# Fault detection of Boolean control networks

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- context-aware systems in smart homes (Kabir et al., ISCE 2014)
- potential games (Cheng, Automatica 2014).

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Genes can be modeled as binary devices that exhibit two transcriptional states: active or inactive ("expressed" or not).

Even more, the state of a gene depends on the activation status of other genes, and such an interaction can be described by means of logical function.

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### Outline of the talk

Motivational examples

- Motivational examples
- Notation and intro to the algebraic representation of Boolean Control Networks

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- Conclusions

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### Sequential logic circuits (1)

In circuit theory, a sequential logic circuit is a logic circuit whose output depends not only on the present value of its input signal(s) but also on the past value of the input(s).

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### Sequential logic circuits (2)

If we denote by  $X_1(t)$  and  $X_2(t)$  the logical states of the upper and lower flip-flops at time t, and by U(t) the Boolean input at time t, then the update of the pair  $(X_1, X_2)$  depending on the value of U follows the state diagram:



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### Sequential logic circuits (3)

This corresponds to the following Boolean control network:

 $\begin{aligned} X_1(t+1) &= [(X_1(t) \lor X_2(t)) \land \bar{U}(t)] \lor [X_1(t) \land \bar{X}_2(t) \land U(t)], \\ X_2(t+1) &= [(\bar{X}_1(t) \lor \bar{X}_2(t)) \land U(t)] \lor [X_1(t) \land X_2(t) \land \bar{U}(t)]. \end{aligned}$ 

Assume that this circuit is part of a complex logical network whose output value Y depends at every time t from the variables  $X_1(t)$  and  $X_2(t)$  and from other logical state variables.

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Assume that this circuit is part of a complex logical network whose output value *Y* depends at every time *t* from the variables  $X_1(t)$  and  $X_2(t)$  and from other logical state variables. A typical problem arising in this kind of circuits is the so-called stuck-in faults: one of logical variables is stuck at 0 or 1, independently of the input sequence.

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How can we model these faults?

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How can we model these faults? How can we detect such faults?

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### Oxidative stress response (1)

Oxidative stress is caused by exposure to reactive oxygen species (ROS) (electrophiles and oxidants).

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Oxidative stress is caused by exposure to reactive oxygen species (ROS) (electrophiles and oxidants). Since oxidative stress contributes to aging and age-related diseases (cancer, cardiovascular disease, chronic inflammation, and neurodegenerative disorders), the body has developed a number of counteractive measures to counterbalance it.

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As a countermeasure, various antioxidant response elements (ARE) are activated.

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### Oxidative stress response (2)

Inside the nucleus, Nrf2 forms heterodimers with small Maf proteins (SMP) which then bind to the ARE and lead to the production of detoxifying enzymes.

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### Oxidative stress response (2)

Inside the nucleus, Nrf2 forms heterodimers with small Maf proteins (SMP) which then bind to the ARE and lead to the production of detoxifying enzymes.

Once the electrophiles have been eliminated, these protein complexes and other proteins named PKC and Bach1 bind to the ARE, and Nrf2 is transported back to the cytoplasm, where it binds with Keap1.

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In [Sridharan et al., BMC Genomics 2012] the following Boolean control network has been proposed for the oxidative stress response:
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$$\begin{aligned} X_1(t+1) &= \bar{X}_6(t) \wedge U(t), \\ X_2(t+1) &= \bar{X}_1(t) \wedge [X_2(t) \vee X_4(t)], \\ X_3(t+1) &= X_1(t) \wedge \bar{X}_6(t), \\ X_4(t+1) &= \bar{X}_2(t) \vee X_3(t), \\ X_5(t+1) &= \bar{X}_1(t), \\ X_6(t+1) &= X_4(t) \wedge [\bar{X}_5(t) \vee \bar{X}_6(t)], \end{aligned}$$

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where  $X_1 = ROS$ ,  $X_2 = Keap1$ ,  $X_3 = PKC$ ,  $X_4 = Nrf2$ ,  $X_5 = Bach1$ ,  $X_6 = ARE$ , U = Stress, and small Maf proteins are always assumed to be expressed (SMP=1).

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### Oxidative stress response (5)

The oxidative response pathway just illustrated interacts with the PI3k/Akt Pathway. A complete model of how the two pathways interact can be found in [Sridharan et al., BMC Genomics 2012].

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For these reasons it is important to understand: How can one detect a fault in the oxidative stress response pathway?

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For these reasons it is important to understand:

How can one detect a fault in the oxidative stress response pathway?

What are the output (measures) we can take, and how can we use them to detect a fault?

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# Notation (1)

•  $\mathcal{B} := \{0, 1\}$  is the set where Boolean variables take values.

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# Notation (2)

• The semi-tensor product  $\ltimes$  between matrices  $L_1 \in \mathcal{B}_{r_1 \times c_1}$  and  $L_2 \in \mathcal{B}_{r_2 \times c_2}$  is defined as

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• There is a bijective correspondence between  $\mathcal{B}$  and  $\mathcal{L}_2$ :

$$X = 1 \longleftrightarrow \mathbf{x} = X^v = \begin{bmatrix} 1\\ 0 \end{bmatrix} \qquad X = 0 \longleftrightarrow \mathbf{x} = X^v = \begin{bmatrix} 0\\ 1 \end{bmatrix}.$$

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It extends to a bijective correspondence between  $\mathcal{B}^n$  and  $\mathcal{L}_{2^n}$  through:

$$X = \begin{bmatrix} X_1 & X_2 & \dots & X_n \end{bmatrix}^\top \longleftrightarrow \mathbf{x} = X_1^v \ltimes X_2^v \ltimes \dots \ltimes X_n^v.$$

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## BCNs: from logic to algebraic representations (1)

A Boolean control network (BCN) is described by the following equations

$$\begin{array}{rcl} X(t+1) &=& f(X(t),U(t)), \\ Y(t) &=& h(X(t)), & t \in \mathbb{Z}_+, \end{array}$$
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 $X(\cdot)$ ,  $U(\cdot)$  and  $Y(\cdot)$  are the Boolean state (dim = n), input (dim = m), and output (dim = p).

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$$\begin{aligned} \mathbf{x}(t+1) &= L \ltimes \mathbf{u}(t) \ltimes \mathbf{x}(t), \quad t \in \mathbb{Z}_+, \\ \mathbf{y}(t) &= H \mathbf{x}(t) \end{aligned}$$
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where  $L \in \mathcal{L}_{2^n \times 2^{(n+m)}}$  and  $H \in \mathcal{L}_{2^p \times 2^n}$ .

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where  $L \in \mathcal{L}_{2^n \times 2^{(n+m)}}$  and  $H \in \mathcal{L}_{2^p \times 2^n}$ . In the following  $N := 2^n, \quad M := 2^m, \quad P := 2^p.$ 

# The scenario (1)

The general problem: Given a BCN, we want to investigate the problem of determining, from its input and output trajectories (but no access to the state), whether a fault has affected the BCN functioning or not.

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#### Assumptions:

A1) The BCN exhibits only two possible configurations:

a non-faulty (NF) and a faulty (F) one.

A2) The fault affects only the state-update, not the output measurements.

### The scenario (2)

Accordingly, we represent the non-faulty BCN as in (2) and the faulty one as

$$\begin{aligned} \mathbf{x}(t+1) &= L^{(F)} \ltimes \mathbf{u}(t) \ltimes \mathbf{x}(t), \\ \mathbf{y}(t) &= H \ltimes \mathbf{x}(t) = H \mathbf{x}(t), \quad t \in \mathbb{Z}_+, \end{aligned}$$
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with  $L^{(F)} \in \mathcal{L}_{N \times NM}$ . We introduce the fault signal  $(\mathbf{f}(t))_{t \in \mathbb{Z}_+}$ , taking values in  $\mathcal{L}_2$ , and assume that  $\mathbf{f}(t) = \delta_2^1$  corresponds to the non-faulty BCN and  $\mathbf{f}(t) = \delta_2^2$  to the faulty one.

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$$\begin{aligned} \mathbf{x}(t+1) &= \tilde{L} \ltimes \mathbf{f}(t) \ltimes \mathbf{u}(t) \ltimes \mathbf{x}(t), \\ \mathbf{y}(t) &= H \ltimes \mathbf{x}(t) = H \mathbf{x}(t), \quad t \in \mathbb{Z}_+. \end{aligned}$$

where  $\tilde{L} := \begin{bmatrix} L & L^{(F)} \end{bmatrix} \in \mathcal{L}_{N \times 2NM}$ .

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Another assumption: A3) the BCN cannot autonomously recover from a fault: once the fault signal switches from  $\delta_2^1$  to  $\delta_2^2$ , it cannot switch back to  $\delta_2^1$ . So, a fault acting at time  $\bar{t}$  is described by a step function

$$\mathbf{f}(t) = \begin{cases} \delta_2^1, & 0 \le t < \bar{t}; \\ \delta_2^2, & t \ge \bar{t}, \end{cases}$$

where  $\bar{t} = +\infty$  in case no fault affects the BCN.
# Meaningful fault (1)

Let  $\mathbf{x}(t; \mathbf{x}_0, \mathbf{u}(\cdot), \mathbf{f}(\cdot))$  and  $\mathbf{y}(t; \mathbf{x}_0, \mathbf{u}(\cdot), \mathbf{f}(\cdot))$  denote the state and output vectors of the BCN (4) at time *t*, when it starts from  $\mathbf{x}(0) = \mathbf{x}_0$  and the input and fault sequences are  $\mathbf{u}(\cdot)$  and  $\mathbf{f}(\cdot)$ , respectively.

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A fault taking place at time  $\overline{t}$ , for certain values of  $\overline{\mathbf{x}} := \mathbf{x}(\overline{t}) \in \mathcal{L}_N$  and  $\mathbf{u}(t), t \geq \overline{t}$ , may not reveal itself, independently of how we choose the output measurements.

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Indeed, the state trajectory generated by the faulty BCN (3) starting from  $\bar{\mathbf{x}}$  at  $t = \bar{t}$ , under the effect of  $\mathbf{u}(\cdot)$ , may coincide with the state trajectory that the non-faulty BCN (2) generates in the same conditions.

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Meaningful fault sequences are the only ones we may hope to detect, by making use of the input and output trajectories.

#### Possible problems

On-line fault detection: the BCN, undergoing normal working conditions, is subject to an arbitrary input, and we want to understand, based on its input-output behavior, if a fault has occurred.

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#### On-line fault detection: Preliminaries

We introduce the set of the admissible input/output trajectories of the non-faulty BCN:

$$\mathfrak{B}_{uy} := \{ (\mathbf{u}(t), \mathbf{y}(t))_{t \in \mathbb{Z}_+} : (\mathbf{u}(t))_{t \in \mathbb{Z}_+} \in (\mathcal{L}_M)^{\mathbb{Z}_+}, \text{and} \\ \exists \mathbf{x}_0 \in \mathcal{L}_N \text{ s.t. } \mathbf{y}(t) = \mathbf{y}(t; \mathbf{x}_0, \mathbf{u}(\cdot), \delta_2^1) \}.$$
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 $\mathfrak{B}_{uy}$  is the set of all pairs  $(\mathbf{u}(t), \mathbf{y}(t))_{t \in \mathbb{Z}_+}$  such that  $(\mathbf{y}(t))_{t \in \mathbb{Z}_+}$  is the output trajectory generated by (2) corresponding to some initial state  $\mathbf{x}(0) = \mathbf{x}_0 \in \mathcal{L}_N$  and to the input  $(\mathbf{u}(t))_{t \in \mathbb{Z}_+}$ .

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### Detectability of a meaningful fault (1)

Definition 2 Given a BCN (4), a state  $\mathbf{x}_0 \in \mathcal{L}_N$ , an input  $(\mathbf{u}(t))_{t \in \mathbb{Z}_+}$ , and a (meaningful) fault sequence  $(\mathbf{f}(t))_{t \in \mathbb{Z}_+}$ ,

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### Detectability of a meaningful fault (2)

We define:

$$X^* := \{ \mathbf{x}^* \in \mathcal{L}_N : \exists \mathbf{u}^* \in \mathcal{L}_M \text{ s.t.} L \ltimes \mathbf{u}^* \ltimes \mathbf{x}^* \neq L^{(F)} \ltimes \mathbf{u}^* \ltimes \mathbf{x}^* \},\$$

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and, for every  $\mathbf{x}^* \in X^*$ ,

 $U^*(\mathbf{x}^*) := \{ \mathbf{u}^* \in \mathcal{L}_M : L \ltimes \mathbf{u}^* \ltimes \mathbf{x}^* \neq L^{(F)} \ltimes \mathbf{u}^* \ltimes \mathbf{x}^* \}.$ 

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Finally,  $\mathcal{U}\mathcal{Y}^*$  denotes the set of input/output trajectories  $(\mathbf{u}(t), \mathbf{y}^{(F)}(t)) \in (\mathcal{L}_M \times \mathcal{L}_P)^{\mathbb{Z}_+}$  generated by the faulty BCN (3) corresponding to some  $\mathbf{x}(0) = \mathbf{x}^* \in X^*$  and to some input  $(\mathbf{u}(t))_{t \in \mathbb{Z}_+}$  with  $\mathbf{u}(0) \in U^*(\mathbf{x}^*)$ .

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#### Detectability of a meaningful fault (3)

Proposition 1 The following facts are equivalent:

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Proposition 1 The following facts are equivalent: i) for every initial condition  $\mathbf{x}_0 \in \mathcal{L}_N$  and every input sequence  $(\mathbf{u}(t))_{t \in \mathbb{Z}_+}$ , every fault that is meaningful (for the specific choice of  $\mathbf{x}_0$  and  $\mathbf{u}$ ) is also detectable (the on-line fault detection problem is solvable);

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### Graph-theoretic characterization (1)

The idea: to introduce a graph that is able to keep in parallel the state-transitions in the non-faulty BCN and in the faulty one, starting from any pair of states and corresponding to any input sequence:

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## Graph-theoretic characterization (1)

The idea: to introduce a graph that is able to keep in parallel the state-transitions in the non-faulty BCN and in the faulty one, starting from any pair of states and corresponding to any input sequence: the NF-F (non-faulty-faulty) directed graph.

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#### Graph-theoretic characterization (2)

The NF-F (non-faulty-faulty) directed graph is defined as  $\mathcal{G} = (\mathcal{V}, \mathcal{E}, C_0, C_1)$ , where

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 $\delta^h_N = L \ltimes \mathbf{u} \ltimes \delta^i_N \text{ and } \delta^k_N = L^{(F)} \ltimes \mathbf{u} \ltimes \delta^j_N.$ 

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From every pair  $(\delta_N^i, \delta_N^j)$  there are *M* outgoing arcs, one for each value of the input **u**.

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#### Graph-theoretic characterization (3)

Proposition 2 Given the BCN (4), let  $\mathcal{G} = (\mathcal{V}, \mathcal{E}, C_0, C_1)$  be the associated NF-F directed graph. The on-line fault detection problem is solvable if and only if

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### Graph-theoretic characterization (3)

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P1) it starts from some vertex pair  $(\mathbf{x}_0, \mathbf{x}^*) \in \mathcal{L}_N \times X^*$ ; P2) the first arc of the path (outgoing from  $(\mathbf{x}_0, \mathbf{x}^*)$ ) is labeled by some  $\mathbf{u}^* \in U^*(\mathbf{x}^*)$ ;

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Off-line fault detection of BCNs

#### Graph-theoretic characterization (3)

Proposition 2 Given the BCN (4), let  $\mathcal{G} = (\mathcal{V}, \mathcal{E}, C_0, C_1)$  be the associated NF-F directed graph. The on-line fault detection problem is solvable if and only if each path in  $\mathcal{G}$  endowed with the properties:

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enters the class  $C_0$  in a finite number of steps.

#### Off-line fault detection: Preliminaries

Proposition 3 The following facts are equivalent: i) the off-line fault detection problem is solvable; ii) there exist  $T \in \mathbb{Z}_+$  and an input  $\hat{\mathbf{u}}(t), t \in [0, T-1]$ , taking values in  $\mathcal{L}_M$ , such that the two sets of output trajectories

$$\begin{split} \hat{\mathcal{Y}}|_{[0,T]} &:= \{ (\mathbf{y}(t))|_{[0,t]} : \exists \mathbf{x}_0 \in \mathcal{L}_N \text{ s.t.} \\ \mathbf{y}(t) &= \mathbf{y}(t; \mathbf{x}_0, \hat{\mathbf{u}}(\cdot), \delta_2^1), \forall t \in [0,T] \} \\ \hat{\mathcal{Y}}^{(F)}|_{[0,T]} &:= \{ (\mathbf{y}(t))|_{[0,t]} : \exists \mathbf{x}_0 \in \mathcal{L}_N \text{ s.t.} \\ \mathbf{y}(t) &= \mathbf{y}(t; \mathbf{x}_0, \hat{\mathbf{u}}(\cdot), \delta_2^2), \forall t \in [0,T] \} \end{split}$$

are disjoint.

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### Algorithm (1)

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Let  $\mathbf{X}_{\tau}^{NF}$  be the set of the states that the non-faulty BCN (2) can reach at time  $\tau$ , under the effect of the input sequence  $\mathbf{u}(t), t \in [0, \tau - 1]$ , meanwhile generating the output  $\mathbf{y}(t), t \in [0, \tau]$ .

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A fault has occurred if and only if there is  $\tau$  such that  $\mathbf{X}_{\tau}^{NF} = \emptyset$ .

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By proceeding in this way, we obtain the sequence of sets  $\mathbf{X}_{\tau}^{NF}$ , whose cardinality decreases with  $\tau$ . If for some  $\tau$  we have  $\mathbf{X}_{\tau}^{NF} = \emptyset$ , a fault has occurred.

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By proceeding in this way, we obtain the sequence of sets  $\mathbf{X}_{\tau}^{NF}$ , whose cardinality decreases with  $\tau$ . If for some  $\tau$  we have  $\mathbf{X}_{\tau}^{NF} = \emptyset$ , a fault has occurred.

Note: at every t, the state  $\delta_N^i$  is compatible with a given output sample  $\mathbf{y}(t) \in \mathcal{L}_P$  if and only if  $[H^\top \mathbf{y}(t)]_i = 1$ .

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# Algorithm (3)



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- \* What if the fault is reversible?
- For the off-line fault detection problem:

\* If solvable, how can we find the most efficient (= the shortest input test sequence)?

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#### Thanks for your attention!

Questions?