Title	Comprehensive Understanding of Gene Regulatory Networks Based on Evolutionary Systems Biology
Sub Title	
Author	松井, 求(Matsui, Motomu)
Publisher	慶應義塾大学湘南藤沢学会
Publication year	2013
Jtitle	生命と情報 No.20 (2013.) ,p.7- 7
JaLC DOI	
Abstract	The evolutionary processes of gene regulatory networks, which form the basis of life systems, remain to be revealed because of the difficulties in conducting studies on highly complex and multilevel biological networks. In this study, I developed novel evolutionary analysis methods contributing to the new field of evolutionary systems biology, which combines the concepts of both systems biology and evolutionary biology. I successfully applied these methods to analyze several important factors related to transcription or translation, such as upstream Open Reading Frames (uORFs) (Chapter2) and transcription factors (TFs) (Chapters3 and 4). At the beginning of this dissertation, I reviewed changes in the approaches to understanding life in the history of biology ; then, I showed that evolutionary systems biology is a particularly effective approach to reconstructing possible evolutionary scenarios of gene regulatory networks based on various large-scale datasets (Chapter1). Next, I performed comprehensive analysis of uORFs, which act as cis regulators of mRNA, by using microarray data on humans and mice. Comparison of transcriptional expression level and RNA decay ratio of mRNAs in a number of different tissues suggested that uORF controlled not only translation efficiency but also mRNA decay rate in a wide range of tissues and species (Chapter2). In chapters3 and 4, several evolutionary analyses or bacterial TFs based on the reconstruction of phylogenetic networks were discussed. I first developed a novel evolutionary analysis method, the TOP-DOWN approach, by integrating step-wise spectral clustering techniques into network theory to solve highly complex structures of sequence similarity networks. The TOP-DOWN approach was applied to the large- scale analysis of the CRP/FNR superfamily, which is one of the major TF families in the bacterial domain, and clarified its comprehensive evolutionary processes in a wide range of bacterial species (Chapter3). Second, I applied the method to analyze all Escherichia coli TFs and all well-annotated bacterial TFs. As a result, I proposed a novel evolutionary model for TF-TF regulatory networks and transcriptional regulatory interactions between TFs and their target genes (Chapter4). These results set up several evolutionary hypotheses regarding transcription and post-transcriptional regulation processes involving uORPs and TFs. Finally, I discussed the contribution of my method to furthering the research of multi-hierarchical biological networks in chapter5.
Notes	慶應義塾大学湘南藤沢キャンパス先端生命科学研究会 2013年度学生論文集 博士論文ダイジェスト
Genre	Technical Report
URL	https://koara.lib.keio.ac.jp/xoonips/modules/xoonips/detail.php?koara_id=KO92001004-00000020-0007

Doctoral Dissertation Digest
Academic Year 2013

Comprehensive Understanding of Gene Regulatory Networks Based on Evolutionary Systems Biology

松井　求

Graduate School of Media and Governance, Systems Biology Program
Keio University

Abstract

The evolutionary processes of gene regulatory networks, which form the basis of life systems, remain to be revealed because of the difficulties in conducting studies on highly complex and multi-level biological networks. In this study, I developed novel evolutionary analysis methods contributing to the new field of evolutionary systems biology, which combines the concepts of both systems biology and evolutionary biology. I successfully applied these methods to analyze several important factors related to transcription or translation, such as upstream Open Reading Frames (uORFs) (Chapter 2) and transcription factors (TFs) (Chapters 3 and 4).

At the beginning of this dissertation, I reviewed changes in the approaches to understanding life in the history of biology; then, I showed that evolutionary systems biology is a particularly effective approach to reconstructing possible evolutionary scenarios of gene regulatory networks based on various large-scale datasets (Chapter 1). Next, I performed comprehensive analysis of uORFs, which act as *cis* regulators of mRNA, by using microarray data on humans and mice. Comparison of transcriptional expression level and RNA decay ratio of mRNAs in a number of different tissues suggested that uORF controlled not only translation efficiency but also mRNA decay rate in a wide range of tissues and species (Chapter 2). In chapters 3 and 4, several evolutionary analyses of bacterial TFs based on the reconstruction of phylogenetic networks were discussed. I first developed a novel evolutionary analysis method, the TOP-DOWN approach, by integrating step-wise spectral clustering techniques into network theory to solve highly complex structures of sequence similarity networks. The TOP-DOWN approach was applied to the large-scale analysis of the CRP/FNR superfamily, which is one of the major TF families in the bacterial domain, and clarified its comprehensive evolutionary processes in a wide range of bacterial species (Chapter 3). Second, I applied the method to analyze all *Escherichia coli* TFs and all well-annotated bacterial TFs. As a result, I proposed a novel evolutionary model for TF-TF regulatory networks and transcriptional regulatory interactions between TFs and their target genes (Chapter 4).

These results set up several evolutionary hypotheses regarding transcription and post-transcriptional regulation processes involving uORFs and TFs. Finally, I discussed the contribution of my method to furthering the research of multi-hierarchical biological networks in chapter 5.

Key words: Post-transcriptional control; Transcription factor; upstream ORF; non-coding RNA; Phylogenetics; Graph theory; Network analysis