Chapter 11
A Synthesis Method of Gene Regulatory Networks Based on Gene Expression by Network Learning

Yoshihiro Mori
Kyoto Institute of Technology, Japan

Yasuaki Kuroe
Kyoto Institute of Technology, Japan

ABSTRACT

Investigating gene regulatory networks is important to understand mechanisms of cellular functions. Recently, the synthesis of gene regulatory networks having desired functions has become of interest to many researchers because it is a complementary approach to understanding gene regulatory networks, and it could be the first step in controlling living cells. In this chapter, we discuss a synthesis problem in gene regulatory networks by network learning. The problem is to determine parameters of a gene regulatory network such that it possesses given gene expression pattern sequences as desired properties. We also discuss a controller synthesis method of gene regulatory networks. Some experiments illustrate the performance of this method.

INTRODUCTION

Investigating gene regulatory networks is important to understand mechanisms and functions of organisms and many researchers have been studied them from various view points. Recently there have been increasing research interests in synthesizing gene regulatory networks and several studies have been done. Those studies are motivated by two ways. One is that the synthesis of gene regulatory networks could be the first step in controlling and monitoring biochemical processes in living cells. The other is that it is a complementary approach to investigating and understanding mechanisms of real gene regulatory networks, that is to say, by synthesizing simple artificial networks and analyzing their behavior

DOI: 10.4018/978-1-60566-685-3.ch011

and functions, one can get some insights into functions of real gene regulatory networks. For example, Elowitz and Leibler (2000); Fung et al. (2005); Tuttle, Salis, Tomshine and Kaznessis (2005) synthesize artificial gene networks having oscillatory behaviors. Analyzing the synthesized networks could give some insights into investigating and understanding oscillatory behavior of organisms, e. g. circadian rhythm. Another example is the study on synthesizing artificial networks having a toggle switch like function (Atkinson, Savageau, Myers and Ninfa (2003); Deans, Cantor and Collins (2007); Gardner, Cantor and Collins (2000)).

Recently, Ichinose and Aihara (2002); Nakayama, Tanaka and Ushio (2006) discuss a synthesis problem in gene regulatory networks having desired properties. In those studies the desired properties are given by expression pattern sequences which describe changes of expression levels of genes. Furthermore, Nakayama et al. (2006) discuss a controller synthesis problem, in which controller gene regulatory networks are synthesized so that an objective gene regulatory network has desired expression pattern sequences.

In this chapter, we discuss the same synthesis problem and the controller synthesis problem of gene regulatory networks, in which the desired properties are given by expression pattern sequences. We present a novel synthesis method by network learning (Mori, Kuroe and Mori 2006). Gene regulatory network models are generally described by nonlinear differential equations and it is difficult to derive a synthesis method directly from nonlinear differential equation models. In order to overcome this difficulty we derive discrete-time networks possessing the equivalent time evolutions of expression pattern sequences to those of the differential equation models. We formulate the synthesis problem as a learning problem of the discrete-time networks and an efficient algorithm to solve the learning problem is derived. If the differential equation models are given by the piecewise linear network model (Glass 1975) with some class of interaction functions, the derived discrete-time networks are equivalent to a class of recurrent high-order neural network(RHONN)s and the synthesis problem is reduced to a learning problem of RHONNs.

The presented synthesis method can be applied to more general models of gene regulatory networks than the model used in Ichinose and Aihara (2002); Nakayama, at el, (2006) and it can be also applied to various synthesis problems. For example, the synthesis method can be extended and applied to the synthesis of gene regulatory networks possessing multiple desired expression pattern sequences, cyclic expression pattern sequences and stable cyclic expression pattern sequences.

BACKGROUND

There are several other studies on analysis and synthesis of gene regulatory networks. For examples, Hasty and Isaacs (2001) consider the gene regulatory network models described by nonlinear differential equations based on chemical reactions and investigate parameter regions such that they possess oscillatory behavior. Rodrigo et al. (2007) propose a synthesis method of gene regulatory network models such that they possess desired behavior, e. g. logical functions. Guido et al., 2006, Weiss et al., 2003 discuss a method for synthesizing rather complex gene regulatory networks by using simple gene regulatory networks as parts of them.

It is expected that the presented synthesis method makes some contributions toward understanding and synthesizing gene regulatory networks. In gene regulatory networks, several models, from simpler ones to detailed ones, have been proposed (Jong 2002). A simplest model is the Boolean network model

Related Content

Improved Model Checking Techniques for State Space Analysis of Gene Regulatory Networks
Hélio C. Pais, Kenneth L. McMillan, Ellen M. Sentovich, Ana T. Freitasand Arlindo L. Oliveira (2010). *Handbook of Research on Computational Methodologies in Gene Regulatory Networks (pp. 386-404).*
www.irma-international.org/chapter/improved-model-checking-techniques-state/38244

How Genetic Algorithms Handle Pareto-Optimality in Design and Manufacturing
N. Chakraborti (2007). *Handbook of Research on Nature-Inspired Computing for Economics and Management (pp. 465-482).*
www.irma-international.org/chapter/genetic-algorithms-handle-pareto-optimality/21146

Innovative Genetic Algorithmic Approach to Select Potential Patches Enclosing Real and Complex Zeros of Nonlinear Equation
Vijaya Lakshmi V. Nadimpalli, Rajeev Wankarand Raghavendra Rao Chillarige (2017). *International Journal of Natural Computing Research (pp. 18-37).*
www.irma-international.org/article/innovative-genetic-algorithmic-approach-to-select-potential-patches-enclosing-real-and-complex-zeros-of-nonlinear-equation/198499

Modeling Fractal Structure of Systems of Cities Using Spatial Correlation Function
Yanguang Chenand Shiguo Jiang (2010). *International Journal of Artificial Life Research (pp. 12-34).*
www.irma-international.org/article/modeling-fractal-structure-systems-cities/38931

Insights Into Simulated Annealing
Khalil Amine (2018). *Handbook of Research on Modeling, Analysis, and Application of Nature-Inspired Metaheuristic Algorithms (pp. 121-139).*
www.irma-international.org/chapter/insights-into-simulated-annealing/187684