Algorithms for Inference of Genetic Networks (AIGNET)

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1 Introduction

Powerful new technologies, such as DNA microarrays, provide simple and economical ways to explore gene expression patterns on a genomic scale[1, 2]. Using comprehensive gene expression data, various approaches are planned to infer genetic networks [3, 4].

In this poster, we propose a system named **AIGNET** (Algorithms for Inference of Genetic Networks), and introduce two top down approaches for inference of genetic networks, which rely on the analysis of state changes and/or temporal responses of gene expression patterns. We show the strategy is flexible and rich in structure.

2 Overview of AIGNET

In general, the outcome of a single model for the inference of complex genetic network architectures is not satisfactory in terms of its power and reliability. Therefore, here we propose AIGNET, and take two approaches, corresponding to two different network models. One is a multi-level digraph approach corresponding to a static Boolean network model, which mainly relies on the analysis of state changes of gene expression patterns resulting from deletion or forcible expression of one gene. The other is an S-system [5] approach corresponding to a dynamic network model, which relies on the analysis of temporal responses of gene expression patterns to perturbations (e.g., heat shock, hormone stimulus) or internal changes (e.g., development). Individual approaches employed in AIGNET are described as follows.

2.1 Multi-level digraph approach

The multi-level digraph approach treats the data representing binary relations of gene expressions. These relations describe the effects of one gene on the expression of the other gene and are mainly provided by the changes of the state of gene expression patterns. Systematical analysis of the binary relations between pairs of genes enables us to reconstruct a possible minimum architecture of the genetic network which is consistent for all the data.

A prototype system of the multi-level digraph approach is implemented with the Python programming language. We shall show the application of this algorithm to various genetic networks.

2.2 S-system approach

Genetic networks are complex nonlinear system and the details of the mechanism at molecular level that govern interactions among system components are generally well not known. The S-system is one of the best formalisms to estimate interaction mechanisms among system components, and enables us to reconstruct genetic network architectures with the experimentally observed time-courses of the patterns of gene expression. The S-system formalism is applied to infer genetic networks, and show the richness in structure of the S-system.

3 Future work

We demonstrated that AIGNET can infer some class of networks that are simple, but large scale genetic network architectures. AIGNET has, however, drawbacks. To overcome them, it is essential to make the collaboration of top down approaches (e.g., multi-level digraph, S-system) and bottom up ones. In the latter strategies, components in a genetic network are inferred from the information of molecular interactions (e.g., interactions between *cis*-elements and trans-acting factors), then the network architecture is constructed step by step, using the components. Therefore, we will integrate various top down and bottom up approaches in AIGNET.

A major focus of our ongoing work is to characterize the flexibility and richness in structure of our two approaches. The results and future plans to infer complex genetic network architectures will be shown. The final goal of this work is to develop an efficient, user-friendly and extensible workbench [6] for analyzing genetic networks.

References

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