AIGNET: A System That Infers Large Scale Genetic Networks

Yukihiro Maki [1] **Shoji Watanabe** [1] **Yukihiro Eguchi** [1]
maki@hq.mki.co.jp sho@hq.mki.co.jp eguchi-y@hq.mki.co.jp
Daisuke Tominaga [2] **Masahiro Okamoto** [2]
dc9702@bse.kyutech.ac.jp okahon@bse.kyutech.ac.jp

[1] Research Institute, Mitsui Knowledge Industry Co., Ltd, 2-7-14 Higashinakano, Nakano-ku, Tokyo 164-8555, Japan
[2] Department of Biochemical Engineering and Science, Kyushu Institute of Technology, 680-4 Kawazu, Iizuka, Fukuoka 820-8502, Japan

1 Introduction

Recent advances of technology in bioinformatics have made gene expression comprehensive and several approaches have been proposed to infer the genetic networks, using such gene data [2, 3]. We previously proposed a system named **AIGNET** (Algorithms for Inference of Genetic Networks) in which either of two completely different network models work independently [4]. One model is a static Boolean network model based on a multi-level digraph approach which can treat a large number of expression data and the other is a dynamic network model such as S-system [1] which can infer the genetic network including a group of interdependent genes. We have demonstrated that AIGNET can infer some class of simple but large-scale genetic networks. However, the reliability and efficiency of these network models obviously depends on the structure of the data given to the system. In the previously proposed AIGNET, it was suggested that these two models should work in a supplementary manner to cover the disadvantage and limitation of individual models. Therefore, to further improve the reliability and efficiency of inference of genetic networks, we developed a new AIGNET in which a combination of these two network models is implemented and works in a cooperative manner. We show that this new AIGNET system becomes more powerful at inferring the large scale genetic networks.

2 Method and Application

The inference process of the combination of the two network models in AIGNET is shown in Fig. 1. First, AIGNET obtains a gene expression matrix by using gene expression time-course data sets. For example, if the concentration of gene i resulting from deletion of gene j gets higher (or lower) than its concentration in normal condition, gene i is set to 1 in this matrix. Second, the static Boolean network model reconstructs the network classified into the genes and some equivalence sets. Third, using the time-course of the genes belonging to each equivalence set and the gene effecting to its set, the S-system approach infers the network architecture of the equivalence set.

In order to examine the effectiveness of this method, as a case study, we made several sets of time-course data corresponding to deletion of one gene, sets of which were numerically calculated using the scheme composed of 30 genes shown in Fig. 1. Given these time-course data sets, the new AIGNET enabled us to reconstruct the same network architecture.

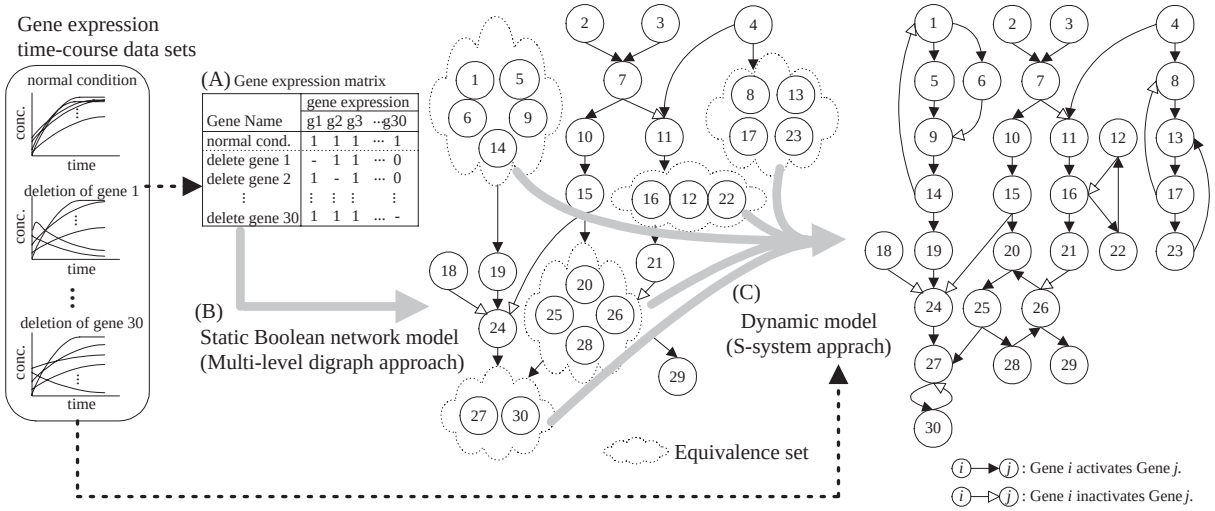

Figure 1: Inference process of a genetic network with the new AIGNET system. (A) Given the gene expression time-course data sets corresponding to the deletion or forcible expression of one gene, AIGNET obtains a gene expression matrix which is provided by the change from the state of normal condition (wildtype) at an arbitrary time. (B) Given this matrix, the static Boolean network model reconstructs the network architecture classified into the genes and some equivalence sets. (C) Using the time-course of the genes related to each equivalence set, the dynamic model (S-system) enables us to infer the genetic network completely.

3 Conclusion

The new AIGNET, in which the static Boolean network model and the dynamic model are implemented, could reconstruct a network architecture composed of 30 genes. Neither of two network models can reconstruct the same network architecture if they work independently, as they did in the previous AIGNET. We verified the effectiveness of this new AIGNET in a artificial genetic network model. Next, we will try to apply AIGNET to experimental data, such as DNA microarrays.

References

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