Identifying a Probabilistic Boolean Threshold Network From Samples

Avraham A. Melkman, Xiaoqing Cheng, Wai-Ki Ching, and Tatsuya Akutsu, *Senior Member, IEEE*

***Abstract*— This paper studies the problem of exactly identifying the structure of a probabilistic Boolean network (PBN) from a given set of samples, where PBNs are probabilistic extensions of Boolean networks. Cheng *et al.* studied the problem while focusing on PBNs consisting of pairs of AND/OR functions. This paper considers PBNs consisting of Boolean threshold functions while focusing on those threshold functions that have unit coefficients. The treatment of Boolean threshold functions, and triplets and n-tuplets of such functions, necessitates a deepening of the theoretical analyses. It is shown that wide classes of PBNs with such threshold functions can be exactly identified from samples under reasonable constraints, which include: 1) PBNs in which any number of threshold functions can be assigned provided that all have the same number of input variables and 2) PBNs consisting of pairs of threshold functions with different numbers of input variables. It is also shown that the problem of deciding the equivalence of two Boolean threshold functions is solvable in pseudopolynomial time but remains co-NP complete.**

***Index Terms*— Network inference, probabilistic Boolean networks (PBNs), threshold functions, threshold networks.**

I. INTRODUCTION

IDENTIFYING the network structure is an important challenge both in neuroscience and in systems biology. Extensive studies have been done for identifying the network structure of a human brain by developing various experimental techniques [1], [2]. However, the human brain's network is too huge to be determined by the current experimental technologies, and thus, computational methods may be helpful to support this big challenge. The identification of the structure of gene regulatory networks has also been extensively studied. Since it is quite difficult to identify the gene regulatory network structure using only experimental technologies, many computational methods have been developed to identify the structure from gene expression time series data [3]–[5].

Manuscript received May 13, 2016; revised October 14, 2016; accepted December 31, 2016. Date of publication January 25, 2017; date of current version March 15, 2018. This work was supported by the Collaborative Research Program of Institute for Chemical Research, Kyoto University. The work of A. A. Melkman was supported by the invitation fellowship from JSPS, Japan. The work of T. Akutsu was supported by JSPS, Japan, under Grant 26540125.

A. A. Melkman is with the Department of Computer Science, Ben-Gurion University of the Negev, Beersheva 84105, Israel (e-mail: melkman@cs.bgu.ac.il).

X. Cheng is with the School of Mathematics and Statistics, Xi'an Jiaotong University, Xi'an 710049, China (e-mail: xiaoqing9054@xjtu.edu.cn).

W.-K. Ching is with the Department of Mathematics, The University of Hong Kong, Hong Kong (e-mail: wching@hku.hk).

T. Akutsu is with the Bioinformatics Center, Institute for Chemical Research, Kyoto University, Kyoto 611-0011, Japan (e-mail: takutsu@kuicr.kyoto-u.ac.jp).

Digital Object Identifier 10.1109/TNNLS.2017.2648039

Various mathematical models have been employed and/or developed for computationally identifying network structures. Among them, the *Boolean network* (BN) is a well-studied discrete mathematical model, which was proposed by Kauffman [6], [7] in 1969 as a model of gene regulatory networks. The BN has also been used in modeling neural networks [8], [9], because neurons are often modeled as Boolean threshold functions. In a BN, each node takes a Boolean value, 0 or 1, at each time step, where each node corresponds to a gene (resp., a neuron), and 1 and 0 mean that genes (resp., neurons) are active and inactive, respectively. In a widely studied synchronous BN, the states of all nodes are updated synchronously according to Boolean functions assigned to nodes.

In order to identify BNs from gene expression time series data, extensive studies have been done based on combinatorial methods [10]–[13] and on algebraic methods [14], [15] with semitensor product [16]. It is known that a BN with n nodes is uniquely determined with high probability from randomly selected $O(\log n)$ state-transition samples if the maximum indegree (i.e., the maximum number of input nodes) is bounded by a constant, whereas $O(2^n)$ samples are required if there is no constraint on the structure of a BN [11], where $\log n$ stands for $\log_2 n$ in this paper. It should be noted that this result is independent of identification algorithms and holds for BNs consisting of Boolean threshold functions with at most K input variables.

While BNs are deterministic, both gene regularity networks [17] and neural networks [18] contain intrinsic stochasticity and observed data also include noise. Therefore, various extensions of BNs have been proposed for including effects of noise or control [19]–[23]. Among them, the *probabilistic BN* (PBN) model has been extensively studied [24]–[27], including recent studies on its control [28]–[31]. In this model, multiple Boolean functions can be assigned to each node and one of them is randomly selected at each time step according to the prescribed probability distribution. Although several studies have been done on the inference of PBNs [24], [27], [32], there had been no result on the sample complexity analogous to the one for BNs.

Recently, Cheng *et al.* [33] studied the number of samples needed to exactly identify the structure of a PBN (i.e., a set of Boolean functions assigned to each node). They showed that there are cases for which it is impossible to uniquely determine a PBN from samples, which is reasonable because of stochasticity of a PBN. However, they also showed that the structure of a PBN can be identified with high probability from

$O(\log n)$ samples for theoretically interesting classes of PBNs of bounded indegree, in particular, a class in which a pair of AND/OR functions with the same number of input variables is assigned to each node under the condition that each variable appears in the pair either positively or negatively (not both). However, their work was limited because: 1) they focused on AND/OR Boolean functions and a very limited subclass of canalyzing functions [34] and 2) at most two functions could be assigned to one node. In order to extend their approach to neural networks, we need to be able to deal with threshold functions. It is to be noted that the class of threshold functions is much wider than that of AND/OR functions [9] and is very different from the subclass of canalyzing functions considered in [33].

In this paper, we describe broad classes of PBNs with threshold functions whose structure can be exactly identified from samples. Hereafter, PBNs with threshold functions are referred to as *probabilistic Boolean threshold networks* (*PBTNs*). As a first step toward this extension, we mainly consider threshold functions with unit coefficients. As in [33], we consider two models for identification: the partial information model (PIM) and the full information model (FIM), but we introduce novel ideas and deeper analyses. We show that broad classes of PBTNs can be exactly identified from samples, in particular the following classes: 1) PBTNs in which any number of threshold functions can be assigned provided all functions assigned to a node have the same number of input variables and satisfy certain reasonable conditions and 2) PBTNs consisting pairs of threshold functions with different numbers of input variables under reasonable conditions, where the PIM and FIM are assumed for 1) and 2), respectively. Furthermore, we show that a certain class of PBTNs with general coefficients can be identified under the PIM; we analyze the number of samples required for identification in both models, and present some biologically relevant class. In addition to the identification problem, we study the problem of deciding the equivalence of two given Boolean threshold functions, because it might be needed to test whether an identified network is intrinsically the same as some known network. We show that the problem is co-NP complete although it can be solved in pseudopolynomial time. Note that a co-NP complete problem is the complement (i.e., exchanging "yes" and "no" in the output) of the corresponding NP complete problem, and that no co-NP complete problem has a polynomial time algorithm unless $P = \mathrm{NP}$ [35].

II. Boolean Threshold Functions

In this paper, we focus on threshold functions on Boolean domains, which have been widely used in theoretical studies on neural networks [9]. Let $x_1, \ldots, x_n$ be Boolean variables. A *Boolean threshold function* f on $x_1, \ldots, x_n$ has the form

$$w_1 x_1 + w_2 x_2 + \cdots + w_n x_n \geq \theta$$

meaning that $f(x_1, \ldots, x_n) = 1$ if $w_1 x_1 + w_2 x_2 + \cdots + w_n x_n \geq \theta$ and otherwise $f(x_1, \ldots, x_n) = 0$, for all $(x_1, \ldots, x_n) \in \{0, 1\}^n$, where w_i and θ are integers. Although the ranges of integers are not fixed in general, we mainly consider identification for the unit coefficient case in which $w_i \in \{0, 1\}$ holds for all i and thus $\theta \in \{1, \ldots, n\}$ holds. Let N denote the maximum value of coefficients w_is and θ. It is known that Boolean threshold functions cover various Boolean functions, which include AND and OR functions, majority functions, and decision lists [9]. For example, an AND function (resp., an OR function) is represented as $x_1 + x_2 + \cdots + x_n \geq n$ (resp., $x_1 + x_2 + \cdots + x_n \geq 1$). Certain types of conditional functions can also be represented as threshold functions, by using the property that $x \rightarrow y$ is equivalent to $\overline{x} \vee y$. For example, $x_1 \wedge x_2 \wedge \cdots \wedge x_k \rightarrow x_n$ is represented as $\overline{x_1} + \overline{x_2} + \cdots + \overline{x_k} + x_n \geq 1$, and $x_1 \vee x_2 \vee \cdots \vee x_k \rightarrow x_n$ is represented as $\overline{x_1} + \overline{x_2} + \cdots + \overline{x_k} + k x_n \geq k$. However, Boolean threshold functions do not cover all conditional functions. For example, $x_1 \oplus x_2 \rightarrow x_3$ is not covered, because exclusive OR ($\oplus$) cannot be represented as a Boolean threshold function [9].

Before considering the identification problem, we consider the problem of deciding the equivalence of two threshold functions. We think that this is a fundamental problem, but we were nevertheless unable to find in the literature a result that explicitly states the complexity of the problem, although [36] gives an efficient algorithm for finding a kind of canonical representation of a Boolean threshold function. First, we present a positive result, i.e., a procedure for deciding the equivalence, that bears some similarity with that of [36].

Proposition 1: The equivalence of two Boolean threshold functions can be decided in time that is polynomial in n and N.

Proof: Suppose that f and g have the forms $w_1 x_1 + \cdots + w_k x_k \geq \theta_1$ and $u_1 x_1 + \cdots + u_h x_h \geq \theta_2$, respectively. We assume without loss of generality that $h = k$ because otherwise we can let $w_i = 0$ for $i > k$ or $u_i = 0$ for $i > h$. Then, equivalence is decided by the following simple recursive procedure. If $k = 1$, we decide the equivalence by examining $x_1 = 0$ and $x_1 = 1$. Otherwise

> $w_1 x_1 + \cdots + w_k x_k \geq \theta_1$ and $u_1 x_1 + \cdots + u_k x_k \geq \theta_2$ are equivalent **if and only if**
> $w_1 x_1 + \cdots + w_{k-1} x_{k-1} \geq \theta_1$ and $u_1 x_1 + \cdots + u_{k-1} x_{k-1} \geq \theta_2$ are equivalent **and**
> $w_1 x_1 + \cdots + w_{k-1} x_{k-1} \geq \theta_1 - w_k$ and $u_1 x_1 + \cdots + u_{k-1} x_{k-1} \geq \theta_2 - u_k$ are equivalent.

The correctness of the procedure is obvious by means of mathematical induction on the number of variables.

The running time of this procedure is polynomial in n and N if it is implemented using dynamic programming while maintaining a table defined by

$$D[j, \theta_1, \theta_2] = \begin{cases} 1, & \text{if } w_1 x_1 + \cdots + w_j x_j \geq \theta_1 \\ & \text{is equivalent to} \\ & u_1 x_1 + \cdots + u_j x_j \geq \theta_2, \\ 0, & \text{otherwise.} \end{cases}$$

■

The above-mentioned algorithm is a pseudopolynomial time one with respect to the input size, because coefficients can be represented by using $O(\log N)$ bits. The following proposition

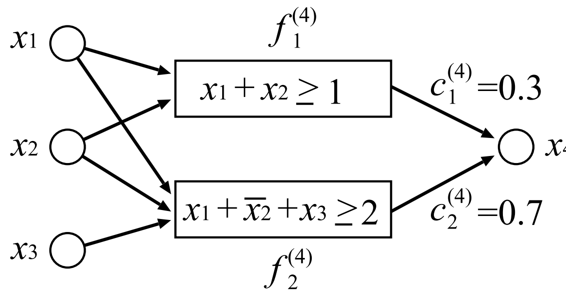


Fig. 1. Example of (part of) a PBTN. In this case, $x_4(t+1)$ is determined by $f_1^{(4)}$ or $f_2^{(4)}$, where $f_1^{(4)}$ and $f_2^{(4)}$ are selected with probability $c_1^{(4)} = 0.3$ and $c_2^{(4)} = 0.7$, respectively.

indicates that probably there does not exist a polynomial time algorithm for the equivalence problem.

Proposition 2: Deciding the equivalence of two Boolean threshold functions is co-NP complete.

Proof: It is straightforward to see that the problem is in co-NP.

In order to show that the problem is co-NP-hard, we consider the subset sum problem, a well-known NP-complete problem [35]. We reduce the complement of the subset problem to the problem of deciding whether two Boolean threshold functions are equivalent.

The subset sum problem asks: given a set of positive integers $A = \{a_1, a_2, \ldots, a_n\}$ and an integer b, is there a 0–1 assignment $x_1, \ldots, x_n$ such that $a_1x_1 + a_2x_2 + \cdots + a_nx_n = b$?

From an instance A of the subset sum problem, we construct two Boolean threshold functions by

$$a_1x_1 + a_2x_2 + \cdots + a_nx_n \geq b$$
$$a_1x_1 + a_2x_2 + \cdots + a_nx_n \geq b + 1.$$

These two functions are equivalent if and only if A does not have a satisfying 0–1 assignment. Since the construction can obviously be done in polynomial time with respect to the size of A, the proposition holds. ■

III. Probabilistic Boolean Threshold Network

Here, we briefly review the definitions of the BN and define PBTN (see also Fig. 1). Throughout this paper, $\mathbf{a}$ denotes a 0–1 bit vector of length n, and $\mathbf{a}_i$ denotes the 0–1 value of its ith bit (i.e., $\mathbf{a} = (\mathbf{a}_1, \ldots, \mathbf{a}_n)$). For a Boolean variable x, a literal is either x or its negation $\overline{x}$.

Definition 3: Let $x_1, \ldots, x_n$ be Boolean variables. An assignment of 0–1 values to the variables will be denoted by a 0–1 bit vector $\mathbf{a} = (\mathbf{a}_1, \ldots, \mathbf{a}_n)$, and the value assigned by $\mathbf{a}$ to a literal ℓ will be denoted $\mathbf{a}(\ell)$, e.g., if $\mathbf{a}_i = 0$ then $\mathbf{a}(x_i) = 0$ and $\mathbf{a}(\overline{x_i}) = 1$.

Since we need to consider negative inputs (i.e., $\overline{x_i}$) in BNs and PBNs, we redefine Boolean threshold functions as follows.

Definition 4: A Boolean function f is a threshold function with (integer) threshold θ if there exists integers w_i such that

$$f(x_1, \ldots, x_n) = 1 \text{ if and only if } \sum_{i \in \{1,\ldots,n\}} w_i \ell_i \geq \theta, \text{for all } (x_1, \ldots, x_n) \in \{0,1\}^n$$

where ℓ_i is either x_i or $\overline{x_i}$.

Henceforth, we will assume that a threshold function f is given by its set of literals, $LIT(f)$, the corresponding weights, and the threshold $\theta(f)$. For example, for f defined by $x_1 + 3\overline{x_2} + 2x_3 \geq 4$, $LIT(f) = \{x_1, \overline{x_2}, x_3\}$, its weights are $(1, 3, 2)$, and $\theta(f) = 4$.

Definition 5: A Boolean threshold network is a directed network with n nodes $x_1, \ldots, x_n$, in which node i has an associated Boolean threshold function $f^{(i)}$. At time step t, node x_i takes on a value $x_i(t)$ that is either 0 or 1, and $x_i(t+1)$ is determined by $x_i(t+1) = f^{(i)}(x_1(t), \ldots, x_n(t))$.

A PBTN is a directed network with n nodes in which node i is associated with a set $F = \{f_1^{(i)}, \ldots, f_{m_i}^{(i)}\}$ of Boolean threshold functions, and with corresponding selection probabilities $c_j^{(i)}$, $\sum_{j=1}^{m_i} c_j^{(i)} = 1$. The value of node x_i at time $t+1$ is determined by

$$x_i(t+1) = f_j^{(i)}(x_1(t), \ldots, x_n(t)) \text{ with probability } c_j^{(i)}$$

where selection of $f_j^{(i)}$ is independent of selections at previous time steps and of selections for other nodes.

Denote $X(t) = (x_1(t), \ldots, x_n(t))$. We focus our attention on the following setup. Suppose we are provided with a set of observations each of which consists of a pair $(X(0), X(1))$. We wish to investigate the conditions under which it is possible to deduce the functions associated with the nodes from these observations and, if so, how many observations are needed. In this paper, we will not attempt to determine the selection probabilities $c^{(i)}$, so that for our purposes duplicate pairs can be unified.

Since at time step t a Boolean threshold function $f_j^{(i)}$ is selected simultaneously with and independently of the selections for the other nodes, we can investigate these questions by looking generically at the dynamics of a single node, as in [33]. Henceforth, we will concentrate, therefore, on the identification of a set F of Boolean threshold functions from a set of samples S each of which is of the form $(\mathbf{a}, \upsilon)$, where $\mathbf{a}$ is an initial assignment to the nodes of the network and υ is the value of the node in question at the next time step. Furthermore, with a slight abuse of notation, we will call a set F of Boolean threshold functions a PBTN.

IV. Two Models

We assume that a class $\mathcal{C}$ of PBTNs is given, and that a set of samples S is generated using some PBTN $F \in \mathcal{C}$, meaning that for each $(\mathbf{a}, \upsilon) \in S$ the value υ belongs to the set $F(\mathbf{a}) = \{f_1(\mathbf{a}), \ldots, f_p(\mathbf{a})\}$. Many PBTNs from the class may be consistent with the sample so generated, in the following sense.

Definition 6: A PBTN $F = \{f_1, \ldots, f_p\}$ is *consistent* with a sample $(\mathbf{a}, \upsilon)$ if $\upsilon \in F(\mathbf{a}) = \{f_1(\mathbf{a}), \ldots, f_p(\mathbf{a})\}$. If F is consistent with every sample in a set of samples S, it is called *consistent with S*.

What we are interested in are classes $\mathcal{C}$ and sample sets S having the property that it is possible to identify from S which PBTN $F \in \mathcal{C}$ it was that generated S. In other words, our purpose is to describe classes $\mathcal{C}$ of PBTNs having the property that there is a unique $F \in \mathcal{C}$ that is consistent with S provided the set of samples S is sufficiently large.

As in [33], we consider two models, the PIM and the *FIM*. Speaking intuitively, in the PIM setting, we require that all observed samples are consistent with the underlying PBN, and no other PBN in the class under consideration could have generated those samples. In the FIM setting, on the other hand, this requirement is relaxed in that it allows for the possibility that other PBNs could have generated the same samples, but requires that, over time, these PBNs should generate in addition different samples that are inconsistent with the underlying PBN. PIM and FIM are defined via identifiability as follows.

Definition 7: S identifies F from among $\mathcal{C}$ under the PIM if F is the only PBTN in $\mathcal{C}$ that is consistent with all samples in S. When the class is clear from the context, we will simply say that S PIM-identifies F.

Under the FIM S identifies F from among $\mathcal{C}$ if it has the following.

1) F is the only PBTN in $\mathcal{C}$ that is consistent with all samples in S.
2) If $(\mathbf{a}, v) \in S$, then $\mathbf{a} \times F(\mathbf{a}) \subseteq S$, i.e., all possible samples $(\mathbf{a}, f(\mathbf{a}))$, $f \in F$ were generated.

When the class is clear from the context, we will say that S FIM-identifies F.

Definition 8: A class $\mathcal{C}$ is identifiable from samples under the PIM, respectively the FIM, if for every $F \in \mathcal{C}$ there is a set of samples that PIM-identifies F, respectively, FIM-identifies, F. We will usually say for short that $\mathcal{C}$ is PIM-identifiable, respectively, FIM-identifiable.

Although the definition of FIM-identifiability is simple, it is far from trivial to determine which classes are FIM-identifiable, as discussed in this paper and in [33].

The central observation that will guide us in exploring the structure of PBTNs is the following Theorem, a rephrasing of [33, Propositions 2 and 3]; for completeness, we provide the proof in the Appendix.

Theorem 9: A class $\mathcal{C}$ of PBTNs is PIM-identifiable if and only if for every $F, G \in \mathcal{C}$, there is an assignment $\mathbf{a}$ such that

$$F(\mathbf{a}) - G(\mathbf{a}) \neq \emptyset. \quad (1)$$

$\mathcal{C}$ is FIM-identifiable if and only if for every $F, G \in \mathcal{C}$, there is an assignment $\mathbf{a}$ such that

$$F(\mathbf{a}) \neq G(\mathbf{a}). \quad (2)$$

Example 10: Let $f_1 = x_1 + x_2 \geq 1$, $f_2 = x_1 + \overline{x_2} + x_3 \geq 2$, $f_3 = x_1 \geq 1$, and $f_4 = x_1 + x_2 + x_3 \geq 3$. Let $F = \{f_1, f_2\}$, $G = \{f_2, f_3\}$, $H = \{f_2, f_4\}$, $\mathcal{C}_1 = \{F, G\}$ and $\mathcal{C}_2 = \{G, H\}$. Then, $\mathcal{C}_1$ is identifiable from samples under FIM but not under PIM, because $G(\mathbf{a}) \subseteq F(\mathbf{a})$ for all $\mathbf{a}$, whereas $\mathcal{C}_2$ is identifiable from samples under both PIM and FIM because $G(\mathbf{a}') - H(\mathbf{a}') = \{1\}$ for $\mathbf{a}' = (1, 1, 0)$ and $H(\mathbf{a}'') - G(\mathbf{a}'') = \{0\}$ for $\mathbf{a}'' = (1, 0, 1)$ (see also Table I).

The theorem highlights the fact that PIM-identifiability of $\mathcal{C}$ requires that, for every $F, G \in \mathcal{C}$, there is an assignment $\mathbf{a}$ and an outcome y such that $y \in F(\mathbf{a})$ but $y \notin G(\mathbf{a})$, whereas FIM-identifiability only requires the existence of an assignment $\mathbf{a}$ such that $F(\mathbf{a}) \neq G(\mathbf{a})$ (so that, for example, $F(\mathbf{a}) \subset G(\mathbf{a})$ is possible). Indeed, if $\mathcal{C}$ is PIM-identifiable, it also is FIM-identifiable but, as we shall see, there are FIM-identifiable classes that are not PIM-identifiable. Although FIM allows identification of wider classes of PBTNs, PIM has a merit as discussed in [33]: we can know whether or not the current set of samples is enough to uniquely determine the network structure. These facts suggest that PIM is more appropriate when the number of samples is small, otherwise FIM is.

TABLE I
EXAMPLE ILLUSTRATING THE DIFFERENCE BETWEEN PIM AND FIM

x_1	0	0	0	0	1	1	1	1
x_2	0	0	1	1	0	0	1	1
x_3	0	1	0	1	0	1	0	1
f_1	0	0	1	1	1	1	1	1
f_2	0	1	0	0	1	1	0	1
f_3	0	0	0	0	1	1	1	1
f_4	0	0	0	0	0	0	0	1
$F = \{f_1, f_2\}$	0	0/1	0/1	0/1	1	1	0/1	1
$G = \{f_2, f_3\}$	0	0/1	0	0	1	1	0/1	1
$H = \{f_2, f_4\}$	0	0/1	0	0	0/1	0/1	0	1

Since our analysis will repeatedly make use of the conditions of the theorem, it will be convenient to employ the following definition.

Definition 11: F is PIM-distinguishable from G if there is an assignment $\mathbf{a}$ such that $F(\mathbf{a}) - G(\mathbf{a}) \neq \emptyset$, and it is FIM-distinguishable from G if $F(\mathbf{a}) \neq G(\mathbf{a})$. We will also say that $\mathbf{a}$ PIM-distinguishes, respectively, FIM-distinguishes, F from G.

Remark 12: F being PIM-distinguishable from G does not imply G is PIM-distinguishable from F.

Throughout this paper, we consider only admissible PBTNs, defined as follows.

Definition 13: Denote $LIT(F) = \cup_{f \in F} LIT(f)$. A PBTN F is admissible if at most one of $\ell, \overline{\ell}$ appears in $LIT(F)$, for all ℓ.

Remark 14: A class may be identifiable even though it contains inadmissible PBTNs.

Example 15: Let $\mathcal{C} = \{F, G\}$ with $F = \{x_1 + x_2 \geq 2,\ \overline{x_1} + x_3 \geq 1\}$, $G = \{\overline{x_1} + x_3 \geq 2,\ x_1 + x_3 \geq 1\}$. Then, the assignment $(x_1, x_2, x_3) = (0, 1, 0)$, PIM-distinguishes F from G, whereas the assignment$(1, 0, 0)$ PIM-distinguishes G from F.

In Sections V - VIII, we present several theorems showing identifiability of various classes of PBTNs under PIM and/or FIM. Fig. 2 shows the relationships among these theorems.

V. PBTNs With Unit Coefficients Under PIM

In this section, we consider identification of PBTNs under the PIM model. For the sake of readability, all the proofs of theorems in Sections V and VI are given in the Appendix. We begin with a simple but important lemma, which can be proven from the fact: if $F \subseteq G$ then $F(\mathbf{a}) - G(\mathbf{a}) = \emptyset$ for all $\mathbf{a}$.

Lemma 16 (Necessary Condition for PIM): A class $\mathcal{C}$ of admissible PBTNs is PIM-identifiable only if it does not contain F and G, such that $F \subseteq G$.

In this section, we restrict attention to those classes $\mathcal{C}$ of admissible PBTNs having the property that for given $F \in \mathcal{C}$,

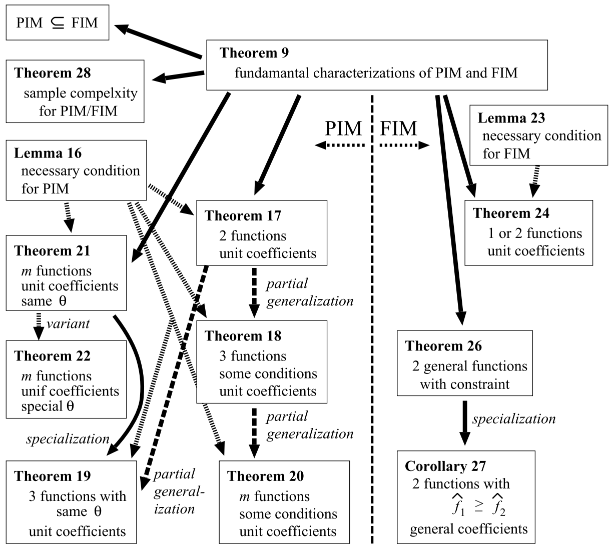


Fig. 2. Relationships among theorems.

all threshold functions $f \in F$ depend on exactly K variables and have unit coefficients (i.e., $w_i \in \{0, 1\}$ for all $i = 1, \ldots, n$).

A. Pairs of Threshold Functions

Our first result constitutes a generalization of [33, Th. 1], which dealt with OR functions and AND functions (the case $\theta_1 = 1$ and $\theta_2 = K$ of Theorem 17).

Theorem 17: Let $1 \leq \theta_1 < \theta_2 \leq K$ be two fixed thresholds, and let $\mathcal{C}$ be a class of admissible PBTNs satisfying the necessary condition for PIM, such that each $F \in \mathcal{C}$ consists of two (not necessarily different) threshold functions with the following properties: every $f \in F$ depends on exactly K variables, has unit coefficients, and has a threshold that is either θ_1 or θ_2. Then, $\mathcal{C}$ is PIM-identifiable.

B. Triplets of Threshold Functions

Theorem 17 can be partially generalized for triplets of threshold functions as follows.

Theorem 18: Let $1 \leq \theta_1 < \theta_3 \leq K$ be two fixed thresholds, and let $\mathcal{C}$ be a class of admissible PBTNs satisfying the necessary condition for PIM, such that each $F = \{f_1, f_2, f_3\} \in \mathcal{C}$ consists of three (not necessarily different) threshold functions with the following properties: every $f \in F$ depends on exactly K variables, has unit coefficients, and has $\theta(f_1) = \theta_1,\ \theta(f_3) = \theta_3$ and $\theta_1 \leq \theta(f_2) \leq \theta_3$. Then, $\mathcal{C}$ is PIM-identifiable if it meets one of the following conditions.

1) $\theta_1 < \theta(f_2) < \theta_3$ for all $F \in \mathcal{C}$, and $f_1 \neq g_1$ or $f_3 \neq g_3$ for all pairs $F, G \in \mathcal{C}$.
2) $1 < \theta_1$ and $\theta_3 < K$, and $|F \cap G| \leq 1$ for all pairs $F, G \in \mathcal{C}$.
3) $F \cap G = \emptyset$ for all pairs $F, G \in \mathcal{C}$.

Note that conditions 2 and 3 permit $f_2 = f_1$ or $f_2 = f_3$.

Theorem 19 is in part a special case of Theorem 21.

Theorem 19: Let $\mathcal{C}$ be a class of admissible PBTNs that satisfies the necessary condition for PIM, and is such that each $F \in \mathcal{C}$ consists of three (not necessarily different) threshold functions that have the same threshold, in addition to all three depending on exactly K variables and having unit coefficients. Then, $\mathcal{C}$ is PIM-identifiable if one of the following holds.

1) $K \geq 4$, or $K \leq 2$.
2) $K = 3$, each $F \in \mathcal{C}$ that has a threshold of 2 consists of three different threshold functions, and if both $F, G \in \mathcal{C}$ have a threshold of 2 then $F \cap G = \emptyset$.

Following is an example of a class of triplet-PBTNs, which is not PIM-identifiable, because the second condition fails to hold, $\theta(F) = \theta(G) = 2$ and $F \cap G \neq \emptyset$

$$F = \{x_1 + x_2 + x_3 \geq 2, x_1 + x_2 + x_4 \geq 2, x_2 + x_3 + x_4 \geq 2\}$$
$$G = \{x_1 + x_2 + x_3 \geq 2, x_1 + x_3 + x_4 \geq 2, x_2 + x_4 + x_5 \geq 2\}.$$

F cannot be PIM-distinguished from G, because $F(\mathbf{a}) = G(\mathbf{a})$ whenever $G(\mathbf{a})$ is a singleton.

C. Partial Generalization to PBTNs Containing m Functions

One sufficient condition for PIM-identifiability of a class $\mathcal{C}$ containing PBTNs of m functions is obtained by generalizing the first condition of Theorem 18.

Theorem 20: Let $1 \leq \theta_1 < \theta_m \leq K$ be two fixed thresholds, and let $\mathcal{C}$ be a class of admissible PBTNs satisfying the necessary condition for PIM, such that each $F \in \mathcal{C}$ consists of m threshold functions with the following properties: every $f \in F$ depends on exactly K variables and has unit coefficients, and the thresholds of F are $\theta(f_1) = \theta_1,\ \theta(f_m) = \theta_m$ and $\theta_1 < \theta(f) < \theta_m,\ f \neq f_1, f_m$. Then, $\mathcal{C}$ is PIM-identifiable if $f_1 \neq g_1$ or $f_m \neq g_m$ for all pairs $F, G \in \mathcal{C}$.

The proof of this theorem is virtually identical to the proof of the first condition of Theorem 18. Another result concerns PBTNs consisting of m threshold functions that all have the same threshold.

Theorem 21: Let $\mathcal{C}$ be a class of admissible PBTNs each of which consists of up to m functions, all depending on exactly K variables, all having unit coefficients, and all having the same threshold θ, with $1 \leq \theta \leq \max\{1, K + 1 - m\}$ or $\min\{m, K\} \leq \theta \leq K$. Then, $\mathcal{C}$ is PIM-identifiable if and only if $\mathcal{C}$ satisfies the necessary condition for PIM.

The ideas of the theorem can be pushed a bit further, as stated in Theorem 22. Note that if $m \geq K$, then $\theta = 2$ and $\theta = K - 1$ do not satisfy the condition of Theorem 21.

Theorem 22: Let $m \geq K$ and let $\theta_1 = 1, \theta_2 = 2$ or $\theta_1 = K - 1, \theta_2 = K$. Let $\mathcal{C}$ be a class of admissible PBTNs each of which consists of exactly m functions, all depending on exactly K variables, having unit coefficients, and having thresholds that are either all θ_1 or all θ_2. Then, $\mathcal{C}$ is PIM-identifiable if and only if $\mathcal{C}$ satisfies the necessary condition for PIM.

VI. PAIRS OF THRESHOLD FUNCTIONS WITH UNIT COEFFICIENTS UNDER FIM

As in Section V, we consider admissible pairs of threshold functions each of which has all unit coefficients. The difference is that in this section, there is no constraint on the permissible thresholds nor is it required that all functions depend on exactly K variables. There is one necessary condition that needs to be imposed, however, to prevent the class from containing pairs that are obviously FIM-indistinguishable, such as $F = \{x_1 \geq 1, x_2 \geq 1\}, G = \{x_1 + x_2 \geq 1, x_1 + x_2 \geq 2\}$.

Lemma 23 (Necessary Condition for FIM): Let $\mathcal{C}$ be a class of admissible PBTNs each of which consists of one or two threshold functions that have unit coefficients. If $\mathcal{C}$ is FIM-identifiable, then it does not contain $F = \{f_1, f_2\}$ and $G = \{g_1, g_2\}$, such that $f_1 = \ell_1 \geq 1$ $f_2 = \ell_2 \geq 1$, $g_1 = \ell_1 + \ell_2 \geq 1$, $g_2 = \ell_1 + \ell_2 \geq 2$, with ℓ_1, ℓ_2 literals.

Note that our definitions imply that $\ell_1 \neq \ell_2$ and $\ell_1 \neq \overline{\ell_2}$. It is easily seen that indeed for the pair of functions of the lemma, $F(\mathbf{a}) = G(\mathbf{a})$ for all $\mathbf{a}$.

This much broader class is FIM-identifiable.

Theorem 24: Let $\mathcal{C}$ be a class of admissible PBTNs each of which consists of one or two threshold functions that have unit coefficients. Then, $\mathcal{C}$ is FIM-identifiable if and only if the necessary condition for FIM holds.

The following example shows that the same class is not PIM-identifiable.

Example 25: The pair $F = \{x_1+x_2+x_3 \geq 1, x_1+x_2+x_4 \geq 2\}$ cannot be distinguished from the pair $G = \{x_1 + x_2 + x_3 \geq 1, x_1 + x_2 + x_4 \geq 3\}$, because $F(\mathbf{a}) \subseteq G(\mathbf{a})$ for all assignments $\mathbf{a}$.

VII. Pairs of Threshold Functions With General Coefficients Under FIM

We have so far focused on unit coefficient cases under both PIM and FIM. It appears difficult to extend the results to threshold functions with general coefficients. With "unit coefficients," only the presence or absence of a literal plays a role. This is technically reflected in the pervasive use of $LIT(f)$ in the analyses and proofs. A more substantial manifestation is the following.

The essence of Theorem 24 is that if $F = \{f_1, f_2\}$ and $G = \{g_1, g_2\}$ are admissible, then there always is an assignment $\mathbf{a}$ such that $F(\mathbf{a}) \neq G(\mathbf{a})$ unless F and G have the forms given in Lemma 23.

With general coefficients, however, a pair having the properties of Lemma 23 can take on many more forms that are hard to catalog. For example, $F'(\mathbf{a}) = G'(\mathbf{a})$ for all $\mathbf{a}$ if $F' = \{2x_1 + x_2 \geq 2, x_1 + 2x_2 \geq 2\}$ and $G' = \{x_1 + x_2 \geq 1, x_1 + x_2 \geq 2\}$. Looking at the bright side, this example does suggest the positive result stated in Corollary 27 of Theorem 26.

Theorem 26: Suppose that for any nonidentical pair $F = \{f_1, f_2\} \in \mathcal{C}, G = \{g_1, g_2\} \in \mathcal{C}$, there does not exist a pair of assignments $(\mathbf{a}, \mathbf{b})$ such that $f_1(\mathbf{a}) = g_1(\mathbf{a}) \neq f_2(\mathbf{a}) = g_2(\mathbf{a})$ and $f_1(\mathbf{b}) = g_2(\mathbf{b}) \neq f_2(\mathbf{b}) = g_1(\mathbf{b})$. Then, $\mathcal{C}$ is FIM-identifiable.

Proof: We prove the theorem by contrapositive. Suppose that $\mathcal{C}$ is not FIM-identifiable. Then, there exists a nonidentical pair (F, G), such that $F(\mathbf{a}) = G(\mathbf{a})$ holds for all assignments $\mathbf{a}$. For each $\mathbf{a}$, $F(\mathbf{a}) = G(\mathbf{a})$ means that one of the following holds:

$$f_1(\mathbf{a}) = g_1(\mathbf{a}) = f_2(\mathbf{a}) = g_2(\mathbf{a}) \quad (\#1)$$
$$f_1(\mathbf{a}) = g_1(\mathbf{a}) \neq f_2(\mathbf{a}) = g_2(\mathbf{a}) \quad (\#2)$$
$$f_1(\mathbf{a}) = g_2(\mathbf{a}) \neq f_2(\mathbf{a}) = g_1(\mathbf{a}). \quad (\#3)$$

If (#1) or (#2) always hold, (f_1, f_2) is identical to (g_1, g_2), which contradicts the assumption that F and G are not identical. Similarly, if (#1) or (#3) always holds, (f_1, f_2) is identical to (g_2, g_1). Therefore, $F(\mathbf{a}) = G(\mathbf{a})$ holds only if (#2) holds for some $\mathbf{a}$ and (#3) holds for another $\mathbf{a}$ for these F and G. ■

To state Corollary 27, we consider the normalized form of a threshold function in which $\theta = 1$. For example, "$2x_1 + x_2 \geq 2$" is normalized to "$x_1 + 0.5x_2 \geq 1$." For a threshold function f, let $\hat{f}$ denote the left-hand side of its normalized function and $\hat{w}_i^f$ denote the coefficient of x_i in $\hat{f}$. For example, for $f = 2x_1 + x_2 \geq 2$, $\hat{f} = x_1 + 0.5x_2$, $\hat{w}_1^f = 1$, and $\hat{w}_2^f = 0.5$. If x_i does not appear in f, we let $\hat{w}_i^f = 0$.

Corollary 27: $\mathcal{C}$ is FIM-identifiable if for any $\{f_1, f_2\} \in \mathcal{C}$, $\hat{w}_i^{f_1} \geq \hat{w}_i^{f_2}$ holds for all i.

Proof: If the condition is satisfied for $\{f_1, f_2\}$, $\{g_1, g_2\} \in \mathcal{C}$, the following hold for all $\mathbf{a}$: $\hat{f}_1(\mathbf{a}) \geq \hat{f}_2(\mathbf{a})$ and $\hat{g}_1(\mathbf{a}) \geq \hat{g}_2(\mathbf{a})$, which means that $f_1(\mathbf{a}) = g_2(\mathbf{a}) \neq f_2(\mathbf{a}) = g_1(\mathbf{a})$ does not hold for any $\mathbf{a}$. ■

The class considered in this corollary bears some similarity with (but is disjoint from) the class consisting of pairs of the form $\{f, f \wedge g\}$, which is discussed in [33] as a biologically relevant one.

VIII. Sample Complexity and Practical Examples

Here, we discuss sample complexity and identifiability of some realistic models of biological networks.

A. Sample Complexity

PBNs that have doublets of functions at the nodes, where for each input sample, one of the two functions is selected with probability 0.5 to generate the output at that node, are considered in [33]. They show, by adapting a result for BNs [11] to PBNs, that some classes of such PBNs can be identified from $O(\log n)$ samples, in the PIM and/or the FIM setting.

Here, we generalize that result so that node k has an L-tuplet of functions, $F^{(k)} = \{f_1^{(k)}, \ldots f_L^{(k)}\}$, and the probability $c_j^{(k)}$ associated with $f_j^{(k)}$ is lower bounded by $c > 0$. Note that in this section, we consider not a single output node but rather all n nodes, so that a sample is of the form $(\mathbf{a}, \mathbf{b})$, with $\mathbf{a}$ and $\mathbf{b}$ n-bit vectors. We assume that each input sample $\mathbf{a}$ is generated uniformly at random, bit by bit, and that the kth bit of the corresponding n-bit output vector $\mathbf{b}$ is obtained by first choosing j according to the underlying probabilities $c_j^{(k)}$, $j \in \{1, \ldots, L\}$, independently of other nodes, and then computing $f_j^{(k)}(\mathbf{a})$. The proof is given in the Appendix.

Theorem 28: Let $\mathcal{C}$ be a class of PBNs consisting of L-tuplets of functions, each of which has at most K inputs, that satisfies the condition of PIM (resp., FIM) of Theorem 9. If, for fixed L and K, $O((1/c) \cdot 2^{2LK} \cdot (2LK + 1 + \alpha) \cdot \log n)$ samples are generated uniformly at random, as described ealier, then the correct PBN can be uniquely identified at all nodes with probability no less than $1 - (1/n^{\alpha})$ under PIM (resp., FIM).

It is to be noted that for $L = 2$, the increase in the sample complexity is not large (only a factor of $(1/2c)$), compared with the case of $c = 0.5$ [33]. The constant factors depending on L and K might be reduced by using the techniques in [13] and [37], which is left as future work.

B. Practical Examples

Kobayashi and Hiraishi [38] considered the following probabilistic model of an apoptosis network:

	$f_1^{(i)}$	$c_1^{(i)}$	$f_2^{(i)}$	$c_2^{(i)}$
$f_j^{(1)}$	$\overline{x_2} + u \geq 2$	0.6	$x_1 \geq 1$	0.4
$f_j^{(2)}$	$\overline{x_1} + x_3 \geq 2$	0.7	$x_2 \geq 1$	0.3
$f_j^{(3)}$	$x_2 + u \geq 1$	0.8	$x_3 \geq 1$	0.2

where x_1, x_2, and x_3 denote the concentration levels (high or low) of the inhibitor of apoptosis proteins, the active caspase 3, and the active caspase 8, and u denotes the concentration level of the tumor necrosis factor (a stimulus), which is regarded as the control input (i.e., an external input). Note that the probabilities $c_j^{(i)}$ are not relevant in this paper. Each function pair can be represented as $\{x_i \geq 1, \sum_{j \neq i} w_j \ell_j \geq \theta_i\}$, where each w_j is 0 or 1, and θ is 1 or 2. Let $\mathcal{C}$ be the class of such function pairs. Clearly, $\mathcal{C}$ satisfies the conditions of Lemma 23. Therefore, we see from Theorem 24 that $\mathcal{C}$ is FIM-identifiable.

It is to be noted that although class $\mathcal{C}$ bears some similarity with the class of complementary canalyzing pairs studied in [33], it is not covered by that class or any other class in [33].

Furthermore, we can show that a wider class of PBNs is PIM-identifiable.

Theorem 29: Let $\mathcal{C}$ be a class of Boolean function pairs of the form $\{x_i, f\}$, where f is any Boolean function not including x_i or $\overline{x_i}$. Then, $\mathcal{C}$ is PIM-identifiable.

Proof: We consider two cases. First, suppose that $F = \{x_i, f\}$ and $G = \{x_i, g\}$ [case (A)]. Since $F \neq G$, there exists $\mathbf{a}$ such that $f(\mathbf{a}) \neq g(\mathbf{a})$. We assume without loss of generality that $f(\mathbf{a}) = 1$ and $g(\mathbf{a}) = 0$. Let $\mathbf{a}_i^0$ (resp., $\mathbf{a}_i^1$) be a bit vector obtained by assigning 0 (resp., 1) to the ith bit in $\mathbf{a}$. Since x_i does not appear in f or g, we have $F(\mathbf{a}_i^1) = \{1\}$, $G(\mathbf{a}_i^1) = \{0, 1\}$, $F(\mathbf{a}_i^0) = \{0, 1\}$, and $G(\mathbf{a}_i^0) = \{0\}$ from which $F(\mathbf{a}_i^0) - G(\mathbf{a}_i^0) \neq \emptyset$ and $G(\mathbf{a}_i^1) - F(\mathbf{a}_i^1) \neq \emptyset$ follow.

Next, suppose that $F = \{x_i, f\}$ and $G = \{x_j, g\}$, where $x_i \neq x_j$ [case (B)]. We will show that $G(\mathbf{a}) - F(\mathbf{a}) \neq \emptyset$ holds for some $\mathbf{a}$. Existence of $\mathbf{a}$ such that $F(\mathbf{a}) - G(\mathbf{a}) \neq \emptyset$ can also be shown in an analogous way. Suppose that f is a constant. We assume without loss of generality that $f = 0$. Then, $G(\mathbf{a}) - F(\mathbf{a}) \neq \emptyset$ holds for $\mathbf{a}$, such that $\mathbf{a}[i] = 0$ and $\mathbf{a}[j] = 1$, where $\mathbf{a}[i]$ denotes the ith bit of $\mathbf{a}$. Otherwise, f is not a constant. Then, for some $\mathbf{a}$, $\mathbf{a}[i] = 0$ and $f(\mathbf{a}) = 0$ hold. If $\mathbf{a}[j] = 0$ holds for all such $\mathbf{a}$, $f(\mathbf{a}) = 0$ implies $\mathbf{a}[j] = 0$, because x_i or $\overline{x_i}$ does not appear in f. For some $\mathbf{a}$, $\mathbf{a}[i] = 1$ and $f(\mathbf{a}) = 1$ also hold. If $\mathbf{a}[j] = 1$ holds for all such $\mathbf{a}$, $f(\mathbf{a}) = 1$ implies $\mathbf{a}[j] = 1$. Therefore, at least one of the following holds.

1) $\mathbf{a}[i] = 0$, $f(\mathbf{a}) = 0$, and $\mathbf{a}[j] = 1$ hold for some $\mathbf{a}$.
2) $\mathbf{a}[i] = 1$, $f(\mathbf{a}) = 1$, and $\mathbf{a}[j] = 0$ hold for some $\mathbf{a}$.
3) $f = x_j$ holds.

If 1) or 2) holds, $G(\mathbf{a}) - F(\mathbf{a}) \neq \emptyset$ holds. Case 3) corresponds to case (A) and thus can be ignored.

Therefore, class $\mathcal{C}$ satisfies the condition of PIM-identifiability of Theorem 9 and the theorem follows. ■

As noted in [38], asynchronous BNs can be represented by PBNs consisting of pairs in the above class $\mathcal{C}$ by replacing f_i assigned to the ith node in a BN with $\{x_i, f_i\}$. Therefore, Theorem 29 implies that all asynchronous BNs without self-loops are PIM-identifiable. Even if there are some self-loops, function pairs can be PIM-identified for all nodes without self-loops, because function pairs can be identified independently for different nodes. Therefore, this result covers a wide range of asynchronous BNs. For example, asynchronous BN models without self-loops have been studied for the following biological processes: T-cell activation (several tens of nodes) [39], differentiation of T-helper cells (23 nodes) [40], and guard cell ABA signal transduction (11 nodes) [41]. Our results imply that these asynchronous BN models are PIM-identifiable. Of course, efficient algorithms should be developed in order to identify practical networks, because theorems in this paper discuss the identifiability based on exhaustive enumeration. It should also be noted that asynchronous BNs with threshold functions have been studied for theoretical analysis of neural networks [42].

IX. Conclusion

We have studied the problem of exactly identifying the structure of a PBTN with unit coefficients and with general coefficients. We proved that broad classes of such PBTNs can be identified from $O(\log n)$ samples. We also showed some impossibility results on extensions of these classes, which somewhat clarified the identifiable classes of PBTNs. These results give a theoretical foundation on computational identification of stochastic biological and neural networks.

One important future direction is to further study the identification of PBTNs with general coefficients. For that purpose, we may need to develop new techniques because most of the present analyses make heavy use of the properties of threshold functions with unit coefficients. Another important future work is to develop efficient algorithms, because the present results are based on implicit enumeration of all possible combinations. Further studies would strengthen the theoretical foundation and might stimulate developments of practical identification methods.

Appendix
Notation

To prove PIM-identifiability, we will typically reason as follows. Given any $F, G \in \mathcal{C}$, we will show how to construct an assignment $\mathbf{a}$ that PIM-distinguishes F from G, i.e., is such that $G(\mathbf{a})$ is a singleton while $F(\mathbf{a}) - G(\mathbf{a}) \neq \emptyset$. The assignment will be partially specified by two sets of literals, say Y and L, and requiring either that $\mathbf{a}(\ell) = 1$ if $\ell \in Y$, and $\mathbf{a}(\ell) = 0$ if $\ell \in L - Y$ or that $\mathbf{a}(\ell) = 0$ if $\ell \in Y$ and $\mathbf{a}(\ell) = 1$ if $\ell \in L - Y$; any literal whose value is not determined by these assignments can be given an arbitrary value, because this value does not figure in the proof. It will therefore be convenient to employ an indicator notation, as follows.

Notation: Denote by $\mathbf{a} \supset \mathbf{1}_Y^L$ *an assignment* $\mathbf{a}$ *such that* $\mathbf{a}(\ell) = 1$ *if* $\ell \in Y$, $\mathbf{a}(\ell) = 0$ *if* $\ell \in L - Y$, *while the values of* $\mathbf{a}(\ell)$ *for* $\ell \notin Y \cup L$ *are irrelevant (as long as they are consistent with the defined values).*

Thus, $\mathbf{a} \supset \mathbf{1}_{L-Y}^{L}$ specifies that $\mathbf{a}(\ell) = 0$ if $\ell \in Y$, $\mathbf{a}(\ell) = 1$ if $\ell \in L - Y$.

Proof of Theorem 9

Proof: Suppose first that condition (1) holds. Then, for each $G \in \mathcal{C}$, $G \neq F$, there is an $\mathbf{a}_G$ such that $\upsilon_G \in F(\mathbf{a}_G) - G(\mathbf{a}_G)$. Let $S = \{(\mathbf{a}_G, \upsilon_G) : G \in \mathcal{C}, G \neq F\}$. Clearly, F is consistent with S, whereas every $G \in \mathcal{C}$, $G \neq F$, is inconsistent with S.

For the converse suppose that $\mathcal{C}$ is PIM-identifiable, and let $F, G \in \mathcal{C}$. Let S be a set of samples that PIM-identifies F. Then, there is a sample $(\mathbf{a}, \upsilon)$ with which F is consistent but G is inconsistent, i.e., $\upsilon \in F(\mathbf{a})$ but $\upsilon \notin G(\mathbf{a})$. Hence, $F(\mathbf{a}) - G(\mathbf{a}) \neq \emptyset$.

Similarly, if condition (2) holds then for each $G \in \mathcal{C}$, $G \neq F$, there is an $\mathbf{a}_G$, such that $F(\mathbf{a}_G) \neq G(\mathbf{a}_G)$. Let $S = \cup_{G \in \mathcal{C}, G \neq F} F(\mathbf{a}_G)$. Clearly, F is consistent with S, and for all $(\mathbf{a}, \upsilon) \in S$ in fact $\mathbf{a} \times F(\mathbf{a}) \subseteq S$. For every $G \in \mathcal{C}$, $G \neq F$, in contrast, there either is a $\upsilon \in F(\mathbf{a}_G) - G(\mathbf{a}_G)$ or a $\upsilon \in G(\mathbf{a}_G) - F(\mathbf{a}_G)$. In the first case, G is inconsistent with $(\mathbf{a}_G, \upsilon)$, and in the second case, $G(\mathbf{a}_G) \not\subseteq S$.

Conversely, if $\mathcal{C}$ is FIM-identifiable and $F, G \in \mathcal{C}$, let S be a set of samples that FIM-identifies F. Then, either G is inconsistent with S, i.e., there is an $(\mathbf{a}, \upsilon)$ such that $\upsilon \in F(\mathbf{a}_G) - G(\mathbf{a}_G)$, or there is $(\mathbf{a}, \upsilon)$ such that $G(\mathbf{a}) \not\subseteq S$, i.e., $\upsilon \in G(\mathbf{a}_G) - F(\mathbf{a}_G)$. In both cases, $F(\mathbf{a}) \neq G(\mathbf{a})$. ■

Proof of Theorem 17

Proof: We will consider separately the possible combinations of thresholds. For brevity, we will denote, for example, the case that f_1, f_2 and g_1 have threshold θ_1 and g_2 has threshold θ_2 by "$\{\theta_1, \theta_1\}$ versus $\{\theta_1, \theta_2\}$." We assume always that $\theta(f_1) \leq \theta(f_2)$, and $\theta(g_1) \leq \theta(g_2)$.

1) $\{\theta_1, \theta_1\}$ versus $\{\theta_2, \theta_2\}$, or $\{\theta_1, \theta_2\}$ versus $\{\theta_2, \theta_2\}$.
Let $Y \subseteq LIT(f_1)$ be such that $|Y| = \theta_1$, and let $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$. Note that the assignment $\mathbf{a}$ is not self-contradictory, because G is admissible, i.e., if $\ell \in LIT(g_1)$, then $\overline{\ell} \notin LIT(g_2)$. Now $1 \in F(\mathbf{a})$ because $|LIT(f_1) \cap Y| = \theta_1$, while $|LIT(g_i) \cap Y| \leq \theta_1 < \theta_2$, $i = 1, 2$, so that $1 \notin G(\mathbf{a})$, and hence, $F(\mathbf{a}) - G(\mathbf{a}) \neq \emptyset$.

2) $\{\theta_1, \theta_2\}$ versus $\{\theta_1, \theta_1\}$, or $\{\theta_2, \theta_2\}$ versus $\{\theta_1, \theta_1\}$.
Let $Z \subseteq LIT(f_2)$ be such that $|Z| = K - \theta_2 + 1$, and let $\mathbf{a} \supset \mathbf{1}_{LIT(G)-Z}^{LIT(G)}$. Then, $0 \in F(\mathbf{a})$, since $|LIT(f_2) - Z| \leq \theta_2 - 1 < \theta_2$, but $0 \notin G(\mathbf{a})$, because $|LIT(g_i) - Z| \geq \theta_2 - 1 \geq \theta_1$, as g_i depends on exactly K variables, $i = 1, 2$.

3) $\{\theta_1, \theta_2\}$ versus $\{\theta_1, \theta_2\}$.
If there is a literal $y \in LIT(f_1) - LIT(g_1) \neq \emptyset$ then let $Y \subseteq LIT(f_1)$ be such that $y \in Y$ and $|Y| = \theta_1$. Let $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$. Then, $1 \in F(\mathbf{a})$, since $|LIT(f_1) \cap Y| = \theta_1$, but $G(\mathbf{a}) = \{0\}$, because $|LIT(g_1) \cap Y| \leq \theta_1 - 1 < \theta_1$, and $|LIT(g_2) \cap Y| \leq \theta_1 < \theta_2$.
If, on the other hand, $LIT(f_1) - LIT(g_1) = \emptyset$, then in fact $LIT(f_1) = LIT(g_1)$, because both functions depend on exactly K variables. Consequently, $f_1 = g_1$, since the two functions have the same threshold. Moreover, necessarily $LIT(f_2) - LIT(g_2) \neq \emptyset$, because otherwise it would follow, similarly, that $f_2 = g_2$. There is therefore a $z \in LIT(f_2) - LIT(g_2)$. Let $Z \subseteq LIT(f_2)$ be such that $|Z| = K - \theta_2 + 1$ and $z \in Z$. Now let $\mathbf{a} \supset \mathbf{1}_{LIT(G)-Z}^{LIT(G)}$. Then, $0 \in F(\mathbf{a})$, since $|LIT(f_2) - Z| \leq \theta_2 - 1 < \theta_2$, but $0 \notin G(\mathbf{a})$, because $|LIT(g_1) - Z| \geq \theta_2 - 1 \geq \theta_1$, and $|LIT(g_2) - Z| \geq \theta_2$.

4) $\{\theta_1, \theta_1\}$ versus $\{\theta_1, \theta_2\}$, or $\{\theta_2, \theta_2\}$ versus $\{\theta_1, \theta_2\}$.
We deal with the two cases together by considering $\{s, s\}$ versus $\{s, t\}$, $s \neq t$, i.e., $s = \theta_1, t = \theta_2$ or $s = \theta_2$, $t = \theta_1$. Note that in the second case, $\theta(g_2) < \theta(g_1)$.
To begin with we prove that there is a literal $z \in LIT(f_1) - LIT(g_1)$. Consider first the possibility that $LIT(f_1) \neq LIT(f_2)$. Then, $|LIT(F)| \geq K + 1 > |LIT(g_1)| = K$, so that $LIT(F) - LIT(g_1) \neq \emptyset$ and without loss of generality, we can assume that $LIT(f_1) - LIT(g_1) \neq \emptyset$. If, on the other hand, $LIT(f_1) = LIT(f_2)$, then $f_1 = f_2$, so that $f_1 \neq g_1$, because of the necessary condition, and in particular $LIT(f_1) - LIT(g_1) \neq \emptyset$.
In case $s = \theta_2$, let $Z \subseteq LIT(f_1)$ with $|Z| = K - s + 1$ be such that $z \in Z$, and let $\mathbf{a} \supset \mathbf{1}_{LIT(G)-Z}^{LIT(G)}$. Then, $0 \in F(\mathbf{a})$, since $|LIT(f_1) - Z| \leq s - 1 < s$, while $G(\mathbf{a}) = \{1\}$, because $|LIT(g_1) - Z| \geq s - 1 \geq t$, and $|LIT(g_2) - Z| \geq s$.
In case $s = \theta_1$, let $Y \subseteq LIT(f_1)$ be such that $y \in Y$ and $|Y| = s$. Letting $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$, it is readily seen that $1 \in F(\mathbf{a})$ but $G(\mathbf{a}) = \{0\}$.

5) $\{\theta_1, \theta_1\}$ versus $\{\theta_1, \theta_1\}$, or $\{\theta_2, \theta_2\}$ versus $\{\theta_2, \theta_2\}$.
We deal with the two cases together by considering $\{t, t\}$ versus $\{t, t\}$, for $t = \theta_1$ or $t = \theta_2$. Observe that for one of $j = 1$ and $j = 2$, there are $z_i \in LIT(f_j) - LIT(g_i)$, $i = 1, 2$, say $j = 1$. Indeed, were that not to be the case then from $LIT(f_1) - LIT(g_i) = \emptyset$ for $i = 1$ or 2, say for $i = 1$, it follows that $f_1 = g_1$, and from $LIT(f_2) - LIT(g_i) = \emptyset$ for $i = 1$ or 2 it follows that $f_2 = g_1$ or $f_2 = g_2$. Neither of the latter eventualities can happen because $f_1 = f_2 = g_1$ violates the necessary condition, while $f_1 = g_1$, $f_2 = g_2$ means that $F = G$.
   a) $1 \leq t \leq K - 1$.
   Let Z contain both z_1 and z_2, $Z \subseteq LIT(f_1)$ and $|Z| = K - t + 1 \geq 2$, and let $\mathbf{a} \supset \mathbf{1}_{LIT(G)-Z}^{LIT(G)}$. Then, $0 \in F(\mathbf{a})$ since $|LIT(f_1) - Z| = t - 1$, while $G(\mathbf{a}) = \{1\}$, because $|LIT(g_i) - Z| \geq t$, $i = 1, 2$.
   b) $2 \leq t \leq K$.
   Let Y contain both z_1 and z_2, $Y \subseteq LIT(f_1)$ and $|Y| = t$, and let $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$. Then, $1 \in F(\mathbf{a})$, since $|LIT(f_1) \cap Y| = t$, while $G(\mathbf{a}) = \{0\}$, because $|LIT(g_i) \cap Y| \leq t - 1$, $i = 1, 2$. ■

Remarks on Theorem 17

Remark 30:

1) Theorem 17 may not be true if some functions do not have exactly K variables, as the following example shows. If $F = \{x_1 \geq 1, x_2 \geq 1\}$, $G = \{x_1 + x_2 \geq 1, x_1 + x_2 \geq 2\}$, then $F(\mathbf{a}) = G(\mathbf{a})$ for all $\mathbf{a}$.

2) Theorem 17 may also not hold if instead of a choice between two thresholds there is a choice between three, as the following example shows. If $F = \{x_1+x_2+x_4 \geq 2, x_2+x_3+x_5 \geq 2\}$, $G = \{x_1+x_2+x_3 \geq 1, x_1+x_2+x_5 \geq 3\}$, then $F(\mathbf{a}) = G(\mathbf{a})$ whenever $G(\mathbf{a})$ is a singleton.
3) In contrast to the previous comment, we note the following special case of Theorem 21 in Section V-C.
Let $\mathcal{C}$ be a class of admissible PBTNs that satisfies the necessary condition for PIM, and is such that each $F \in \mathcal{C}$ consists of two (not necessarily different) threshold functions that have the *same* threshold, in addition to both depending on exactly K variables and having unit coefficients. Then, $\mathcal{C}$ is PIM-identifiable.
Note that here the common threshold of F is not restricted to two values.

Proof of Theorem 18

Proof: Suppose the first condition holds, and consider a pair $F, G \in \mathcal{C}$. If $f_1 \neq g_1$ let $Y \subseteq LIT(f_1)$ be such that $|Y| = \theta_1$ and $Y \cap \big(LIT(f_1) - LIT(g_1)\big) \neq \emptyset$, and let $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$. Then, $1 \in F(\mathbf{a})$, while $|Y \cap LIT(g_1)| \leq \theta_1 - 1$ means that $g_1(\mathbf{a}) = 0$, and $|Y \cap LIT(g_i)| \leq \theta_1 < \theta(g_i)$ means that also $g_i(\mathbf{a}) = 0$, $i = 2, 3$. Hence, $G(\mathbf{a}) = \{0\}$. The proof for the case $f_3 \neq g_3$ is similar: there must be a set $Z \subseteq LIT(f_3)$, $|Z| = K - \theta_3 + 1$, such that $Z \cap \big(LIT(f_3) - LIT(g_3)\big) \neq \emptyset$. Defining $\mathbf{a} \supset \mathbf{1}_{LIT(G)-Z}^{LIT(G)}$, it is easily seen that $0 \in F(\mathbf{a})$ but $G(\mathbf{a}) = \{1\}$.

Conditions (2) and (3) are different ways of imposing more stringent restrictions in order to deal with the difficulty that arises when $\theta(g_2) = \theta_1$ or $\theta(g_2) = \theta_3$. If (3) holds, then the previous proof is again applicable, because it ensures that both $f_1 \neq g_1$ and $f_3 \neq g_3$. Even if $\theta(g_2) = \theta_3$, the previous proof for the case $f_1 \neq g_1$ is still applicable, because $\theta(g_1) < \theta(g_2)$.

If (2) holds and, say, $f_3 = g_3$, then we know that $f_1 \neq g_1$ and $f_1 \neq g_2$, so that there are $y_i \in LIT(f_1) - LIT(g_i)$, $i = 1, 2$. Since $\theta_1 \geq 2$, there is $Y \subseteq LIT(f_1)$ with $|Y| = \theta_1$, such that $Y \supset \{y_1, y_2\}$. Letting $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$, it is again seen that $1 \in F(\mathbf{a})$, while $G(\mathbf{a}) = \{0\}$. ■

Remarks on Theorem 18

Remark 31:

1) The first two conditions cannot be weakened to permit both $f_1 = g_1$ and $f_3 = g_3$.
Consider $f_1 = g_1 \equiv x_1 + x_2 + x_3 + x_4 + x_5 \geq 2$, $f_3 = g_3 \equiv x_1 + x_2 + x_3 + x_4 + x_5 \geq 4$, $f_2 \equiv x_1 + x_2 + x_3 + x_4 + x_5 \geq 3$, $g_2 \equiv x_1 + x_2 + x_4 + x_5 + x_6 \geq 3$. It is readily seen that $F(\mathbf{a}) = G(\mathbf{a})$ if $|G(\mathbf{a})| = 1$.
2) The third condition cannot be weakened to permit $f_1 = g_1$ or $f_3 = g_3$.
Here, these are two counterexamples. In the first, $f_1 = g_1 \equiv x_1 + x_2 + x_3 \geq 2$, $f_2 \equiv x_2 + x_3 + x_4 \geq 3$, $f_3 \equiv x_1 + x_2 + x_3 \geq 3$, $g_2 \equiv x_1 + x_2 + x_4 \geq 3$, and $g_3 \equiv x_1 + x_3 + x_4 \geq 3$.
In the second $f_1 \equiv x_1+x_2+x_3 \geq 1$, $f_2 \equiv x_3+x_4+x_5 \geq 2$, $f_3 = g_3 \equiv x_1 + x_3 + x_5 \geq 3$, $g_1 \equiv x_1 + x_2 + x_4 \geq 1$, and $g_2 \equiv x_2 + x_3 + x_5 \geq 1$.
In both cases, it can be verified that $F(\mathbf{a}) = G(\mathbf{a})$ if $|G(\mathbf{a})| = 1$.
3) In the first counterexample of the previous comment, the absence of an assignment that PIM-distinguishes F from G is the result of the fact that $\theta(f_2) = \theta(f_3) = \theta(g_2) = \theta(g_3) = K = 3$ and $\big(LIT(f_2) \cup LIT(f_3)\big) - \big(LIT(g_2) \cup LIT(g_3)\big) = \emptyset$. Similarly, in the second, counterexample $\theta(f_1) = \theta(g_1) = \theta(g_2) = 1$ and $LIT(f_1) - \big(LIT(g_2) \cup LIT(g_3)\big) = \emptyset$.
It *is* possible to weaken the third condition as follows: if $\theta_1 = 1$, then for all $F, G \in \mathcal{C}$ such that $\theta(g_2) = 1$ and $f_3 = g_3$ it holds that $LIT(f_1) - \big(LIT(g_1) \cup LIT(g_2)\big) \neq \emptyset$, or, if also $\theta(f_2) = 1$, that $LIT(f_2) - \big(LIT(g_1) \cup LIT(g_2)\big) \neq \emptyset$. And if $\theta_3 = K$, then for all $F, G \in \mathcal{C}$ such that $\theta(g_2) = 3$ and $f_1 = g_1$ it holds that $LIT(f_3) - \big(LIT(g_2) \cup LIT(g_3)\big) \neq \emptyset$, or, if also $\theta(f_2) = 3$, that $LIT(f_2) - \big(LIT(g_2) \cup LIT(g_3)\big) \neq \emptyset$.

Proof of Theorem 19

Proof: The first condition follows from Theorem 21. Consider, then, $K = 3$ and $F, G \in \mathcal{C}$. Denote by $\theta(F)$ the threshold that is common to all $f \in F$. If $\theta(F) \neq \theta(G)$ or $\theta(F) = \theta(G) \neq 2$, then the proofs of these cases given in the section proof of Theorem 21 in the Appendix apply here as well. It remains to examine the case $\theta(F) = \theta(G) = 2$.

Observe that $|LIT(f_i) \cap LIT(g_j)| \leq 2$, $i, j = 1, 2, 3$, since $F \cap G = \emptyset$. The following cases are exhaustive.

1) $|LIT(f_i) \cap LIT(g_j)| \leq 1$ for some i, j.
Without loss of generality assume $i = j = 1$. If also $|LIT(f_1) \cap LIT(g_2)| \leq 1$, let $y \in LIT(f_1) - LIT(g_3)$ and if $|LIT(f_1) \cap LIT(g_3)| \leq 1$, let $y \in LIT(f_1) - LIT(g_2)$. Let $z \in LIT(f_1) - \{y\}$, set $Y = \{y, z\}$ and note that $|LIT(g_j) \cap Y| \leq 1$, $j = 1, 2, 3$.
Otherwise, $|LIT(f_1) \cap LIT(g_2)| = |LIT(f_1) \cap LIT(g_3)| = 2$, and it follows that there is a $y \in LIT(f_1)$, such that $y \in LIT(g_2) \cap LIT(g_3)$. Let $Y = LIT(f_1) - \{y\}$ and note that again $|LIT(g_j) \cap Y| \leq 1$, $j = 1, 2, 3$.
Letting $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$, it is seen that $1 \in F(\mathbf{a})$, while $G(\mathbf{a}) = \{0\}$, i.e., that F is PIM-distinguishable from G.
2) $|LIT(f_i) \cap LIT(g_j)| = 2$, $i, j = 1, 2, 3$, and for some i, j_1, j_2, $|LIT(f_i) \cap LIT(g_{j_1}) \cap LIT(g_{j_2})| = 2$.
Without loss of generality, assume $i = j_1 = 1, j_2 = 2$. Let $y \in LIT(f_1) - LIT(g_1)$, and $z \in LIT(f_1) - LIT(g_3)$. Setting $Y = \{y, z\}$, note that $|LIT(g_j) \cap Y| \leq 1$, $j = 1, 2, 3$. Thus, $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$ PIM-distinguishes F from G.
3) $|LIT(f_i) \cap LIT(g_j)| = 2$, $i, j = 1, 2, 3$, and $|LIT(f_i) \cap LIT(g_{j_1}) \cap LIT(g_{j_2})| = 1$ for all i, j_1, j_2.
We prove that this case cannot occur. Let $LIT(f_1) = \{y_1, y_2, y_3\}$. Then, $LIT(g_1) = \{y_1, y_2, \ell_1\}$, $LIT(g_2) = \{y_1, y_3, \ell_2\}$, and $LIT(g_3) = \{y_2, y_3, \ell_3\}$, with $\ell_i \notin \{y_1, y_2, y_3\}$, $i = 1, 2, 3$.
Observe that the multiset obtained by adjoining $LIT(g_1)$, $LIT(g_2)$, and $LIT(g_3)$ consists of two copies each of y_1, y_2, and y_3, in addition to ℓ_1, ℓ_2, and ℓ_3.

At the same, this multiset can also be viewed as containing two copies of each of the literals in the set $LIT(f_2) = \{z_1, z_2, z_3\}$. But $LIT(f_1) \neq LIT(f_2)$, and hence, one of the pair of copies must involve ℓ_is, i.e., $\ell_i = \ell_j$ for some $i \neq j$.

Suppose, without loss of generality, that $\ell_1 = \ell_2$. The preconditions of this case imply that one of the z_is is ℓ_1, and the other two are y_is, in fact $LIT(f_2) = \{y_1, y_3, \ell_1\}$, and $\ell_3 \neq \ell_1$.

However, the multiset can also be viewed as containing two copies of each of the literals in the set $LIT(f_3)$, and reasoning as before we reach the conclusion that $LIT(f_3) = \{y_1, y_3, \ell_1\} = LIT(f_2)$ when $\ell_1 = \ell_2$. This contradicts the prerequisite that F consists of three different threshold functions. ∎

Proof of Theorem 21

Proof: The proof is an adaptation of the cases $\{t, t\}$ versus $\{t, t\}$, and $\{s, s\}$ versus $\{t, t\}$ of Theorem 17 to the present setting.

1) $t = \theta(F) = \theta(G)$.

For at least one of $j = 1, \ldots, m$, there are $z_i \in LIT(f_j) - LIT(g_i), i = 1, \ldots, m$, say $j = 1$. Where there no such j then for each j, there is an i_j such that $f_j = g_{i_j}$, which means that $F \subseteq G$.

a) $1 \leq t \leq \max\{1, K + 1 - m\}$.

Let $Z \subseteq LIT(f_1)$ with $|Z| = K - t + 1$ be such that $z_i \in Z,\ i = 1, \ldots m$, and let $\mathbf{a}$ be an assignment such that $\mathbf{a}(\ell) = 0$ if $\ell \in Z$ and $\mathbf{a}(\ell) = 1$ if $\ell \in LIT(G) - Z$. Then, $w_{f_1}(\mathbf{a}) = |LIT(f_1) - Z| = t - 1$, while $w_g(\mathbf{a}) = |LIT(g) - Z| \geq t$ for all $g \in G$, so that $0 \in F(\mathbf{a})$, while $G(\mathbf{a}) = \{1\}$. Note that $|\{z_1, \ldots, z_m\}| \leq K$ even if $m > K$, because all z_i are in $LIT(f_1)$; in particular, if $t = 1$, then $Z = LIT(f_1)$ regardless of the value of m.

b) $\min\{m, K\} \leq t \leq K$.

Let $Y \subseteq LIT(f_1)$ with $|Y| = t$ such that $z_i \in Y,\ i = 1, \ldots m$, and let $\mathbf{a}$ be an assignment such that $\mathbf{a}(\ell) = 1$ if $\ell \in Y$ and $\mathbf{a}(\ell) = 0$ if $\ell \in LIT(G) - Y$. Then, $w_{f_1}(\mathbf{a}) = |LIT(f_1) \cap Y| = t$, while $w_g(\mathbf{a})|LIT(g) \cap Y| \leq t - 1$ for all $g \in G$, so that $1 \in F(\mathbf{a})$ while $G(\mathbf{a}) = \{0\}$.

2) $\theta(F) = s \neq t = \theta(G)$.

In case $s < t$, let Y be any subset of $LIT(f_1)$ such that $|Y| = s$, and let $\mathbf{a}$ be an assignment such that $\ell(\mathbf{a}) = 1$ if $\ell \in Y$ and $\ell(\mathbf{a}) = 0$ if $\ell \in LIT(G) - Y$. Then, $|LIT(f_1) \cap Y| = s$ so that $1 \in F(\mathbf{a})$, while $|LIT(g_i) \cap Y| \leq s < t,\ i = 1, \ldots, m$, so that $G(\mathbf{a}) = \{0\}$, and $F(\mathbf{a}) - G(\mathbf{a}) \neq \emptyset$.

In case $s > t$, let Z be a subset of $LIT(f_1)$ such that $|Z| = K - s + 1$, and let $\mathbf{a}$ be an assignment such that $\mathbf{a}(\ell) = 0$ if $\ell \in Z$ and $\mathbf{a}(\ell) = 1$ if $\ell \in LIT(G) - Z$. Then, $|LIT(f_1) - Z| \leq s - 1$ so that $0 \in F(\mathbf{a})$, but $|LIT(g_i) - Z| \geq s - 1 \geq t,\ i = 1, \ldots, m$. Hence, $G(\mathbf{a}) = \{1\}$. ∎

Remarks on Theorem 21

Remark 32:

1) If the class $\mathcal{C}$ contains only AND-PBTNs ($\theta = K$) and OR-PBTNs ($\theta = 1$), then it is PIM-identifiable for all m (provided all functions depend on exactly K variables).
2) If $m \leq K \div 2 + 1$, then $\mathcal{C}$ is PIM-identifiable without any restriction on possible θs.
3) There is no straightforward generalization of Theorem 17 to the case that $\mathcal{C}$ contains PBTNs with a mixture of thresholds. Here, it is an example for $m = 3,\ K = 2$ and thresholds $\theta_1 = 1,\ \theta_2 = 2$

$$F = \{x_1 + x_2 \geq 2, x_2 + x_3 \geq 2, x_3 + x_4 \geq 2\}$$
$$G = \{x_1 + x_3 \geq 2, x_2 + x_4 \geq 2, x_1 + x_3 \geq 1\}.$$

To verify that F is not PIM-distinguishable from G observe that $0 \in F(\mathbf{a})$ means that at least one of $\mathbf{a}_1, \mathbf{a}_2, \mathbf{a}_3$, and $\mathbf{a}_4$ is assigned 0, so that $0 \in G(\mathbf{a})$, and that there exists no assignment $\mathbf{a}$ such that $1 \in F(\mathbf{a})$ while $G(\mathbf{a}) = \{0\}$, because the latter implies that both $\mathbf{a}_1 = \mathbf{a}_3 = 0$. However, the assignment $\mathbf{a} = (1, 0, 0, 0)$ FIM-distinguishes the two PBTNs.

Proof of Theorem 24

Proof: We base the proof on condition 2 of Theorem 9, and show that given an $F = \{f_1, f_2\} \in \mathcal{C}$ and any other $G = \{g_1, g_2\} \in \mathcal{C},\ F \neq G$, there is an assignment $\mathbf{a}$ such that $F(\mathbf{a}) \neq G(\mathbf{a})$. In doing so, we assume that $\theta(f_1) \leq \theta(f_2),\ \theta(g_1) \leq \theta(g_2)$, and $\theta(f_1) \leq \theta(g_1)$.

1) $f_1 = g_1$ or $f_2 = g_2$, i.e., $F \cap G \neq \emptyset$.

Assume, for example, $f_1 = g_1$ and $f_2 \neq g_2$, the proof for $f_2 = g_2$ and $f_1 \neq g_1$ being entirely similar. If $\theta(f_2) < \theta(g_2)$, then let $Y \subseteq LIT(f_2)$ have size $\theta(f_2)$, and let $\mathbf{a} \supset \mathbf{1}_Y^{LIT(g_2)}$. Then, $f_2(\mathbf{a}) = 1$ while $g_2(\mathbf{a}) = 0$. If $\theta(f_2) = \theta(g_2)$, then necessarily $LIT(f_2) \neq LIT(g_2)$ because $f_2 \neq g_2$. This means that $LIT(f_2) - LIT(g_2) \neq \emptyset$ or $LIT(g_2) - LIT(f_2) \neq \emptyset$. Assume the former, let $y \in LIT(f_2) - LIT(g_2)$, let Y be a subset of $LIT(f_2)$ of size $\theta(f_2)$ such that $y \in Y$, and let $\mathbf{a} \supset \mathbf{1}_Y^{LIT(g_2)}$. Then, $f_2(\mathbf{a}) = 1$, while $|LIT(g_2) \cap Y| < \theta(g_2)$ means that $g_2(\mathbf{a}) = 0$.

Consequently, in both cases, $F(\mathbf{a}) \neq G(\mathbf{a})$, regardless of the value of $f_1(\mathbf{a})$.

Note that included in this case is the possibility that $F = \{f_1\}$, i.e., $f_2 = f_1$, a possibility which was excluded in the PIM setting.

In the following cases, we can therefore assume that $f_j \neq g_i, i = 1, 2,\ j = 1, 2$.

2) $\theta(f_1) < \theta(g_1)$.

Let Y be an arbitrary subset of $LIT(f_1)$ of size $\theta(f_1)$, and let $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$. The admissibility of G ensures that such an assignment exists. Then, $f_1(\mathbf{a}) = 1$, while $|Y \cap LIT(g_i)| < \theta(g_i)$ means that $g_i(\mathbf{a}) = 0,\ i = 1, 2$. Hence, $F(\mathbf{a}) \neq G(\mathbf{a})$.

3) $\theta(f_1) = \theta(g_1) < \min\{\theta(f_2), \theta(g_2)\}$.

$LIT(f_1) \neq LIT(g_1)$ because $f_1 \neq g_1$. Assume without loss of generality that $LIT(f_1) - LIT(g_1) \neq \emptyset$, define

Y as in the previous case but impose the additional requirement that $Y \cap \big(LIT(f_1) - LIT(g_1)\big) \neq \emptyset$. It follows as above that $f_1(\mathbf{a}) = 1$ and $g_i(\mathbf{a}) = 0$, $i = 1, 2$.

4) $\theta(f_1) = \theta(g_1) = \theta(f_2) = t < \theta(g_2)$.
   a) $LIT(g_1) - LIT(F) \neq \emptyset,\ t \geq 1$.
      Let $Y \subseteq LIT(g_1)$ be of size t with $Y \cap \big(LIT(g_1) - LIT(F)\big) \neq \emptyset$. Arguing as in case 3, it is easily seen that $g_1(\mathbf{a}) = 1$ and $f_i(\mathbf{a}) = 0$, $i = 1, 2$.
   b) $LIT(F) - LIT(g_1) \neq \emptyset,\ t \geq 1$.
      Assume without loss of generality that $LIT(f_1) - LIT(g_1) \neq \emptyset$. Let $Y \subseteq LIT(f_1)$ be of size t with $Y \cap \big(LIT(f_1) - LIT(g_1)\big) \neq \emptyset$. Arguing as in case 3, it is easily seen that $f_1(\mathbf{a}) = 1$ and $g_i(\mathbf{a}) = 0,\ i = 1, 2$.
   c) $LIT(F) = LIT(g_1)$, $t \geq 2$.
      There exist $y_i \in LIT(g_1) - LIT(f_i)$, because $g_1 \neq f_1,\ g_1 \neq f_2$. Let $Y \subseteq LIT(g_1)$ be of size t with $y_i \in Y,\ i = 1, 2$. Arguing as in case 3, it is easily seen that $g_1(\mathbf{a}) = 1$ and $f_i(\mathbf{a}) = 0,\ i = 1, 2$.
   d) $LIT(F) = LIT(g_1)$, $t = 1$, and $\theta(g_2) > 2$.
      With y_i defined as in the previous item, let $Y = \{y_1, y_2\}$. Note that $y_1 \in LIT(f_2),\ y_2 \in LIT(f_1)$, because $LIT(F) = LIT(g_1)$. Hence, $|Y \cap LIT(f_i)| = 1$, and so $g_1(\mathbf{a}) = f_i(\mathbf{a}) = 1,\ i = 1, 2$, while $g_2(\mathbf{a}) = 0$. Note that $|LIT(g_1)| \geq 2$ because $LIT(g_1) = LIT(F)$, and $f_1 \neq f_2$.
   e) $LIT(F) = LIT(g_1)$, $t = 1$, $\theta(g_2) = 2$, and $LIT(f_1) \cap LIT(f_2) \neq \emptyset$.
      Let $y \in LIT(f_1) \cap LIT(f_2)$, and $\mathbf{a} \supset \mathbf{1}_{\{y\}}^{LIT(g_2)}$. Then, $g_1(\mathbf{a}) = f_i(\mathbf{a}) = 1,\ i = 1, 2$ while $g_2(\mathbf{a}) = 0$.
   f) $LIT(F) = LIT(g_1), t = 1, \theta(g_2) = 2, LIT(f_1) \cap LIT(f_2) = \emptyset$, and $LIT(g_1) \neq LIT(g_2)$.
      If there exists $y \in LIT(g_1) - LIT(g_2)$, then $y \in LIT(f_1)$ or $y \in LIT(f_2)$, but not both, say $y \in LIT(f_1),\ y \notin LIT(f_2)$.Let $y' \in LIT(f_2)$, and let $\mathbf{a} \supset \mathbf{1}_{\{y,y'\}}^{LIT(g_2)}$. Then, $g_1(\mathbf{a}) = f_i(\mathbf{a}) = 1,\ i = 1, 2$, while $g_2(\mathbf{a}) = 0$.
      If $LIT(g_1) \cap LIT(g_2) = \emptyset$, then trivially there is an assignment, such that $g_1(\mathbf{a}) = f_i(\mathbf{a}) = 0,\ i = 1, 2$ while $g_2(\mathbf{a}) = 1$.
      If none of these occurs, then there exist $y \in LIT(g_2) - LIT(g_1)$ and $y' \in LIT(g_1) \cap LIT(g_2)$, and for an assignment $\mathbf{a}$ such that $\mathbf{a}(y) = \mathbf{a}(y') = 1$ and $\mathbf{a}(\ell) = 0$ if $\ell \in LIT(F) - \{y'\}$, $g_1(\mathbf{a}) = g_2(\mathbf{a}) = 1$, while $f_1(\mathbf{a}) \neq f_2(\mathbf{a})$.
   g) $LIT(F) = LIT(g_1) = LIT(g_2)$, $t = 1$, $\theta(g_2) = 2$, $LIT(f_1) \cap LIT(f_2) = \emptyset$, and $LIT(f_1) \geq 2$ or $LIT(f_2) \geq 2$.
      If, say, $LIT(f_1) \geq 2$, then $F(\mathbf{a}) = \{0, 1\} \neq G(\mathbf{a}) = \{1\}$ for the assignment $\mathbf{a}$ that assigns 1 to all literals in $LIT(f_1)$ and 0 to all literals in $LIT(f_2)$.

5) $\min\{\theta(f_1), \theta(g_1)\} = \max\{\theta(f_2), \theta(g_2)\} = t$.
   a) $LIT(F) - LIT(G) \neq \emptyset$ or $LIT(G) - LIT(F) \neq \emptyset$.
      Suppose, for example, that there is a $y \in LIT(f_1) - LIT(G) \neq \emptyset$. Let $Y \subseteq LIT(f_1)$ be such that $|Y| = t$ and $y \in Y$, and let $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$. Then, $f_1(\mathbf{a}) = 1$ while $|Y \cap LIT(g_i)| < t$, $i = 1, 2$, means that $G(\mathbf{a}) = \{0\}$.
   b) $LIT(F) = LIT(G)$ and $t \geq 2$.
      If there are $y_1 \in LIT(f_1) - LIT(g_1) \neq \emptyset$ and $y_2 \in LIT(f_1) - LIT(g_2) \neq \emptyset$ let $Y \subseteq LIT(f_1)$ have size t with $\{y_1, y_2\} \subseteq Y$, and let $\mathbf{a} \supset \mathbf{1}_Y^{LIT(G)}$. Then, $g_i(\mathbf{a}) = 0$ since $|LIT(g_i) \cap Y| \leq t - 1,\ i = 1, 2$, while $f_1(\mathbf{a}) = 1$.
      Let us examine next the case that the previous condition does not hold, say $LIT(f_1) - LIT(g_1) = \emptyset$, which means that $LIT(f_1)$ is a strict subset of $LIT(g_1)$, $LIT(g_1) - LIT(f_1) \neq \emptyset$, because $f_1 \neq g_1$. If also $LIT(g_1) - LIT(f_2) \neq \emptyset$ then, reasoning as above, it is possible to construct an assignment $\mathbf{a}$ such that $f_j(\mathbf{a}) = 0,\ j = 1, 2$, while $g_1(\mathbf{a}) = 1$.
      If, on the other hand, $LIT(g_1) - LIT(f_2) = \emptyset$, then $LIT(g_1)$ is a strict subset of $LIT(f_2)$, $LIT(f_2) - LIT(g_1) \neq \emptyset$, so that $LIT(f_1) \subset LIT(g_1) \subset LIT(f_2)$. Recalling that $LIT(F) = LIT(G)$, we conclude that $LIT(f_2)$ cannot be a strict subset of $LIT(g_2)$, i.e., $LIT(f_2) - LIT(g_2) \neq \emptyset$. It is therefore possible to construct an assignment $\mathbf{a}$ such that $g_i(\mathbf{a}) = 0,\ i = 1, 2$, while $f_2(\mathbf{a}) = 1$.
   c) $LIT(F) = LIT(G)$ and $t = 1$.
      i) $LIT(f_1) \cap LIT(f_2) \neq LIT(g_1) \cap LIT(g_2)$.
         Say there exists a $y \in \big(LIT(f_1) \cap LIT(f_2)\big) - \big(LIT(g_1) \cap LIT(g_2)\big)$. Let $\mathbf{a} \supset \mathbf{1}_{\{y\}}^{LIT(G)}$. Then, $f_1(\mathbf{a}) = f_2(\mathbf{a}) = 1$, while $g_1(\mathbf{a}) \neq g_2(\mathbf{a})$.
      ii) $LIT(f_1) \cap LIT(f_2) = LIT(g_1) \cap LIT(g_2) = I$.
         Let us deal first with the cases that one of $LIT(f_i) = I, i = 1$ or one of $LIT(g_j) = I, j = 1, 2$, say $LIT(f_1) = I$. Then, $LIT(f_2) - I = \big(LIT(g_1) - I\big) \cup \big(LIT(g_2) - I\big)$ (because $LIT(F) = LIT(G)$), none of these three sets is empty (because $f_1 \neq g_i, i = 1, 2$) and $\big(LIT(g_1) - I\big) \cap \big(LIT(g_2) - I\big) = \emptyset$. Consequently, there are $y_i \in \big(LIT(f_2) - I\big) \cap \big(LIT(g_i) - I\big),\ i = 1, 2$. Let $Y = \{y_1, y_2\}$, and observe that $|Y \cap LIT(f_2)| = 2, |Y \cap LIT(g_i)| = 1, i = 1, 2$ and $|Y \cap LIT(f_1)| = 0$. Thus, for any assignment, $\mathbf{a} \supset \mathbf{1}_{\{y_1,y_2\}}^{I}$. $f_2(\mathbf{a}) = 1$, and $g_i(\mathbf{a}) = 1,\ i = 1, 2$, while $f_1(\mathbf{a}) = 0$.
         Assuming next that $LIT(f_j) - I \neq \emptyset,\ j = 1, 2$ and $LIT(g_i) - I \neq \emptyset,\ i = 1, 2$, consider the case that there are $y_j \in \big(LIT(f_j) - I\big) \cap \big(LIT(g_1) - I\big),\ j = 1, 2$. Then, for any assignment $\mathbf{a}$ such that $\mathbf{a}(y_j) = 1,\ j = 1, 2$ and $\mathbf{a}(\ell) = 0$, if $\ell \in LIT(G) - \{y_1, y_2\}$, $f_j(\mathbf{a}) = 1,\ j = 1, 2$, and $g_1(\mathbf{a}) = 1$, while $g_2(\mathbf{a}) = 0$

because $\big(LIT(g_1) - I\big) \cap \big(LIT(g_2) - I\big) = \emptyset$. If, on the other hand, $\big(LIT(f_j) - I\big) \cap \big(LIT(g_1) - I\big) = \emptyset$ for $j = 1$ or $j = 2$, say $\big(LIT(f_1) - I\big) \cap \big(LIT(g_1) - I\big) = \emptyset$, then $\big(LIT(f_2) - I\big) \cap \big(LIT(g_1) - I\big) \neq \emptyset$, because $LIT(g_1) - I \neq \emptyset$ (and $LIT(F) = LIT(G)$). $\big(LIT(f_1) - I\big) \cap \big(LIT(g_1) - I\big) = \emptyset$ also implies that $LIT(f_2) - LIT(g_1) \neq \emptyset$. The reason is that otherwise $LIT(f_2) \subseteq LIT(g_1)$, and since $LIT(f_2)$ cannot be a strict subset of $LIT(g_1)$ (because $LIT(F) = LIT(G)$ and $LIT(f_1) \cap LIT(g_1) = I$), this would imply that $LIT(f_2) = LIT(g_1)$, i.e., $f_2 = g_1$ which we assumed was not the case. Now $LIT(f_2) - LIT(g_1) \neq \emptyset$ taken together with $LIT(f_2) - LIT(G) = \emptyset$ shows that $\big(LIT(f_2) - I\big) \cap \big(LIT(g_2) - I\big) \neq \emptyset$. In summary, we have proven that there are $y_i \in \big(LIT(f_2) - I\big) \cap \big(LIT(g_i) - I\big)$, $i = 1, 2$. Thus, for any assignment $\mathbf{a} \supset \mathbf{1}^G_{\{y_1, y_2\}}$. $f_2(\mathbf{a}) = 1$, and $g_i(\mathbf{a}) = 1$, $i = 1, 2$, while $f_1(\mathbf{a}) = 0$.

Proof of Theorem 28

Proof: We prove the theorem for the case of PIM; the FIM case can be proved in the same manner. Suppose that $F = \{f_1, f_2, \ldots, f_L\}$ is the underlying function tuple for the kth node in a PBN and that $G = \{g_1, \ldots, g_L\}$ is another possible function tuple for the same node. It is seen from the proof of Theorem 9 that if all possible 0–1 assignments on a set I of input nodes to $f_1, \ldots, f_L$ and to $g_1, \ldots, g_L$, and all possible corresponding values output by $f_1, \ldots, f_L$ are given, the inconsistency of $G(\neq F)$ can be detected.

We refer to this condition as Condition C1. Note that there are at most KL input nodes to $f_1, \ldots, f_L$ and another KL to $g_1, \ldots, g_L$, for a grand total of at most $2KL$.

Since we do not know I in advance, we consider all possible I with $|I| = 2KL$. The probability that $\mathbf{a}_i = 1$ does not hold for some $i \in \{1, \ldots, 2KL\}$ or f_j is not selected (for any fixed $j \in \{1, \ldots, L\}$) in a given sample $(\mathbf{a}, \mathbf{b})$ is at most $1 - c \cdot 1/2^{2KL}$, and thus, the probability that the same condition does not hold in any m samples is at most $(1 - c \cdot 1/2^{2KL})^m$. Since the number of combinations of $2KL$ variables is less than n^{2KL}, the number of functions assigned per node is L, and the number of 0-1 assignments on $2KL$ bits is 2^{2KL}, the probability that Condition C1 does not hold is bounded above by $L \cdot 2^{2KL} \cdot n^{2KL} \cdot \big(1 - c \cdot 1/2^{2KL}\big)^m$. Since there are n nodes, the probability that Condition C1 does not hold for one or more nodes is bounded above by

$$p_{K,L,n,m} = L \cdot 2^{2KL} \cdot n^{2KL+1} \cdot \left(1 - c \cdot \frac{1}{2^{2KL}}\right)^m.$$

By taking $\log(\cdots)$ of both sides and using $\ln(1 - x) \leq -x$, it is seen that $p_{K,L,n,m} \leq p$ holds if

$$m > \frac{1}{c} \cdot \ln 2 \cdot 2^{2KL} [\log L + 2KL + (2KL + 1)\log n - \log p].$$

Setting $p = 1/n^{\alpha}$, the theorem holds. ■

References

[1] R. W. Baughman, R. Farkas, M. Guzman, and M. F. Huerta, “The national institutes of health blueprint for neuroscience research,” *J. Neurosci.*, vol. 26, no. 41, pp. 10329–10331, 2006.

[2] J. W. Lichtman and W. Denk, “The big and the small: Challenges of imaging the brain’s circuits,” *Science*, vol. 334, pp. 618–623, Nov. 2011.

[3] K. H. Cho, S. M. Choo, S. H. Jung, J. R. Kim, H. S. Choi, and J. Kim, “Reverse engineering of gene regulatory networks,” *IET Syst. Biol.*, vol. 1, no. 3, pp. 149–163, May 2007.

[4] M. Hecker, S. Lambeck, S. Toepfer, E. van Someren, and R. Guthke, “Gene regulatory network inference: Data integration in dynamic models—A review,” *Biosystems*, vol. 96, no. 1, pp. 86–103, 2009.

[5] G. Karlebach and R. Shamir, “Modelling and analysis of gene regulatory networks,” *Nature*, vol. 9, pp. 770–780, Oct. 2008.

[6] S. A. Kauffman, “Metabolic stability and epigenesis in randomly constructed genetic nets,” *J. Theoret. Biol.*, vol. 22, no. 3, pp. 437–467, 1969.

[7] S. A. Kauffman, *The Origins of Order: Self-Organization and Selection in Evolution.* New York, NY, USA: Oxford Univ. Press, 1993.

[8] L. P. Wang, E. E. Pichler, and J. Ross, “Oscillations and chaos in neural networks: An exactly solvable model,” *Proc. Nat. Acad. Sci. USA*, vol. 87, no. 23, pp. 9467–9471, 1990.

[9] M. Anthony, *Discrete Mathematics of Neural Networks, Selected Topics*. Philadelphia, PA, USA: SIAM, 2001.

[10] S. Liang, S. Fuhrman, and R. Somogyi, “REVEAL, a general reverse engineering algorithm for inference of genetic network architectures,” in *Proc. Pacific Symp. Biocomput.*, 1998, pp. 18–29.

[11] T. Akutsu, S. Miyano, and S. Kuhara, “Identification of genetic networks from a small number of gene expression patterns under the Boolean network model,” in *Proc. Pacific Symp. Biocomput.*, 1999, pp. 17–28.

[12] R. Laubenbacher and B. Stigler, “A computational algebra approach to the reverse engineering of gene regulatory networks,” *J. Theor. Biol.*, vol. 229, no. 4, pp. 523–537, Aug. 2004.

[13] T. J. Perkins and M. T. Hallett, “A trade-off between sample complexity and computational complexity in learning Boolean networks from time-series data,” *IEEE/ACM Trans. Comput. Biol. Bioinform.*, vol. 7, no. 1, pp. 118–128, Jan. 2010.

[14] D. Cheng, H. Qi, and Z. Li, “Model construction of Boolean network via observed data,” *IEEE Trans. Neural Netw.*, vol. 22, no. 4, pp. 525–536, Apr. 2011.

[15] X. Zhang, H. Han, and W. Zhang, “Identification of Boolean networks using premined network topology information,” *IEEE Trans. Neural Netw. Learn. Syst.*, doi: 10.1109/TNNLS.2015.2499446.

[16] D. Cheng and H. Qi, “State–space analysis of Boolean networks,” *IEEE Trans. Neural Netw.*, vol. 21, no. 4, pp. 584–594, Apr. 2010.

[17] T. S. Gardner and J. J. Collins, “Gene regulation: Neutralizing noise in gene networks,” *Nature*, vol. 405, pp. 520–521, Jun. 2000.

[18] C. Allen and C. F. Stevens, “An evaluation of causes for unreliability of synaptic transmission,” *Proc. Nat. Acad. Sci. USA*, vol. 91, no. 22, pp. 10380–10383, 1994.

[19] E. N. Miranda and N. Parga, “Noise effects in the Kauffman model,” *Europhys. Lett.*, vol. 10, no. 4, pp. 293–298, 1989.

[20] T. Akutsu, S. Miyano, and S. Kuhara, “Inferring qualitative relations in genetic networks and metabolic pathways,” *Bioinformatics*, vol. 16, no. 8, pp. 727–734, 2000.

[21] T. P. Peixoto, “Redundancy and error resilience in Boolean networks,” *Phys. Rev. Lett.*, vol. 104, p. 048701, Jan. 2010.

[22] H. Chen, J. Liang, T. Huang, and J. Cao, “Synchronization of arbitrarily switched Boolean networks,” *IEEE Trans. Neural Netw. Learn. Syst.*, doi 10.1109/TNNLS.2015.2497708.

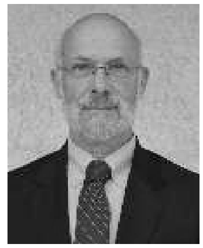
[23] Y. Liu, H. Chen, and B. Wu, “Controllability of Boolean control networks with impulsive effects and forbidden states,” *Math. Methods Appl. Sci.*, vol. 37, no 1, pp. 1–9, Jan. 2014.

[24] I. Shmulevich, E. R. Dougherty, S. Kim, and W. Zhang, “Probabilistic Boolean networks: A rule-based uncertainty model for gene regulatory networks,” *Bioinformatics*, vol. 18, no. 2, pp. 261–274, 2001.

[25] I. Shmulevich and E. R. Dougherty, *Probabilistic Boolean Networks: The Modeling and Control of Gene Regulatory Networks*. Philadelphia, PA, USA: SIAM, 2010.

[26] Y. Xiao, “A tutorial on analysis and simulation of Boolean gene regulatory network models,” *Current Genomics*, vol. 10, no. 7, pp. 511–525, 2009.

[27] P. Trairatphisan, A. Mizera, J. Pang, A. A. Tantar, J. Schneider, and T. Sauter, "Recent development and biomedical applications of probabilistic Boolean networks," *Cell Commun. Signaling*, vol. 11, p. 46, Jul. 2013.
[28] Y. Zhao and D. Cheng, "On controllability and stabilizability of probabilistic Boolean control networks," *Sci. China Inf. Sci.*, vol. 57, p. 012202, Dec. 2014.
[29] R. Li, M. Yang, and T. Chu, "State feedback stabilization for probabilistic Boolean networks," *Automatica*, vol. 50, no. 4, pp. 1272–1278, 2014.
[30] Y. Liu, H. Chen, J. Lu, and B. Wu, "Controllability of probabilistic Boolean control networks based on transition probability matrices," *Automatica*, vol. 52, pp. 340–345, Feb. 2015.
[31] H. Li, Y. Wang, and P. Guo, "State feedback based output tracking control of probabilistic Boolean networks," *Inf. Sci.*, vols. 349–350, pp. 1–11, Jul. 2006.
[32] S. Marshall, L. Yu, Y. Xiao, and E. R. Dougherty, "Inference of a probabilistic Boolean network from a single observed temporal sequence," *EURASIP J. Bioinform. Syst. Biol.*, vol. 2007, p. 32454, Dec. 2007.
[33] X. Cheng, T. Mori, Y. Qiu, W.-K. Ching, and T. Akutsu, "Exact identification of the structure of a probabilistic Boolean network from samples," *IEEE/ACM Trans. Comput. Biol. Bioinf.*, vol. 13, no. 6, pp. 1107–1116, Nov. 2016.
[34] S. E. Harris, B. K. Sawhill, A. Wuensche, and S. Kauffman, "A model of transcriptional regulatory networks based on biases in the observed regulation rules," *Complexity*, vol. 7, no. 4, pp. 23–40, Mar. 2002.
[35] M. R. Garey and D. S. Johnson, *Computers and Intractability*. New York, NY, USA: Freeman, 1979.
[36] T. Gowda, S. Vrudhula, and G. Konjevod, "Combinational equivalence checking for threshold logic circuits," in *Proc. ACM Great Lakes Symp. (VLSI)*, 2007, pp. 102–107.
[37] J. Lawrence, R. N. Kacker, Y. Lei, D. R. Kuhn, and M. Forbes, "A survey of binary covering arrays," *Electron. J. Combinat.*, vol. 18, no. 1, p. 84, Jul. 2011.
[38] K. Kobayashi and K. Hiraishi, "An integer programming approach to optimal control problems in context-sensitive probabilistic Boolean networks," *Automatica*, vol. 47, no. 6, pp. 1260–1264, Jun. 2011.
[39] S. Klamt, J. Saez-Rodriguez, J. A. Lindquist, L. Simeoni, and E. D. Gilles, "A methodology for the structural and functional analysis of signaling and regulatory networks," *BMC Bioinform.*, vol. 7, p. 56, Feb. 2006.
[40] A. Garg, A. D. Cara, I. Xenarios, L. Mendoza, and G. De Micheli, "Synchronous versus asynchronous modeling of gene regulatory networks," *Bioinformatics*, vol. 24, no. 17, pp. 1917–1925, 2008.
[41] A. Saadatpour, I. Albert, and R. Albert, "Attractor analysis of asynchronous Boolean models of signal transduction networks," *J. Theoret. Biol.*, vol. 266, no. 4, pp. 641–656, Oct. 2010.
[42] N. Alon, "Asynchronous threshold networks," *Graphs Combinat.*, vol. 1, no. 1, pp. 305–310, 1985.



Avraham A. Melkman received the B.Sc. degree in mathematics and physics from The Hebrew University of Jerusalem, Jerusalem, Israel, in 1965, and the Ph.D. degree in physics from the University of California at Berkeley, Berkeley, CA, USA, in 1971.

From 1971 to 1976, he was with the Applied Mathematics Institute, The Hebrew University of Jerusalem. In 1976, he was a Visiting Scientist with the Thomas J. Watson Research Center, Yorktown Heights, NY, USA. He joined the Department of Computer Science, Ben-Gurion University of the Negev, Beersheba, Israel in 1977, becoming an Associate Professor in 1987. His current research interests include bioinformatics and algorithms.

Xiaoqing Cheng received the B.E. degree from the Department of Mathematics, University of Science and Technology of China, Hefei, China, in 2012, and the Ph.D. degree from The University of Hong Kong, Hong Kong, in 2016.

She is currently an Assistant Professor with the School of Mathematics and Statistics, Xi'an Jiaotong University, Xi'an, China. Her current research interests include bioinformatics and data mining.

Wai-Ki Ching received the B.Sc. degree (Hons.) and the M.Phil. degree from The University of Hong Kong, Hong Kong, and the Ph.D. degree from the Chinese University of Hong Kong, Hong Kong.

He is currently a Professor and the Head of the Department of Mathematics, The University of Hong Kong. He is also a Visiting Fellow with Hughes Hall, Cambridge University, Cambridge, U.K., and a Visiting Professor with the Beijing University of Chemical Technology, Beijing, China. His current research interests include stochastic modeling, matrix computations, the applications of mathematical models and numerical algorithms in solving problems related to Markov chains, bioinformatics, mathematical finance, and management science.

Tatsuya Akutsu (SM'–) received the B.E. and M.E. degrees in aeronautics and the D.E. degree in information engineering from the University of Tokyo, Tokyo, Japan, in 1984, 1986, and 1989, respectively.

He has been a Professor with the Bioinformatics Center, Institute for Chemical Research, Kyoto University, Kyoto, Japan, since 2001. His current research interests include bioinformatics and discrete algorithms.