Minimum-Time Control of Boolean Networks

Dmitriy Laschov and Michael Margaliot

Abstract

Boolean networks (BNs) are discrete-time dynamical systems with Boolean state-variables. BNs are recently attracting considerable interest as computational models for biological systems and, in particular, as models of gene regulating networks. Boolean control networks (BCNs) are Boolean networks with Boolean inputs. We consider the problem of steering a BCN from a given state to a desired state in minimal time. Using the algebraic state-space representation (ASSR) of BCNs we derive several necessary conditions, stated in the form of maximum principles (MPs), for a control to be time-optimal. In the ASSR every state and input vector is a canonical vector. Using this special structure yields an explicit state-feedback formula for all time-optimal controls. To demonstrate the theoretical results, we develop a BCN model for the genetic switch controlling the lambda phage development upon infection of a bacteria. Our results suggest that this biological switch is designed in a way that guarantees minimal time response to important environmental signals.

Index Terms

Logical systems, variational analysis, necessary condition for optimality, time-optimal control, systems biology, gene regulation networks, lambda switch.

I. INTRODUCTION

A Boolean network (BN) is a discrete-time dynamical system with Boolean state-variables. For example, cellular automata, with two possible states per cell, are a particular case of BNs. Here the state of every variable at time $k+1$ is determined by the state of its spatial neighbors at time k [70]. BNs have a long history [23], [24] and they have been used as models for different systems including: simple artificial neural networks [36], social interactions between

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simple agents, the emergence of social consensus, the influence of mass media on public opinion, and the role of peer influence in maintaining law and order [33].

More recently, BNs have gained renewed interest as models for biological systems. The underlying assumption is that certain biological variables can be approximated as having just two possible levels of operation (i.e., ON and OFF). S. A. Kauffman [42] modeled a gene as a binary device, and studied the behavior of large, randomly constructed nets of these binary genes. Kauffman's simulations suggest that if each network node has two or three inputs, then the dynamical behavior of the network demonstrates order and stability. Kauffman also related the behavior of the random nets to various cellular control processes including cell differentiation. The key idea being to view each stable attractor of the BN as representing one possible cell type.

Kauffman's pioneering ideas stimulated research in several directions including: (1) theoretical analysis of the dynamics of BNs, especially using tools from the fields of complex systems and statistical physics (see, e.g. [4], [6], [27], [28], [43], [56], [68]); and (2) modeling various biological processes using BNs. This is a vast area of research and we review below only a few examples.

BNs seem especially suitable for modeling genetic regulation networks where the ON (OFF) state corresponds to the transcribed (quiescent) state of the gene. There are several other motivations [39] for using BNs in this context, including the fact that many metabolic and genetic networks demonstrate some form of bi-stability. An important example are epigenetic switches (see, e.g. [66]). Specific examples of genetic regulation networks modeled using BNs include: the cell-cycle regulatory network of the budding yeast [51]; the yeast transcriptional network [41]; the network controlling the segment polarity genes in the fly *Drosophila melanogaster* [5], [14]; and the ABC network determining floral organ cell fate in Arabidopsis [29] (see also [13]).

BNs were also used for modeling other cellular processes. In this context, the two possible logic states may represent the open/closed state of an ion channel, basal/high activity of an enzyme, two possible conformational states of a protein, etc. Specific examples include: a detailed model for the complex cellular signaling network controlling stomatal closure in plants [52], and a model of the molecular pathway between two neurotransmitter systems, the dopamine and glutamate receptors [34]. Szallasi and Liang [75] discuss the use of BNs in modeling carcinogenesis and for analyzing the effect of therapeutic intervention (see also [40]).

BNs have also been used to address more general problems that may have important implications to biological and cellular systems. For example, the trade-off between functional complexity and robustness (see [55], [60] and the references therein).

Despite their simplicity, BNs provide an efficient tool for modeling large-scale biological networks [12], [37]. These models are able to reproduce the main characteristics of the biological system dynamics: attractors of the BN correspond to stationary biological states; large attraction basins indicate robustness of the biological state; and so on.

Modeling using BNs requires only coarse-grained qualitative information (e.g., an interaction between two genes is either activating or inhibiting). Many other models, for example, those based on differential equations, require knowledge of numerous parameter values (e.g., rate constants). For a general exposition on various approaches for modeling gene regulation networks, see [10].

Modeling a biological system involves considerable uncertainty. This is due to the noise and perturbations that affect the biological system, and inaccuracies of the measuring equipment. One approach for tackling this uncertainty is by using *Probabilistic Boolean Networks* (PBNs) [72], [73]. These may be viewed as a collection of (deterministic) BNs combined with a probabilistic switching rule determining which network is active at each time instant.

BNs with (binary) inputs are referred to as *Boolean Control Networks* (BCNs). For example, the value of the input at time k can represent whether a certain medicine is administered or not, or whether a ceratin environmental condition is hazardous or not at time k. PBNs with inputs have been used to design and analyze therapeutic intervention strategies. Several methods have been proposed including flipping the state of a single gene [74]; changing the Boolean interaction functions [67]; and finding a control sequence that steers the network from an undesirable location (e.g., corresponding to a diseased state) to a desirable one (e.g., corresponding to a healthy state). The latter type of problems can be cast as stochastic optimal control problems, and solved numerically using dynamic programming [26], [54] and Markov chains methods both in the finite and infinite-horizon case [25], [65].

Daizhan Cheng and his colleagues developed an *algebraic state-space representation* (ASSR) of BCNs using the semi-tensor product of matrices. This representation proved useful for addressing control-theoretic problems for BCNs. Examples include the analysis of disturbance decoupling [16], controllability and observability [19], [48], realization theory [18], and more [20],

[21], [15]. See the recent monograph [22] for a detailed presentation.

Here we make use of the ASSR to study *minimum-time* controls for BCNs. Time-optimal controls are important in the context of BCNs that model biological systems. For example, a natural problem is to determine a control that steers the BCN from an initial condition (that corresponds to a diseased state) to a desired condition (that corresponds to a healthy state) in *minimal time*.

In continuous-time control systems, a time-optimal control typically steers the state to the boundary of the reachable set, and can thus be characterized using the celebrated Pontryagin maximum principle (PMP) (see, e.g. [2], [11], [69], [53]). The analysis of time-optimal controls in discrete-time systems is more difficult, as the idea of an infinitesimal control perturbation, that is used in deriving the PMP, cannot be applied. The analysis of time-optimal controls for discrete-time systems is thus usually based on successively computing the reachable set at time $k = 0, 1, 2, \dots$ (see, e.g. [44]).

In this paper we derive several necessary conditions for a control to be time-optimal. These conditions are stated in the form of maximum principles (MPs). Let I_j denote the $j \times j$ identity matrix. In the ASSR, the state vector $x(k)$ of a BCN with n state variables is a column of I_{2^n} for any time k. Similarly, the input vector $u(k)$ is a column of I_{2^m}, where m is the number of input variables. In other words, both $x(k)$ and $u(k)$ are *canonical* vectors. Using this special structure leads to MPs that are more explicit than their analogues for general discrete-time systems. In fact, one of these MPs can be used to iteratively compute *all* the time-optimal controls. Surprisingly, perhaps, it also provides a *state-feedback* expression for the time-optimal controls.

BCNs are in fact discrete-time positive linear switched systems, and our approach is motivated by the simple proof of a special case of the PMP used in the variational analysis of continuous-time switched systems [57] (see also [58], [71], [59]). This variational approach was also extended to analyze discrete-time switched systems (see [9], [62], [63] and the references therein).

Some related work includes the following. Ref. [47] considers a Mayer-type optimal control problem for single-input BCNs, and describes a necessary condition for optimality in the form of an MP. This was extended to multi-input BCNs in [49]. BNs and BCNs have a natural graph-theoretic representation (see, e.g. [80]). Zhao [79] used this representation and the Floyd-Warshall algorithm to address an infinite-horizon Mayer-type optimal control problem. Akutsu et al. [3] showed that control problems for BCNs are in general NP-hard. Determining whether a BN with a (binary) output is observable is also NP-hard [50].

It is important to note that the ASSR of a BCN with n state variables and m control variables includes a binary matrix with dimensions $2^n \times 2^{n+m}$. Thus, an inherent drawback of the ASSR is that any algorithm based on it has exponential time complexity. However, the computational complexity results referred to above suggest that, unless $P = NP$, most control problems for general BCNs cannot be solved in polynomial time.

The theoretical results are demonstrated using a biological system known as the λ *switch* [66]. The λ phage is a virus that grows on a bacterium. Upon infection of the bacterium, the phage injects its chromosome into the bacterium cell. The virus can then follow one of two different pathways: *lysogeny* or *lysis*. In the lysogenic state, the phage integrates its genome into the bacterium's DNA and passively replicates as a part of the host bacterium. In the lytic state, the phage's DNA is extensively replicated, new phages are formed within the bacterium, and after about 45 minutes the bacterium lyses and releases about 100 new phages.

The two possible pathways are the result of expressing different sets of genes. The molecular mechanism responsible for the lysogeny/lysis decision is known as the λ switch. Various computational models for the λ switch have been suggested based on different tools including a stochastic kinetic model [8], differential equations [46], the logical method of R. Thomas [76], and also BNs [38]. As noted in [78], the lambda switch is of special interest as it allows to investigate how a biological system controls gene expression, DNA replication, and other crucial processes *in response to environmental signals*. This suggests that a computational model of the switch should treat the environmental signals as inputs.

We derive a simple BCN model for the λ switch. The Boolean input represents whether the total environmental conditions are "favorable" or not. Analysis of the time-optimal controls in this BCN suggests that the transition from the initial state right after infection to either the lysogenic state or the lytic state takes place in a *time-optimal* manner.

The remainder of this paper is organized as follows. Section II reviews BCNs and their ASSR. Section III defines the minimum-time optimal control problem and details our main results. In section IV, some of theoretical results are demonstrated using a BCN model of the λ switch.

II. Boolean control networks

Let $S = \{\text{True}, \text{False}\}$. A BCN is a discrete-time logical dynamical control system in the form

$$\begin{aligned} x_1(k+1) &= f_1(x_1(k), \dots, x_n(k), u_1(k), \dots, u_m(k)), \\ &\vdots \\ x_n(k+1) &= f_n(x_1(k), \dots, x_n(k), u_1(k), \dots, u_m(k)), \end{aligned} \tag{1}$$

where $x_i, u_i \in S$, and each f_i is a Boolean function, i.e. $f_i : S^{n+m} \to S$.

A BCN with m inputs is a *Boolean switched system* switching between 2^m possible subsystems, where each subsystem is a BN, and with the value of the control determining which subsystem is active at every time step. To demonstrate this, consider the two-state, two-input BCN

$$\begin{aligned} x_1(k+1) &= x_1(k) \vee [x_2(k) \wedge u_1(k)], \\ x_2(k+1) &= x_2(k) \wedge u_2(k). \end{aligned} \tag{2}$$

The control $u = \begin{bmatrix} u_1 & u_2 \end{bmatrix}^T$ may attain one of four values: $\{TT, TF, FT, FF\}$, where T $[F]$ is shorthand for True [False]. With each of these possible values we can associate a corresponding dynamics, i.e. a subsystem. For example, when $u_1(k) = u_2(k) = T$ the corresponding subsystem is

$$\begin{aligned} x_1(k+1) &= x_1(k) \vee x_2(k), \\ x_2(k+1) &= x_2(k). \end{aligned}$$

In the ASSR, each subsystem becomes a positive linear system, so the BCN becomes a discrete-time positive linear switched system (PLSS). For more on PLSSs, see e.g. [35], [31], [61], [32], [30] and the references therein.

Control-theoretic problems for BCNs are best addressed in the algebraic state-space representation (ASSR) derived by Daizhan Cheng and his colleagues [22]. This representation uses the semi-tensor product of matrices.

A. Semi-tensor product

Given two positive integers a, b, let $\text{lcm}(a, b)$ denote the *least common multiple* of a and b. For example, $\text{lcm}(6, 8) = 24$. Let I_j denote the $j \times j$ identity matrix.

Definition 1. *The* semi-tensor product *of $A \in \mathbb{R}^{m \times n}$ and $B \in \mathbb{R}^{p \times q}$ is*

$$A \ltimes B = (A \otimes I_{\alpha/n})(B \otimes I_{\alpha/p}),$$

where $\alpha = \text{lcm}(n, p)$, and $\otimes$ denotes the Kronecker product.

Note that $(A \otimes I_{\alpha/n}) \in \mathbb{R}^{(m\alpha/n)\times\alpha}$ and $(B \otimes I_{\alpha/p}) \in \mathbb{R}^{\alpha\times(q\alpha/p)}$, so $(A \ltimes B) \in \mathbb{R}^{(m\alpha/n)\times(q\alpha/p)}$.

Remark 1. *If $n = p$, then $A \ltimes B = (A \otimes I_1)(B \otimes I_1) = AB$. Thus, the semi-tensor product is a generalization of the standard matrix product that provides a way to multiply two matrices with arbitrary dimensions. Intuitively, this is based on first modifying A, B to two matrices $(A \otimes I_{\alpha/n})$, $(B \otimes I_{\alpha/p})$ of compatible dimensions, and then calculating their standard matrix product.*

Example 1. *If $a, b \in \mathbb{R}^2$, then*

$$\begin{aligned} a \ltimes b &= (a \otimes I_2)(b \otimes I_1) \\ &= \begin{bmatrix} a_1 & 0 \\ 0 & a_1 \\ a_2 & 0 \\ 0 & a_2 \end{bmatrix} b \\ &= \begin{bmatrix} a_1b_1 & a_1b_2 & a_2b_1 & a_2b_2 \end{bmatrix}^T . \end{aligned}$$

■

Various properties of the semi-tensor product are analyzed in [17]. For our purposes, it is sufficient to note that this product is associative

$$A \ltimes (B \ltimes C) = (A \ltimes B) \ltimes C,$$

and distributive

$$(A + B) \ltimes C = (A \ltimes C) + (B \ltimes C).$$

B. Algebraic representation of Boolean functions

Let e_n^i denote the ith column of the identity matrix I_n. Represent the Boolean values True and False by $e_2^1 = \begin{bmatrix} 1 \\ 0 \end{bmatrix}$ and $e_2^2 = \begin{bmatrix} 0 \\ 1 \end{bmatrix}$, respectively. Then any Boolean function of n variables $f : S^n \to S$ can be equivalently represented as a mapping $\bar{f} : \{e_2^1, e_2^2\}^n \to \{e_2^1, e_2^2\}$. With some abuse of notation, we identify $\bar{f}$ with f. In other words, from here on a Boolean variable x_i is always a vector in $\{e_2^1, e_2^2\}$.

Theorem 1. *[20] Let $f : \{e_2^1, e_2^2\}^n \to \{e_2^1, e_2^2\}$ be a Boolean function. There exists a unique binary matrix $M_f \in \{0,1\}^{2\times 2^n}$ such that*

$$f(x_1, \dots, x_n) = M_f \ltimes x_1 \ltimes \cdots \ltimes x_n.$$

M_f is called the structure matrix *of f.*

Remark 2. *To provide some intuition on this representation, consider the case $n = 2$, i.e. $f = f(x_1, x_2)$. Recall that $x_i \in \{e_2^1, e_2^2\}$, so $x_1 = \begin{bmatrix} v & \bar{v} \end{bmatrix}^T$ and $x_2 = \begin{bmatrix} w & \bar{w} \end{bmatrix}^T$, with $v, w \in \{0,1\}$. Hence,*

$$x_1 \ltimes x_2 = \begin{bmatrix} vw & v\bar{w} & \bar{v}w & \bar{v}\bar{w} \end{bmatrix}^T, \tag{3}$$

i.e. $x_1 \ltimes x_2$ contains all the possible minterms *of v and w. Recall that any Boolean function may be represented as a sum of some minterms of its variables (see, e.g. [45]). This is known as the sum of products (SOP) representation. The multiplication $M_f \ltimes x_1 \ltimes x_2$ provides such a representation. Note that* (3) *implies that $(x_1 \ltimes x_2) \in \{e_4^1, \dots, e_4^4\}$. Indeed, one and only one minterm is 1 and all the others must be 0.*

Example 2. *Consider the function $g(x_1, x_2) = x_1 \wedge x_2$. It is straightforward to verify that*

$g(x_1, x_2) = M_g \ltimes x_1 \ltimes x_2$, *with* $M_g = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 1 & 1 \end{bmatrix}$. *For example,*

$$\begin{aligned} M_g \ltimes e_2^1 \ltimes e_2^2 &= M_g \ltimes \begin{bmatrix} 0 & 1 & 0 & 0 \end{bmatrix}^T \\ &= M_g \begin{bmatrix} 0 & 1 & 0 & 0 \end{bmatrix}^T \\ &= \begin{bmatrix} 0 & 1 \end{bmatrix}^T, \\ &= e_2^2, \end{aligned}$$

corresponding to (*True* $\wedge$ *False*) $=$ *False.* ■

C. Algebraic representation of BCNs

Since the dynamics of BCNs is described by a set of Boolean functions, the semi-tensor product can be used to provide an ASSR of BCNs.

Theorem 2. *[21] Consider a BCN with state variables* $x_1, \dots, x_n$ *and inputs* $u_1, \dots, u_m$, *with* $x_i, u_i \in \{e_2^1, e_2^2\}$. *Denote* $x(k) = x_1(k) \ltimes \cdots \ltimes x_n(k)$ *and* $u(k) = u_1(k) \ltimes \cdots \ltimes u_m(k)$. *There exists a unique matrix* $L \in \{0,1\}^{2^n \times 2^{n+m}}$ *such that*

$$x(k+1) = L \ltimes u(k) \ltimes x(k). \tag{4}$$

The matrix L *is called the* transition matrix *of the BCN.*

Algorithms for converting a BCN in the form (1) to its ASSR (4), and vice versa, may be found in [20], [19].

Remark 3. *The intuition behind this representation is very similar to the algebraic representation of a single Boolean function using the semi-tensor product. The vector* $u(k) \ltimes x(k)$ *includes all the possible minterms of the input and state variables, and* (4) *amounts to a description of (every minterm of) the next state in terms of the current state and inputs.*

Note that since $u(k) = u_1(k) \ltimes \cdots \ltimes u_m(k)$, with $u_i(k) \in \{e_2^1, e_2^2\}$, $u(k) \in \{e_{2^m}^1, \dots, e_{2^m}^{2^m}\}$. For example, if $m = 3$, $u_1(k) = e_2^1$, $u_2(k) = e_2^2$, and $u_3(k) = e_2^2$, then $u(k) = e_8^4$.

III. Main results

A fundamental problem for all dynamical control systems is to determine a control that is optimal in some sense. For a final time $N > 0$, let $\mathbb{U}^N$ denote the set of admissible controls of (4), i.e. the set of all sequences $\{u(0), \dots, u(N-1)\}$, with $u(i) \in \{e^1_{2^m}, \dots, e^{2^m}_{2^m}\}$. For an admissible control u, let $x(k; u, x_0)$ denote the solution of (4) with $x(0) = x_0$ at time k.

Problem 1. *Consider a BCN in the ASSR* (4)*. Fix an arbitrary initial condition* $x(0) = x_0 \in \{e^1_{2^n}, \dots, e^{2^n}_{2^n}\}$ *and a desired state* $z \in \{e^1_{2^n}, \dots, e^{2^n}_{2^n}\}$*. Suppose that there exists a time* $N > 0$ *and a control* $u \in \mathbb{U}^N$ *that steers the BCN from* $x(0) = x_0$ *to* $x(N; u, x_0) = z$*. Let* N^* *be the* minimal time *for which there exists a control* $u^* \in \mathbb{U}^{N^*}$ *steering the BCN from* $x(0) = x_0$ *to* $x(N^*; u^*, x_0) = z$*. Find* N^* *and a time-optimal control.*

A. Time-optimality implies Mayer-type optimality

Our first result is based on a simple observation, namely, that a time-optimal control is also a solution of a suitable Mayer-type optimal control problem. Indeed, suppose that $u^* \in \mathbb{U}^{N^*}$ is a time-optimal control. Define a cost functional $J : \mathbb{N} \times \mathbb{U}^{N^*} \to \{0, 1\}$ by $J(N; u) = z^T x(N; u)$. Note that since both z and $x(N; u)$ are columns of I_{2^n}, J can attain only the values zero or one. Since

$$\begin{aligned} J(N^*; u^*) &= z^T x(N^*; u^*) \\ &= z^T z \\ &= 1, \end{aligned}$$

u^* maximizes $J(N^*; u)$. Hence, u^* must satisfy the MP for a Mayer-type optimal control problem stated in [49, Thms. 3 and 4]. This yields the following result.

Corollary 1. *Suppose that* $u^* \in \mathbb{U}^{N^*}$ *is a minimum-time control for Problem 1, and let* x^* *denote the corresponding trajectory of* (4)*. Let the* adjoint $\lambda : \{0, 1, \dots, N^*\} \to \mathbb{R}^{2^n}$ *be the solution of*

$$\begin{aligned} \lambda(k) &= (L \ltimes u^*(k))^T \lambda(k+1), \\ \lambda(N^*) &= z. \end{aligned} \tag{5}$$

Define 2^m switching functions $\alpha_i : \{0, 1, \dots, N^*\} \to \mathbb{R}$, $i = 1, \dots, 2^m$, *by*

$$\alpha_i(k) = \lambda^T(k+1) \ltimes L \ltimes e^i_{2^m} \ltimes x^*(k).$$

Fix an arbitrary $s \in \{0, 1, \dots, N^* - 1\}$. *If there exists an index* i *such that* $\alpha_i(s) > \alpha_j(s)$ *for all* $j \neq i$, *then*

$$u^*(s) = e^i_{2^m}. \tag{6}$$

Furthermore, if there exists a subset of indexes $I = \{i_1, \dots, i_l\}$ *such that* $\alpha_{i_1}(s) = \dots = \alpha_{i_l}(s)$ *and* $\alpha_{i_1}(s) > \alpha_j(s)$ *for all* $j \notin I$, *then*

$$u^*(s) \in \{e^{i_1}_{2^m}, \dots, e^{i_l}_{2^m}\},$$

and any control in the form

$$w(j) = \begin{cases} v, & \text{if } j = s, \\ u^*(j), & \text{otherwise}, \end{cases} \tag{7}$$

with $v \in \{e^{i_1}_{2^m}, \dots, e^{i_l}_{2^m}\}$, *is a time-optimal control.*

The next example demonstrates an application of this MP.

Example 3. *Consider the three-state, one-input BCN*

$$\begin{aligned} x_1(k+1) &= x_2(k), \\ x_2(k+1) &= x_3(k), \\ x_3(k+1) &= u(k). \end{aligned} \tag{8}$$

Suppose that $x_1(0) = x_2(0) = x_3(0) =$ *False, and that we are interested in finding a control that steers this BCN to* $x_1(N^*) = x_2(N^*) = x_3(N^*) =$ *True in minimal time* N^* *(if it exists). By inspection, we see that* $N^* = 3$, *and that the unique optimal control is* $u^*(k) =$ *True for* $k \in \{0, 1, 2\}$. *We will show that this conclusion can also be deduced using the MP. In the ASSR,* $n = 3$, $m = 1$,

$$L = \begin{bmatrix} e^1_8 & e^3_8 & e^5_8 & e^7_8 & e^1_8 & e^3_8 & e^5_8 & e^7_8 & e^2_8 & e^4_8 & e^6_8 & e^8_8 & e^2_8 & e^4_8 & e^6_8 & e^8_8 \end{bmatrix}, \tag{9}$$

$x(0) = e_8^8$, *and* $z = e_8^1$. *Since* $\lambda(N^*) = e_8^1$ *(see* (5)*), we begin by calculating*

$$\begin{aligned}\alpha_1(N^*-1) &= \lambda^T(N^*) \ltimes L \ltimes e_2^1 \ltimes x^*(N^*-1) \\ &= \begin{bmatrix}1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\end{bmatrix} \ltimes e_2^1 \ltimes x^*(N^*-1) \\ &= \begin{bmatrix}1 & 0 & 0 & 0 & 1 & 0 & 0 & 0\end{bmatrix} \ltimes x^*(N^*-1) \\ &= \begin{bmatrix}1 & 0 & 0 & 0 & 1 & 0 & 0 & 0\end{bmatrix} x^*(N^*-1).\end{aligned}$$

Similarly,

$$\begin{aligned}\alpha_2(N^*-1) &= \lambda^T(N^*) \ltimes L \ltimes e_2^2 \ltimes x^*(N^*-1) \\ &= \begin{bmatrix}1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\end{bmatrix} \ltimes e_2^2 \ltimes x^*(N^*-1) \\ &= 0.\end{aligned}$$

Thus $\alpha_1(N^*-1) \geq \alpha_2(N^*-1)$. *If the inequality here is strict, then the MP implies that* $u^*(N^*-1) = e_2^1$. *If* $\alpha_1(N^*-1) = \alpha_2(N^*-1)$, *then* (7) *implies that there exists an optimal control satisfying* $u^*(N^*-1) = e_2^1$. *Now* (5) *yields*

$$\begin{aligned}\lambda(N^*-1) &= (L \ltimes e_2^1)^T \ltimes e_8^1 \\ &= \begin{bmatrix}1 & 0 & 0 & 0 & 1 & 0 & 0 & 0\end{bmatrix}^T,\end{aligned}$$

so

$$\begin{aligned}\alpha_1(N^*-2) &= \lambda^T(N^*-1) \ltimes L \ltimes e_2^1 \ltimes x^*(N^*-2) \\ &= \begin{bmatrix}1 & 0 & 1 & 0 & 1 & 0 & 1 & 0\end{bmatrix} x^*(N^*-2),\end{aligned}$$

and

$$\begin{aligned}\alpha_2(N^*-2) &= \lambda^T(N^*-1) \ltimes L \ltimes e_2^2 \ltimes x^*(N^*-2) \\ &= 0.\end{aligned}$$

Hence, $\alpha_1(N^*-2) \geq \alpha_2(N^*-2)$, *and thus the MP implies that there exists an optimal control satisfying* $u^*(N^*-2) = e_2^1$. *Proceeding in this way, we find that* $u^*(k) = e_2^1$, $k \in \{0, 1, 2\}$, *is a* *candidate for a time-optimal control.* ■

B. Maximum principle for time-optimal controls

It is straightforward to find a control u that steers the BCN in Example 3 to $x(4) = z = e_8^1$. Hence, this u maximizes the cost functional $J(4;u) = z^T x(4;u)$ and thus satisfies the MP in Corollary 1. However, this control is certainly not time-optimal. The next result provides more specific information on controls that are indeed time-optimal.

Theorem 3. *Suppose that $u^* \in \mathbb{U}^{N^*}$ is a minimum-time control for Problem 1, and let x^* denote the corresponding trajectory of* (4)*. Define the* adjoint $\lambda : \{0, 1, \dots, N^*\} \to \mathbb{R}^{2^n}$ *as in* (5)*. Then for any $k, p \in \{0, 1, \dots, N^*\}$, with $k < p$,*

$$\lambda^T(p)x^*(p) = 1, \tag{10}$$

and

$$\lambda^T(p)x^*(k) = 0. \tag{11}$$

Proof: First note that iterating (4) shows that for any $k \geq j \geq 0$,

$$x(k; u, x_0) = C(k, j; u) \ltimes x(j; u, x_0), \tag{12}$$

where

$$C(k, j; u) = \begin{cases} L \ltimes u(k-1) \ltimes L \ltimes u(k-2) \ltimes \cdots \ltimes L \ltimes u(j), & k > j, \\ I_{2^n}, & k = j. \end{cases} \tag{13}$$

We refer to the $2^n \times 2^n$ matrix $C(k, j; u)$ as the transition matrix from time j to time k corresponding to the control u. Note that (13) implies that for any $k \geq l \geq j$,

$$C(k, j; u) = C(k, l; u) \ltimes C(l, j; u).$$

Fix an arbitrary $p \in \{0, 1, \dots, N^* - 1\}$. Then

$$\begin{aligned} 1 &= z^T x^*(N^*) \\ &= z^T C(N^*, p+1; u^*) x^*(p+1) \\ &= z^T C(N^*, p+1; u^*) \ltimes L \ltimes u^*(p) \ltimes x^*(p). \end{aligned}$$

It is straightforward to verify that (5) implies that $\lambda^T(p+1) = z^T C(N^*, p+1; u^*)$, so

$$\begin{aligned} 1 &= \lambda^T(p+1) \ltimes L \ltimes u^*(p) \ltimes x^*(p) \\ &= \lambda^T(p+1) L \ltimes u^*(p) \ltimes x^*(p) \\ &= \left((L \ltimes u^*(p))^T \lambda(p+1) \right)^T \ltimes x^*(p) \\ &= \lambda^T(p) x^*(p), \end{aligned}$$

where the second equation follows from Remark 1. This proves (10). To prove (11) we use the time optimality of u^*. Seeking a contradiction, assume that there exist $k < p$ such that $\lambda^T(p)x^*(k) \neq 0$. It follows from (5) that each entry of $\lambda(k)$ is nonnegative, so $\lambda^T(p)x^*(k) > 0$, that is,

$$z^T C(N^*, p; u^*) C(k, 0; u^*) x_0 > 0.$$

Since the transition matrix must map any column of I_{2^n} to a column of I_{2^n}, this implies that $C(N^*, p; u^*) C(k, 0; u^*) x_0 = z$. In other words, the control sequence

$$\{u^*(N^*-1), u^*(N^*-2), \dots, u^*(p), u^*(k-1), u^*(k-2), \dots, u^*(0)\}$$

steers the BCN from $x(0) = x_0$ to $x(N^* + k - p) = z$. Since $k < p$, $N^* + k - p < N^*$, and this contradicts the fact that N^* is the minimal time required to steer the BCN from x_0 to z. This completes the proof of Theorem 3. ■

Example 4. *Consider again the time-optimal control problem in Example 3. We already know that $N^* = 3$ and that $u^*(k) = e_2^1$, $k = 0, 1, 2$, is a time-optimal control. A calculation yields*

$$x^*(0) = e_8^8, \quad x^*(1) = e_8^7, \quad x^*(2) = e_8^5, \quad x^*(3) = e_8^1,$$

and

$$\lambda(3) = e_8^1, \quad \lambda(2) = e_8^1 + e_8^5, \quad \lambda(1) = e_8^1 + e_8^3 + e_8^5 + e_8^7, \quad \lambda(0) = \sum_{j=1}^{8} e_8^j.$$

so (10) *and* (11) *indeed hold.*

Now consider the control u given by $u(0) = e_2^2$, and $u(k) = e_2^1$ for $k = 1, 2, 3$. This control *yields*

$$x(0) = e_8^8, \;\; x(1) = e_8^8, \;\; x(2) = e_8^7, \;\; x(3) = e_8^5, \;\; x(4) = e_8^1,$$

so it steers the state to the desired final condition at time $N = 4$*. Clearly, this control is* not *time optimal. Let us show that this may be deduced from Theorem 3. Solving* (5) *for* $N^* = 4$ *and the control* u *yields*

$$\lambda(4) = e_8^1, \;\; \lambda(3) = e_8^1 + e_8^5, \;\; \lambda(2) = e_8^1 + e_8^3 + e_8^5 + e_8^7, \;\; \lambda(1) = \lambda(0) = \sum_{j=1}^{8} e_8^j.$$

so $\lambda^T(1)x(0) = 1$ *and this violates* (11). ■

C. Determining the optimal time using the generalized adjoint

The adjoint and the switching functions depend on (the generally unknown) u^* and x^*. This is of course a typical feature of MPs. In what follows, we define a modified adjoint vector that does not depend on the optimal control u^*. This allows us to derive a stronger MP.

We introduce some notation from the binary algebra of binary matrices that will be used later on; for more details, see [22, Chapter 11]. Let $P \in \{0,1\}^{m \times n}$ and $Q \in \{0,1\}^{p \times q}$ be two matrices. If $n = p$, the *Boolean product* of P and Q, denoted $P \odot Q$, is a $(m \times q)$ binary matrix defined by

$$(P \odot Q)_{ij} = \bigvee_{k=1}^{n} (p_{ik} \wedge q_{kj}). \tag{14}$$

In other words, the standard matrix multiplication but with logical and [logical or] replacing the standard product [sum] operation. The kth *Boolean power* of A, denoted $A^{[k]}$, is the Boolean product of k factors of A (e.g., $A^{[3]} = A \odot A \odot A$). The *Boolean semi-tensor product* of P and Q is

$$P \ltimes_B Q = (P \otimes I_{\alpha/n}) \odot (Q \otimes I_{\alpha/p}), \tag{15}$$

where $\alpha = \operatorname{lcm}(n, p)$.

Let 1_j [0_j] denote the column vector of length j with all entries equal to 1 [0]. For a time $k \geq 0$ and a state $z \in \{e_{2^n}^1, \dots, e_{2^n}^{2^n}\}$, let $B(k; z)$ denote the set of all states $x_0 \in \{e_{2^n}^1, \dots, e_{2^n}^{2^n}\}$ such that there exists a control u steering the BCN from $x(0) = x_0$ to $x(k) = z$. Define

$$l(k; z) = \sum_{x \in B(k;z)} x,$$

i.e., the sum of all states in $B(k; z)$ (If $B(k; z) = \emptyset$ then we define $l(k; z) = 0_{2^n}$.) Note that since any $x \in B(k; z)$ is a canonical vector, $l(k; z) \in \{0, 1\}^{2^n}$.

The next result provides a simple algebraic expression for $l(k; a)$.

Proposition 4. *For any* $z \in \{e^1_{2^n}, \dots, e^{2^n}_{2^n}\}$ *and any* $k \geq 1$*,*

$$l(k; z) = (Q^{[k]})^T \odot z, \tag{16}$$

where

$$Q = L \ltimes_B 1_{2^m}. \tag{17}$$

Note that (15) implies that $Q = (L \otimes I_1) \odot (1_{2^m} \otimes I_{2^n})$, so $Q \in \mathbb{R}^{2^n \times 2^n}$.

Proof: By induction on k. Consider the case $k = 1$. By definition, $B(1; z)$ is the set of all states x_0 such that there exist a control steering (4) from $x(0) = x_0$ to $x(1) = z$. Assume for the moment that $B(1; z) \neq \emptyset$. Fix an arbitrary $x_0 \in B(1; z)$. Then there exist $s \geq 1$ control values $w^1, \dots, w^s$ that steer x_0 to z, that is,

$$z = L \ltimes w^i \ltimes x_0, \quad i \in \{1, \dots, s\}, \tag{18}$$

Since each control value is a column of I_{2^m}, there exist $t = 2^m - s$ different control values v^j such that

$$z \neq L \ltimes v^j \ltimes x_0, \quad j \in \{1, \dots, t\}. \tag{19}$$

Note that the term on the right-hand side of this inequality must be a column of I_{2^n}. Therefore, a Boolean semi-tensor multiplication of (18) and (19) from the left by z^T yields

$$\begin{aligned} 1 &= z^T \ltimes_B L \ltimes w^i \ltimes x_0, && i \in \{1, \dots, s\}, \\ 0 &= z^T \ltimes_B L \ltimes v^j \ltimes x_0, && j \in \{1, \dots, t\}. \end{aligned} \tag{20}$$

Since each control value is a different column of I_{2^m}, summing up this set of $s + t = 2^m$

equations yields

$$s = z^T \ltimes_B L \ltimes 1_{2^m} \ltimes x_0.$$

Since $s \geq 1$ and z, x_0 are canonical vectors, this implies that

$$\begin{aligned} 1 &= z^T \ltimes_B L \ltimes_B 1_{2^m} \ltimes x_0 \\ &= z^T \ltimes_B Q \ltimes x_0. \end{aligned} \tag{21}$$

It is straightforward to verify that $z^T \ltimes_B Q$ is a binary vector. Since Eq. (21) holds for any $x_0 \in B(1; z)$, this implies that $(z^T \ltimes_B Q)^T = \bigvee_{x_0 \in B(1;z)} x_0$. Since $z \in \mathbb{R}^{2^n}$ and $Q \in \mathbb{R}^{2^n \times 2^n}$, $Q^T \ltimes_B z = Q^T \odot z$, so

$$l(1; z) = Q^T \odot z. \tag{22}$$

Recall that we assumed that $B(1; z) \neq \emptyset$. If $B(1; z) = \emptyset$, then the second equation in (20) holds for $t = 2^m$ and *any* $x_0 \in \{e^1_{2^n}, \dots e^{2^n}_{2^n}\}$. Arguing as above yields $0 = z^T \ltimes_B Q \ltimes x_0$, so $z^T \ltimes_B Q$ is the zero vector, and (22) holds in this case as well. This proves (16) for $k = 1$.

Assume that (16) holds for some $k \geq 1$. For the induction step, consider

$$\begin{aligned} (Q^T)^{[k+1]} \odot z &= (Q^T)^{[k]} \odot (Q^T \odot z), \\ &= (Q^T)^{[k]} \odot \bigvee_{x_0 \in B(1;z)} x_0, \\ &= \bigvee_{x_0 \in B(1;z)} (Q^T)^{[k]} \odot x_0, \\ &= \bigvee_{x_0 \in B(1;z)} \bigvee_{y_0 \in B(k;x_0)} y_0, \end{aligned} \tag{23}$$

where the last step follows from the induction hypothesis. Clearly, the term in (23) is just $l(k+1; z)$. ∎

Example 5. *Consider the three-state, one-input BCN*

$$\begin{aligned} x_1(k+1) &= x_2(k), \\ x_2(k+1) &= x_3(k), \\ x_3(k+1) &= u(k) \vee [x_2(k) \wedge x_3(k)]. \end{aligned} \tag{24}$$

Suppose that the desired state is $z = (\mathit{True}, \mathit{True}, \mathit{True})^T$. The ASSR is given by $n = 3$, $m = 1$, $z = e_8^1$, and

$$L = \begin{bmatrix} e_8^1 & e_8^3 & e_8^5 & e_8^7 & e_8^1 & e_8^3 & e_8^5 & e_8^7 & e_8^1 & e_8^4 & e_8^6 & e_8^8 & e_8^1 & e_8^4 & e_8^6 & e_8^8 \end{bmatrix}. \tag{25}$$

Thus,

$$\begin{aligned} Q &= L \ltimes_B \begin{bmatrix} 1 & 1 \end{bmatrix}^T \\ &= \begin{bmatrix} e_8^1 & e_8^3 + e_8^4 & e_8^5 + e_8^6 & e_8^7 + e_8^8 & e_8^1 & e_8^3 + e_8^4 & e_8^5 + e_8^6 & e_8^7 + e_8^8 \end{bmatrix}, \end{aligned} \tag{26}$$

and (16) *yields*

$$\begin{aligned} l(1; z) &= Q^T \odot e_8^1 = e_8^1 + e_8^5, \\ l(2; z) &= (Q^{[2]})^T \odot e_8^1 = e_8^1 + e_8^3 + e_8^5 + e_8^7, \\ l(3; z) &= (Q^{[3]})^T \odot e_8^1 = \sum_{i=1}^{8} e_8^i. \end{aligned}$$ ■

Fig. 1 depicts the trajectories of this BCN, where each node is a state in the ASSR, and edges denote time transitions between the states. For $z = e_8^1$, it is easy to see from this figure that indeed $l(1; z) = e_8^1 + e_8^5$, $l(2; z) = e_8^1 + e_8^3 + e_8^5 + e_8^7$ and $l(k; z) = \sum_{i=1}^8 e_8^i$ for all $k \geq 3$.

It is interesting to note that Zhao et al. [80] defined a matrix $M = L \ltimes 1_{2^m}$. They used this matrix for controllability analysis. That is similar, yet different, from the matrix Q defined in (17).

We can now restate Theorem 3 in a different, and more explicit, form.

Theorem 5. *Suppose that $u^* \in \mathbb{U}^{N^*}$ is a minimum-time control for Problem 1, and let x^* denote*

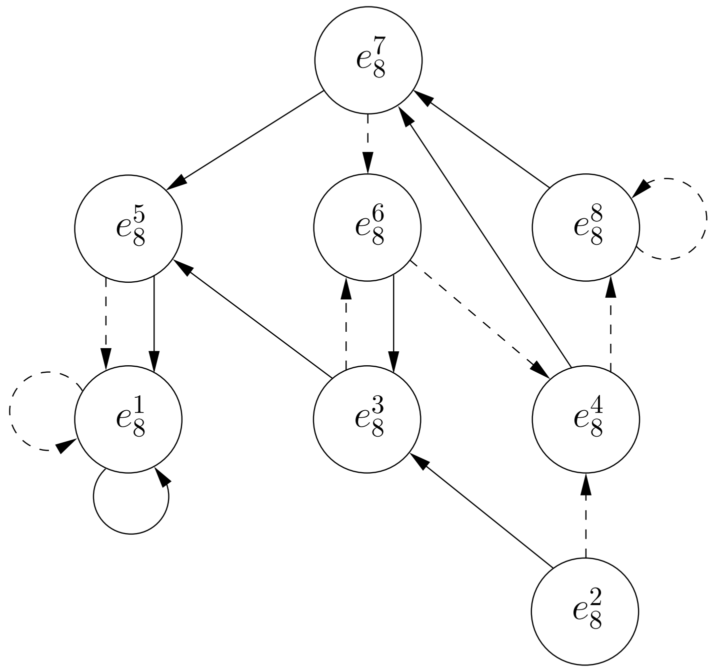

Fig. 1. Trajectories of the BCN in Example 5. A solid [dashed] line denotes the transition corresponding to $u(k) = e_2^1$ [$u(k) = e_2^2$].

the corresponding trajectory of (4). *Let* $\eta : \{0, 1, \dots, N^*\} \to \mathbb{R}^{2^n}$ *be the solution of*

$$\begin{aligned} \eta(k) &= Q^T \odot \eta(k+1), \\ \eta(N^*) &= z. \end{aligned} \tag{27}$$

Then for any $k, p \in \{0, 1, \dots, N^*\}$, *with* $k < p$,

$$\eta^T(p)x^*(p) = 1, \tag{28}$$

and

$$\eta^T(p)x^*(k) = 0. \tag{29}$$

Note that η, unlike the adjoint λ in Theorem 3, does not depend on u^*, and so we can easily calculate $\eta(k)$ for $k = N^*, N^* - 1, \dots, 0$.

Proof: It follows from (27) that $\eta(N^* - k) = (Q^{[k]})^T \odot z$, so (16) yields $\eta(N^* - k) = l(k; z)$.

Thus,

$$\begin{aligned}\eta^T(p)x^*(p) &= [l(N^* - p; z)]^T x^*(p) \\ &= [\sum_{x_0 \in B(N^*-p;z)} x_0]^T x^*(p)\end{aligned}$$

for all $p \in \{0, 1, \ldots, N^*\}$. Since $x^*(p) \in B(N^* - p; z)$ this proves (28). To prove (29), fix arbitrary $k, p \in \{0, 1, \ldots, N^*\}$ with $k < p$. Seeking a contradiction, assume that $\eta^T(p)x^*(k) > 0$, that is,

$$[\sum_{x_0 \in B(N^*-p;z)} x_0]^T x^*(k) > 0.$$

Since each $x_0 \in B(N^* - p; z)$ and $x^*(k)$ are canonical vectors, this implies that $x^*(k) \in B(N^* - p; z)$. In other words, there exists a control u that steers the BCN from $x^*(k)$ to z in $N^* - p$ time steps. But u^*, which is time optimal, does the same in $N^* - k$ time steps. Since $k < p$ this is a contradiction. This proves (29). ■

For $k = 0$ and $p > 0$, Eq. (29) becomes

$$\eta^T(p)x^*(0) = 0. \tag{30}$$

On the other-hand, Eq. (28) yields

$$\eta^T(0)x^*(0) = 1. \tag{31}$$

This implies that given the initial condition $x(0)$, we can explicitly determine the minimal time N^* by calculating $\eta^T(N^*)x^*(0)$, $\eta^T(N^* - 1)x^*(0)$, and so on until the first value k such that $\eta^T(N^* - k)x^*(0) = 1$. Then $N^* - k = 0$ so $N^* = k$.

Example 6. *Consider again the three-state, one-input BCN from Example 5 with $x_1(0) = x_2(0) = x_2(0) =$ False. In the ASSR, $x(0) = e_8^8$, $z = e_8^1$, and L is given in* (25)*. We now use Theorem 5 to find N^*. A calculation yields $\eta(N^*) = z = e_8^1$, so $\eta(N^*))^T x_0 = (e_8^1)^T e_8^8 = 0$; $\eta(N^*-1) = e_8^1 + e_8^5$, so $(\eta(N^*-1))^T x_0 = 0$; $\eta(N^*-2) = e_8^1 + e_8^3 + e_8^5 + e_8^7$, so $(\eta(N^*-2))^T x_0 = 0$; and $\eta(N^* - 3) = \sum_{i=1}^{8} e_8^i$, so $(\eta(N^* - 3))^T x_0 = 1$. We conclude that $N^* = 3$. Fig. 2 depicts the possible trajectories of the BCN up to time $k = 3$. Each node corresponds to a possible value of $x(i)$ at time $i \in \{0, 1, 2, 3\}$. It may be seen that indeed $N^* = 3$.* ■

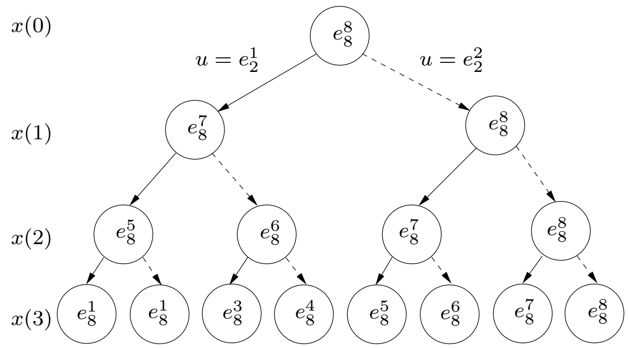

Fig. 2. Trajectories of the BCN in Example 6. Each node depicts the value of $x(i)$ for either $u(i-1) = e_2^1$ (solid line) or $u(i-1) = e_2^2$ (dashed line).

D. State-feedback representation of time-optimal controls

The next result shows that using the *generalized adjoint* η it is possible to provide a kind of *state-feedback* expression for *all* the time-optimal controls. We require one more tool, introduced by Cheng and Qi in [20].

Proposition 6. *[20] For two integers $i, j > 0$, define the* swap matrix $W_{[i,j]} \in \mathbb{R}^{(ij)\times(ij)}$ *by*

$$W_{[i,j]} = \begin{bmatrix} I_i \otimes (e_j^1)^T \\ I_i \otimes (e_j^2)^T \\ \vdots \\ I_i \otimes (e_j^j)^T \end{bmatrix}.$$

Then for any $x \in \mathbb{R}^i$ and $y \in \mathbb{R}^j$,

$$W_{[i,j]} \ltimes x \ltimes y = y \ltimes x. \tag{32}$$

In other words, the swap matrix allows swapping the roles of x and y in the semi-tensor product.

Given the BCN (4), let $H = LW_{[2^n,2^m]}$. Note that this implies that $H \in \mathbb{R}^{2^n \times 2^{m+n}}$.

Theorem 7. *Suppose that there exists a time-optimal control $u^* \in \mathbb{U}^{N^*}$ that solves Problem 1, and let x^* denote the corresponding trajectory of* (4)*. Fix an arbitrary time $p \in \{0, 1, \dots, N^*-1\}$ and let $r = x^*(p)$. Suppose that there exist exactly s different control values $\{v^1(p), \dots, v^s(p)\}$*

such that $v^i(p)$ *steers* (4) *from* $x(p) = r$ *to a point* $x(p+1)$ *satisfying*

$$x(p+1) \in B(N^* - (p+1); z). \tag{33}$$

Then

$$\sum_{i=1}^{s} v^i(p) = (H \ltimes x^*(p))^T \eta(p+1). \tag{34}$$

Note that (33) implies that $v^i(p)$, $i \in \{1, \dots, s\}$, is an *optimal* control value, as it steers the BCN to a point from which it is possible to reach z in $N^* - (p+1)$ time steps. As we will see below, Theorem 7 allows to iteratively determine *all* the time-optimal controls.

Proof: By the proof of Theorem 5,

$$1 = \eta^T(p+1)(L \ltimes v^i(p) \ltimes x^*(p)), \tag{35}$$

for all $i \in \{1, \dots, s\}$. Using the definition of H yields

$$\begin{aligned} 1 &= \eta^T(p+1)(H \ltimes x^*(p) \ltimes v^i(p)) \\ &= q^T(p) \ltimes v^i(p), \end{aligned} \tag{36}$$

where $q^T(p) = (\eta^T(p+1)H) \ltimes x^*(p)$. Since $(\eta^T(p+1)H) \in \mathbb{R}^{1\times 2^{n+m}}$ and $x^*(p) \in \mathbb{R}^{2^n}$, $q^T(p) = (\eta^T(p+1)H)(x^*(p) \otimes I_{2^m})$, so $q^T(p) \in \mathbb{R}^{1\times 2^m}$. Thus (36) becomes

$$1 = q^T(p)v^i(p). \tag{37}$$

Recall that $v^i(p)$ is a column of I_{2^m}, i.e. for any i there exists a $j = j(i) \in \{1, \dots, 2^m\}$ such that $v^i(p) = e^j_{2^m}$. It follows from (37) that $q_{j(i)}(p) = 1$ for all i. Furthermore, all the other entries of $q(p)$ must be zero, as otherwise (37) will imply (see (35)) that

$$\eta^T(p+1)(L \ltimes w \ltimes x^*(p)) > 0$$

for some control value w with $w \notin \{v^1(p), \dots, v^s(p)\}$. But this contradicts the definition of the set of control values $\{v^1(p), \dots, v^s(p)\}$. We conclude that (37) implies that

$$q(p) = \sum_{i=1}^{s} v^i(p),$$

so

$$\sum_{i=1}^{s} v^i(p) = ((\eta^T(p+1)H) \ltimes x^*(p))^T$$
$$= (H \ltimes x^*(p))^T \eta(p+1),$$

and this completes the proof. ■

Remark 4. *Note that the* state-feedback *solution* (34) *at time p depends on both $x^*(p)$ and $\eta(p+1)$. But the term $\eta(p+1)$ can be explicitly calculated using* (27)*.*

The next example demonstrates an application of Theorem 7.

Example 7. *Consider again the three-state, one-input BCN in Example 5 with $x_1(0) = x_2(0) = x_3(0) =$ False, and desired final state $z = e_8^1$. The matrix H is*

$$\begin{aligned} H &= LW_{[8,2]} \\ &= L \begin{bmatrix} I_8 \otimes (e_2^1)^T \\ I_8 \otimes (e_2^2)^T \end{bmatrix} \\ &= \begin{bmatrix} e_8^1 & e_8^1 & e_8^3 & e_8^4 & e_8^5 & e_8^6 & e_8^7 & e_8^8 & e_8^1 & e_8^1 & e_8^3 & e_8^4 & e_8^5 & e_8^6 & e_8^7 & e_8^8 \end{bmatrix}. \end{aligned}$$

We already found that $N^* = 3$, and that

$$\eta(3) = e_8^1, \quad \eta(2) = e_8^1 + e_8^5, \quad \eta(1) = e_8^1 + e_8^3 + e_8^5 + e_8^7$$

(see Example 6). Eq. (34) *with $p = 0$ yields*

$$\sum_{i=1}^{s_0} v^i(0) = (H \ltimes x^*(0))^T \eta(1) = e_2^1, \tag{38}$$

where s_0 is the number of different control values that steer the BCN from $x^*(0)$ to a state $x(1)$ in $B(N^*-1; z)$. This implies that $s_0 = 1$, and that the only optimal control value at time 0 is e_2^1. The corresponding state is $x^*(1) = L \ltimes e_2^1 \ltimes x^*(0) = e_8^7$. Now (34) *with $p = 1$ yields $\sum_{i=1}^{s_1} v^i(1) = (H \ltimes x^*(1))^T \eta(2) = e_2^1$, so the only optimal control value at time 1 is e_2^1, and $x^*(2) = L \ltimes e_2^1 \ltimes x^*(1) = e_8^5$. Finally,* (34) *with $p = 2$ yields $\sum_{i=1}^{s_2} v^i(2) = (H \ltimes x^*(2))^T \eta(3) = e_2^1 + e_2^2$. This implies that both e_2^1 and e_2^2 are optimal control values at time 2. We conclude that there exist two time-*

optimal controls $\{v^1(2), v^1(1), v^1(0)\} = \{e_2^1, e_2^1, e_2^1\}$ *and* $\{v^2(2), v^2(1), v^2(0)\} = \{e_2^2, e_2^1, e_2^1\}$. *This agrees with the trajectories depicted in Fig. 2.* ■

IV. A BIOLOGICAL EXAMPLE: THE λ SWITCH

The λ phage is a virus that grows on a bacterium. To ensure successful propagation, the virus had to develop efficient mechanisms of precise response to changes in the physiology of its host. This was achieved by a specific genetic switch that allows this virus to choose the most effective developmental pathway for the given environmental conditions.

Upon infection of the bacterium, the phage injects its chromosome into the bacterium cell. The virus can then follow one of two different pathways: *lysogeny* or *lysis*.[1] In the lysogenic state, the phage integrates its genome into the bacterium's DNA and passively replicates with the bacterium. In the lytic state, the phage's DNA is extensively replicated, new phages are formed within the bacterium, and after about 45 minutes the bacterium lyses and releases about 100 new phages. The phage may switch from the lysogenic state to the lytic state. This is a kind of *SOS* response initiated when the host cell experiences DNA damage. This happens, for example, if the bacteria is exposed to ultraviolet (UV) light (see Fig. 3).

The two possible pathways are the result of expressing different sets of genes. The molecular mechanism responsible for the lysogeny/lysis decision is known as the λ *switch* [66]. Bistable switches are common motifs in gene regulation networks [7], and the λ switch provides a convenient test case, as the virus is one of nature's simplest organisms.

A. Lambda phage decision circuit

The biomolecular mechanisms behind the lambda switch are generally known [66], [78], [1], [76], [77], [64]. Two genes, cI and cro, directly affect this decision. When cI is ON [OFF] and cro is OFF [ON], the phage is in the lysogenic [lytic] state. Whether or not gene cI will be switched on, and, thus, whether or not lysogenic state will be established, depends on a subtle control process in which five phage genes, cI, cro, cII, $cIII$, and N, and the environmental state play a prominent role.

Immediately after infection genes cro and N are activated, and their induced proteins begin to accumulate. Gene N exerts a positive control on cII and $cIII$ genes and is itself under negative

[1]From the Greek, *Lysis*, act of loosening. *Lysogenic*, capable of producing or undergoing lysis.

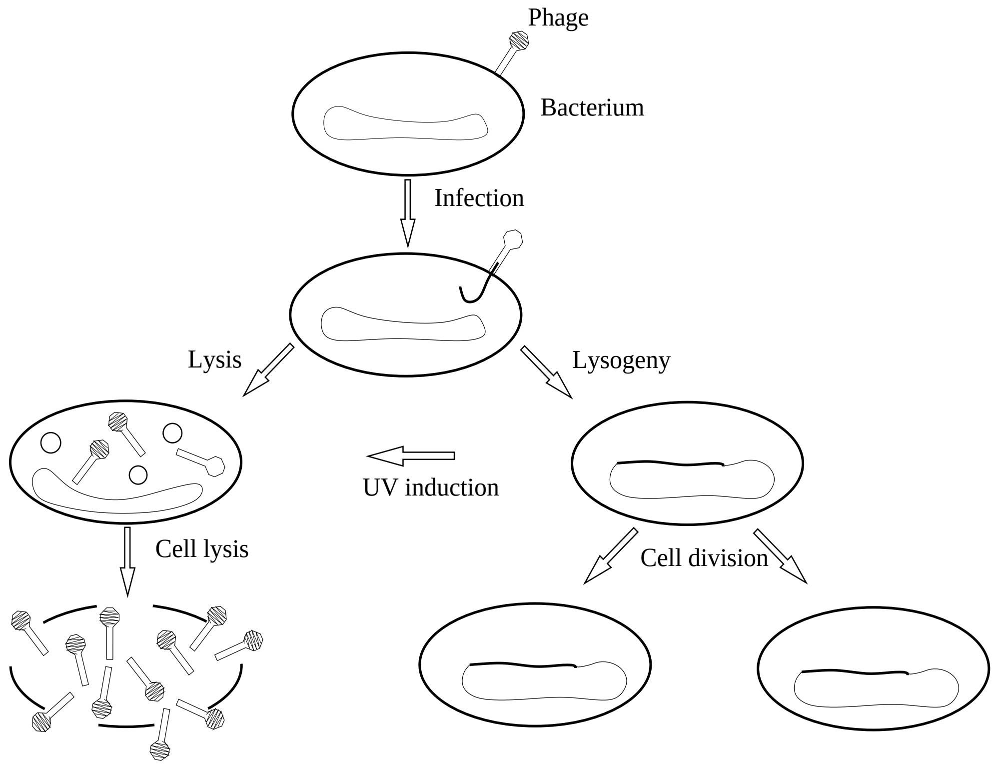

Fig. 3. Two developmental pathways: lytic and lysogenic.

control of cI and cro. The most important factor in the lysis/lysogenization decision is actually the CII protein, as its activity dictates the level of cI. The $CIII$ protein also helps to establish lysogeny; its role is to protect CII from degradation.

Several environmental conditions including concentration of nutrition, growth rate, temperature, and multiplicity of infection can influence the cII and $cIII$ genes. If the environmental conditions are favorable, then the cII and $cIII$ genes are highly active, and the cII gene product turns the cI gene on. The cI gene inhibits all other genes including cro, and the lysogenic state is established. If the environmental conditions are not favorable, then genes cII, $cIII$ are not activated, the cro gene remains a active and its product represses the cI gene. Thus, the lytic state is established.

The gene interactions are summarized in Fig. 4, where u is a binary input that represents whether the sum of environmental conditions is favorable or not.

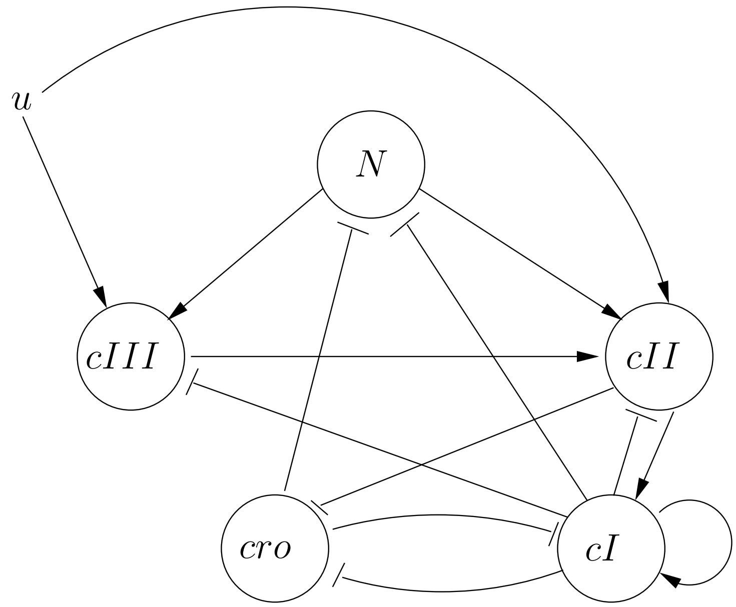

Fig. 4. Gene interactions for the λ switch. The edges represent either activatory ($\rightarrow$) or inhibitory ($\perp$) interactions.

B. BCN model of the lambda switch

We derive a simple BCN model for the lambda switch based on the assumption that the effect of activators and inhibitors is never additive, but rather inhibitors are dominant. Each gene is modeled using a Boolean variable where state ON [OFF] of the gene corresponds to the logical state True [False] of the variable. This yields

$$\begin{aligned} N(k+1) &= (\neg cI(k)) \wedge (\neg cro(k)), \\ cI(k+1) &= (\neg cro(k)) \wedge (cI(k) \vee cII(k)), \\ cII(k+1) &= (\neg cI(k)) \wedge u(k) \wedge (N(k) \vee cIII(k)), \\ cIII(k+1) &= (\neg cI(k)) \wedge u(k) \wedge N(k), \\ cro(k+1) &= (\neg cI(k)) \wedge (\neg cII(k)), \end{aligned} \tag{39}$$

where $\neg$ denotes logical negation. The input $u(k)$ is True [False] if the environmental conditions are favorable [not favorable] at time k.

The Boolean interaction functions are constructed from the verbal description of the interactions between the genes described above. For example, since cI suppresses all other genes, the right-hand side of the equations for $N(k+1), cII(k+1), cIII(k+1)$ and $cro(k+1)$ includes a logical and with the term $(\neg cI(k))$.

Remark 5. *Our model considers what happens immediately after infection and thus does not take into account some known interactions that control long time behavior. For example, it is known that both cI and cro auto-regulate themselves in order to limit the concentration values of the corresponding proteins, once they reach high values. We also ignore the negative control of cII by Cro that takes place only at high concentration of Cro [76]. A third simplification is that we consider a single control input. Indeed, as was discussed above several different external factors affect the lytic/lysogenic decision process. However, we model their total effect using a single control that can inhibit the expression of the cII or cIII genes (see [78]).*

We assume from here on that the initial condition right after infection is $N(0) = cI(0) = cII(0) = cIII(0) = cro(0) =$ False, i.e., all genes are not expressed.

C. Algebraic representation of the BCN

Recall that in the ASSR every Boolean variable may attain the values e_2^1 or e_2^2. Let $x(k) = N(k) \ltimes cI(k) \ltimes cII(k) \ltimes cIII(k) \ltimes cro(k)$. The ASSR of (39) is given by (4) with $n = 5$, $m = 1$, and

$$\begin{aligned} L = e_{32}[\; & 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 24 \;\; 26 \;\; 2 \;\; 26 \;\; 2 \;\; 25 \;\; 9 \;\; 25 \;\; 9 \\ & 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 24 \;\; 28 \;\; 4 \;\; 32 \;\; 8 \;\; 27 \;\; 11 \;\; 31 \;\; 15 \\ & 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 8 \;\; 32 \;\; 8 \;\; 31 \;\; 15 \;\; 31 \;\; 15 \\ & 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 24 \;\; 32 \;\; 8 \;\; 32 \;\; 8 \;\; 31 \;\; 15 \;\; 31 \;\; 15 \;\;]. \end{aligned} \tag{40}$$

This notation means that the first column of L is e_{32}^{32}, the second column is e_{32}^{24} and so on. The initial condition is $x(0) = x_{init} = e_{32}^{32}$.

To verify the model, we first consider the BNs obtained from this BCN for the case of a constant control.

1) Constant control: For $u(k) \equiv e_2^1$, the BCN becomes the BN

$$x(k+1) = L_1 x(k), \tag{41}$$

with

$$L_1 = e_{32}[\begin{array}{cccccccccccccccc} 32 & 24 & 32 & 24 & 32 & 24 & 32 & 24 & 26 & 2 & 26 & 2 & 25 & 9 & 25 & 9 \\ 32 & 24 & 32 & 24 & 32 & 24 & 32 & 24 & 28 & 4 & 32 & 8 & 27 & 11 & 31 & 15 \end{array}].$$

This BN admits two equilibrium points: e_{32}^{24} and e_{32}^{31}. Note that $e_{32}^{24} = e_2^2 \ltimes e_2^1 \ltimes e_2^2 \ltimes e_2^2 \ltimes e_2^2$. This corresponds to all the genes turned OFF except for cI which is ON, i.e. the lysogenic state, so we denote $x_{lysogenic} = e_{32}^{24}$. Similarly, $e_{32}^{31} = e_2^2 \ltimes e_2^2 \ltimes e_2^2 \ltimes e_2^2 \ltimes e_2^1$. This corresponds to all the genes turned OFF except for cro which is ON. This is the lytic state, so we denote $x_{lytic} = e_{32}^{31}$. For the initial condition $x(0) = x_{init}$, the trajectory of (41) satisfies $x(5) = e_{32}^{24}$ (and thus $x(k) = e_{32}^{24}$ for any $k \geq 5$). This seems reasonable as it implies that for a constant signal of favorable environmental conditions the BCN converges to the lysogenic state.

For $u(k) \equiv e_2^2$, the BCN becomes the BN $x(k+1) = L_2 x(k)$ with

$$L_2 = e_{32}[\begin{array}{cccccccccccccccc} 32 & 24 & 32 & 24 & 32 & 24 & 32 & 24 & 32 & 8 & 32 & 8 & 31 & 15 & 31 & 15 \\ 32 & 24 & 32 & 24 & 32 & 24 & 32 & 24 & 32 & 8 & 32 & 8 & 31 & 15 & 31 & 15 \end{array}].$$

This BN admits the same two equilibrium points as (41), i.e. $x_{lysogenic}$ and x_{lytic}. For the initial condition $x(0) = x_{init}$, the corresponding trajectory satisfies $x(2) = e_{32}^{31}$ (and thus $x(k) = e_{32}^{31}$ for any $k \geq 2$). This seems reasonable as it implies that for a constant signal of unfavorable environmental conditions the BCN converges to the lytic state.

We now apply the theoretical results in this paper to determine time-optimal controls that steer the BCN (39) from x_{init} to either x_{lytic} or $x_{lysogenic}$.

D. Minimum-time control in the λ switch

To apply Thm. 7 we calculate

$$\begin{aligned} Q =& L \ltimes_B \begin{bmatrix} 1 & 1 \end{bmatrix}^T \qquad (42) \\ =& [e_{32}^{32} \;\; e_{32}^{24} \;\; e_{32}^{32} \;\; e_{32}^{24} \;\; e_{32}^{32} \;\; e_{32}^{24} \;\; e_{32}^{32} \;\; e_{32}^{24} \;\; e_{32}^{26} + e_{32}^{32} \;\; e_{32}^{2} + e_{32}^{8} \;\; e_{32}^{26} + e_{32}^{32} \\ & e_{32}^{2} + e_{32}^{8} \;\; e_{32}^{25} + e_{32}^{31} \;\; e_{32}^{9} + e_{32}^{15} \;\; e_{32}^{25} + e_{32}^{31} \;\; e_{32}^{9} + e_{32}^{15} \;\; e_{32}^{32} \;\; e_{32}^{24} \;\; e_{32}^{32} \;\; e_{32}^{24} \;\; e_{32}^{32} \\ & e_{32}^{24} \;\; e_{32}^{32} \;\; e_{32}^{24} \;\; e_{32}^{28} + e_{32}^{32} \;\; e_{32}^{4} + e_{32}^{8} \;\; e_{32}^{32} \;\; e_{32}^{8} \;\; e_{32}^{27} + e_{32}^{31} \;\; e_{32}^{11} + e_{32}^{15} \;\; e_{32}^{31} \;\; e_{32}^{15}], \end{aligned}$$

and

$$
\begin{aligned}
H &= LW_{[32,2]} \\
&= L \begin{bmatrix} I_{32} \otimes (e_2^1)^T \\ I_{32} \otimes (e_2^2)^T \end{bmatrix} \\
&= e_{32}[32\ 32\ 24\ 24\ 32\ 32\ 24\ 24\ 32\ 32\ 24\ 24\ 32\ 32\ 24\ 24 \\
&\quad 26\ 32\ 2\ 8\ 26\ 32\ 2\ 8\ 25\ 31\ 9\ 15\ 25\ 31\ 9\ 15\ 32\ 32\ 24 \\
&\quad 24\ 32\ 32\ 24\ 24\ 32\ 32\ 24\ 24\ 32\ 32\ 24\ 24\ 28\ 32\ 4\ 8 \\
&\quad 32\ 32\ 8\ 8\ 27\ 31\ 11\ 15\ 31\ 31\ 15\ 15].
\end{aligned}
$$

1) Time-minimal transition to the lytic state: Let u^*_{lytic} be a time-optimal control steering the BCN from x_{init} to x_{lytic} in minimal time N^*_{lytic}. We find N^*_{lytic} using Theorem 5. Here $\eta(N^*_{lytic}) = x_{lytic} = e_{32}^{31}$, so $(\eta(N^*_{lytic}))^T x_{init} = (e_{32}^{31})^T e_{32}^{32} = 0$; $\eta(N^*_{lytic}-1) = Q^T \odot \eta(N^*_{lytic}) = e_{32}^{13} + e_{32}^{15} + e_{32}^{29} + e_{32}^{31}$, so again $(\eta(N^*_{lytic}-1))^T x_{init} = 0$; $\eta(N^*_{lytic}-2) = Q^T \odot \eta(N^*_{lytic}-1) = e_{32}^{13} + e_{32}^{14} + e_{32}^{15} + e_{32}^{16} + e_{32}^{29} + e_{32}^{30} + e_{32}^{31} + e_{32}^{32}$, so $(\eta(N^*_{lytic}-2))^T x_{init} = 1$, and we conclude that $N^*_{lytic} = 2$. We can now use Theorem 7 to iteratively determine all the time-optimal controls:

$$\sum_{i=1}^{s_0} u^*_{lytic}(0) = (H \ltimes x^*(0))^T \eta(1) = e_2^1 + e_2^2,$$

so there are two time-optimal values at time 0. The corresponding state for both these values is is $x^*(1) = e_{32}^{15}$. Since $e_{32}^{15} = e_2^1 \ltimes e_2^2 \ltimes e_2^2 \ltimes e_2^2 \ltimes e_2^1$, this implies that for $x(0) = x_{init}$ the state $x(1)$ does not depend on the environmental conditions and corresponds to genes N and cro ON, and all other genes OFF. Now

$$\sum_{i=1}^{s_1} u^*_{lytic}(1) = (H \ltimes x^*(1))^T \eta(2) = e_2^2,$$

so there exists a unique time-optimal control value at time 1. The corresponding trajectory is, as expected, $x^*(2) = e_{32}^{31}$. Thus, time step $k = 1$ is critical for the switching decision and if at this time step the environmental conditions are unfavorable, the virus immediately switches to the lytic state.

2) Time-minimal transition to the lysogenic state: We start with calculating the minimal time $N^*_{lysogenic}$ using Theorem 5. A calculation of $\eta(N^*_{lysogenic}), \eta(N^*_{lysogenic}-1), \dots$ until the first value k such that $(\eta(N^*_{lysogenic}-k))^T x_{init} = 1$ yields $k=5$, so $N^*_{lysogenic}=5$.

Now applying Theorem 7 yields

$$\begin{aligned}
\sum_{i=1}^{s_0} u^*_{lys}(0) &= (H \ltimes x^*(0))^T \eta(1) = e_2^1 + e_2^2, \quad x^*(1) = e_{32}^{15},\\
\sum_{i=1}^{s_1} u^*_{lys}(1) &= (H \ltimes x^*(1))^T \eta(2) = e_2^1, \quad x^*(2) = e_{32}^{25},\\
\sum_{i=1}^{s_2} u^*_{lys}(2) &= (H \ltimes x^*(2))^T \eta(3) = e_2^1, \quad x^*(3) = e_{32}^{28},\\
\sum_{i=1}^{s_3} u^*_{lys}(3) &= (H \ltimes x^*(3))^T \eta(4) = e_2^1 + e_2^2, \quad x^*(4) = e_{32}^{8},\\
\sum_{i=1}^{s_4} u^*_{lys}(4) &= (H \ltimes x^*(4))^T \eta(5) = e_2^1 + e_2^2, \quad x^*(5) = e_{32}^{24}.
\end{aligned}$$

We conclude that any control u^* satisfying $u^*(1) = u^*(2) = e_2^1$ is time-optimal. Thus, there exist 8 different time-optimal controls steering the BCN from $x(0) = x_{init}$ to $x(N^*_{lysogenic}) = x_{lysogenic}$ and they all yield the same trajectory, namely, $x^* = \{x^*(5), x^*(4), x^*(3), x^*(2), x^*(1), x^*(0)\} = \{e_{32}^{24}, e_{32}^{8}, e_{32}^{28}, e_{32}^{25}, e_{32}^{15}, e_{32}^{32}\}$. In particular the control $u^* = \{e_2^1, e_2^1, e_2^1, e_2^1, e_2^1\}$, corresponding to a set of 5 consecutive favorable environmental conditions, is time-optimal. Here time steps $k = 1, 2$ are critical for the switching decision, and if the environmental conditions at these times are favorable, then the virus will be steered to the lysogenic state.

From a biophysical point of view, these results suggest that the lambda switch is designed in a way that guarantees a swift as possible response to the environmental conditions. This seems reasonable and agrees with the biological findings. Indeed, Wegrzyn & Wegrzyn [78] note that "The lysis-versus-lysogenization decision has to be made shortly after infection and is crucial for effective propagation of the phage λ."

V. CONCLUSION

BNs and BCNs are recently attracting considerable interest as computational models for biological networks. We considered the following problem. Given an initial state x_0 and a desired state z, find a time-optimal control steering the BCN from x_0 to z (if it exists). This problem may have important applications in the context of biological systems modeled using BCNs. Indeed, intervention protocols may require transferring a biological network from an undesirable state to a desirable one in minimal time. Also, it is possible that biological networks evolved to respond in a time-minimal manner to important external or internal conditions.

Using the algebraic state-space representation of BCNs, we derived several MPs that provide necessary conditions for time-optimality. The canonical structure of the state vectors in this representation allows the derivation of an explicit state-feedback formula for all the time-optimal controls.

Some of the theoretical results were demonstrated using a new BCN model for the lambda switch, with the input representing the environmental conditions sensed by the phage at the time of infection. Analysis of time-optimal controls suggests that the switch is designed in a way that guarantees a fast response to the environmental conditions inside the bacterium.

As a topic for further research, we note that MPs combined with Lie-algebraic ideas have been used to derive nice-reachability-type results for discrete-time linear switched systems (see [62] and the references therein). It may be interesting to try and develop similar results for BCNs.

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