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# Controllability of time-delayed Boolean multiplex control networks under asynchronous stochastic update

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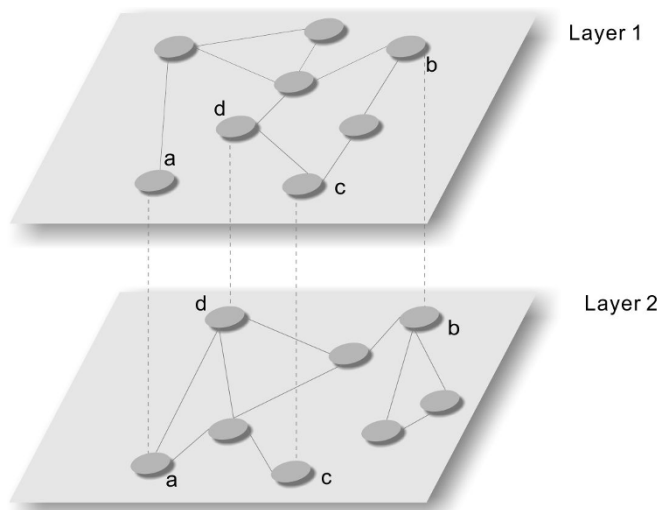
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In this article, the controllability of asynchronous Boolean multiplex control networks (ABMCNs) with time delay is studied. Firstly, dynamical model of Boolean multiplex control networks is constructed, which is assumed to be under Harvey' asynchronous update and time delay is introduced both in states and controls. By using of semi-tensor product (STP) approach, the logical dynamics is converted into an equivalent algebraic form by obtaining the control-depending network transition matrices of delayed system. Secondly, a necessary and sufficient condition is proved that only control-depending fixed points of the studied dynamics can be controlled with probability one. Thirdly, respectively for two types of controls, the controllability of dynamical control system is investigated. When initial states and time delay are given, formulae are obtained to show a) the reachable set at time  $s$  under specified controls; b) the reachable set at time  $s$  under arbitrary controls; c) the reachable probabilities to different destination states. Furthermore, an approach is discussed to find a precise control sequence which can steer dynamical system into a specified target with the maximum reachable probability. Examples are shown to illustrate the feasibility of the proposed scheme.

**B**oolean networks (BNs), as a class of simplified discrete models, are widely applied to reveal the generic properties of biological systems in an integrative and holistic manner. In 1969, random Boolean networks (RBNs), also known as  $N$ - $K$  models, were originally proposed by Stuart Kauffman<sup>1</sup>. This classic model consists of  $N$  nodes representing genes, each of which receives inputs from  $K$  randomly selected neighbors. The nodes on networks are characterized by two qualitative values, usually referred to logical 0 and 1, to present the active and repressing states of genes, respectively. Boolean rules assigned to nodes are employed to indicate the mutual regulations among genes. Based on synchronous update, at each time  $t$ , the state of each node on network is determined by the Boolean rule and  $K$  inputs at the previous time  $t-1$ . During the past few decades, Boolean networks have been used to unveil characteristics of complex systems and abundant of results have been achieved, such as dynamical behaviors of BNs<sup>2,3</sup>, efficient attractor-seeking algorithms<sup>4-6</sup>, biological control<sup>7,8</sup> and some applications in biological research<sup>9-11</sup>.

Biological information operates on multiple hierarchical levels of living organization<sup>12</sup>. From the viewpoint of systems biology, system-level analysis of biological regulation requires the interactions of genes on a holistic level, rather than the characteristics of isolated parts of an organism<sup>13</sup>. As mentioned in Ref. 14, "*the same gene or biochemical species can be involved in a regulatory interaction, in a metabolic reaction, or in another signaling pathway*". Therefore, to understand the intricate variability of biological systems, where many hierarchical levels and interactions coexist, a new level of description is required. Meanwhile, multiplex networks as an extension of complex networks were firstly proposed by Mucha in 2010<sup>15</sup>, which is composed of several layered networks interrelated with each other shown in Fig. 1. Each layer in multiplex networks could have particular features and dynamical processes. Interconnections between layers are represented by some special nodes on behave of different roles participating in multiple layers of interactions. Different from the traditional sense of coupling, the final states of those common nodes at each time step are determined by all of involved layers. During the past four years, a variety of studies based on multiplex networks have been achieved, including network topology and dynamic properties<sup>16</sup>, diffusion dynamics<sup>17,18</sup> and game theory<sup>19,20</sup>, etc. It's noteworthy that multiplex networks provide a novel way to construct the multilevel models of biochemical systems and be better depict a richer structure of interactions.

To incorporate mutual regulations of genes observed in the real biological system, Boolean networks as abstract models are employed to investigate dynamical properties of systems. For a certain degree of simplification,



**Figure 1 | Illustration of multiplex networks with two layers.** Nodes a, b, c, d are identical in both layer 1 and layer 2.

synchronous update scheme is adopted in the previous studies of RBNs, which is based on an assumption that update scheme isn't an essential factor on the consideration of dynamical behaviors. However, regulated entities can't implement the interactions and renew their states simultaneously at each time step by following a synchronized clock. As the studies in Ref. 21, "*factors such as mRNA and protein synthesis, degradation and transport times mean that the system is replete with delays of varying amounts, and genes are activated or inhibited in a fundamentally asynchronous manner*", that means there are multiple timescales should be considered in the biological systems. Asynchronous Boolean networks (ABNs) were firstly proposed by Harvey et al.<sup>22</sup>, followed by a series of related studies. In<sup>23</sup>, Greil et al. illustrated that the growth of the mean number and size of attractors in asynchronous critical BNs are in strong contrast to the synchronous version. Furthermore, dynamics of critical BNs under deterministic asynchronous update was also studied<sup>24</sup>; in<sup>25</sup>, Saadatpour et al. carried out a comparative study on the attractors of a signal transduction network modelled by BNs under synchronous and asynchronous updating schemes; in<sup>26</sup>, Tournier and Chaves investigated dynamics of the interconnection of two ABNs by directly analyzing the properties of two individual modules, that can be applied to analyze the multicellular modeling and high dimensional model; in<sup>27</sup>, asynchronous stochastic Boolean networks were proposed to investigate dynamical behaviors of a T-helper network; in<sup>28</sup>, Jack et al. simulated quantitative cellular responses of signal transduction in a single cell by means of asynchronous threshold BNs. The previous results were presented to verify the asynchronous update is more plausible for many cases of biological systems. Therefore, studies of BNs under asynchronous stochastic update are meaningful and applicable.

From system-level understanding of biological systems, to find a mechanisms that systematically control the states of regulatory entities can be implemented to minimize malfunctions and provide potential therapeutic targets for treatment of disease<sup>29,30</sup>. Boolean control networks (BCNs) as dynamical control systems provide an efficient approach to carry out theoretical and numerical analysis<sup>31</sup>. Controllability, roughly speaking, which is to steer a control system from an arbitrary initial state to an arbitrary final state by using the set of admissible controls, is one of the fundamental concepts at the onset of control theory infiltrating into the research of gene regulatory networks (GRNs)<sup>32,33</sup>. Over the past few years, controllability of BCNs have been receiving considerable attention, such as controllability and observability of BCNs<sup>34</sup>; controllability of BCNs with time-invariant delay<sup>35</sup> and time-variant delay<sup>36</sup> as well as time delay

involved both in states and controls<sup>37</sup>; controllability of  $\mu$ -th order BCNs<sup>38</sup> and the approach to transform  $\mu$ -th order BCNs to equivalent time-variant BCNs<sup>39</sup>; studies on controllability of BCNs via the Perron-Frobenius theory<sup>40</sup>, etc. The previous works were based on an independent network, which represents the assembly of genes or other entities to fulfil a specified function. With the in-depth of research, it is necessary to further study how the interplay among multiple interdependent networks affects dynamical behaviors of system. Compared with the traditional models, Boolean multiplex networks have more complex topology structure and higher holistic level which can provide a more generalized model to be better in conformity with the development of biology. Moreover, most of the previous studies on controllability of BCNs were assumed to be updated under synchronous scheme, i.e. the studied models are deterministic systems. As the above discussion, asynchronous update is closer to the real situation, based on which studies on BNs can be more likely to obtain the essential properties of biological systems. In<sup>41</sup>, the reachable sets of Boolean multiplex networks under asynchronous update scheme at time  $s$  were revealed, where the asynchronous scheme was based on randomly chosen update nodes at each time step. However, Due to signal propagation delays in the environment, a propagation delay  $\tau$  can be seen as a particular form of asynchronous phenomenon existing in the processes of transcription and translation in biological systems<sup>42</sup> or information propagation in society systems<sup>43</sup>. Hence, we think it's valuable to extend the related research into the field of asynchronous Boolean multiplex networks with time delay.

In this article, controllability of ABMCNs with time delay is discussed. The dynamical model of Boolean multiplex control networks is constructed by introducing inputs as controls into the model proposed by Cozzo et al.<sup>14</sup>. For obtaining the more general results, time delay is involved both in states and inputs<sup>44</sup>. Harvey's update scheme, i.e. only one node could be randomly chosen to renew its state at each time step, is implemented. In<sup>45</sup>, as a kind of non-deterministic system, the controllability of probabilistic Boolean networks was discussed, in which the concept of controllable probability was firstly proposed. But, authors just showed the sufficiency of the controllability with probability but not verify the necessary. In our work, a necessary and sufficient condition is proved that only control-depending fixed points of asynchronous delayed system can be controlled with probability one, which provide the theoretical basis to discuss the controllability of non-deterministic system from the perspective of probability. Based on the algebraic representation of the studied model, controllability of delayed system is to be analytically discussed respectively for two types of controls, i.e. free Boolean control sequences and the controls satisfying certain logical rule. When initial state sequence and time delay are given, we discuss the formulae to calculate reachable sets at time  $s$  under specified or free controls, as well as the reachable probabilities to different destination states. Furthermore, we are to illustrate the method to determine specific controls which can drive dynamical system to a given target with the maximum reachable probability.

This article is organized as follows. In Preliminaries, semi-tensor product as mathematic tools applied in this article is briefly introduced. In Main Results, the studied model of ABMCNs with time delay is firstly proposed and converted into linear form. Based on two types of controls, the controllability of dynamical control system is discussed. Some examples are shown to illustrate the main results. Finally, a concluding remark is given.

## Preliminaries

In this section, STP of matrix is briefly introduced, by means of which logical dynamics can be converted into an equivalent algebraic form.

**Definition 1** (<sup>31</sup>):

- 1) Let  $X$  be a row vector of dimension  $np$ , and  $Y$  be a column vector of dimension  $p$ . Then we split  $X$  into  $p$  equal-size blocks as  $X^i$ ,



$X^2, \dots, X^p$ , which are  $1 \times n$  rows. Define the STP, denoted by  $\ltimes$ , as

$$\begin{cases} X \ltimes Y = \sum_{i=1}^p X^i Y_i \in \mathbb{R}^n, \\ Y^T \ltimes X^T = \sum_{i=1}^p Y_i (X^i)^T \in \mathbb{R}^n. \end{cases}$$

- 2) Let  $A \in M_{m \times n}$  and  $B \in M_{p \times q}$ . If either  $n$  is a factor of  $p$ , say  $nt = p$  and denote it as  $A \ltimes_t B$ , or  $p$  is a factor of  $n$ , say  $n = pt$  and denote it as  $A \gtimes_t B$ , then we define the STP of  $A$  and  $B$ , denoted by  $C = A \ltimes B$ , as the following:  $C$  consists of  $m \times q$  blocks as  $C = (C^j)$  and each block is

$$C^{ij} = A^i \ltimes B_j, \quad i = 1, \dots, m, \quad j = 1, \dots, q$$

where  $A^i$  is the  $i$ -th row of  $A$  and  $B_j$  is the  $j$ -th column of  $B$ .

**Example 1:** Let  $A = \begin{bmatrix} 1 & 2 & 3 & 5 \\ 0 & -1 & 4 & 6 \end{bmatrix}$  and  $B = \begin{bmatrix} 2 & 4 \\ 1 & -2 \end{bmatrix}$ . Then, one can obtain

$$\begin{aligned} A \ltimes B &= \begin{bmatrix} (1 \ 2) \times 2 + (3 \ 5) \times 1 & (1 \ 2) \times 4 + (3 \ 5) \times (-2) \\ (0 \ -1) \times 2 + (4 \ 6) \times 1 & (0 \ -1) \times 4 + (4 \ 6) \times (-2) \end{bmatrix} \\ &= \begin{bmatrix} 5 & 9 & -2 & -2 \\ 4 & 4 & -8 & -16 \end{bmatrix} \end{aligned}$$

**Remark 1:** It is noted that when  $n = p$ , STP of  $A$  and  $B$  turns into the conventional matrix product. So, STP can be seen as a generalization of the conventional matrix product and all the fundamental properties of matrix product, such as distributive rule, associative rule, etc, still hold.

And, it can be verified that for two column vectors  $X \in \mathbb{R}^m$  and  $Y \in \mathbb{R}^n$ ,  $X \ltimes Y \in \mathbb{R}^{mn}$ .

Some related properties of STP are collected as follows:

**Proposition 1:** Assume  $A \gtimes_t B$ , then (where  $\otimes$  refers to the Kronecker product,  $I_t$  is the identity matrix)

$$A \ltimes B = A(B \otimes I_t).$$

Assume  $A \ltimes_t B$ , then

$$A \ltimes B = (A \otimes I_t)B.$$

**Proposition 2:** Assume  $A \in M_{m \times n}$  is given,

- 1) Let  $Z \in \mathbb{R}^t$  be a row vector. Then,

$$A \ltimes Z = Z \ltimes (I_t \otimes A).$$

- 2) Let  $Z \in \mathbb{R}^t$  be a column vector. Then,

$$Z \ltimes A = (I_t \otimes A) \ltimes Z.$$

For statement ease, some notations used in this article are defined as follows.

- $\delta_n^r$  denotes the  $r$ -th column of the  $n \times n$  identity matrix  $I_n$  and  $\Delta_n := \{\delta_n^r | 1 \leq r \leq n\}$ , which is the set of all  $n$  columns of  $I_n$ .
- A matrix  $A \in M_{n \times m}$  can be called a logical matrix if  $A = [\delta_n^{i_1}, \delta_n^{i_2}, \dots, \delta_n^{i_m}]$ , which is briefly denoted by  $A = \delta_n [i_1, i_2, \dots, i_m]$ . And the set of  $n \times m$  logical matrices is denoted by  $\mathcal{L}_{n \times m}$ .

Next, we define the swap matrix  $W_{[m,n]}$ , let  $X \in \mathbb{R}^m$  and  $Y \in \mathbb{R}^n$  be two column vectors

$$W_{[m,n]}XY = YX,$$

where  $W_{[m,n]}$  is a  $mn \times mn$  matrix labeled columns by  $(11, 12, \dots, 1n, \dots, m1, m2, \dots, mn)$  and rows by  $(11, 21, \dots, m1, \dots, 1n, 2n, \dots, mn)$ , the elements in position  $((I, J), (i, j))$  is

$$w_{(I,J),(i,j)} = \begin{cases} 1, & I=i \text{ and } J=j \\ 0, & \text{otherwise} \end{cases}.$$

$W_{[m,n]}$  is briefly denoted by  $W_{[m]}$ .

Assume  $X_n = x_1 \ltimes x_2 \ltimes \dots \ltimes x_n \triangleq \ltimes_{i=1}^n x_i$  and  $x_i(t) \in \Delta_2$ , we can get  $x_n^2(t) = \Phi_n x_n(t)$ , where  $\Phi_n = \prod_{i=1}^n I_{2^{i-1}} \otimes [(I_2 \otimes W_{[2,2^{n-i}]})M_r]$ . Here,  $M_r = \delta_4[1,4]$ , which is power-reducing matrix and it can be verified that  $P^2 = M_r P, \forall P \in \Delta_2$ .

In order to get the matrix expression of logical dynamics, the Boolean values should be denoted as vectors  $\text{True} = 1 \sim \delta_2^1$  and  $\text{False} = 0 \sim \delta_2^2$ . And the following lemma is fundamental for the matrix expression of logical functions.

**Lemma 1**<sup>31</sup>: Any logical function  $f(x_1, x_2, \dots, x_r)$  with logical arguments  $x_1, x_2, \dots, x_r \in \Delta_2$ , can be expressed in a multi-linear form as

$$f(x_1, x_2, \dots, x_r) = M_f \ltimes_{i=1}^r x_i$$

where  $M_f \in 2 \times 2^r$  is unique, which is called the structure matrix of logical function  $f$ .

More details on STP can be found in Ref. 31. In the following, the matrix products are assumed to be STP and the symbol  $\ltimes$  is omitted if no confusion arises.

## Main Results

**Algebraic expression of asynchronous Boolean multiplex control networks with time delay.** Regulatory entities in multiplex take part in several layers of networks, the states of which on different layers evolve independently. However, a final deterministic state of each entity should be obtained at the end of each time step determined by all of values on involved layers.

For a Boolean multiplex network with  $\tilde{n}$  nodes and  $\tilde{k}$  layers, assume  $x_i^l(t)$ ,  $l \in \{1, 2, \dots, \tilde{k}\}$  accounts for the state of node  $i$  on layer  $l$  at time  $t$ . When time delay  $\tau$  is considered in states, one can obtain

$$x_i^l(t+1) = f_i^l(\tilde{x}_1(t-\tau), \tilde{x}_2(t-\tau), \dots, \tilde{x}_{\tilde{n}}(t-\tau)), \quad i = 1, 2, \dots, \tilde{n}; \quad l = 1, 2, \dots, \tilde{k}, \quad (1)$$

where  $f_i^l$  is the update function of node  $i$  on layer  $l$ . Furthermore, assume  $\tilde{x}_i(t)$ ,  $i \in \{1, 2, \dots, \tilde{n}\}$  represents the overall state of node  $i$  at time  $t$ . Refer to<sup>14</sup>, we can get

$$\tilde{x}_i(t+1) = \tilde{f}_i(x_1^1, x_1^2, \dots, x_{\tilde{n}}^{\tilde{k}}), \quad i = 1, 2, \dots, \tilde{n}, \quad (2)$$

where  $\tilde{f}_i$  is the canalizing function. Boolean functions are canalizing if whenever the canalizing variable takes a given value, the function always yields the same output, irrespective of the values of other variables<sup>14</sup>. Note that, strictly speaking, there exists an interval between the renewal of the value of node  $i$  on layer  $l$ , say  $x_i^l(t)$ , and the overall state  $\tilde{x}_i(t)$  in the whole multiplex. In the following discussion, based on an assumption that the interval between the above two states is instantaneous, the same time step  $t$  is used for both of them.

Next, we introduce  $\tilde{m}$  controls with time delay  $\tau$  into system (1), the corresponding dynamical control system can be described as

$$\begin{aligned} x_i^l(t+1) &= \hat{f}_i^l(u_1(t-\tau), \dots, u_{\tilde{m}}(t-\tau), \tilde{x}_1(t-\tau), \dots, \tilde{x}_{\tilde{n}}(t-\tau)), \\ i &= 1, 2, \dots, \tilde{n}; \quad l = 1, 2, \dots, \tilde{k}, \end{aligned} \quad (3)$$

where  $u_i(t)$ ,  $i = 1, 2, \dots, \tilde{m}$  are controls and  $\hat{f}_i^l$  is the update rule of node  $i$  on layer  $l$  with controls.



By means of Lemma 1, a structure matrix  $M_i^l$  can be calculated for each logical rule  $\hat{f}_i^l$ , based on which one can obtain the algebraic form of Eq.(3) as follows.

$$x_i^l(t+1) = M_i^l u(t-\tau) \tilde{x}(t-\tau), \quad i=1,2,\dots,\tilde{n}; \quad l=1,2,\dots,\tilde{k}, \quad (4)$$

where  $\tilde{x}(t) = \times_{i=1}^{\tilde{n}} \tilde{x}_i(t)$ ,  $u(t) = \times_{i=1}^{\tilde{m}} u_i(t)$ . Subsequently, the algebraic representation of Eq.(2) can be obtained as

$$\begin{aligned} \tilde{x}_i(t+1) &= \tilde{M}_i M_i^1 u(t-\tau) \tilde{x}(t-\tau) M_i^2 u(t-\tau) \tilde{x}(t-\tau) \dots M_i^{\tilde{k}} u(t-\tau) \tilde{x}(t-\tau) \\ &= L_i u(t-\tau) \tilde{x}(t-\tau), \quad i=1,2,\dots,\tilde{n} \end{aligned} \quad (5)$$

where  $\tilde{M}_i$  is the structure matrix of logical function  $\tilde{f}_i$  and  $L_i = \tilde{M}_i \times_{j=1}^{\tilde{k}} \left( 2^{(j-1)(\tilde{m}+\tilde{n})} \otimes M_i^j \right) \cdot \Phi_{\tilde{m}+\tilde{n}}^{k-1}$ .

Under Harvey's asynchronous update, at each time step  $t$ , only one node is at random chosen for update. Hence, one can obtain

$$\begin{cases} \tilde{x}_i(t+1) = L_i u(t-\tau) \tilde{x}(t-\tau), & i \in \{1,2,\dots,\tilde{n}\} \\ \tilde{x}_j(t+1) = \tilde{x}_j(t-\tau), & j \neq i, j=1,2,\dots,\tilde{n} \end{cases}, \quad (6)$$

Multiplying all the  $\tilde{n}$  equations of system (6), one can get

$$\begin{aligned} \tilde{x}(t+1) &= \tilde{x}_1(t-\tau), \dots, \\ \tilde{x}_{i-1}(t-\tau) L_i u(t-\tau) \tilde{x}(t-\tau) \tilde{x}_{i+1}(t-\tau), \dots, \tilde{x}_{\tilde{n}}(t-\tau) \\ &= (I_{2^{i-1}} \otimes L_i) W_{[2^{\tilde{m}}, 2^{i-1}]} u(t-\tau) \tilde{x}_1(t-\tau), \dots, \\ \tilde{x}_{i-1}(t-\tau) \tilde{x}(t-\tau) \tilde{x}_{i+1}(t-\tau), \dots, \tilde{x}_{\tilde{n}}(t-\tau) \\ &= (I_{2^{i-1}} \otimes L_i) W_{[2^{\tilde{m}}, 2^{i-1}]} u(t-\tau) \Phi_{i-1} \tilde{x}_1(t-\tau), \dots, \\ \tilde{x}_{i-1}(t-\tau) \tilde{x}_i(t-\tau) \Phi_{\tilde{n}-i} \tilde{x}_{i+1}(t-\tau), \dots, \tilde{x}_{\tilde{n}}(t-\tau) \\ &= (I_{2^{i-1}} \otimes L_i) W_{[2^{\tilde{m}}, 2^{i-1}]} (I_{2^{\tilde{m}}} \otimes \Phi_{i-1}) (I_{2^{i+\tilde{m}}} \otimes \Phi_{\tilde{n}-i}) u(t-\tau) \tilde{x}(t-\tau) \\ &\triangleq \hat{L}_i u(t-\tau) \tilde{x}(t-\tau), \end{aligned}$$

where  $\hat{L}_i = (I_{2^{i-1}} \otimes L_i) W_{[2^{\tilde{m}}, 2^{i-1}]} (I_{2^{\tilde{m}}} \otimes \Phi_{i-1}) (I_{2^{i+\tilde{m}}} \otimes \Phi_{\tilde{n}-i})$  is called as the control-dependent network transition matrix, which involves all of the state transfer information of a dynamical control system.

In the following, respectively for two kinds of controls, the controllability of ABMCNs with time delay is to be discussed:

- 1) Controls come from a free Boolean sequence. Precisely, at time  $t$ ,  $\tilde{m}$  controls are freely designed and described as  $u(t) = \times_{i=1}^{\tilde{m}} u_i(t)$ .
- 2) The controls are determined by certain logical rules, which can be called input control networks:

$$\begin{cases} u_1(t+1) = g_1(u_1(t-\tau), u_2(t-\tau), \dots, u_{\tilde{m}}(t-\tau)), \\ u_2(t+1) = g_2(u_1(t-\tau), u_2(t-\tau), \dots, u_{\tilde{m}}(t-\tau)), \\ \vdots \\ u_{\tilde{m}}(t+1) = g_{\tilde{m}}(u_1(t-\tau), u_2(t-\tau), \dots, u_{\tilde{m}}(t-\tau)), \end{cases} \quad (7)$$

where  $g_i : \{0,1\}^{\tilde{m}} \rightarrow \{0,1\}$ ,  $i=1,2,\dots,\tilde{m}$  are logical rules.

**Deterministic controllability of asynchronous Boolean multiplex control networks with time delay.** Synchronous BNs are deterministic dynamical systems, however, under Harvey's asynchronous update scheme,  $\tilde{n}$  different update choices can be randomly chosen with the same probability at each time step. Correspondingly, when logical system is converted into linear form, there are  $\tilde{n}$  different control-dependent network transition matrices  $\hat{L}_i$ ,  $i \in \{1,2,\dots,\tilde{n}\}$ . Say, the average probability for each transition matrix is  $\Pr\{\hat{L}_i\} = 1/\tilde{n}$ . Then, one can obtain

$$\bar{L} = \frac{1}{\tilde{n}} \sum_{i=1}^{\tilde{n}} \hat{L}_i. \quad (8)$$

**Definition 2:** Consider system (6) with time delay  $\tau$ , given an initial state sequence  $\tilde{x}(t) \in \Delta_{2^{\tilde{n}}}$ ,  $t = -\tau, -\tau+1, \dots, 0$ , the destination state  $\tilde{x}_d \in \Delta_{2^{\tilde{n}}}$  is said to be controllable with probability one at time  $s > 0$ , if a group of controls  $u(t)$ ,  $t = s - (1+\tau), s - 2(1+\tau), \dots, s - \lceil s/\tau + 1 \rceil(1+\tau)$  can be found such that  $\Pr\{\times_{i=1}^{\tilde{n}} \tilde{x}_i(s) = \tilde{x}_d\} = 1$ . Noted that  $\lceil a \rceil$  is the smallest integer larger than or equal to  $a$ , for instance,  $\lceil 5.1 \rceil = 6$ .

**Remark 2:** When time delay  $\tau$  and time  $s$  are given, according to the discussed model, i.e. Eq. (1), the previous location should be  $s - (1+\tau)$ , continue to induce, one can obtain  $s - 2(1+\tau)$ ,  $s - 3(1+\tau), \dots$ . Since an initial state sequence  $\tilde{x}(t) \in \Delta_{2^{\tilde{n}}}$ ,  $t = -\tau, -\tau+1, \dots, 0$  is given, one can verify that location  $s - \lceil s/\tau + 1 \rceil(1+\tau)$  should be in the scope of  $t = -\tau, -\tau+1, \dots, 0$ , i.e. the initial state would be  $\tilde{x}(\rho)$ ,  $\rho = s - (\tau+1)\lceil s/\tau + 1 \rceil$ .

**Definition 3:** As to system (6) with time delay  $\tau$ , when a control  $u \in \Delta_{2^{\tilde{m}}}$  exists such that state  $\tilde{x}_f \in \Delta_{2^{\tilde{n}}}$  holds  $\tilde{x}_f = \hat{L}_i u \tilde{x}_f$ ,  $\forall i \in \{1,2,\dots,\tilde{n}\}$ ,  $\tilde{x}_f$  is said to be a control-dependent fixed point.

**Theorem 1:** Consider system (6) with time delay  $\tau$ , when an initial state sequence  $\tilde{x}(t) \in \Delta_{2^{\tilde{n}}}$  ( $t = -\tau, -\tau+1, \dots, 0$ ) is given, the destination state  $\tilde{x}_d \in \Delta_{2^{\tilde{n}}}$  is said to be controllable at time  $s > 0$  with probability one, only and if only state  $\tilde{x}_d$  is a control-dependent fixed point.

**Proof:**

(Sufficiency) Assume the destination state  $\tilde{x}_d \in \Delta_{2^{\tilde{n}}}$  is a control-dependent fixed point of system (6) with time delay  $\tau$ . According to Definition 3, a control  $u \in \Delta_{2^{\tilde{m}}}$  can be found that  $\Pr\{\times_{i=1}^{\tilde{n}} \tilde{x}_i(s) = \tilde{x}_d | \times_{i=1}^{\tilde{n}} \tilde{x}_i(s-\tau-1) = \tilde{x}_d\} = 1$ . Consequently, we can find a group of controls  $u(t) = u$ ,  $t = s - (1+\tau), s - 2(1+\tau), \dots, s - \lceil s/\tau + 1 \rceil(1+\tau)$ . Then, one can obtain  $\Pr\{\times_{i=1}^{\tilde{n}} \tilde{x}_i(s) = \tilde{x}_d\} = 1$  from the initial state  $\tilde{x}(s - (\tau+1)\lceil s/\tau + 1 \rceil)$ . So,  $\tilde{x}_d$  can be controllable from itself with probability one at time  $s$ .

(Necessity) When the destination state  $\tilde{x}_d$  is said to be controllable with probability one at time  $s > 0$  from initial state  $\tilde{x}(s - (\tau+1)\lceil s/\tau + 1 \rceil)$ ,  $\tilde{x}_d$  should be proved to be a control-dependent fixed point. Firstly, we assume  $\tilde{x}(s - \tau - 1) \neq \tilde{x}(s)$ . According to Definition 2, a control  $u(s - \tau - 1)$  can be found that  $\Pr\{\times_{i=1}^{\tilde{n}} \tilde{x}_i(s) = \tilde{x}_d | \times_{i=1}^{\tilde{n}} \tilde{x}_i(s - \tau - 1) = \tilde{x}(s - \tau - 1)\} = 1$ , which means  $\tilde{x}(s) = L_{i_1} u(s - \tau - 1) \tilde{x}(s - \tau - 1) = L_{i_2} u(s - \tau - 1) \tilde{x}(s - \tau - 1)$ , where  $i_1, i_2 \in \{1, 2, \dots, \tilde{n}\}$  and  $i_1 \neq i_2$ . When  $\tilde{x}(s) = L_{i_1} u(s - \tau - 1) \tilde{x}(s - \tau - 1)$ , considering the rule of Harvey's update scheme, there should be only one node  $\tilde{x}_{i_1}(s - \tau - 1) \neq \tilde{x}_{i_1}(s)$  and the rest elements  $\tilde{x}_j(s - \tau - 1) = \tilde{x}_j(s)$ ,  $j \neq i_1, j = 1, 2, \dots, \tilde{n}$ . And when  $\tilde{x}(s) = L_{i_2} u(s - \tau - 1) \tilde{x}(s - \tau - 1)$ , there should be only one node  $\tilde{x}_{i_2}(s - \tau - 1) \neq \tilde{x}_{i_2}(s)$  and the rest elements  $\tilde{x}_j(s - \tau - 1) = \tilde{x}_j(s)$ ,  $j' \neq i_2, j' = 1, 2, \dots, \tilde{n}$ . The two results are contradictory. So the above assumption can't be held. Say,  $\tilde{x}(s - \tau - 1)$  should be equal to  $\tilde{x}(s)$ . Deduce the rest from this, one can obtain  $\tilde{x}(s) = \tilde{x}(s - i'(\tau + 1))$ ,  $i' \in \mathbb{R}^+$ ,  $s - i'(\tau + 1) \geq -\tau$ . According to Definition 3, it can be proved that  $\tilde{x}_d$  should be a control-dependent fixed point of system (6) with time delay  $\tau$ .

This completes the proof.

From the above results, we can conclude that, as to system (6) with time delay  $\tau$ , when two states  $\tilde{x}_0, \tilde{x}_d \in \Delta_{2^{\tilde{n}}}$  are given and  $\tilde{x}_0 \neq \tilde{x}_d$ ,  $\tilde{x}_d$  can't be controllable from  $\tilde{x}_0$  with probability one. Hence, it is necessary and reasonable to discuss the controllability of the studied model from the perspective of probability.

**Controllability of asynchronous Boolean multiplex control networks with time delay via free Boolean sequence.** In this section, controls are assumed to be free Boolean sequences, based on which the controllability of studied model is discussed.





**Definition 4:** Given the initial state sequence  $\mathbf{x}(t) \in \Delta_{2^n}$ ,  $t = -\tau, -\tau+1, \dots, 0$  and the destination state  $\tilde{\mathbf{x}}_d \in \Delta_{2^n}$ , system (6) with time delay  $\tau$  is said to be controllable to  $\tilde{\mathbf{x}}_d$  with probability at time  $s > 0$ , if a group of controls  $\mathbf{u}(t)$ ,  $t = s - (1 + \tau), s - 2(1 + \tau), \dots$ ,  $s - \lceil s/\tau + 1 \rceil(1 + \tau)$  can be found such that  $\Pr\{\times_{i=1}^n \tilde{\mathbf{x}}_i(s) = \tilde{\mathbf{x}}_d\} > 0$ .

When the initial states and a control sequence are specified, the following approach can be used to calculate the reachable set with probability at time  $s$ .

Before the next discussions, we define two operations:

- 1)  $\Lambda(\delta_n^r) = r$ , furthermore, when  $C' = \{\delta_n^{i_1}, \delta_n^{i_2}, \dots, \delta_n^{i_p}\}$ ,  $\Lambda(C') = \{i_1, i_2, \dots, i_p\}$ . Correspondingly,  $\bar{\Lambda}(r)_n = \delta_n^r$  and  $\Lambda(\{i_1, i_2, \dots, i_p\})_n = \{\delta_n^{i_1}, \delta_n^{i_2}, \dots, \delta_n^{i_p}\}$ . For instance,  $\Lambda(\delta_8^2) = 2$  and  $\Lambda(2)_8 = \delta_8^2$ .
- 2) Let column vector  $\mathbf{X} \in \mathbb{R}^m$ , all of row indices of  $\mathbf{X}$  in which row elements aren't equal to zero compose a set denoted by  $\Omega(\mathbf{X})$ . For example,  $\mathbf{X} = [1, 0, 2, 1]^T$  and  $\Omega(\mathbf{X}) = \{1, 3, 4\}$ .

**Theorem 2:** For system (6) with time delay  $\tau$ , given the initial state sequence  $\tilde{\mathbf{x}}(t) \in \Delta_{2^n}$ ,  $t = -\tau, -\tau+1, \dots, 0$  and controls  $\mathbf{u}(t)$ ,  $t = -\tau, -\tau+1, \dots, s-1$ , the destination state  $\tilde{\mathbf{x}}_d$  is reachable with probability at time  $s$ , iff

$$\tilde{\mathbf{x}}_d \in \bar{\Lambda}\left(\Omega\left(\text{Col}(\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho))\right)\right)_{2^n}, \quad (9)$$

where  $\tilde{\mathbf{L}} = \bar{\mathbf{L}}\mathbf{W}_{[2^n, 2^m]}$ ,  $\bar{\mathbf{L}} = \frac{1}{n} \sum_{i=1}^n \hat{\mathbf{L}}_i$ ,  $\rho = s - \lceil s/\tau + 1 \rceil(\tau + 1)$ ,  $\times_{i=0}^{\lceil s/\tau + 1 \rceil - 1} \mathbf{u}(\rho + i(\tau + 1)) = \delta_{2^{m\lceil s/\tau + 1 \rceil}}^\varphi$  and  $\text{Col}(\cdot)_\varphi$  represent the  $\varphi$ -th column of matrix.

**Proof:** By means of STP, system (6) with time delay  $\tau$  can be rewritten as

$$\tilde{\mathbf{x}}(t+1) = \hat{\mathbf{L}}_i \mathbf{W}_{[2^n, 2^m]} \tilde{\mathbf{x}}(t-\tau) \mathbf{u}(t-\tau). \quad (10)$$

At time  $t$ , since each node in multiplex has the same probability to be chosen for update, one can obtain the overall expected value of  $\tilde{\mathbf{x}}(t)$  as

$$\begin{aligned} \mathbf{Ex}(t+1) &= \frac{1}{n} \sum_{i=1}^n \hat{\mathbf{L}}_i \mathbf{W}_{[2^n, 2^m]} \mathbf{Ex}(t-\tau) \mathbf{u}(t-\tau) \\ &\triangleq \tilde{\mathbf{L}} \mathbf{Ex}(t-\tau) \mathbf{u}(t-\tau). \end{aligned} \quad (11)$$

Since time delay  $\tau$  is involved both in states and controls, the location of the initial state which evolves into the destination state  $\tilde{\mathbf{x}}(s)$  is  $s - \lceil s/\tau + 1 \rceil(\tau + 1)$ . To expand the above formula and yields

$$\begin{aligned} \mathbf{Ex}(1) &= \tilde{\mathbf{L}} \mathbf{Ex}(0-\tau) \mathbf{u}(0-\tau) = \tilde{\mathbf{L}} \tilde{\mathbf{x}}(-\tau) \mathbf{u}(-\tau), \\ \mathbf{Ex}(2) &= \tilde{\mathbf{L}} \mathbf{Ex}(1-\tau) \mathbf{u}(1-\tau) = \tilde{\mathbf{L}} \tilde{\mathbf{x}}(1-\tau) \mathbf{u}(1-\tau), \\ &\vdots \\ \mathbf{Ex}(\tau) &= \tilde{\mathbf{L}} \mathbf{Ex}(-1) \mathbf{u}(-1) = \tilde{\mathbf{L}} \tilde{\mathbf{x}}(-1) \mathbf{u}(-1), \\ \mathbf{Ex}(\tau+1) &= \tilde{\mathbf{L}} \mathbf{Ex}(0) \mathbf{u}(0) = \tilde{\mathbf{L}} \tilde{\mathbf{x}}(0) \mathbf{u}(0), \\ \mathbf{Ex}(\tau+2) &= \tilde{\mathbf{L}} \mathbf{Ex}(1) \mathbf{u}(1) = \tilde{\mathbf{L}}^2 \tilde{\mathbf{x}}(-\tau) \mathbf{u}(-\tau) \mathbf{u}(1), \\ &\vdots \\ \mathbf{Ex}(s) &= \tilde{\mathbf{L}} \mathbf{Ex}(s-1-\tau) \mathbf{u}(s-1-\tau) = \\ &\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho) \mathbf{u}(\rho) \mathbf{u}(\rho + \tau + 1) \cdots \mathbf{u}(s-1-\tau), \end{aligned}$$

where  $\rho = s - \lceil s/\tau + 1 \rceil(\tau + 1)$ .

This completes the proof.

When the initial states are given and controls are freely chosen, we provide the following approach to calculate the reachable set with probability at time  $s$ . Assume  $X_0 = \{\tilde{\mathbf{x}}(t) | t = -\tau, -\tau+1, \dots, 0\}$  is the set of initial states, we denote by  $R(X_0)_{s,\tau}$  the reachable set from set  $X_0$  with time delay  $\tau$  at time  $s$  under arbitrary controls.

**Lemma 2:** For system (6) with time delay  $\tau$ ,  $X_0 = \{\tilde{\mathbf{x}}(t) | t = -\tau, -\tau+1, \dots, 0\}$  is the set of initial states. Controls  $\mathbf{u}(t)$ ,  $t = -\tau, -\tau+1, \dots, s-1$  can be freely chosen, one can obtain

$$R(X_0)_{s,\tau} = \{\delta_{2^n}^i | \text{Row}(\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho))_i \neq 0\}, \quad (12)$$

where  $\tilde{\mathbf{L}} = \bar{\mathbf{L}}\mathbf{W}_{[2^n, 2^m]}$ ,  $\bar{\mathbf{L}} = \frac{1}{n} \sum_{i=1}^n \hat{\mathbf{L}}_i$ ,  $\rho = s - \lceil s/\tau + 1 \rceil(\tau + 1)$  and  $\text{Row}(\cdot)_i$  represents the  $i$ -th row of matrix.

**Proof:**

1) Assume state  $\delta_{2^n}^r \in R(X_0)_{s,\tau}$ ,  $\text{Row}(\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho))_r \neq 0$  should be proofed.

Since the destination state  $\delta_{2^n}^r$  is reachable with probability at time  $s$ , one can find a sequence of controls  $\times_{i=0}^{\lceil s/\tau + 1 \rceil - 1} \mathbf{u}(\rho + i(\tau + 1)) = \delta_{2^{m\lceil s/\tau + 1 \rceil}}^\varphi$  to steer the system from initial state  $\tilde{\mathbf{x}}(\rho)$  to the destination states  $\delta_{2^n}^r$ . Correspondingly, based on Theorem 2, it's easy to get the element in the position  $(r, \varphi)$  of matrix  $\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho)$  should be non-zero, which means the  $\varphi$ -th element of row vector  $\text{Row}(\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho))_r$  is non-zero.

2) When  $\text{Row}(\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho))_r \neq 0$ , we can assume the  $\varphi$ -th element of row vector  $\text{Row}(\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho))_r$  is non-zero. According to Theorem 2, by means of  $\mathbf{u} = \delta_{2^{m\lceil s/\tau + 1 \rceil}}^\varphi$ , the destination states  $\delta_{2^n}^r$  is reachable with probability at time  $s$ . Furthermore,  $\mathbf{u} = \delta_{2^{m\lceil s/\tau + 1 \rceil}}^\varphi$  can be decomposed into a sequence of controls as  $\mathbf{u}(\rho), \mathbf{u}(\rho + \tau + 1), \dots, \mathbf{u}(s-1-\tau)$ .

This completes the proof.

And, when a control sequence is given, we also can obtain the specific reachable probability from certain initial states to a given destination state  $\tilde{\mathbf{x}}_d$  at time  $s$ .

**Lemma 3:** For system (6) with time delay  $\tau$ , assume the initial state sequence as  $\tilde{\mathbf{x}}(t) \in \Delta_{2^n}$ ,  $t = -\tau, -\tau+1, \dots, 0$  and controls as  $\times_{i=0}^{\lceil s/\tau + 1 \rceil - 1} \mathbf{u}(\rho + i(\tau + 1)) = \delta_{2^{m\lceil s/\tau + 1 \rceil}}^\varphi$ . The reachable probability from the initial states to the destination state  $\tilde{\mathbf{x}}_d = \delta_{2^n}^\beta$  at time  $s$  is

$$\Pr\{\tilde{\mathbf{x}}(s) = \delta_{2^n}^\beta\} = (\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho))_{\beta, \varphi}, \quad (13)$$

where  $\tilde{\mathbf{L}} = \bar{\mathbf{L}}\mathbf{W}_{[2^n, 2^m]}$ ,  $\bar{\mathbf{L}} = \frac{1}{n} \sum_{i=1}^n \hat{\mathbf{L}}_i$ ,  $\rho = s - \lceil s/\tau + 1 \rceil(\tau + 1)$  and  $(\cdot)_{i,j}$  is the element at position  $(i, j)$  of matrix.

**Remark 3:** Entry  $(\beta, \varphi)$  of matrix  $\tilde{\mathbf{L}}^{\lceil s/\tau + 1 \rceil} \tilde{\mathbf{x}}(\rho)$  indicate the state transfer information of dynamics from initial state  $\tilde{\mathbf{x}}(\rho)$  under control sequence  $\delta_{2^{m\lceil s/\tau + 1 \rceil}}^\varphi$  after  $\lceil s/\tau + 1 \rceil$  time steps to destination state  $\delta_{2^n}^\beta$ .

**Controllability of asynchronous Boolean multiplex control networks with time delay via input control networks.** Based on STP of matrix, the linear representation of system (7) can be obtained as

$$\mathbf{u}(t+1) = \mathbf{G}\mathbf{u}(t-\tau), \quad (14)$$

where  $\mathbf{G} \in \mathcal{L}_{2^m \times 2^m}$  is the network transient matrix of input control network.

**Definition 5:** Consider system (6) with input control network (7) and time delay  $\tau$ , when initial state  $\tilde{\mathbf{x}}_0 \in \Delta_{2^n}$  and destination state  $\tilde{\mathbf{x}}_d \in \Delta_{2^n}$  are given,  $\tilde{\mathbf{x}}_d$  is said to be controllable with probability from  $\tilde{\mathbf{x}}_0$  at time  $s$ , if an initial control  $\mathbf{u}_0 \in \Delta_{2^m}$  can be found such that



$$\Pr(\times_{i=1}^{\tilde{n}} \tilde{x}_i(s) = \tilde{x}_d | \times_{i=1}^{\tilde{n}} \tilde{x}_i(\rho) = \tilde{x}_0, \times_{i=1}^{\tilde{m}} u_i(\rho) = u_0) > 0,$$

where  $\rho = s - \lceil s/\tau + 1 \rceil(\tau + 1)$ .

**Theorem 3:** For system (6) with input control network (7) and time delay  $\tau$ , the destination state  $\tilde{x}_d$  is controllable with probability from initial state  $\tilde{x}_0$  under initial control  $u_0$  at time  $s$  iff

$$\tilde{x}_d \in \bar{\Lambda}(\Omega(\Theta^G(s, \tau) W_{[2\tilde{n}, 2\tilde{m}]} \tilde{x}(\rho) u(\rho)))_{2\tilde{n}}, \quad (15)$$

where  $\Theta^G(s, \tau) = \bar{L}(G(I_{\tilde{m}} \otimes \bar{L})\Phi_{\tilde{m}})^{(\lceil s/\tau + 1 \rceil - 1)}$ ,  $\bar{L} = \frac{1}{\tilde{n}} \sum_{i=1}^{\tilde{n}} L_i$ ,  $\rho = s - \lceil s/\tau + 1 \rceil(\tau + 1)$ .

**Proof:**

One can obtain

$$\begin{aligned} Ex(1) &= \bar{L}u(-\tau)Ex(-\tau) = \bar{L}u(-\tau)\tilde{x}(-\tau), \\ Ex(2) &= \bar{L}u(1-\tau)Ex(1-\tau) = \bar{L}u(1-\tau)\tilde{x}(1-\tau), \\ &\vdots \\ Ex(\tau+1) &= \bar{L}u(0)Ex(0) = \bar{L}u(0)\tilde{x}(0), \\ Ex(\tau+2) &= \bar{L}u(1)Ex(1) = \bar{L}Gu(-\tau)\bar{L}u(-\tau)\tilde{x}(-\tau) \\ &= \bar{L}G(I_{\tilde{m}} \otimes \bar{L})\Phi_{\tilde{m}}u(-\tau)\tilde{x}(-\tau), \\ Ex(\tau+3) &= \bar{L}u(2)Ex(2) = \bar{L}Gu(1-\tau)\bar{L}u(1-\tau)\tilde{x}(1-\tau) \\ &= \bar{L}G(I_{\tilde{m}} \otimes \bar{L})\Phi_{\tilde{m}}u(1-\tau)\tilde{x}(1-\tau), \\ &\vdots \\ Ex(s) &= \bar{L}u(s-1-\tau)Ex(s-1-\tau) \\ &= \bar{L}Gu(s-2(\tau+1))\bar{L}u(s-2(\tau+1))Ex(s-2(\tau+1)) \\ &= \bar{L}G(I_{\tilde{m}} \otimes \bar{L})\Phi_{\tilde{m}}u(s-2(\tau+1))Ex(s-2(\tau+1)) \\ &= \bar{L}(G(I_{\tilde{m}} \otimes \bar{L})\Phi_{\tilde{m}})^2 u(s-3(\tau+1))Ex(s-3(\tau+1)) \\ &\vdots \\ &= \bar{L}(G(I_{\tilde{m}} \otimes \bar{L})\Phi_{\tilde{m}})^{(\lceil s/\tau + 1 \rceil - 1)} u(\rho)\tilde{x}(\rho) \\ &\triangleq \Theta^G(s, \tau) W_{[2\tilde{n}, 2\tilde{m}]} \tilde{x}(\rho) u(\rho) \end{aligned}$$

This completes the proof.

**Lemma 4:** For system (6) with input control network (7) and time delay  $\tau$ , when the initial control  $u_0$  can be freely chosen, the set of states which are reachable with probability from initial states  $X_0 = \{\tilde{x}(t) | t = -\tau, -\tau+1, \dots, 0\}$  at time  $s$  is

$$R(X_0)_{s, \tau} = \left\{ \delta_{2\tilde{n}}^i \text{Row}(\Theta^G(s, \tau) W_{[2\tilde{n}, 2\tilde{m}]} \tilde{x}(\rho))_i \neq 0 \right\},$$

where  $\rho = s - \lceil s/\tau + 1 \rceil(\tau + 1)$ .

**Lemma 5:** For system (6) with input control network (7) and time delay  $\tau$ , the probability from the initial states  $X_0 = \{\tilde{x}(t) | t = -\tau, -\tau+1, \dots, 0\}$  to the destination state  $\tilde{x}_d$  under initial control  $u_0$  at time  $s$  is

$$\Pr(\times_{i=1}^{\tilde{n}} \tilde{x}_i(s) = \tilde{x}_d | \times_{i=1}^{\tilde{n}} \tilde{x}_i(\rho) = \tilde{x}_0, \times_{i=1}^{\tilde{m}} u_i(\rho) = u_0) = (\Theta^G(s, \tau) W_{[2\tilde{n}, 2\tilde{m}]} \tilde{x}_0 u_0)_{\Lambda(\tilde{x}_d), 1},$$

where  $\rho = s - \lceil s/\tau + 1 \rceil(\tau + 1)$ .

## Examples

**Example 1** Consider Boolean multiplex control network (16) with  $\tilde{k} = 2$  layers,  $\tilde{n} = 4$  nodes and  $\tilde{m} = 1$  control shown in Fig 2. Assume

system (16) is under Harvey's asynchronous update and time delay  $\tau$  both in states and controls.

$$\begin{aligned} \text{Layer 1 : } & \begin{cases} x_1^1(t+1) = x_3^1(t-\tau) \wedge u_1(t-\tau) \\ x_2^1(t+1) = x_3^1(t-\tau) \rightarrow x_1^1(t-\tau) \\ x_3^1(t+1) = x_1^1(t-\tau) \vee \neg u_1(t-\tau) \end{cases} \\ \text{Layer 2 : } & \begin{cases} x_2^2(t+1) = \neg x_4^2(t-\tau) \vee u_1(t-\tau) \\ x_3^2(t+1) = x_2^2(t-\tau) \leftrightarrow x_4^2(t-\tau) \\ x_4^2(t+1) = x_3^2(t-\tau) \wedge \neg u_1(t-\tau) \end{cases} \end{aligned} \quad (16)$$

where  $\neg, \vee, \wedge, \rightarrow$  and  $\leftrightarrow$  represent the logical functions of negation, disjunction, conjunction, implication and equivalence, respectively. Correspondingly, one can obtain the algebraic representation of logical functions as  $\vee \sim M_d = \delta_2[1, 1, 1, 2]$ ,  $\neg \sim M_n = \delta_2[1, 2]$ ,  $\wedge \sim M_c = \delta_2[1, 2, 2, 2]$ ,  $\rightarrow \sim M_{im} = \delta_2[1, 2, 1, 1]$  and  $\leftrightarrow \sim M_e = \delta_2[1, 2, 2, 1]$ .

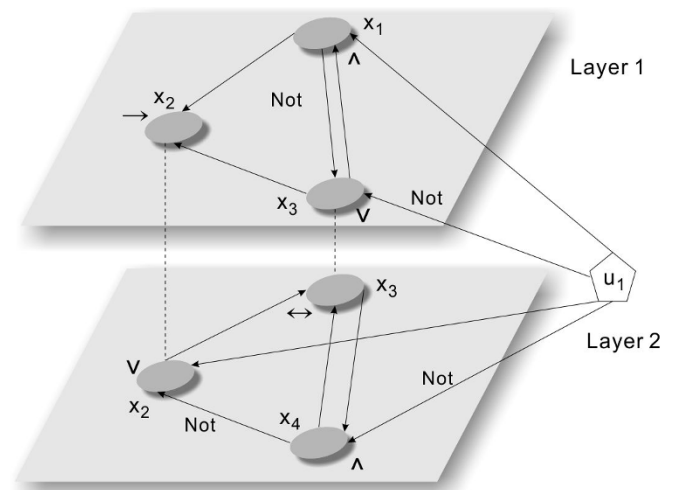
Based on the above discussion, we define  $\tilde{x}(t) = \times_{i=1}^{\tilde{n}} \tilde{x}_i(t)$  and  $\tilde{u}(t) = \times_{i=1}^{\tilde{m}} u_i(t)$ . And, as to the canalizing function  $\tilde{f}_i, i \in \{1, 2, \dots, \tilde{n}\}$ , without loss of the generality, we choose disjunction function, i.e.  $\tilde{M}_i = M_d, i \in \{1, 2, \dots, \tilde{n}\}$ . The control  $u_1(t)$  in system (16) is free Boolean variable. In the following, the controllability of ABMCNs (16) with time delay  $\tau$  is to be discussed. Firstly, we calculate the control-depending network transition matrix of system. Note that, at time  $t$ ,  $\tilde{x}_l(t) = x_l^l(t)$ ,  $l \in \{1, 2, \dots, \tilde{k}\}$ .

Case 1: at time  $t$ , when node 1 is selected for update,

$$\begin{aligned} \tilde{x}(t+1) &= M_c x_3^1(t-\tau) u_1(t-\tau) \tilde{x}_2(t-\tau) \tilde{x}_3(t-\tau) \tilde{x}_4(t-\tau) \\ &= M_c (I_2 \otimes W_{[8,2]}) W_{[2]} (I_2 \otimes M_r) E_d W_{[2,16]} u_1(t-\tau) \tilde{x}_1(t-\tau) \\ &\quad \tilde{x}_2(t-\tau) \tilde{x}_3(t-\tau) \tilde{x}_4(t-\tau) \\ &\triangleq \hat{L}_1 u(t-\tau) \tilde{x}(t-\tau). \end{aligned}$$

Case 2: at time  $t$ , when node 2 is selected for update,

$$\begin{aligned} \tilde{x}(t+1) &= \tilde{x}_1(t-\tau) M_d M_i x_3^1(t-\tau) x_1^1(t-\tau) M_d M_n x_4^2(t-\tau) u_1(t-\tau) \tilde{x}_3(t-\tau) \tilde{x}_4(t-\tau) \\ &= (I_2 \otimes M_d) (I_2 \otimes M_i) (I_8 \otimes M_d) (I_8 \otimes M_n) (I_{16} \otimes W_{[4,2]}) (I_2 \otimes W_{[2]}) \\ &\quad (I_4 \otimes W_{[2]}) (I_2 \otimes M_r) (I_4 \otimes M_r) E_d W_{[2]} W_{[2,16]} u_1(t-\tau) \tilde{x}_1(t-\tau) \tilde{x}_2(t-\tau) \tilde{x}_3(t-\tau) \tilde{x}_4(t-\tau) \\ &\triangleq \hat{L}_2 u(t-\tau) \tilde{x}(t-\tau). \end{aligned}$$



**Figure 2 |** An asynchronous Boolean multiplex control network with time delay (16).





Case 1: at time  $t$ , when node  $\tilde{A}$  is selected for update,

$$\begin{aligned}\tilde{X}(t+1) &= M_p M_p M_p M_n D^1(t-\tau) B^1(t-\tau) M_c D^1(t-\tau) B^1(t-\tau) u_1(t-\tau) \tilde{B}(t-\tau) \tilde{D}(t-\tau) \tilde{A}'(t-\tau) \\ &= M_p M_p M_p M_n (I_4 \otimes M_c) (I_{16} \otimes W_{[8,2]}) (I_4 \otimes W_{[4,2]}) W_{[8,2]} M_r M_r (I_2 \otimes M_r M_r) E_d W_{[2,16]} \\ &\quad E_d W_{[2]} u_1(t-\tau) u_2(t-\tau) \tilde{A}(t-\tau) \tilde{B}(t-\tau) \tilde{D}(t-\tau) \tilde{A}'(t-\tau) \triangleq \hat{L}_1 u(t-\tau) \tilde{X}(t-\tau).\end{aligned}$$

Case 2: at time  $t$ , when node  $\tilde{B}$  is selected for update,

$$\begin{aligned}\tilde{X}(t+1) &= \tilde{A}(t) M_d M_c A^1(t-\tau) u_2(t-\tau) A^2(t-\tau) \tilde{D}(t-\tau) \tilde{A}'(t-\tau) \\ &= (I_2 \otimes M_d M_c) (I_2 \otimes W_{[8,2]}) (I_4 \otimes W_{[2]}) W_{[2]} (I_8 \otimes M_r M_r) E_d W_{[4,2]} \\ &\quad E_d u_1(t-\tau) u_2(t-\tau) \tilde{A}(t-\tau) \tilde{B}(t-\tau) \tilde{D}(t-\tau) \tilde{A}'(t-\tau) \triangleq \hat{L}_2 u(t-\tau) \tilde{X}(t-\tau).\end{aligned}$$

Case 3: at time  $t$ , when node  $\tilde{D}$  is selected for update,

$$\begin{aligned}\tilde{X}(t+1) &= \tilde{A}(t-\tau) \tilde{B}(t-\tau) M_d B^1(t-\tau) M_d B^2(t-\tau) u_1(t-\tau) \tilde{A}'(t-\tau) \\ &= (I_4 \otimes M_d) (I_8 \otimes M_d) (I_{16} \otimes W_{[2]}) (I_2 \otimes M_r M_r) \\ &\quad E_d W_{[4,2]} W_{[2,16]} E_d W_{[2]} u_1(t-\tau) u_2(t-\tau) \tilde{A}(t-\tau) \tilde{B}(t-\tau) \tilde{D}(t-\tau) \tilde{A}'(t-\tau) \\ &\triangleq \hat{L}_3 u(t-\tau) \tilde{X}(t-\tau).\end{aligned}$$

Case 4: at time  $t$ , when node  $\tilde{A}'$  is selected for update,

$$\begin{aligned}\tilde{X}(t+1) &= \tilde{A}(t-\tau) \tilde{B}(t-\tau) \tilde{D}(t-\tau) M_p M_p M_p D^2(t-\tau) B^2(t-\tau) M_c D^2(t-\tau) B^2(t-\tau) u_2(t-\tau) \\ &= (I_8 \otimes M_p M_p M_p) (I_{32} \otimes M_c) (I_4 \otimes W_{[2,4]}) (I_8 \otimes W_{[2,8]}) (I_2 \otimes M_r M_r) \\ &\quad (I_4 \otimes M_r M_r) E_d W_{[8,2]} W_{[2,16]} E_d u_1(t-\tau) u_2(t-\tau) \tilde{A}(t-\tau) \tilde{B}(t-\tau) \tilde{D}(t-\tau) \tilde{A}'(t-\tau) \\ &\triangleq \hat{L}_4 u(t-\tau) \tilde{X}(t-\tau)\end{aligned}$$

Assume time step  $s = 9$  and time delay  $\tau = 3$ , randomly choose the initial states as  $\tilde{X}(-3) = \delta_{16}^4 \sim (1, 1, 0, 0)$ ,  $\tilde{X}(-2) = \delta_{16}^5 \sim (1, 0, 1, 1)$ ,  $\tilde{X}(-1) = \delta_{16}^6 \sim (1, 0, 1, 0)$  and  $\tilde{X}(0) = \delta_{16}^7 \sim (1, 0, 0, 1)$ . One can obtain  $\rho = s - \lceil s/\tau + 1 \rceil (\tau + 1) = -3$  and the initial state  $\tilde{X}_0 = \tilde{X}(\rho) = \delta_{16}^4$ . According to Theorem 3, we can calculate that

$$\begin{cases} \Theta^G(9, 3) = \bar{L}(G(I_{\bar{m}} \otimes \bar{L})\Phi_{\bar{m}})^{(\lceil s/\tau + 1 \rceil - 1)} = \bar{L}(G(I_2 \otimes \bar{L})\Phi_2)^{(\lceil 9/4 \rceil - 1)} \\ \Phi_2 = (I_2 \otimes W_{[2]}) M_r (I_2 \otimes M_r) = \delta_{16}[1, 6, 11, 16] \\ \bar{L} = \frac{1}{4} \sum_{i=1}^4 \hat{L}_i \end{cases}$$

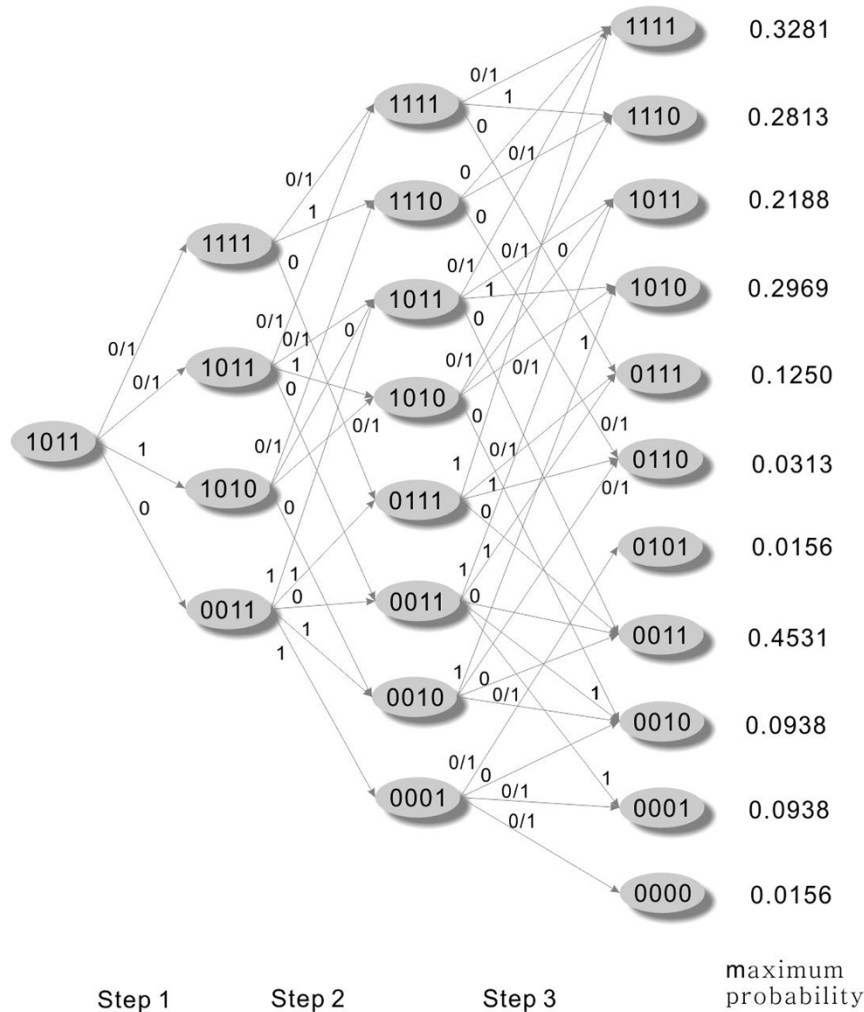


Figure 3 | The state transfer graph of system (16) from initial state (1011) in 3 steps.





$$\Theta^G(9,3)W_{[2^4,2^2]}\tilde{X}_0 = \begin{pmatrix} 0.0469 & 0 & 0.0938 & 0 \\ 0.1406 & 0.1406 & 0.2656 & 0.25 \\ 0.0938 & 0 & 0.0625 & 0 \\ 0 & 0.1406 & 0.1250 & 0.2969 \\ 0 & 0 & 0 & 0 \\ 0.0469 & 0 & 0.0938 & 0.0469 \\ 0 & 0 & 0 & 0 \\ 0.0938 & 0.1406 & 0.0625 & 0.1094 \\ 0.0156 & 0 & 0.0156 & 0 \\ 0.1719 & 0.1094 & 0.0781 & 0.0781 \\ 0.0938 & 0 & 0.0625 & 0 \\ 0.1875 & 0.3594 & 0 & 0.0781 \\ 0 & 0 & 0 & 0 \\ 0.0156 & 0 & 0.0313 & 0.0156 \\ 0 & 0 & 0 & 0.0156 \\ 0.0938 & 0.1094 & 0.1094 & 0.1094 \end{pmatrix}. \quad (20)$$

Using Lemma 4, when the initial control  $u_0$  is free, except three unreachable states  $\delta_{16}^5$ ,  $\delta_{16}^7$  and  $\delta_{16}^{13}$ , all of the rest states can be reachable from initial state  $\tilde{X}_0 = \tilde{X}(\rho) = \delta_{16}^4$  at time  $s = 9$  with time delay  $\tau = 3$ . Furthermore, when initial control  $u_\rho$  is assumed to be specified, for instance,  $u_\rho = (u_1(\rho), u_2(\rho)) = (1, 0) \sim \delta_4^2$ , one can obtain the corresponding reachable set as follows.

$$\bar{\Lambda}(\Omega(\Theta^G(9,3)W_{[2^4,2^2]}\tilde{X}(\rho)u_\rho))_{2^4} = \{\delta_{16}^2, \delta_{16}^4, \delta_{16}^8, \delta_{16}^{10}, \delta_{16}^{12}, \delta_{16}^{16}\}.$$

Note that states  $\delta_{16}^2 \sim (1, 1, 1, 0)$ ,  $\delta_{16}^4 \sim (1, 1, 0, 0)$  and  $\delta_{16}^8 \sim (1, 0, 0, 0)$  can be reached with the same probability 0.1406 from initial state  $\tilde{X}(\rho) = \delta_{16}^4$  under initial control  $u_\rho = (1, 0)$  at time  $s = 9$  with time delay  $\tau = 3$ . Similarly, destination states  $\delta_{16}^{10} \sim (0, 1, 1, 0)$  and  $\delta_{16}^{16} \sim (0, 0, 0, 0)$  can be reached with the same probability 0.1094, which is also the minimum reachable probability compared with the rest reachable states. Correspondingly, we can obtain the maximum reachable probability belonging to state  $\delta_{16}^{12} \sim (0, 1, 0, 0)$  is 0.3594.

In some applications, such as the therapeutic intervention, normally a final target is clear, i.e. an expected state for biological system is given. Hence, we should find a specific control sequence to steer system from the initial state to target with the maximum probability. Based on the above discussion, an approach can be obtained. Assume a required target at time  $s = 9$  with time delay  $\tau = 3$  is  $\tilde{X}_d = \delta_{16}^2 \sim (1, 1, 1, 0)$ . By using of matrix (20), we can get the maximum reachable probability is 0.2656 at the Row 2 and Column 3. According to Theorem 3 and Lemma 5, we can calculate the initial control  $u_0 = \delta_4^3 \sim (0, 1)$ , i.e.  $u_1(0) = 0$  and  $u_2(0) = 1$ .

## Conclusions

In this article, inputs as controls are introduced into Boolean multiplex networks under asynchronous stochastic update, meanwhile, time delay as additional factor is considered both in states and inputs of system. By means of STP approach, the above logical dynamics is converted into algebraic form and the controllability of dynamics is discussed. Firstly, it is proved that only control-depending fixed points can be controlled with probability one, which means the discussion of controllability of asynchronous Boolean control networks should be in terms of probabilities. Subsequently, respectively for two kinds of controls, formulae to calculate the reachable set from an initial state to a destination state under specified controls or arbitrary

controls are provided, as well as the approach to obtain the specific reachable probabilities from an initial state to different destination states. Moreover, we also present how to find a precise control sequence which can steer dynamics into a given target with the maximum reachable probability.

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## Author contributions

L.C., W.X.Y. devised the model and carried out theoretical analysis. L.C. and L.H. implemented numerical simulations. L.C., W.X.Y. and L.H. wrote the main text of the manuscript.

## Additional information

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