Generic Gene Expression System for Modeling Complex Gene Regulation Network Using E-CELL System

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1 Introduction

We present a general framework for modeling gene expression using the E-CELL system, a general purpose cell simulator developed at Keio University. Using the framework, we modeled and simulated the following three gene regulation systems: the *lac* operon and the *ara* operon of *E. coli*, and the lytic-lysogenic switch network in bacteriophage λ.

We have previously constructed a detailed model [1] of the gene expression system as a part of the "virtual" cell with 127 genes [2]. The previous model faithfully reflected the gene expression system of *M. genitalium*, involving more than 100 objects including various subunits, factors, amino acids, nucleotides, tRNAs and their ligases. However, in order to simulate complex gene regulation systems with a large number of genes, a more abstract and simpler model is desired for the sake of efficiency. The gene expression system used in this work consists of the following four basic elements. 1) Production of RNAs and proteins, 2) Regulation of expression by various factors, 3) Time delay between regulation and production, and 4) Sigmoidal curve of product increase over time. All gene expressions are reduced to these four elements.

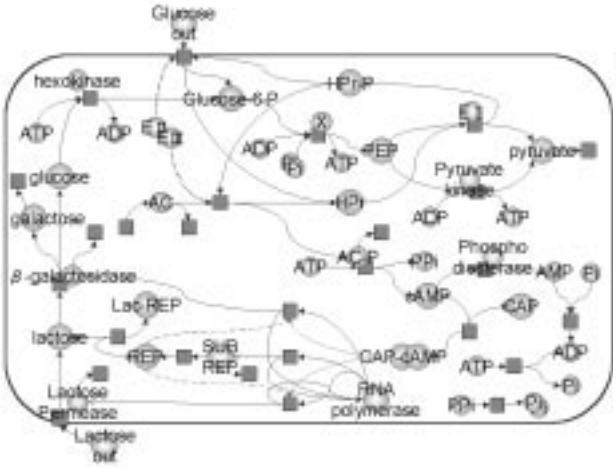

Figure1: The integrated model of the *lac* operon and glycolysis

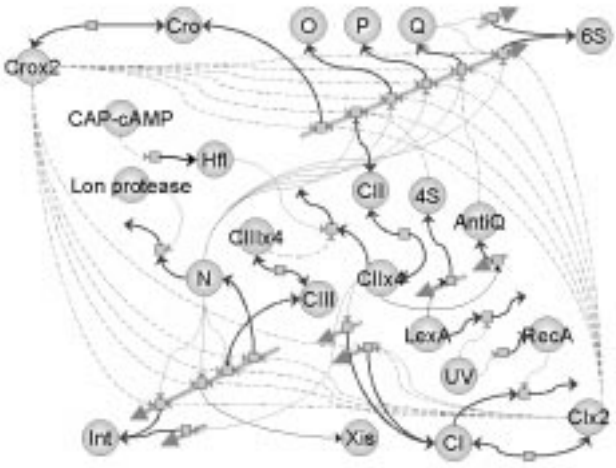

Figure2: The lytic-lysogenic switch network of bacteriophage λ

2 *E. coli*'s *lac* operon and *ara* operon

Based on the framework described above, we have modeled gene regulation systems of the *lac* operon and the *ara* operon in *E. coli*. We are currently integrating the *lac* operon model with the glycolysis pathway (Fig. 1), so that we can simulate *E. coli*'s sugar metabolism and regulation with lactose and glucose. The *ara* operon model is also being integrated with the pentose phosphate cycle. Results of these simulations will be compared and analyzed with experimental data reported in the literature [3].

3 Lytic-lysogenic switch network of bacteriophage λ

As a more complex gene regulation system, we are modeling the lytic-lysogenic switch network of bacteriophage λ (Fig. 2). The model of the lytic-lysogenic switch network includes the effects of glucose deprivation, ultraviolet light, and multiplicity of infection (MOI).

Since the E-CELL system allows the user to easily substitute individual reactions, several variations of gene expression models of bacteriophage λ reported in the literature [4, 5] will be constructed and compared using the E-CELL system.

Acknowledgments

This work was supported in part by Japan Science and Technology Corporation, Eizai Research Institute and a Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science, Sports and Culture of Japan.

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