

# Complexity of limit-cycle problems in Boolean networks

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## Abstract

Boolean networks are a general model of interacting entities, with applications to biological phenomena such as gene regulation. Attractors play a central role, and the schedule of entities update is *a priori* unknown. This article presents results on the computational complexity of problems related to the existence of update schedules such that some limit-cycle lengths are possible or not. We first prove that given a Boolean network updated in parallel, knowing whether it has at least one limit-cycle of length  $k$  is **NP**-complete. Adding an existential quantification on the block-sequential update schedule does not change the complexity class of the problem, but the following alternation brings us one level above in the polynomial hierarchy: given a Boolean network, knowing whether there exists a block-sequential update schedule such that it has no limit-cycle of length  $k$  is **NP<sup>NP</sup>**-complete.

## 1 Introduction

Boolean networks (BNs) were introduced by McCulloch and Pitts in the 1940s through the well known formal neural networks [17] that are specific BNs governed by a multi-dimensional threshold function. Informally, BNs are finite dynamical systems in which entities having Boolean states may interact with each other over discrete time. After their introduction, neural networks were studied in depth from the mathematical standpoint. Among the main works on them are the introduction by Kleene of finite automata and regular expression [16], first results on the dynamical behaviors of linear feedback shift register [13] and linear networks [8]. These researches led Kauffman and Thomas (independently) from the end of the 1960s to develop the use of BNs in the context of biological networks modeling [15, 27], which has paved the way to numerous applied works at the interface between molecular biology, computer science and discrete mathematics. In parallel, theoretical developments were done in the framework of linear algebra and numerical analysis by Robert [24], and in that of dynamical system theory and computational models, which constitutes the lens through which we look at BNs in this paper.

In this context, numerous studies have already been led and have brought very important results. Considering that a BN can be defined as a collection of local Boolean

# The Complexity Of Boolean Networks

**Jin-Ying Zhang**



## **The Complexity Of Boolean Networks:**

**The Complexity of Boolean Networks** Paul E. Dunne, 1988      **Size-time Complexity of Boolean Networks for Prefix Computations** Gianfranco Bilardi, Franco P. Preparata, 1987      **Efficient Algorithms** Susanne Albers, Helmut Alt, Stefan Näher, 2009-09-01 This Festschrift volume published in honor of Kurt Mehlhorn on the occasion of his 60th birthday contains 28 papers that demonstrate how the field of algorithmics has developed and matured in the decades since Mehlhorn's first book on the subject in 1977

**Complex Networks & Their Applications IX** Rosa M. Benito, Chantal Cherifi, Hocine Cherifi, Esteban Moro, Luis Mateus Rocha, Marta Sales-Pardo, 2021-01-04 This book highlights cutting edge research in the field of network science offering scientists researchers students and practitioners a unique update on the latest advances in theory and a multitude of applications It presents the peer reviewed proceedings of the IX International Conference on Complex Networks and their Applications COMPLEX NETWORKS 2020 The carefully selected papers cover a wide range of theoretical topics such as network models and measures community structure network dynamics diffusion epidemics and spreading processes resilience and control as well as all the main network applications including social and political networks networks in finance and economics biological and neuroscience networks and technological networks

**Handbook of Research on Computational Methodologies in Gene Regulatory Networks** Das, Sanjoy, Caragea, Doina, Welch, Stephen, Hsu, William H., 2009-10-31 This book focuses on methods widely used in modeling gene networks including structure discovery learning and optimization Provided by publisher

**SOFSEM 2021: Theory and Practice of Computer Science** Tomáš Bureš, Riccardo Dondi, Johann Gamper, Giovanna Guerrini, Tomasz Jurdziński, Claus Pahl, Florian Sikora, Prudence W.H. Wong, 2021-01-20 This book contains the invited and contributed papers selected for presentation at SOFSEM 2021 the 47th International Conference on Current Trends in Theory and Practice of Computer Science which was held online during January 25-28 2021 hosted by the Free University of Bozen Bolzano Italy The 33 full and 7 short papers included in the volume were carefully reviewed and selected from 100 submissions They were organized in topical sections on foundations of computer science foundations of software engineering foundations of data science and engineering and foundations of algorithmic computational biology The book also contains 5 invited papers

**An improved complexity hierarchy on the Boolean network complexity and formula size of Boolean functions** Ingo Wegener, 1984

**Thinking About Biology** Wilfred Stein, Francisco J. Varela, 2018-03-08 This book discusses the emergence of life the development of the individual and the study of the interaction between individuals and species It gives the student of theoretical biology some idea of the flavor of current research in the field

**Proceedings of the Twenty-seventh Annual ACM Symposium on Theory of Computing**, 1995

**Logical Modeling of Cellular Processes: From Software Development to Network Dynamics** Matteo Barberis, Tomáš Helikar, 2019-08-16 Mathematical models have become invaluable tools for understanding the intricate dynamic behavior of complex biochemical and biological systems Among computational strategies logical modeling

has been recently gaining interest as an alternative approach to address network dynamics. Due to its advantages including scalability and independence of kinetic parameters, the logical modeling framework is becoming increasingly popular to study the dynamics of highly interconnected systems such as cell cycle progression, T cell differentiation, and gene regulation. Novel tools and standards have been developed to increase the interoperability of logical models, which can now be employed to respond to a variety of biological questions. This Research Topic brings together the most recent and cutting edge approaches in the area of logical modeling, including among others novel biological applications, software development, and model analysis techniques.

**Size-time Complexity of Boolean Networks for Prefix Computation** Cornell University, Department of Computer Science, G. Bilardi, F. P. Preparata, 1987. The prefix problem consists of computing all the products  $x_0 x_1 \dots x_{j-1}$  given a sequence  $X = x_0 x_1 \dots x_{N-1}$  of elements in a semigroup. In this paper we completely characterize the size-time complexity of computing prefixes with boolean networks, which are synchronized interconnections of boolean gates and one-bit storage devices. This complexity crucially depends upon a property of the underlying semigroup, which we call cycle freedom: no cycle of length greater than one in the Cayley graph of the semigroup. Denoting by  $S$  and  $T$  size and computation time respectively, we have  $S = \Theta(N)$ ,  $T = O(N \log N)$  for non-cycle-free semigroups, and  $S = \Theta(N)$ ,  $T = O(N)$  for cycle-free semigroups. In both cases,  $T = O(N \log N)$ .

**Quantitative Assessment and Validation of Network Inference Methods in Bioinformatics** Benjamin Haibe-Kains, Frank Emmert-Streib, 2015-04-14. Scientists today have access to an unprecedented arsenal of high-tech tools that can be used to thoroughly characterize biological systems of interest. High-throughput omics technologies enable the generation of enormous quantities of data at the DNA, RNA, epigenetic, and proteomic levels. One of the major challenges of the post-genomic era is to extract functional information by integrating such heterogeneous, high-throughput genomic data. This is not a trivial task, as we are increasingly coming to understand that it is not individual genes but rather biological pathways and networks that drive an organism's response to environmental factors and the development of its particular phenotype. In order to fully understand the way in which these networks interact or fail to do so in specific states, disease, for instance, we must learn both the structure of the underlying networks and the rules that govern their behavior. In recent years, there has been an increasing interest in methods that aim to infer biological networks. These methods enable the opportunity for better understanding the interactions between genomic features and the overall structure and behavior of the underlying networks. So far, such network models have been mainly used to identify and validate new interactions between genes of interest. But ultimately, one could use these networks to predict large-scale effects of perturbations, such as treatment by multiple targeted drugs. However, currently, we are still at an early stage of comprehending methods and approaches providing a robust statistical framework to quantitatively assess the quality of network inference and its predictive potential. The scope of this Research Topic in Bioinformatics and Computational Biology aims at addressing these issues by investigating the various complementary approaches to quantify the quality of network

models These validation techniques could focus on assessing quality of specific interactions global and local structures and predictive ability of network models These methods could rely exclusively on in silico evaluation procedures or they could be coupled with novel experimental designs to generate the biological data necessary to properly validate inferred networks

**Proceedings of the Twenty-sixth Annual ACM Symposium on the Theory of Computing** ,1994 *Journal of the Association for Computing Machinery* **JOURNAL OF THE ASSOCIATION FOR COMPUTING MACHINERY**,1989 **SIAM Journal on Computing** Society for Industrial and Applied Mathematics,2001 *International Congress of Mathematicians, Kyoto, Japan, August 21-29,1990: Plenary lectures, section lectures, ICMI lectures* ,1990 **Complex Systems** ,2007

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