

# Preface

Motivated by the Human Genome Project, a new view of biology, called systems biology, is emerging [5]. Systems biology does not investigate individual genes, proteins or cells in isolation. Rather, it studies the behavior and relationships of all of the cells, proteins, DNA and RNA in a biological system called a cellular network. The most active networks may be those associated with genetic regulation, which regulate the growth, replication, and death of cells in response to changes in the environment.

How do these genetic regulatory networks function? In the early 1960s Jacob and Monod showed that any cell contains a number of “regulatory” genes that act as switches and which can turn each another on and off. This shows that a genetic network is of “on–off” type [7].

Boolean networks, first introduced by Kauffman, have become powerful tools for describing, analyzing, and simulating cellular networks [2, 3]. Hence, they have received much attention, not only from the biology community, but also from researchers with backgrounds in physics, systems science, etc.

The purpose of this book is to present a new approach to the investigation of Boolean (control) networks. In this new approach, a logical relation is expressed as an algebraic equation, and a logical dynamical system, such as a Boolean network, is converted into a standard discrete-time linear system. Similarly, a Boolean control network is converted into a discrete-time bilinear system. In this way, various tools for solving conventional algebraic equations and dealing with difference or differential equations can be used to solve logic-based problems. Under this framework, the topological structures of Boolean networks are revealed via the structures of their network transition matrices. The state space, subspaces, etc., are then defined as sets of logical functions. This framework makes the state-space approach to dynamical (control) systems applicable to Boolean (control) networks. Using this new technique, we investigate the properties and control design of Boolean networks. Many basic problems in control theory are studied, such as controllability, observability, realization, stabilization, disturbance decoupling and optimal control.

The fundamental tool in this approach is a new matrix product, called the semi-tensor product (STP). The STP of matrices is a generalization of the conventional

matrix product to the case where the dimension-matching condition is not satisfied. That is, we extend the matrix product  $AB$  to the case where the column number of  $A$  and the row number of  $B$  are different. This generalization preserves all the major properties of the conventional matrix product.

Using the STP, a logical function can be converted into a multilinear mapping, called the matrix expression of logical relations. Under this construction, the dynamics of a Boolean network can be expressed as a conventional discrete-time linear system. In the light of this linear expression, certain major features of the topology of a Boolean network, such as fixed points, cycles, transient time, and basins of attractors, can be easily revealed via a set of formulas.

When the control of a Boolean network is considered, the bilinear system representation of a Boolean control network makes it possible to apply most techniques developed in modern control theory to the analysis and synthesis of a Boolean control network.

The main contents of this book are as follows.

Chapter 1 consists of a brief introduction to propositional logic. This is very elementary and involves only the propositional logic required in this book. A reader who is familiar with mathematical logic can skip it.

In Chap. 2 we introduce some basic concepts and properties of the STP, which is the principal tool used in this book. The STP is a generalization of the conventional matrix product in cases where the dimension-matching requirement for the factor matrices fails. This generalization preserves the major properties of the conventional matrix product.

In Chap. 3 we consider the matrix expression of logical relations. Identifying  $T$  (true) and  $F$  (false) with vectors  $[1, 0]^T$  and  $[0, 1]^T$ , respectively, a logical variable becomes a 2-dimensional vector variable. Using the STP, a logical function can be expressed as a multilinear mapping with respect to its logical arguments so that each logical function is uniquely determined by a matrix, called its structure matrix.

Chapter 4 is devoted to solving logical equations. Using the matrix expression of logic a system of logical equations can be converted into a linear algebraic equation. Ignoring the complexity of computation, the solution of systems of logical equations becomes theoretically equivalent to the solution of algebraic equations, which can be achieved with straightforward computation.

Chapter 5 considers the linear expression of Boolean networks. Using the technique developed in previous chapters, the dynamics of a Boolean network is converted into a conventional discrete-time linear system. In the light of this linear expression, the topological structures of Boolean networks are investigated via their transition matrices. Formulas are obtained to calculate the fixed points, cycles of different lengths, transient period, and the basin of each attractor.

The input-state structures of Boolean control networks are studied in Chap. 6. The compounded structure of cycles in input-state space is obtained. This approach is applied to the analysis of Boolean networks with cascading structure. The “rolling gear” structure of cycles is revealed, which explains the phenomenon that tiny attractors can determine the vast order of the network [4].

Chapter 7 presents a technique to build the dynamic model of a Boolean network via observed data. Instead of building the logical dynamics of a Boolean network, we first identify its algebraic form, so the conversion of the algebraic form of a Boolean network back to its logical form is first investigated. After a general model construction technique is introduced, several special cases are studied, including the known network graph case, the least in-degree model, the uniform model, etc. The problem of dealing with data containing errors is also discussed.

In Chap. 8 a systematic state-space description is developed. The state space (and its subspaces) of a Boolean (control) network are defined in a dual way, i.e., they are defined as sets of logical functions. It is shown that this description is very convenient in revealing the properties of Boolean networks and in the control design of Boolean control networks.

Chapter 9 is devoted to Boolean control networks. Using linear expressions, it is shown that Boolean control networks can be converted into linear control systems. Some basic control problems such as controllability and observability of Boolean control networks are then investigated via their equivalent forms for linear control systems.

Chapter 10 considers the realization problem of Boolean control networks. First, coordinate transformations are considered, and then the Kalman decomposition of Boolean input–output networks is proposed. Using the Kalman decomposition, the minimum realization of a Boolean input–output mapping is obtained.

The stability and stabilization problem is discussed in Chap. 11. The applicable set from metric-based convergence analysis [6] is enlarged by the use of coordinate transformations. Based on the analysis of the network transition matrix, necessary and sufficient conditions are then obtained for stability and stabilization by either open-loop control or closed-loop control. Several examples are included.

Chapter 12 considers the disturbance decoupling problem. First, the output-friendly subspace is introduced. Formulas and algorithms are provided to construct a minimum regular subspace, which is called the “friend” of output  $y$ . The design technique for constructing the feedback and solving the disturbance decoupling problem is presented. To construct a constant stabilizing control, the canalizing mapping, which is a generalization of the canalizing function, is proposed and its main properties are revealed.

In Chap. 13 we consider the coordinate-independent geometric structure of Boolean (control) networks. Based on this structure, the feedback decomposition of Boolean control networks is studied. The input-state decomposition, including cascading and parallel decompositions, and input–output decomposition of Boolean control networks are investigated, and necessary and sufficient conditions are presented.

Chapter 14 deals with the multivalued logic which could provide a more precise description for real networks such as gene regulation networks, etc. The structure of  $k$ -valued logical networks is first investigated. Controllability and observability of  $k$ -valued logical networks are then considered. In fact, almost all the arguments and results about Boolean networks can be extended to the  $k$ -valued logic setting.

Chapter 15 considers the optimal control of Boolean control networks. To deal with Boolean (or  $k$ -valued) games with  $s$ -memory, higher-order Boolean (control) networks are introduced, and their algebraic forms are also presented. The one-to-one correspondence between the cycles of the original network and the cycles of its algebraic form is established. The optimal control problem is then investigated and the optimal control is designed.

Chapter 16 introduces a useful tool, called the input-state incidence matrix, which is an algebraic description of the input-state transfer graph. Controllability and observability of Boolean control networks are revisited and some further results are presented. The topological structures of Boolean control networks with free controls are also investigated. Finally, the results are extended to mix-valued logical dynamical systems.

Chapter 17 investigates the identification of Boolean control networks. First, a new observability condition is obtained which provides a way to construct the initial state of a trajectory from its input–output data. A necessary and sufficient condition for identifiability is then presented. A numerical algorithm is proposed for practical application.

Chapter 18 considers an application to game theory. We consider a game with finitely many players and where each player has finitely many possible actions. When the game is infinitely repeated, a strategy using finite memory becomes a logical dynamical system. Hence, the results obtained for Boolean or logical networks are applicable to finding Nash or sub-Nash solutions for the infinitely repeated games.

The primary objects of this book are deterministic Boolean networks, but in Chap. 19 we provide a brief introduction to random Boolean networks. Basic concepts are presented and then the steady-state distribution of a random Boolean network is investigated. Finally, the stabilization of a random Boolean network is studied. Recently, random Boolean networks have been the subject of much research, and so a detailed discussion is beyond the scope of this work.

Appendix A explains relevant numerical calculations. A software toolbox for the algorithms is available at <http://lsc.amss.ac.cn/~dcheng/>.

Appendix B contains proofs of some key properties of the semi-tensor product, which are translated from [1], with the permission of Science Press.

This book is self-contained. The prerequisites for its use are linear algebra and some basic knowledge of the control theory of linear systems. The manuscript was originally prepared when the first author was visiting Kyoto University. The first author would like to express his hearty thanks to Professor Yutaka Takahashi for his proof-reading and useful suggestions for parts of the manuscript. The manuscript has been used as lecture notes in a series of seminars organized jointly by the Academy of Mathematics and Systems Science, Tsinghua University, and Peking University. Many colleagues and students attending these seminars have contributed to this book via useful discussions, suggestions, and corrections. Particularly, Dr. Yin Zhao helped in the preparation of Chaps. 15–17. Dr. Yifen Mu, Dr. Zhenning Zhang, Dr. Yin Zhao, Dr. Xiangru Xu, and Dr. Jiangbo Zhang helped with the final galley proof of the manuscript. The authors are also indebted to Mr. Oliver Jackson for his warmhearted support.

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