Average sensitivity of nested canalizing multivalued functions

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Abstract

We prove that the average sensitivity of nested canalizing multivalued functions is bounded above by a constant. In doing so, we introduce a generalization of nested canalizing multivalued functions, which we call weakly nested canalizing, for which this upper bound holds.

1 Introduction

Boolean canalizing functions are Boolean functions $f : (\mathbb{Z}/2\mathbb{Z})^n \to \mathbb{R}$ such that at least one input variable, say x_i ($1 \leqslant i \leqslant n$), has a value $a = 0$ or 1 which determines the value of $f(x)$. Nested canalizing (NC) functions are a "recursive" version of canalizing functions: an NC function f is canalizing as above and moreover its restriction $f\restriction_{x_i \neq a}$ is itself NC.

These classes of Boolean functions have been introduced by Kauffman [3, 4] to formalize the "canalizing" behaviour observed in some discrete systems. This idea is also at the basis of Waddington's work in embryology: he described an epigenetic landscape guiding embryogenesis by canalizing configurations [19].

NC functions are particularly interesting because they have "low complexity". The average sensitivity $\mathbf{AS}(f)$ (also called influence or total influence) of a Boolean function f is a measure of its complexity. It can be defined in several ways, in particular via Fourier-Walsh analysis. It is related to spectral concentration, learning properties, decision tree complexity [10]. For arbitrary Boolean functions, $\mathbf{AS}(f) = \mathcal{O}(n)$, but some functions have significantly smaller average sensitivity. For NC functions, $\mathbf{AS}(f)$ is bounded above by a constant [7, 6].

NC functions are notably used as appropriate rules in Boolean models of gene regulatory networks [17]. The dynamical systems in biological networks are far from random, and it has been shown that NC functions ensure expected stability properties [3, 5] and are indeed predominant in large databases of Boolean gene networks [15].

In most cases Boolean variables are sufficient, but for some situations this description is too crude, and it may be necessary to consider other levels. To model such a situation correctly, multivalued variables have been introduced [18]. Then it is necessary to consider multivalued functions $f : (\mathbb{Z}/k\mathbb{Z})^n \to \mathbb{Z}/k\mathbb{Z}$ for some $k \geqslant 2$. The notion of average sensitivity generalizes to the multivalued setting [10], and multivalued NC functions are defined in [8, 9]. Very little is known about their spectral properties. In [1], a variant of average sensitivity, the normalized average c-sensitivity, is defined for multivalued functions, and used to measure the stability of networks made of NC functions.

A natural question is whether the average sensitivity of NC multivalued functions is bounded above by a constant, too. We prove in Theorem 3 that this is the case. We actually show that the upper bound holds for a more general class of functions, which we call weakly nested canalizing, and at the same time this enables us to establish the upper bound in a simpler way than in [7] for Boolean NC functions.

2 Nested canalizing multivalued functions

Let k, n be positive integers, $k \geqslant 2$. $\mathbb{Z}/k\mathbb{Z}$ is the ring of integers modulo k.

Following [8, 9, 1], we shall say that $f : (\mathbb{Z}/k\mathbb{Z})^n \to \mathbb{Z}/k\mathbb{Z}$ is *canalizing with respect to coordinate* i *and* $(a, b) \in \mathbb{Z}/k\mathbb{Z} \times \mathbb{Z}/k\mathbb{Z}$ if there exists a function $g : (\mathbb{Z}/k\mathbb{Z})^n \to \mathbb{Z}/k\mathbb{Z}$ different from the constant b such that

$$f(x) = \begin{cases} b & \text{if } x_i = a \\ g(x) & \text{if } x_i \neq a. \end{cases}$$

We shall simply say that f is *canalizing* if it is canalizing with respect to some i, a, b.

A *segment* is a subset of $\mathbb{Z}/k\mathbb{Z}$ of the form $\{0, \dots, i\}$ or $\{i, \dots, k-1\}$.

Let $\sigma \in \mathfrak{S}_n$ be a permutation, $A_1, \dots, A_n$ be segments, and $c_1, \dots, c_{n+1} \in \mathbb{Z}/k\mathbb{Z}$ be such that $c_n \neq c_{n+1}$. Then f is said to be *nested canalizing (NC)* *with respect to* σ, $A_1, \ldots, A_n$, $c_1, \ldots, c_{n+1}$ if

$$f(x) = \begin{cases} c_1 & \text{if } x_{\sigma(1)} \in A_1 \\ c_2 & \text{if } x_{\sigma(1)} \notin A_1, x_{\sigma(2)} \in A_2 \\ \vdots & \quad \vdots \\ c_n & \text{if } x_{\sigma(1)} \notin A_1, \ldots, x_{\sigma(n-1)} \notin A_{n-1}, x_{\sigma(n)} \in A_n \\ c_{n+1} & \text{if } x_{\sigma(1)} \notin A_1, \ldots, x_{\sigma(n-1)} \notin A_{n-1}, x_{\sigma(n)} \notin A_n. \end{cases}$$

We shall simply say that f is *NC* if it is NC with respect to some σ, $A_1, \ldots, A_n$, $c_1, \ldots, c_{n+1}$.

2.1 Weakly nested canalizing multivalued functions

In Theorem 3, we shall give an upper bound on average sensitivity which holds not only for NC functions, but for the more general class of weakly nested canalizing functions, which we define now.

Let n be a positive integer. For each $i \in \{1, \ldots, n\}$, Ω_i is a finite set of cardinality $k_i > 0$, $\Omega = \prod_i \Omega_i$, and $f : \Omega \to \mathbb{R}$. Note that we do not require $k_i \geqslant 2$ for all i. If $k_j = 1$ for some j, f could be viewed as a function with one less variable, *i.e.* as a function on $\prod_{i \neq j} \Omega_i$, but we still consider it as a function defined on $\prod_i \Omega_i$.

We shall say that f is *weakly canalizing with respect to coordinate* i *and* $(a, b) \in \Omega_i \times \mathbb{R}$ if $f(x) = b$ whenever $x_i = a$, and simply that it is *weakly canalizing* if it is weakly canalizing with respect to some i, a, b.

Note that this definition differs slightly from the usual definition by the absence of condition on the values of f for $x_i \neq a$: we do not require the existence of some x such that $x_i \neq a$ and $f(x) \neq b$. In particular, constant functions are weakly canalizing, though not canalizing.

If f is canalizing with respect to i, a, b and $k_i \geqslant 2$, we shall consider

$$f\restriction_{x_i \neq a} : \Omega \cap \{x \mid x_i \neq a\} \to \mathbb{R},$$

the restriction of f to the set of $x \in \Omega$ such that $x_i \neq a$.

The class of weakly nested canalizing on $\Omega = \prod_i \Omega_i$ is then defined by induction on the cardinality $|\Omega| = \prod_i k_i$ of Ω:

- If $|\Omega| = 1$, *i.e.* $k_i = 1$ for all i, any $f : \Omega \to \mathbb{R}$ is *weakly nested canalizing (WNC) on* Ω.
- If $|\Omega| > 1$, $f : \Omega \to \mathbb{R}$ is *WNC on* Ω if it is weakly canalizing with respect to some i, a, b such that $k_i \geqslant 2$ and $f\restriction_{x_i \neq a}$ is WNC on $\Omega \cap \{x \mid x_i \neq a\}$, a strict subset of Ω.

Intuitively, a function $f : \Omega \to \mathbb{R}$ is WNC if its domain Ω can be "peeled" by successively removing coordinate hyperplanes (defined by equations of the form $x_i = a$) whose points are mapped by f to the same value, whence the following characterization:

Proposition 1. *Letting $K = \sum_i k_i$, f is WNC if and only if there exist a function $v : \{1, \ldots, K\} \to \{1, \ldots, n\}$ and numbers $a_i \in \Omega_{v(i)}$ and $b_i \in \mathbb{R}$ for each $i \in \{1, \ldots, K\}$ such that:*

$$f(x) = \begin{cases} b_1 & \textit{if } x_{v(1)} = a_1 \\ b_2 & \textit{if } x_{v(1)} \neq a_1, x_{v(2)} = a_2 \\ \vdots & \quad \vdots \\ b_K & \textit{if } x_{v(1)} \neq a_1, \ldots, x_{v(K-1)} \neq a_{K-1}, x_{v(K)} = a_K. \end{cases}$$

In decomposing an NC function $f : (\mathbb{Z}/k\mathbb{Z})^n \to \mathbb{Z}/k\mathbb{Z}$, each coordinate $i \in \{1, \ldots, n\}$ is considered exactly once (in some order prescribed by a permutation σ) and the value of f is fixed for $x_{\sigma(i)}$ in some segment A_i. This can be realized by successively fixing the value of f for each $\alpha \in A_i$, and therefore, the class of WNC functions contains the class of NC functions, as stated in the following Proposition:

Proposition 2. *If $f : (\mathbb{Z}/k\mathbb{Z})^n \to \mathbb{Z}/k\mathbb{Z}$ is NC, then it is WNC.*

Proof. Assume f is NC with respect to σ, $A_1, \ldots, A_n$, $c_1, \ldots, c_{n+1}$. For each $i \in \{1, \ldots, n\}$, let

$$A_i = \{\alpha_i^1, \ldots, \alpha_i^{|A_i|}\}$$
$$(\mathbb{Z}/k\mathbb{Z}) \setminus A_i = \{\alpha_i^{1+|A_i|}, \ldots, \alpha_i^k\}$$

with $\alpha_i^1 < \cdots < \alpha_i^{|A_i|}$ and $\alpha_i^{1+|A_i|} < \cdots < \alpha_i^k$. This defines $K = nk$ numbers $\alpha_i^j \in \mathbb{Z}/k\mathbb{Z}$. For each $i \in \{1, \ldots, n\}$ and $j \in \{1, \ldots, k\}$, let

$$\beta_i^j = \begin{cases} c_i & \text{if } j \leqslant |A_i| \\ c_{n+1} & \text{otherwise.} \end{cases}$$

To comply with the characterization of WNC functions (Proposition 1), we relabel the numbers α_i^j, β_i^j by identifying the list

$$\alpha_1^1, \ldots, \alpha_1^{|A_1|}, \ldots, \alpha_n^1, \ldots, \alpha_n^{|A_i|}, \alpha_1^{1+|A_1|}, \ldots, \alpha_1^k, \ldots, \alpha_n^{1+|A_n|}, \ldots, \alpha_n^k$$

as the list $a_1, \ldots, a_K$, and by identifying similarly the list

$$\beta_1^1, \ldots, \beta_1^{|A_1|}, \ldots, \beta_n^1, \ldots, \beta_n^{|A_n|}, \beta_1^{1+|A_1|}, \ldots, \beta_1^k, \ldots, \beta_n^{1+|A_n|}, \ldots, \beta_n^k$$

as the list $b_1, \ldots, b_K$. Call φ this relabeling, mapping $r \in \{1, \ldots, K\}$ to the pair $\varphi(r) = (i, j)$ such that $a_r = \alpha_i^j$ and $b_r = \beta_i^j$. For instance, $\varphi(1) = (1, 1)$ and $\varphi(K) = (n, k)$. Then finally, a function $v : \{1, \ldots, K\} \to \{1, \ldots, n\}$ is defined by $v(r) = \sigma(i)$ if $\varphi(r) = (i, j)$. Then f clearly enjoys the characterization of WNC functions, with the choice of function v and numbers a_r, b_r. $\square$

2.2 Examples

- As we have already observed, constant functions from $(\mathbb{Z}/k\mathbb{Z})^n$ to $\mathbb{Z}/k\mathbb{Z}$ are WNC but not NC.

- In decomposing a WNC function $f : (\mathbb{Z}/k\mathbb{Z})^n \to \mathbb{Z}/k\mathbb{Z}$, it is possible to "peel" a coordinate hyperplane defined on some coordinate i (*i.e.* by some equation $x_i = a$), then a coordinate hyperplane defined on j, and later a coordinate hyperplane defined on i again. This is because of the recursive definition of WNC functions, and gives more freedom in the construction of WNC functions than in the construction of NC functions.

  For instance, the functions min and max : $(\mathbb{Z}/k\mathbb{Z})^2 \to \mathbb{Z}/k\mathbb{Z}$ are not NC, as observed in [1]. However, an easy induction on k shows that they are WNC. For instance, $\min = \min_k : \{0, \ldots, k-1\}^2 \to \{0, \ldots, k-1\}$ is weakly canalizing with respect to $1, 0, 0$, $\min_k\restriction_{x_1 \neq 0}$ is weakly canalizing with respect to $2, 0, 0$, and $\min_k\restriction_{x_1 \neq 0, x_2 \neq 0}$ is identical to the function $\min_{k-1} : \{1, \ldots, k-1\}^2 \to \{1, \ldots, k-1\}$, which is WNC.

- Also, in constructing a WNC function $f : (\mathbb{Z}/k\mathbb{Z})^n \to \mathbb{Z}/k\mathbb{Z}$, the values a used to define $f(x)$ for $x_i = a$ need not be extremal values (initially 0 or $k-1$), they can be intermediate values: $0 < a < k-1$.

  For instance, the function from $\mathbb{Z}/3\mathbb{Z}$ to $\mathbb{Z}/3\mathbb{Z}$ defined by $0 \mapsto 0, 1 \mapsto 1, 2 \mapsto 0$ is not NC because it is canalizing with respect to either the intermediate value 1 (for its unique variable), or the values 0 and 2 (which do not form a segment). But any function from $\mathbb{Z}/k\mathbb{Z}$ to $\mathbb{Z}/k\mathbb{Z}$ is WNC.

2.3 NC functions and genetic networks

We have already mentioned that canalizing functions are significantly predominant in gene network modellings [15], and that networks with nested canalyzing rules are stable [5]. In this context, one is interested in the discrete-time asynchronous evolution of the expression levels of n genes, where "asynchronous" means that at each time step, the level of at most one gene can change. Moreover the expression level of each gene belongs to a finite set, typically $\{0,1\}$ or $\{0,1,2\}$.

The following example is inspired from the logical modelling of the phage lambda, a biological model widely studied to understand the decision between lysis and lysogenization [11, 16, 12]. It involves two genes, CI and Cro. CI is either expressed or not, and its expression level is therefore modelled by a Boolean variable, Cro can take 3 values $\{0,1,2\}$. This simple model is sufficient to display both multistability (representing lysis and lysogeny fates) and oscillations (lysogeny state) [13, 14].

In state $x = (x_{CI}, x_{Cro}) \in \mathbb{Z}/2\mathbb{Z} \times \mathbb{Z}/3\mathbb{Z}$, the next value of CI is given by the following function $f_{CI} : \mathbb{Z}/2\mathbb{Z} \times \mathbb{Z}/3\mathbb{Z} \to \mathbb{Z}/2\mathbb{Z}$:

$$f_{CI}(x) = \begin{cases} 0 & \text{if } x_{Cro} \geqslant 1 \\ 1 & \text{otherwise.} \end{cases}$$

For instance, in state $(1,2)$, the next value of CI can be 0 because $f_{CI}(1,2) = 0$, and in state $(0,2)$, the value of CI cannot change because $f_{CI}(0,2) = 0$. Similarly, the next value of Cro is given by a function $f_{Cro} : \mathbb{Z}/2\mathbb{Z} \times \mathbb{Z}/3\mathbb{Z} \to \mathbb{Z}/3\mathbb{Z}$. However, the following two choices for f_{Cro}:

$$f^1_{Cro}(x) = \begin{cases} 0 & \text{if } x_{CI} = 1 \\ 1 & \text{if } x_{CI} = 0 \text{ and } x_{Cro} = 2 \\ 2 & \text{otherwise} \end{cases}$$

$$f^2_{Cro}(x) = \begin{cases} 1 & \text{if } x_{Cro} = 2 \\ 0 & \text{if } x_{Cro} \neq 2 \text{ and } x_{CI} = 1 \\ 2 & \text{otherwise} \end{cases}$$

give rise to the same asynchronous trajectories, represented by the following graph, where vertices are states of the system (x_{CI}, x_{Cro}) and arrows link two consecutive states:

$$
\begin{tikzcd}
(0,2) \arrow[d, leftrightarrow] & (1,2) \arrow[l] \arrow[d] \\
(0,1) & (1,1) \arrow[l] \arrow[d] \\
(0,0) \arrow[u] \arrow[r] & (1,0)
\end{tikzcd}
$$

These two functions do not have the same canalizing property: f^1_{Cro} is NC, f^2_{Cro} is only WNC. Thus, in this example two functions that represent the same asynchronous dynamics do not have the same canalizing properties. The observations of [5] can thus be an assistance for modelling the biological system, a task known to be difficult, as the number of network-compatible functions is enormous.

3 Average sensitivity of WNC multivalued functions

Following [10, Chapter 8], we shall take the following definition of average sensitivity.

First, Fourier decomposition is generalized to non Boolean domains. Let $\Omega = \prod_{i=1}^n \Omega_i$ be as above, with $|\Omega_i| = k_i$. On the vector space of real-valued functions defined on Ω, an inner product is given by $\langle f, g\rangle = \mathbf{E}_x[f(x)g(x)]$, where $\mathbf{E}$ denotes the expectation. Here, $x \in \Omega$ and we assume independent uniform probability distributions on the Ω_i. A *Fourier basis* is an orthonormal basis $(\varphi_\alpha)_{\alpha\in\prod_i\{0,\ldots,k_i\}}$ such that $\varphi_{(0,\ldots,0)} = 1$. It is not difficult to see that a Fourier basis always exists, although it is not unique.

Then, fix a Fourier basis (φ_α). The *Fourier coefficients of* $f : \Omega \to \mathbb{R}$ are $\widehat{f}(\alpha) = \langle f, \varphi_\alpha\rangle$, and $E_i f = \sum_{\alpha_i=0} \widehat{f}(\alpha)\varphi_\alpha$ turns out to be independent of the basis. for all $i \in \{1, \ldots, n\}$, let the *ith coordinate Laplacian operator* L_i be the linear operator defined by $L_i f = f - E_i f$.

Finally, the *influence of coordinate* i *on* f is defined by $\mathbf{Inf}_i[f] = \langle f, L_i f\rangle$, and the *average sensitivity* (also called *influence* or *total influence*) of f is then $\mathbf{AS}[f] = \sum_i \mathbf{Inf}_i[f]$.

By Plancherel's theorem (see [10]), we have

$$\mathbf{Inf}_i[f] = \sum_{\alpha_i\neq 0} \widehat{f}(\alpha)^2 = \mathbf{E}_x[\mathbf{Var}_{y_i}[f(x_1, \ldots, x_{i-1}, y_i, x_{i+1}, \ldots, x_n)]],$$

where $\mathbf{Var}$ denotes the variance ($\mathbf{Var}[g] = \mathbf{E}[g^2] - \mathbf{E}[g]^2$) and $y_i \in \Omega_i$. The above equality makes clear that the definition of influence of multivalued functions generalizes the Boolean case, as expected.

Now, for an arbitrary $f : \Omega \to [0, M]$, we have $\mathbf{Var}_i[f](x) \leqslant (M/2)^2$ for all i, therefore $\mathbf{Inf}_i[f] \leqslant M^2/4$ for all i and $\mathbf{AS}[f] \leqslant n \cdot M^2/4 = \mathcal{O}(n)$.

For WNC functions, this upper bound can be greatly improved. In the Boolean case, [7] proves (by a different method from ours) that $\mathbf{AS}[f] \leqslant 2$ for NC $\{-1, +1\}$-valued functions. This bound is improved in [6], where it is proved that $\mathbf{AS}[f] \leqslant 4/3$. For NC functions $f : \{0,1\}^n \to \{0,1\}$, the result in [7] means $\mathbf{AS}[f] \leqslant 1/2$.

Theorem 3 generalizes this result, by establishing that, in the more general multivalued case, the average sensitivity of WNC functions is bounded above by a constant.

Theorem 3. *Let $\Omega = \prod_{i=1}^n \Omega_i$ where each Ω_i has cardinality $k_i > 0$. Let $f : \Omega \to [0, M]$ and $\kappa = \max_i (k_i - 1)/k_i < 1$. If f is WNC (in particular if it is NC), then*

$$\mathbf{AS}[f] \leqslant \frac{M^2}{4(1-\kappa)}.$$

Proof. We prove this by induction on $\sum_i k_i$. If $k_i = 1$ for all i, the inequality holds trivially: actually $\mathbf{AS}[f] = 0$. Now assume f is canalizing with respect to j, a, b, with $k_j \geqslant 2$, and let $f' = f\restriction_{x_j \neq a}$. Let Ω' be the set of $x \in \Omega$ such that $x_j \neq a$, so that $f' : \Omega' \to \mathbb{R}^+$. The induction hypothesis is $\mathbf{AS}[f'] \leqslant M'^2/(4(1-\kappa'))$, with

$$\begin{aligned} M' &= \max_{x \in \Omega'} f'(x) = \max_{x \in \Omega'} f(x) \leqslant M \\ \kappa' &= \max\left\{ \frac{k_j - 2}{k_j - 1}, \max_{i \neq j} \frac{k_i - 1}{k_i} \right\} \leqslant \kappa. \end{aligned}$$

Note that the induction hypothesis implies $\mathbf{AS}[f'] \leqslant M^2/(4(1-\kappa))$. We shall use the notation $\mathbf{Var}_i[f](x) = \mathbf{Var}_{y_i}[f(x_1, \ldots, x_{i-1}, y_i, x_{i+1}, \ldots, x_n)]$. Then $\mathbf{AS}[f] = \mathbf{E}_x[\sum_i \mathbf{Var}_i[f](x)]$ and

$$\begin{aligned} \mathbf{AS}[f] \cdot \prod_i k_i &= \sum_x \sum_i \mathbf{Var}_i[f](x) \\ &= \sum_{x_j = a} \mathbf{Var}_j[f](x) + \sum_{x_j \neq a} \left(\mathbf{Var}_j[f](x) + \sum_{i \neq j} \mathbf{Var}_i[f](x) \right) \end{aligned}$$

since $f(x)$ is constant when $x_j = a$, so that $\mathbf{Var}_i[f](x) = 0$ for $i \neq j$. Furthermore, $\mathbf{Var}_j[f](x)$ is independent of x_j, and on the other hand, $\mathbf{Var}_i[f](x)$

$= \mathbf{Var}_i[f'](x)$ if $x_j \neq a$ and $i \neq j$. Thus

$$\mathbf{AS}[f] \cdot \prod_i k_i = k_j \cdot \sum_{x_j = a} \mathbf{Var}_j[f](x) + \sum_{x \in \Omega'} \sum_{i \neq j} \mathbf{Var}_i[f'](x).$$

Since $0 \leqslant f(x) \leqslant M$ for all x, we have $\mathbf{Var}_j[f](x) \leqslant M^2/4$. Therefore

$$\begin{aligned}\mathbf{AS}[f] \cdot \prod_i k_i &\leqslant k_j \cdot \prod_{i \neq j} k_i \cdot M^2/4 + \sum_{x \in \Omega'} \sum_{i=1}^{n} \mathbf{Var}_i[f'](x) \\ &= \prod_i k_i \cdot M^2/4 + \mathbf{AS}[f'] \cdot (k_j - 1) \cdot \prod_{i \neq j} k_i\end{aligned}$$

and

$$\mathbf{AS}[f] \leqslant \frac{M^2}{4} + \mathbf{AS}[f'] \cdot \frac{k_j - 1}{k_j} \leqslant \frac{M^2}{4} + \kappa \cdot \mathbf{AS}[f'].$$

To conclude the proof, it suffices to observe that $\mathbf{AS}[f'] \leqslant M^2/(4(1-\kappa))$ implies $\mathbf{AS}[f] \leqslant M^2/(4(1-\kappa))$. $\square$

In the Boolean case, $\kappa = 1/2$ and $M = 1$, so that the upper bound $M^2/(4(1-\kappa))$ equals $1/2$ and the above result is a generalization of the result in [7]. The proof is also significantly simpler than the one in [7]. It can be easily checked that in the Boolean case, our argument on variance essentially amounts to compute the fraction of edges in the Hamming cube $\{0,1\}^n$ which are boundary edges (*i.e.* edges (x, y) with $f(x) \neq f(y)$).

An obvious question is whether the bound $M^2/(4(1-\kappa))$ can be improved for multivalued WNC, or at least NC, functions, along the lines of [6].

References

[1] C. Kadelka, Y. Li, J. Kuipers, J. O. Adeyeye, and R. Laubenbacher. Multistate nested canalizing functions and their networks. *Theoret. Comput. Sci.*, 675:1–14, 2017.

[2] C. Kadelka, R. Laubenbacher, D. Murrugarra, A. Veliz-Cuba, and M. Wheeler. Decomposition of Boolean networks: An approach to modularity of biological systems. *arXiv:2206.04217*, 2022.

[3] S. A. Kauffman. *The origins of order: Self organization and selection in evolution.* Oxford University Press, 1993.

[4] S. Kauffman, C. Peterson, B. Samuelsson, and C. Troein. Random Boolean network models and the yeast transcriptional network. *Proc. Natl. Acad. Sci.*, 100(25), 2003.

[5] S. Kauffman, C. Peterson, B. Samuelsson, and C. Troein. Genetic networks with canalyzing Boolean rules are always stable. *Proc. Natl. Acad. Sci.*, 101(49), 2004.

[6] J. G. Klotz, R. Heckel, and S. Schober. Bounds on the average sensitivity of nested canalizing functions. *Plos One*, 8(5), 2013.

[7] Y. Li, J. O. Adeyeye, D. Murrugarra, B. Aguilar, and R. Laubenbacher. Boolean nested canalizing functions: A comprehensive analysis. *Theoret. Comput. Sci.*, 481:24–36, 2013.

[8] D. Murrugarra and R. Laubenbacher. Regulatory patterns in molecular interaction networks. *J. Theor. Biol.*, 288:66–72, 2011.

[9] D. Murrugarra and R. Laubenbacher. The number of multistate nested canalyzing functions. *Physica D: Nonlinear Phenomena*, 241(10):929–938, 2012.

[10] R. O'Donnell. *Analysis of Boolean functions.* Cambridge University Press, 2014.

[11] M. Ptachne. *A genetic switch. Phage lambda and higher organisms.* Blackwell Science, 1992.

[12] É. Remy and P. Ruet. From minimal signed circuits to the dynamics of Boolean regulatory networks. *Bioinformatics*, 24:i220–i226, 2008.

[13] É. Remy, P. Ruet, and D. Thieffry. Graphic requirements for multistability and attractive cycles in a Boolean dynamical framework. *Adv. Appl. Math.*, 41(3):335–350, 2008.

[14] P. Ruet. Local cycles and dynamical properties of Boolean networks. *Math. Struct. Comput. Sci.*, 26(4):702–718, 2016.

[15] A. Subbaroyan, O. C. Martin, and A. Samal. Minimum complexity drives regulatory logic in Boolean models of living systems. *PNAS Nexus*, 1:1–12, 2022.

[16] D. Thieffry and R. Thomas. Dynamical behaviour of biological regulatory networks II. Immunity control in bacteriophage lambda. *Bull. Math. Biol.*, 57:277–295, 1995.

[17] R. Thomas. Boolean formalization of genetic control circuits. *J. Theor. Biol.*, 42:563–585, 1973.

[18] R. Thomas. Regulatory networks seen as asynchronous automata: a logical description. *J. Theor. Biol.*, 153:1–23, 1991.

[19] C.H. Waddington. Canalization of development and the inheritance of acquired characters. *Nature*, 150:563–565, 1942.

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