2. Definitions and notations

Let $a \in \{\mathtt{0}, \mathtt{1}\}$. We define $\overline{a}$ by $\overline{\mathtt{0}} = \mathtt{1}$ and $\overline{\mathtt{1}} = \mathtt{0}$. For a finite set A, the notation $\#A$ designs the cardinal of A.

In the following $\mathcal{C}$ designs a finite set of elements called *components* (*genes* in biological applications). The elements of $\{0,1\}^{\mathcal{C}}$ are called the *configurations* of $\mathcal{C}$. One can think about $\mathcal{C}$ as a set of random variables taking values in $\{0,1\}$ and about a configuration as a realization of this set of variables.

Let $A \subset \mathcal{C}$ and $x \in \{0,1\}^{\mathcal{C}}$. We note $\overline{x}^A$, the element of $\{0,1\}^{\mathcal{C}}$ defined for all $\beta \in \mathcal{C}$ by $\overline{x}^A_\beta = \overline{x_\beta}$ if $\beta \in A$ and $\overline{x}^A_\beta = x_\beta$ otherwise. For a component $\alpha \in \mathcal{C}$, the notation $\overline{x}^\alpha$ stands for $\overline{x}^{\{\alpha\}}$.

Let x and y be two configurations. We note $\Delta(x,y)$ the subset of components differentiating x and y, formally: $\Delta(x,y) = \{\alpha \in \mathcal{C} \mid x_\alpha \neq y_\alpha\}$. Basically, we have $x = \overline{y}^{\Delta(x,y)}$ and $y = \overline{x}^{\Delta(x,y)}$.

2.1. Asynchronous Boolean dynamics

An *asynchronous Boolean dynamics* is an oriented graph represented by a pair $\langle \mathcal{C}, \mathcal{E} \rangle$ where $\mathcal{C}$ is a finite set of components and $\mathcal{E}$ is the set of the edges of the graph. The set of vertices of $\langle \mathcal{C}, \mathcal{E} \rangle$ is $\{0,1\}^{\mathcal{C}}$. The set $\mathcal{E}$ is a subset of $\{(x, \overline{x}^\alpha) \mid x \in \{0,1\}^{\mathcal{C}} \text{ and } \alpha \in \mathcal{C}\}$ (the "asynchronous" character). Since each edge has the form $(x, \overline{x}^\alpha)$, α will be referred as the component of the edge $(x, \overline{x}^\alpha)$. In [5], the authors introduce a Boolean function $f_{\langle \mathcal{C}, \mathcal{E} \rangle}$ from $\{0,1\}^{\mathcal{C}}$ to $\{0,1\}^{\mathcal{C}}$ which somehow summarizes the asynchronous Boolean dynamics $\langle \mathcal{C}, \mathcal{E} \rangle$: for all $x \in \{0,1\}^{\mathcal{C}}$ and all $\alpha \in \mathcal{C}$, $f_{\langle \mathcal{C}, \mathcal{E} \rangle}(x)$ is defined by $f_{\langle \mathcal{C}, \mathcal{E} \rangle}(x)_\alpha = \overline{x_\alpha}$ if $(x, \overline{x}^\alpha) \in \mathcal{E}$ and $f_{\langle \mathcal{C}, \mathcal{E} \rangle}(x)_\alpha = x_\alpha$ otherwise.

A configuration x is said *stationary* (resp. *unreachable*) in $\langle \mathcal{C}, \mathcal{E} \rangle$ if there is no component $\alpha \in \mathcal{C}$ such that $(x, \overline{x}^\alpha) \in \mathcal{E}$ (resp. $(\overline{x}^\alpha, x) \in \mathcal{E}$).

A *path* in $\langle \mathcal{C}, \mathcal{E} \rangle$ is a sequence of vertices such that from each vertex of the sequence there is an edge of $\mathcal{E}$ to the next vertex in the sequence. A *cycle* is a path where the starting vertex is also the ending vertex.

2.2. From dynamics to regulatory graph

The *regulatory graph* of a given asynchronous Boolean dynamics $\langle \mathcal{C}, \mathcal{E} \rangle$ is an oriented graph $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ where the set of vertices is $\mathcal{C}$ and the edges are signed, *i.e.* labelled by $\{+,-\}$. Following the way of [5], we define the set of edges of $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ by putting an edge from α to β if there is a configuration $x \in \{0,1\}^{\mathcal{C}}$ such that $f_{\langle \mathcal{C}, \mathcal{E} \rangle}(x)_\beta \neq f_{\langle \mathcal{C}, \mathcal{E} \rangle}(\overline{x}^\alpha)_\beta$. Component β is said regulated by α, and α is a regulator of β. This edge from α to β is positive if $x_\alpha = f_{\langle \mathcal{C}, \mathcal{E} \rangle}(x)_\beta$ and negative otherwise.

The set of edges of $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ can be equivalently defined directly from the asynchronous Boolean dynamics. In the case where $\alpha \neq \beta$, we have $\alpha \xrightarrow{s} \beta$ if there exists a configuration $x \in \{0,1\}^{\mathcal{C}}$ such that $(x, \overline{x}^\beta) \in \mathcal{E}$, $(\overline{x}^\alpha, \overline{x}^{\{\alpha,\beta\}}) \notin \mathcal{E}$ with $s = +$ if $x_\alpha \neq x_\beta$ and $s = -$ if $x_\alpha = x_\beta$. In the case of auto-regulation (*i.e.* where $\alpha = \beta$), we have a positive auto-regulation $\alpha \overset{+}{\circlearrowleft}$ if there is a configuration x such that both $(x, \overline{x}^\alpha) \notin \mathcal{E}$ and $(\overline{x}^\alpha, x) \notin \mathcal{E}$ and a negative auto-regulation $\alpha \overset{-}{\circlearrowleft}$ if both $(x, \overline{x}^\alpha) \in \mathcal{E}$ and $(\overline{x}^\alpha, x) \in \mathcal{E}$.

A component β can be regulated by a component α in more than one way: we can have both $\alpha \xrightarrow{+} \beta$ and $\alpha \xrightarrow{-} \beta$ in $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$. In this last case we say the regulation of α on β is *multiple*. Conversely if only one signed edge among $\alpha \xrightarrow{+} \beta$ and $\alpha \xrightarrow{-} \beta$ belongs to $\mathcal{G}_{\langle \mathcal{C},\mathcal{E}\rangle}$, the regulation of α on β is said *univocal*.

Let us remark that under this definition a component α can be not regulated at all. This is the case when for all configurations $x \in \{\mathtt{0},\mathtt{1}\}^{\mathcal{C}}$, we have $(x, \overline{x}^{\alpha}) \notin \mathcal{E}$ if $x_\alpha = \mathtt{0}$ (resp. if $x_\alpha = \mathtt{1}$) and $(x, \overline{x}^{\alpha}) \in \mathcal{E}$ if $x_\alpha = \mathtt{1}$ (resp. if $x_\alpha = \mathtt{0}$). Such a component α is said to be an *input* of $\langle \mathcal{C},\mathcal{E}\rangle$.

For a component α we note $\mathcal{I}(\alpha)$ and $\mathcal{O}(\alpha)$ the set of components which regulate α and the set of components which are regulated by α respectively. We have $\mathcal{I}(\alpha) = \{\beta \in \mathcal{C} \mid \beta \xrightarrow{-} \alpha \text{ or } \beta \xrightarrow{+} \alpha\}$ and $\mathcal{O}(\alpha) = \{\beta \in \mathcal{C} \mid \alpha \xrightarrow{-} \beta \text{ or } \alpha \xrightarrow{+} \beta\}$.

Naturally *path* and *cycle* have the same significations as precedently. The *sign* of a path is defined as the product of the signs of its edges. Basically a path is positive if and only if it contains an even number of negative edges.

A *circuit* of the regulatory graph is a cycle in which vertices occur only once. René Thomas has conjectured that some behaviors are closely related to the presence of circuits in the regulatory graph [6, 13, 14].

3. Stationarity

Lemma 1. *Let $\langle \mathcal{C},\mathcal{E}\rangle$ be an asynchronous Boolean dynamics, a configuration $x \in \{\mathtt{0},\mathtt{1}\}^{\mathcal{C}}$, a subset $\mathcal{D} \subseteq \mathcal{C}$ and a map $\mathrm{p} : \mathcal{D} \to \mathcal{D}$. If for all $\delta \in \mathcal{D}$, we have $\mathrm{p}(\delta) \xrightarrow{s} \delta$ with $s = -$ if $x_\delta \neq x_{\mathrm{p}(\delta)}$ and $s = +$ otherwise, for each component $\alpha \in \mathcal{D}$ there exist a component $\beta \in \mathcal{D}$ occurring in a positive circuit involving only components of $\mathcal{D}$ and a path from β to α in $\mathcal{G}_{\langle \mathcal{C},\mathcal{E}\rangle}$.*

Proof. Let $\alpha \in \mathcal{D}$ and consider the sequence $(\mathrm{p}^k(\alpha))_{k\geq 0}$ of components of $\mathcal{D}$. Since $\mathcal{D}$ is finite, there are an integer j and a positive integer ℓ such that $\mathrm{p}^j(\alpha) = \mathrm{p}^{j+\ell}(\alpha)$ and $\#\{\mathrm{p}^{j+k}(\alpha) \mid 0 \leq k < \ell\} = \ell$ (*i.e.* a component does not occur more than once in the finite sequence $\mathrm{p}^j(\alpha)$, $\mathrm{p}^{j+1}(\alpha)$, $\ldots$, $\mathrm{p}^{j+\ell-1}(\alpha)$). By setting $\beta = \mathrm{p}^j(\alpha)$ there is a path from β to α and we have a circuit $\mathrm{p}^0(\beta)$, $\mathrm{p}^1(\beta)$ $\ldots$, $\mathrm{p}^\ell(\beta)$. Moreover the number of times we observe a negative edge in this circuit is necessary even, since for $0 \leq i < \ell$, $\mathrm{p}^i(\beta) \xrightarrow{-} \mathrm{p}^{i+1}(\beta)$ if $x_{\mathrm{p}^i(\beta)} \neq x_{\mathrm{p}^{i+1}(\beta)}$. This gives the conclusion of the lemma.

Theorem 1. *Let $\langle \mathcal{C},\mathcal{E}\rangle$ be an asynchronous Boolean dynamics. If $\langle \mathcal{C},\mathcal{E}\rangle$ contains a stationary configuration then for all components $\alpha \in \mathcal{C}$, one of the following assertions holds:*

1. *α is an input of $\mathcal{G}_{\langle \mathcal{C},\mathcal{E}\rangle}$,*
2. *α occurs in a positive circuit of $\mathcal{G}_{\langle \mathcal{C},\mathcal{E}\rangle}$,*
3. *there exists a component $\beta \in \mathcal{C}$ verifying one of the two preceding assertions and a path from β to α in $\mathcal{G}_{\langle \mathcal{C},\mathcal{E}\rangle}$.*

Proof. We assume that x is a stationary configuration of $\langle \mathcal{C},\mathcal{E}\rangle$. We have $(x, \overline{x}^{\gamma}) \notin \mathcal{E}$ for all $\gamma \in \mathcal{C}$.

Let α be a component of $\mathcal{C}$. If α is an input, Assertion 1 holds. Otherwise there exists at least a configuration u with $u_\alpha = x_\alpha$ such that $(u, \overline{u}^{\alpha}) \in \mathcal{E}$. This

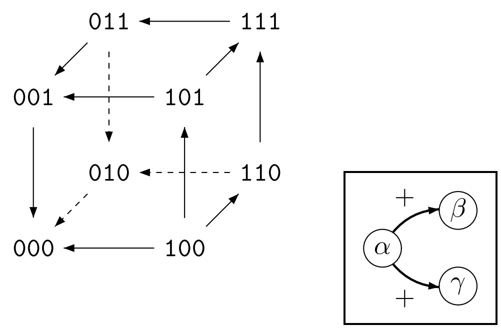

Figure 1: An asynchronous Boolean dynamics with a stationary state 000 (configurations are displayed following the order $\alpha\beta\gamma$). Its corresponding regulatory graph contains an input α regulating the components β and γ.

configuration u can be written as $\overline{x}^D$ where $D = \Delta(x, u)$ (remark that $\alpha \notin D$). Possibly by replacing D by one of its subset, one can assume that for all $\gamma \in D$, $(\overline{x}^{D\setminus\{\gamma\}}, \overline{x}^{D\setminus\{\gamma\}\cup\{\alpha\}}) \notin \mathcal{E}$ and $(\overline{x}^D, \overline{x}^{D\cup\{\alpha\}}) \in \mathcal{E}$. Since $(x, \overline{x}^\alpha) \notin \mathcal{E}$, the set D such defined cannot be empty. One can choose a component γ in D such that $\gamma \xrightarrow{s} \alpha$, with, by definition, $s = -$ if $\overline{x}^D_\gamma = \overline{x}^D_\alpha$ and $s = +$ otherwise. From $\gamma \in D$ and $\alpha \notin D$, we get $\overline{x}^D_\gamma \neq x_\gamma$ and $\overline{x}^D_\alpha = x_\alpha$. It comes $s = -$ if $x_\gamma \neq x_\alpha$ and $s = +$ otherwise.

In summary, one can associate to all $\alpha \in \mathcal{C}$ which is not an input, a component $\mathrm{p}(\alpha)$ such that $\mathrm{p}(\alpha) \xrightarrow{s} \alpha$ where $s = -$ if $x_\alpha \neq x_{\mathrm{p}(\alpha)}$. For a component $\alpha \in \mathcal{C}$, let us consider the sequence $(\mathrm{p}^i(\alpha))_{i\geq 0}$. For all k such that $\mathrm{p}^k(\alpha)$ is defined, there is by construction a path from $\mathrm{p}^k(\alpha)$ to α in $\mathcal{G}_{\langle\mathcal{C},\mathcal{E}\rangle}$. We have to consider two possibilities:

- there is an integer k such that $\mathrm{p}^k(\alpha)$ is an input ($\mathrm{p}^\ell(\alpha)$ is then undefined for $\ell > k$). The component $\mathrm{p}^k(\alpha)$ verifies Assertion 1 which ends the proof with the preceding remark.

- $\mathrm{p}^k(\alpha)$ is defined for all integers k and p is a map from $\{\mathrm{p}^k(\alpha) \mid k \in \mathbb{N}\}$ to $\{\mathrm{p}^k(\alpha) \mid k \in \mathbb{N}\}$. Lemma 1 allows us to the conclude.

Figures 1 and 2 illustrate the situations reported by Theorem 1.

Remark 1. *If $\langle\mathcal{C},\mathcal{E}\rangle$ is an input-free asynchronous Boolean dynamics having a stationary configuration then $\mathcal{G}_{\langle\mathcal{C},\mathcal{E}\rangle}$ contains a positive circuit.*

The ideas of Theorem 1 can be applied to give a short and self-contained proof of the first Thomas' rule in the Boolean framework. This rule was first proved in this framework by Remy *et al.* [5]. Their proof was based upon a result from [15] about the discrete Jacobian of a Boolean function applied to $f_{\langle\mathcal{C},\mathcal{E}\rangle}$. Using Lemma 1 leads finally to a necessary condition stronger than the one required in the first Thomas' rule.

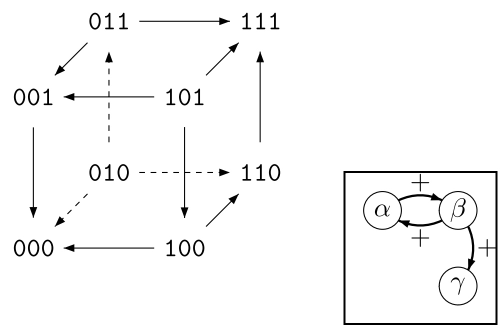

Figure 2: An asynchronous Boolean dynamics with stationary states 000 and 111 (configurations are displayed following the order $\alpha\beta\gamma$). Its corresponding regulatory graph contains a positive circuit (α, β) and β regulates γ.

Theorem 2. *Let $\langle \mathcal{C}, \mathcal{E} \rangle$ be an asynchronous Boolean dynamics. If $\langle \mathcal{C}, \mathcal{E} \rangle$ contains two stationary configurations x and y then for each component $\alpha \in \Delta(x, y)$ there exist a component $\beta \in \Delta(x, y)$ occurring in a positive circuit involving only components of $\Delta(x, y)$ and a path from α to β in $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$. In particular $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ contains at least a positive circuit involving a subset of $\Delta(x, y)$.*

Proof. Let x and y be two stationary configurations. The arguments of this proof are essentially the same as for Theorem 1: we show there is a map p from $\Delta(x, y)$ to $\Delta(x, y)$ satisfying the assumption needed by Lemma 1. For all $\alpha \in \Delta(x, y)$, $x_\alpha \neq y_\alpha$ and we have two possibilities:

1. $(\overline{y}^\alpha, y) \notin \mathcal{E}$,
2. $(\overline{y}^\alpha, y) \in \mathcal{E}$.

In the first case there is a positive auto-regulation over α since we have also $(y, \overline{y}^\alpha) \notin \mathcal{E}$ (for the stationarity of y) and we set $\mathrm{p}(\alpha) = \alpha$.

Let us assume we are in the second case. Since $(\overline{y}^\alpha, y) \in \mathcal{E}$ there is a subset D of $\Delta(x, y)$ not containing α such that for all $\gamma \in D$, $(\overline{x}^{D\setminus\{\gamma\}}, \overline{x}^{D\setminus\{c\}\cup\{\alpha\}}) \notin \mathcal{E}$ and $(\overline{x}^D, \overline{x}^{D\cup\{\alpha\}}) \in \mathcal{E}$. Thus one can choose a component $\mathrm{p}(\alpha) \in D \subseteq \Delta(x, y)$ such that $\mathrm{p}(\alpha) \xrightarrow{s} \alpha$ where $s = -$ if $x_\alpha \neq x_{\mathrm{p}(\alpha)}$ and $s = +$ otherwise.

Finally we have defined a map p such that for all components $\alpha \in \Delta(x, y)$ two possibilities arises:

1. if $\mathrm{p}(\alpha) = \alpha$ then $\alpha \overset{+}{\circlearrowleft}$ (in this case we have $x_\alpha = x_{\mathrm{p}(\alpha)}$),
2. if $\mathrm{p}(\alpha) \neq \alpha$ then $\mathrm{p}(\alpha) \xrightarrow{s} \alpha$ where $s = -$ if $x_\alpha \neq x_{\mathrm{p}(\alpha)}$ and $s = +$ otherwise.

In all cases the map p satisfies the hypothesis of Lemma 1 which give us the conclusion.

As said above, the necessary condition for multi-stationarity of Theorem 2 is stronger than the condition which just requires the existence of a positive circuit

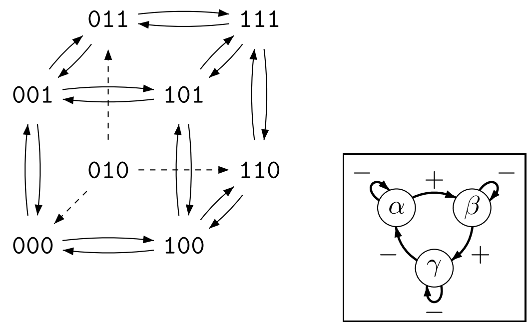

Figure 3: An asynchronous Boolean dynamics with an unreachable state 010 (configurations are displayed following the order $\alpha\beta\gamma$). Its corresponding regulatory graph contains only negative circuits.

stated in the first Thomas' rule. In particular, x and y being two stationary configurations, this condition involves all the components of $\Delta(x, y)$: even if all these components are not necessarily directly included in a positive circuit, they are always influenced through a chain of regulations by an element of a positive circuit (Figure 2).

Despite the fact that the situation can appear symmetrical, the existence of one or two unreachable configurations does not imply that the regulatory graph contains a positive circuit. Nevertheless the ideas used for studying stationary configurations can also be applied to show the existence of circuits but their signs cannot be specified. Let us apply some of the steps of the proof of Theorem 1 to this situation.

We assume that there is an unreachable configuration x (*i.e.* $(\overline{x}^{\gamma}, x) \notin \mathcal{E}$ for all $\gamma \in \mathcal{C}$). Let α be a component of $\mathcal{C}$. If α is not an input, there exists at least a configuration u with $u_\alpha = x_\alpha$ such that $(\overline{u}^{\alpha}, u) \in \mathcal{E}$. This configuration u can be written as $\overline{x}^{D}$ where $D = \Delta(x, u)$ (remark that again $\alpha \notin D$). Possibly by replacing D by one of its subset, one can assume that for all $\gamma \in D$, $(\overline{x}^{D\setminus\{\gamma\}\cup\{\alpha\}}, \overline{x}^{D\setminus\{\gamma\}}) \notin \mathcal{E}$ and $(\overline{x}^{D\cup\{\alpha\}}, \overline{x}^{D}) \in \mathcal{E}$. Since $(\overline{x}^{\alpha}, x) \notin \mathcal{E}$, the set D such defined cannot be empty. Thus one can choose a component γ in D such that $\gamma \xrightarrow{s} \alpha$, with, by definition, $s = -$ if $\overline{x}_{\gamma}^{D\cup\{\alpha\}} = \overline{x}_{\alpha}^{D\cup\{\alpha\}}$ and $s = +$ otherwise. Since $\overline{x}_{\gamma}^{D\cup\{\alpha\}} \neq x_\gamma$ and $\overline{x}_{\alpha}^{D\cup\{\alpha\}} \neq x_\alpha$, it comes $s = -$ if $x_\gamma = x_\alpha$ and $s = +$ otherwise.

In summary, one can associate to all $\alpha \in \mathcal{C}$ which is not an input, a component $\mathrm{p}(\alpha)$ such that $\mathrm{p}(\alpha) \xrightarrow{s} \alpha$ where $s = -$ if $x_\alpha = x_{\mathrm{p}(\alpha)}$. Unfortunately, this property is slightly different to the one required in Lemma 1 and even if it ensures the existence of a circuit, this one is not necessarily positive, as shown in the example of Figure 3.

4. Combination of circuits

4.1. Multiple regulators

Here we are interested in studying the behavior of a component η regulated by several components (under certain properties), that is describing for which configurations x, we have $(x, \overline{x}^\eta) \in \mathcal{E}$. Let $\langle \mathcal{C}, \mathcal{E} \rangle$ be an asynchronous Boolean dynamics and η a component of $\mathcal{C}$. We recall that $\mathcal{I}(\eta)$ designs the set of regulators of η. In particular if y and y' are two configurations of $\{0,1\}^{\mathcal{C}}$ such that $y_\alpha = y'_\alpha$ for all $\alpha \in \mathcal{I}(\eta) \cup \{\eta\}$ we have $(y, \overline{y}^\eta) \in \mathcal{E}$ if and only if $(y', \overline{y'}^\eta) \in \mathcal{E}$. We define the two following subsets of (partial) configurations of $\mathcal{I}(\eta) \cup \{\eta\}$:

$$
\begin{aligned}
E_0^\eta &= \{y \in \{0,1\}^{\mathcal{I}(\eta)\cup\{\eta\}} \mid y_\eta = 0 \text{ and } (x, \overline{x}^\eta) \notin \mathcal{E} \text{ for all } x \in \{0,1\}^{\mathcal{C}} \\
&\qquad \text{such that } x_\alpha = y_\alpha \text{ for all } \alpha \in \mathcal{I}(\eta) \cup \{\eta\}\} \\
E_1^\eta &= \{y \in \{0,1\}^{\mathcal{I}(\eta)\cup\{\eta\}} \mid y_\eta = 1 \text{ and } (x, \overline{x}^\eta) \notin \mathcal{E} \text{ for all } x \in \{0,1\}^{\mathcal{C}} \\
&\qquad \text{with } x_\alpha = y_\alpha \text{ for all } \alpha \in \mathcal{I}(\eta) \cup \{\eta\}\}
\end{aligned}
$$

Remark 2. *For a component $\alpha \neq \eta$, we have $\alpha \xrightarrow{s} \eta$ if there exists a configuration $x \in \{0,1\}^{\mathcal{I}(\eta)\cup\{\eta\}}$ such that either $x \in E_0^\eta$ and $\overline{x}^\alpha \notin E_0^\eta$, with $s = +$ if $x_\alpha = 1$ and $s = -$ otherwise, or $x \in E_1^\eta$ and $\overline{x}^\alpha \notin E_1^\eta$, with $s = +$ if $x_\alpha = 0$ and $s = -$ otherwise.*

If η is not auto-regulated then, for any $x \in \{0,1\}^{\mathcal{I}(\eta)\cup\{\eta\}}$, we have $x \in E_0^\eta$ if and only if $\overline{x}^\eta \notin E_1^\eta$. It comes that if η is not auto-regulated then a component α regulates η with sign s if and only if there exist a configuration $x \in \{0,1\}^{\mathcal{I}(\eta)\cup\{\eta\}}$ such that $x \in E_0^\eta$, $\overline{x}^\alpha \notin E_0^\eta$, $x_\alpha = 1$ if $s = +$ and $x_\alpha = 0$ otherwise.

If η is a component such that all the regulations on it are univocal, we define the configuration u^η of $\{0,1\}^{\mathcal{I}(\eta)\cup\{\eta\}}$ by:

- $u^\eta_\eta = 0$,
- for all $\alpha \in \mathcal{I}(\eta)_{\setminus\{\eta\}}$, $u^\eta_\alpha = 0$ if $\alpha \xrightarrow{+} \eta$ and $u^\eta_\alpha = 1$ otherwise.

Lemma 2. *Let $\langle \mathcal{C}, \mathcal{E} \rangle$ be an asynchronous Boolean dynamics and η a component of $\mathcal{C}$ which is not auto-regulated, not an input and such that all the regulations on it are univocal. We have $u^\eta \in E_0^\eta$ and $\overline{u^\eta} \in E_1^\eta$.*

Proof. Let us assume that $u^\eta \notin E_0^\eta$. Since η is not an input and is not auto-regulated, there exists a component $\alpha \neq \eta$ such that $\alpha \xrightarrow{s_{\alpha\eta}} \eta$. From Remark 2, it implies there exists a configuration $x \in \{0,1\}^{\mathcal{I}(\eta)\cup\{\eta\}}$ such that $x \in E_0^\eta$, $\overline{x}^\alpha \notin E_0^\eta$, $x_\alpha = 1$ if $s_{\alpha\eta} = +$ and $x_\alpha = 0$ otherwise. With the definition of η, we have $x_\alpha \neq u^\eta_\alpha$ thus $x \neq u^\eta$. From the fact $u^\eta \notin E_0^\eta$ and $x \in E_0^\eta$, there exists a configuration $y \in E_0^\eta$ and a component $\gamma \in \Delta(u^\eta, x) \subset \mathcal{I}(\eta)$ such that $y_\gamma = u^\eta_\gamma = 0$, $y \notin E_0^\eta$ and $\overline{y}^\gamma \in E_0^\eta$. From Remark 2, we get $\gamma \xrightarrow{-} \eta$ and a contradiction with the definition of u^η.

A symmetrical argument proves that $\overline{u^\eta} \in E_1^\eta$.

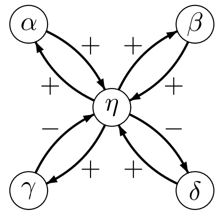

Figure 4: A regulatory flower-graph over components $\{\eta, \alpha, \beta, \gamma, \delta\}$ which contains two positive and two negative circuits.

Lemma 3. *Let $\langle \mathcal{C}, \mathcal{E} \rangle$ be an asynchronous Boolean dynamics and η a component of $\mathcal{C}$ which is not auto-regulated and such that all the regulations on it are univocal. For all $\mathcal{D} \subseteq \mathcal{I}(\eta)$, if $\overline{u^\eta}^{\mathcal{D}} \in E_0^\eta$ then, $\forall \mathcal{F} \subset \mathcal{D}$, $\overline{u^\eta}^{\mathcal{F}} \in E_0^\eta$.*

Proof. We know by Lemma 2 that $u^\eta \in E_0^\eta$; suppose $\overline{u^\eta}^{\mathcal{D}} \in E_0^\eta$ and $\overline{u^\eta}^{\mathcal{F}} \notin E_0^\eta$ with $\mathcal{F} \subset \mathcal{D} \subseteq \mathcal{I}(\eta)$. There exist a subset $\mathcal{F}'$ with $\mathcal{F} \subseteq \mathcal{F}' \subset \mathcal{D}$, and a component $\alpha \in \mathcal{D}_{\setminus \mathcal{F}'}$ such that $\overline{u^\eta}^{\mathcal{F}'} \notin E_0^\eta$ and $\overline{u^\eta}^{\mathcal{F}' \cup \alpha} \in E_0^\eta$. With Remark 2, this implies $\alpha \xrightarrow{+} \eta$ if $u_\alpha^\eta = 1$ and $\alpha \xrightarrow{-} \eta$ otherwise. This leads to a contradiction with the definition of u^η and the assumption that all the regulations on η are univocal.

Remark 3. *Let* f *be the Boolean function defined from $\{0,1\}^{\mathcal{I}(\eta)}$ to $\{0,1\}$ by* $\mathrm{f}(b) = 1$ *if $\overline{u^\eta}^{\mathcal{D}} \in E_0^\eta$ where $\mathcal{D} = \{\alpha \in \mathcal{I}(\eta) \mid b_\alpha = 1\}$. Lemma 3 means that* f *is a monotone Boolean function.*

It follows the number of possible behaviors of a component η univocally regulated, that is the number of possible sets E_0^η (and E_1^η), is closely related to the number of monotone Boolean functions over $\#\mathcal{I}(\eta)$ variables which is known as the $\#\mathcal{I}(\eta)^{\text{th}}$ Dedekind number [16]. Note that the number of possible behaviors with k regulators is smaller than the k^{th} Dedekind number: the sets E_0^η are constrained by the fact the regulation of each component has to be observed, thus not all the monotone Boolean functions over $\#\mathcal{I}(\eta)$ variables correspond to a set E_0^η. Relation between the number of possible dynamics behaviors and Dedekind numbers was informally pointed out in [17].

4.2. Flower-graphs

Definition 1. *A regulatory graph $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ is a* flower-graph *if there is a particular component $\eta \in \mathcal{C}$ such that $\mathcal{E} = \{\eta \overset{s_{\eta\alpha}}{\to} \alpha \mid \alpha \in \mathcal{C}_{\setminus \eta}\} \cup \{\alpha \overset{s_{\alpha\eta}}{\to} \eta \mid \alpha \in \mathcal{C}_{\setminus \eta}\}$ where $s_{\eta\alpha}, s_{\alpha\eta} \in \{-, +\}$ for all component $\alpha \in \mathcal{C}_{\setminus \eta}$.*

An example of flower-graph is pictured in Figure 4. Remark that in a flower-graph, the component η is not auto-regulated and all the regulations on η are univocal: Lemmas 2 and 3 apply on η.

Theorem 3. *Let $\langle \mathcal{C}, \mathcal{E} \rangle$ be an asynchronous Boolean dynamics. If $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ is a flower-graph then $\langle \mathcal{C}, \mathcal{E} \rangle$ contains at most two stationary configurations. In the particular case $\langle \mathcal{C}, \mathcal{E} \rangle$ does contain two stationary configurations, they are complementary. More precisely:*

1. *if $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ contains only positive circuits then $\langle \mathcal{C}, \mathcal{E} \rangle$ contains two stationary configurations;*
2. *if $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ contains only negative circuits then $\langle \mathcal{C}, \mathcal{E} \rangle$ has no stationary configuration;*
3. *if $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ contains a unique negative circuit and at least one positive circuit, then $\langle \mathcal{C}, \mathcal{E} \rangle$ contains at least one stationary configuration;*
4. *if $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ contains a unique positive circuit and at least one negative circuit, then $\langle \mathcal{C}, \mathcal{E} \rangle$ contains at most one stationary configuration.*

PROOF. Remark that for a dynamics $\langle \mathcal{C}, \mathcal{E} \rangle$ such that $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ is a flower-graph, we have $\mathcal{I}(\eta) \cup \{\eta\} = \mathcal{C}$ and in particular u^η is a configuration of $\mathcal{C}$.

Let v be the configuration of $\mathcal{C}$ defined by:

- $v_\eta = 0$,
- for all $\alpha \in \mathcal{C}_{\setminus \eta}$ we have $v_\alpha = 0$ if $s_{\eta,\alpha} = +$, and $v_\alpha = 1$ otherwise.

Since for all $\alpha \in \mathcal{C}_{\setminus \eta}$, η is the unique regulator of α, for all configuration $x \in \{0,1\}^{\mathcal{C}}$, we have $(x, \overline{x}^\alpha) \in \mathcal{E}$ if and only if $x_\alpha = x_\eta$ or if and only if $x_\alpha \neq x_\eta$, depending on the sign of the regulation of η over α. It follows the configurations v and $\overline{v}$ are the only configurations for which we have $(v, \overline{v}^\alpha) \notin \mathcal{E}$ and $(\overline{v}, \overline{v}^{\mathcal{C}_{\setminus \alpha}}) \notin \mathcal{E}$ for all components $\alpha \neq \eta$. Clearly, no other configuration can be stationary. If $v \in E_0^\eta$, we have $(v, \overline{v}^\eta) \notin \mathcal{E}$ and v is a stationary configuration. Symmetrically, if $\overline{v} \in E_1^\eta$, then $\overline{v}$ is stationary.

In the case where $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ contains only positive circuits, we have $v = u^\eta$ and $\overline{v} = \overline{u^\eta}$. Lemma 2 ensures both $v \in E_0^\eta$ and $\overline{v} \in E_1^\eta$. These two configurations are stationary and Assertion 1 is proved.

In the case where $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ contains only negative circuits, we have $v = \overline{u^\eta}^{\mathcal{C}_{\setminus \eta}}$ and $\overline{v} = \overline{u^\eta}^\eta$. Since η is not auto-regulated and $\overline{u^\eta} \in E_1^\eta$ (Lemma 2), we have $(\overline{u^\eta}^{\mathcal{C}_{\setminus \eta}}, \overline{u^\eta}) \in \mathcal{E}$ and v is not stationary. In the same way we have $(\overline{u^\eta}^\eta, u^\eta) \in \mathcal{E}$ which makes $\overline{v}$ not stationary and ends the proof of Assertion 2.

Let us assume we are in the case of Assertion 3, *i.e.* there is a unique negative circuit involving η and a component $\alpha \neq \eta$, as well as at least a positive circuit. We have $v = \overline{u^\eta}^\alpha$ and $\overline{v} = \overline{u^\eta}^{\mathcal{C}_{\setminus \alpha}}$. If we assume there is no stationary configuration, which occurs only if $v \notin E_0^\eta$ and $\overline{v} \notin E_1^\eta$, Lemma 3 implies that for all $\mathcal{D} \subset \mathcal{C}$ we have $\overline{u^\eta}^{\mathcal{D}} \in E_0^\eta$ if and only if $\alpha \notin \mathcal{D}$. In other words, we have $(x, \overline{x}^\eta) \in \mathcal{E}$ if and only if $x_\alpha \neq u_\alpha^\eta$. It implies that α is the unique component regulating η which contradicts the existence of a positive circuit.

Assertion 4 is proved in a symmetrical way.

A dynamics corresponding to a regulatory flower-graph which contains both more than two positive circuits and more than two negative circuits, may actually have zero, one or two stationary configurations. An example is given in

Figure 5 were we display three dynamics over the same set of five components. These three dynamics are all associated to the regulatory flower-graph displayed in Figure 4 and contain respectively zero, one and two stationary configurations.

4.3. Two transformations

Definition 2. *Let $\langle \mathcal{C}, \mathcal{E} \rangle$ be an asynchronous Boolean dynamics such that there exists a component $\beta \in \mathcal{C}$ verifying:*

- $\mathcal{I}(\beta) = \{\alpha\}$ *where $\alpha \neq \beta$ and the regulation of α on β is univocal (its sign is noted $s_{\alpha\beta}$),*
- $\mathcal{O}(\beta) \cap \mathcal{O}(\alpha)$ *is either empty or equal to $\{\alpha\}$.*

The transformation T_β associates to $\langle \mathcal{C}, \mathcal{E} \rangle$ the asynchronous Boolean dynamics $\langle \mathcal{C}, \mathcal{E}' \rangle$ where the set of edge $\mathcal{E}'$ is derived from $\mathcal{E}$ in the following way:

- *for all $(x, \overline{x}^\gamma) \in \mathcal{E}$ with $\gamma \notin \mathcal{O}(\beta)_{\setminus\{\alpha\}}$, $(x, \overline{x}^\gamma) \in \mathcal{E}'$;*
- *for all $(x, \overline{x}^\gamma) \in \mathcal{E}$ with $\gamma \in \mathcal{O}(\beta)_{\setminus\{\alpha\}}$,*
  - *if $(\overline{x}^\beta, \overline{x}^{\{\beta,\gamma\}}) \in \mathcal{E}$ then $(x, \overline{x}^\gamma) \in \mathcal{E}'$;*
  - *if $(\overline{x}^\beta, \overline{x}^{\{\beta,\gamma\}}) \notin \mathcal{E}$ – since α does not regulate γ, it implies $(\overline{x}^\alpha, \overline{x}^{\{\alpha,\gamma\}}) \in \mathcal{E}$ and $(\overline{x}^{\{\alpha,\beta\}}, \overline{x}^{\{\alpha,\beta,\gamma\}}) \notin \mathcal{E}$ – then the edges $(x, \overline{x}^\gamma)$ and $(\overline{x}^\alpha, \overline{x}^{\{\alpha,\gamma\}})$ of $\mathcal{E}$ are replaced in $\mathcal{E}'$ by:*
    - *$(\overline{x}^\alpha, \overline{x}^{\{\alpha,\gamma\}})$ and $(\overline{x}^{\{\alpha,\beta\}}, \overline{x}^{\{\alpha,\beta,\gamma\}})$ if $s_{\alpha\beta} = +$ and $x_\alpha \neq x_\beta$ or if $s_{\alpha\beta} = -$ and $x_\alpha = x_\beta$;*
    - *$(x, \overline{x}^\gamma)$ and $(\overline{x}^\beta, \overline{x}^{\{\beta,\gamma\}})$ otherwise.*

Lemma 4. *The regulatory graph $\mathcal{G}_{T_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)}$ is obtained from $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ by replacing each regulation of the form $\beta \xrightarrow{s} \gamma$ with $\gamma \in \mathcal{O}(\beta)_{\setminus\{\alpha\}}$ by a regulation $\alpha \xrightarrow{s_{\alpha\beta}s} \gamma$, the other regulations being unchanged.*

Proof. This is a direct consequence of Definition 2, and in particular of the way the set of edges of $T_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)$ is derived. Let consider $\beta \xrightarrow{s} \gamma$ with $\gamma \neq \alpha$, a regulation of $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$. By definition this regulation occurs if and only if there is a configuration $x \in \{0, 1\}^\mathcal{C}$ such that $(x, \overline{x}^\gamma) \in \mathcal{E}$, $(\overline{x}^\beta, \overline{x}^{\{\beta,\gamma\}}) \notin \mathcal{E}$ and $x_\beta \neq x_\gamma$ if $s = +$ or $x_\beta = x_\gamma$ if $s = -$. Remark that we have also $(\overline{x}^\alpha, \overline{x}^{\{\alpha,\gamma\}}) \in \mathcal{E}$ and $(\overline{x}^{\{\alpha,\beta\}}, \overline{x}^{\{\alpha,\beta,\gamma\}}) \notin \mathcal{E}$ (for α does not regulate γ).

By considering the way the edges $(x, \overline{x}^\gamma)$ and $(\overline{x}^\alpha, \overline{x}^{\{\alpha,\gamma\}})$ of $\mathcal{E}$ are replaced in $\mathcal{E}'$, we get in all cases a regulation of the form $\alpha \xrightarrow{s_{\alpha\beta}s} \gamma$ in $\mathcal{G}_{T_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)}$ and the regulation of β on γ cannot anymore be observed over configurations x and $\overline{x}^\alpha$.

Lemma 5. *The regulatory graph $\mathcal{G}_{T_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)}$ contains the same number of positive (resp. negative) circuits as $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$.*

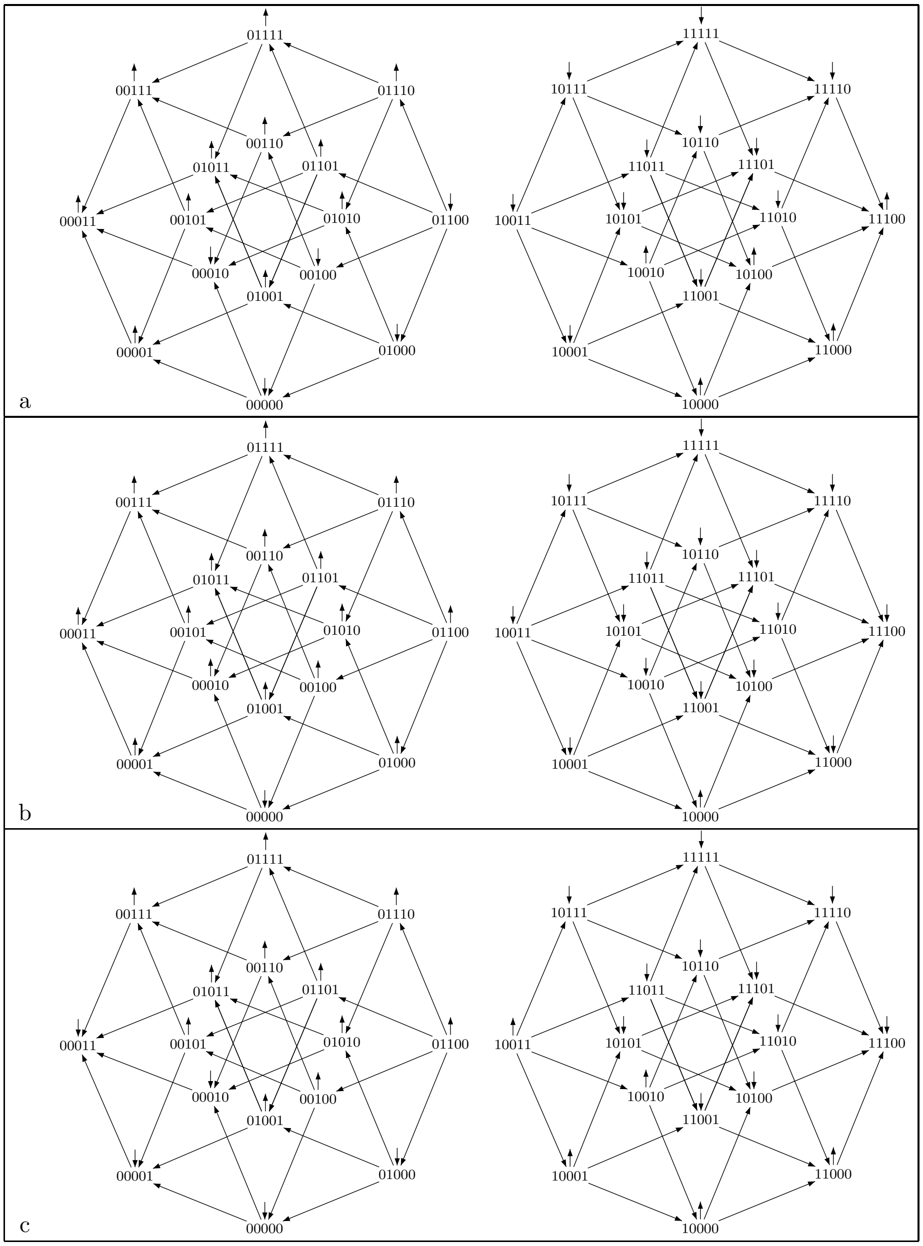

Figure 5: Three dynamics which all correspond the regulatory graph of Figure 4. Coordinates of configurations are displayed following the order $\eta\alpha\beta\gamma\delta$. We have $u^\eta = 00000$ and $v = 00011$. In order to make the pictures clearer, the edges $(x, \overline{x}^\eta)$ are figured by incoming or outgoing vertical arrows: an outgoing vertical arrow above x comes always with an incoming vertical arrow above $\overline{x}^\eta$ and indicates there is an edge $(x, \overline{x}^\eta)$. Dynamics (a) has no stationary configuration. Dynamics (b) has a single stationary configuration: $\overline{v}$. Dynamics (c) has two stationary configurations: v and $\overline{v}$.

PROOF. It is enough to remark that, since applying T_β on $\langle \mathcal{C}, \mathcal{E} \rangle$ requires $\mathcal{I}(\beta) = \{\alpha\}$, if β occurs in a circuit of $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$, it is necessary preceded by α. Then Lemma 4 shows that each regulatory circuit of $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ has a unique counterpart in $\mathcal{G}_{T_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)}$ which has the same sign and reciprocally.

Lemma 6. *A configuration $y \in \{0,1\}^{\mathcal{C}}$ is stationary in $\langle \mathcal{C}, \mathcal{E} \rangle$ if and only if y is stationary in $T_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)$.*

PROOF. Let y be a stationary configuration in $\langle \mathcal{C}, \mathcal{E} \rangle$. We have $(y, \overline{y}^\gamma) \notin \mathcal{E}$ for all $\gamma \in \mathcal{C}$. With the definition of $\langle \mathcal{C}, \mathcal{E}' \rangle = T_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)$, we cannot have $(y, \overline{y}^\delta) \in \mathcal{E}'$ if $\delta \notin \mathcal{O}(\beta)_{\setminus \{\alpha\}}$. Let $\gamma \in \mathcal{O}(\beta)_{\setminus \{\alpha\}}$. Let us first remark that since $\alpha \overset{s_{\alpha\beta}}{\to} \beta$ is the only regulation with β as target, both in $\langle \mathcal{C}, \mathcal{E} \rangle$ and $T_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)$, if y is stationary in $\langle \mathcal{C}, \mathcal{E} \rangle$, then we have either $y_\alpha = y_\beta$ with $s_{\alpha\beta} = +$ or $y_\alpha \neq y_\beta$ with $s_{\alpha\beta} = -$.

We have $(y, \overline{y}^\delta) \notin \mathcal{E}$. From Definition 2, the only conditions in which we could have $(y, \overline{y}^\delta) \in \mathcal{E}'$ should be $(\overline{y}^\beta, \overline{y}^{\{\beta,\delta\}}) \in \mathcal{E}$ and $s_{\alpha\beta} = +$ with $y_\alpha \neq y_\beta$ or $s_{\alpha\beta} = -$ with $y_\alpha = y_\beta$ which we showed not consistent with the stationarity of y.

Definition 3. *Let $\langle \mathcal{C}, \mathcal{E} \rangle$ be an asynchronous Boolean dynamics. Assume there exists a component $\beta \in \mathcal{C}$ such that $\mathcal{O}(\beta) = \emptyset$. The transformation P_β associates to $\langle \mathcal{C}, \mathcal{E} \rangle$ the asynchronous Boolean dynamics $\langle \mathcal{C}_{\setminus \{\beta\}}, \mathcal{E}' \rangle$ where $\mathcal{E}'$ is defined by: for all $x \in \{0,1\}^{\mathcal{C}_{\setminus \{\beta\}}}$ and $\gamma \in \mathcal{C}_{\setminus \{\beta\}}$, $(x, \overline{x}^\gamma) \in \mathcal{E}'$ if there is $y \in \{0,1\}^{\mathcal{C}}$ with $y_\delta = x_\delta$ for all $\delta \in \mathcal{C}_{\setminus \{\beta\}}$ and $(y, \overline{y}^\gamma) \in \mathcal{E}$.*

Lemma 7. *The regulatory graph $\mathcal{G}_{P_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)}$ is obtained from $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ by removing the vertex β. In particular it contains the same number of positive (resp. negative) circuits as $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$.*

PROOF. This lemma is a direct consequence of the fact that, since $\mathcal{O}(\beta) = \emptyset$, we have $(\overline{y}^\beta, \overline{y}^{\{\beta,\delta\}}) \in \mathcal{E}$ if and only if $(y, \overline{y}^\delta) \in \mathcal{E}$ for all component $\delta \neq \beta$.

Lemma 8. *Let y be a stationary configuration in $\langle \mathcal{C}, \mathcal{E} \rangle$. The (unique) configuration x of $P_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)$ which is such that $x_\delta = y_\delta$ for all $\delta \in \mathcal{C}_{\setminus \{\beta\}}$ is stationary. Reciprocally, if x is a stationary configuration in $P_\beta(\langle \mathcal{C}, \mathcal{E} \rangle)$, then at most one configuration among y and y' is stationary, where y and y' are the configurations of $\{0,1\}^{\mathcal{C}}$ defined by $y'_\delta = y_\delta = x_\delta$ for all $\delta \in \mathcal{C}_{\setminus \{\beta\}}$, $y'_\beta = 0$ and $y_\beta = 1$.*

PROOF. First assertion of the lemma comes with the same argument as the preceding lemma. The second one is a direct consequence from the fact that β is not auto-regulated ($\mathcal{O}(\beta)$ is assumed empty). Thus, for all x, we have either $(x, \overline{x}^\beta) \in \mathcal{E}$ or $(\overline{x}^\beta, x) \in \mathcal{E}$.

4.4. Hub-graphs

Definition 4. *A regulatory graph $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ is a* hub-graph *if*

1. *all the regulations of $\mathcal{G}_{\langle \mathcal{C}, \mathcal{E} \rangle}$ are univocal;*
2. *there is a particular component η, called the hub, such that:*

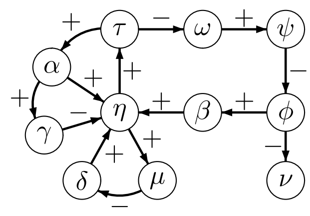

Figure 6: A regulatory hub-graph which contains two positive and two negative circuits and is related to the flower-graph displayed in Figure 4.

- *η is the only component which can have more than one regulator;*
- *for all components $\gamma \in \mathcal{C}$, there is a path from η to γ in $\mathcal{G}_{\langle \mathcal{C},\mathcal{E}\rangle}$;*
- *η is not auto-regulated.*

An example of hub-graph is displayed in Figure 6. Basically, a flower-graph is a hub-graph. The two preceding transformations allow us to associate to all hub-graphs some related flower-graphs.

Lemma 9. *Let $\langle \mathcal{C},\mathcal{E}\rangle$ be an asynchronous Boolean dynamics whose regulatory graph is a hub-graph. There exists a flower-graph $\langle \mathcal{C}',\mathcal{E}'\rangle$ such that*

- *$\mathcal{G}_{\langle \mathcal{C}',\mathcal{E}'\rangle}$ contains the same number of positive and negative circuits as $\mathcal{G}_{\langle \mathcal{C},\mathcal{E}\rangle}$.*
- *$\langle \mathcal{C}',\mathcal{E}'\rangle$ contains the same number of stationary configurations as $\langle \mathcal{C},\mathcal{E}\rangle$.*

Proof. Let $\mathcal{G}_{\langle \mathcal{C},\mathcal{E}\rangle}$ be a hub-graph and η its multi-regulated node. We define for all $\alpha \in \mathcal{C}$ the distance $\mathrm{d}_{\langle \mathcal{C},\mathcal{E}\rangle}(\eta,\alpha)$ by the number of edges of the shortest path from η to α in $\mathcal{G}_{\langle \mathcal{C},\mathcal{E}\rangle}$. With Definition 4, this distance is well defined for all components of $\mathcal{C}$.

Assume there is at least a component $\gamma \in \mathcal{C}$ such that $\mathrm{d}_{\langle \mathcal{C},\mathcal{E}\rangle}(\eta,\alpha) > 1$. It implies there exists a component $\beta \neq \eta$ in $\mathcal{O}(\eta)$ such that $\mathcal{O}(\beta)_{\setminus\{\eta\}} \neq \emptyset$. Since η is the only multi-regulated component, β is only regulated by η and we have $\mathcal{O}(\beta) \cap \mathcal{O}(\eta) = \emptyset$ (η is assumed not auto-regulated). Consequently, we can apply the transformation T_β to $\langle \mathcal{C},\mathcal{E}\rangle$. A direct consequence of Lemma 4 is that the corresponding regulatory graph obtained is still a hub-graph. Again from Lemma 4, it comes that for all $\alpha \in \mathcal{C}$, we have $\mathrm{d}_{T_\beta(\langle \mathcal{C},\mathcal{E}\rangle)}(\eta,\alpha) \leq \mathrm{d}_{\langle \mathcal{C},\mathcal{E}\rangle}(\eta,\alpha)$, and for at least a component δ (in particular for all components δ in $\mathcal{O}(\beta)_{\setminus\{\eta\}}$) we have $\mathrm{d}_{T_\beta(\langle \mathcal{C},\mathcal{E}\rangle)}(\eta,\alpha) < \mathrm{d}_{\langle \mathcal{C},\mathcal{E}\rangle}(\eta,\alpha)$.

The preceding considerations show that if we apply iteratively such transformations while there exists a component γ with $\mathrm{d}_{\langle \mathcal{C},\mathcal{E}\rangle}(\eta,\alpha) > 1$, we end up with a hub-graph such that each component different from η is at distance 1 to η (*i.e.* regulated by η). This situation leaves two possibilities for all $\gamma \neq \eta$: either $\mathcal{O}(\gamma) = \eta$, or $\mathcal{O}(\gamma) = \emptyset$. For all components γ in this second case, we apply the transformation P_γ and finally obtain a flower-graph.

By applying Lemmas 5 and 7, we prove that $\mathcal{G}_{\langle\mathcal{C},\mathcal{E}\rangle}$ and the final regulatory flower-graph have the same number of positive and negative circuits. The second item (the same number of stationary configurations) comes with Lemmas 6 and 8.

For instance, if we apply iteratively T_τ, T_α, T_ω, T_ψ, T_ϕ, T_μ and P_ν on a dynamics associated to the hub-graph of Figure 6, we obtain a dynamics corresponding to the flower-graph of Figure 4.

Finally Lemma 9 allows us to transpose the results of Theorem 3 to hub-graphs.

Corollary 1. *Let $\langle\mathcal{C},\mathcal{E}\rangle$ be an asynchronous Boolean dynamics. If $\mathcal{G}_{\langle\mathcal{C},\mathcal{E}\rangle}$ is a hub-graph then $\langle\mathcal{C},\mathcal{E}\rangle$ contains at most two stationary configurations. In the particular case $\langle\mathcal{C},\mathcal{E}\rangle$ does contain two stationary configurations, they are complementary. More precisely:*

1. *if $\mathcal{G}_{\langle\mathcal{C},\mathcal{E}\rangle}$ contains only positive circuits then $\langle\mathcal{C},\mathcal{E}\rangle$ contains two stationary configurations;*
2. *if $\mathcal{G}_{\langle\mathcal{C},\mathcal{E}\rangle}$ contains only negative circuits then $\langle\mathcal{C},\mathcal{E}\rangle$ has no stationary configuration;*
3. *if $\mathcal{G}_{\langle\mathcal{C},\mathcal{E}\rangle}$ contains a unique negative circuit and at least one positive circuit, then $\langle\mathcal{C},\mathcal{E}\rangle$ contains at least one stationary configuration;*
4. *if $\mathcal{G}_{\langle\mathcal{C},\mathcal{E}\rangle}$ contains a unique positive circuit and at least one negative circuit, then $\langle\mathcal{C},\mathcal{E}\rangle$ contains at most one stationary configuration.*

5. Conclusion

Knowing only the pairwise regulations between components appears to be insufficient to accurately predict properties of a dynamics, even in the case where all the regulations are univocal. It comes essentially from the fact that there are so many ways, growing roughly like the k^{th} Dedekind number, for k components to combine their respective influences when regulating a common target. If we have necessary conditions over the regulatory networks for specific dynamics features like the existence of stationary configuration(s), finding properties of regulatory graphs which comes always with given features of the corresponding dynamics is really a challenging problem, except in the case each component has at most one regulator, like in simple circuits. The main source of freedom for dynamics with regard to the underlying regulatory networks comes from components with multiple regulators and not from components regulating many targets.

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