

Computer Simulation of Gene Expression by Cell-cell Interaction Involved in Development of *Drosophila*'s Eye

Mineo Morohashi¹ Hiroaki Kitano²
moro@aa.cs.keio.ac.jp kitano@csl.sony.co.jp

¹ Department of Computer Science, Keio University
3-14-1 Kohoku-ku Hiyoshi, Yokohama 223, Japan

² Sony Computer Science Laboratory Inc.
3-14-13 Higashi-Gotanda, Shinagawa-ku, Tokyo 141, Japan

Abstract

*In this paper, we describe an overview of a computer simulation system which is designed to simulate the gene expression, and their interaction during development of *Drosophila*'s eye. There are numbers of genes which involve in the development of eye, and each of those have been well investigated by biologists. Using the simulation, we consider that complex dynamics of specific cascades of genes can be investigated in detail, and possibly enable us to shed lights on currently unclear interactions.*

1 Introduction

In the field of developmental biology, large amounts of knowledge have been accumulated by various kinds of biological experiments [1]. While these efforts have continued to provide more detailed data, we shall move forward to obtain more integrated understanding of biological phenomena. We believe that well designed computer simulation combined with other powerful computational technique provides viable approach. Synthesizing the fraction of data, it would be possible to observe the phenomena from macro viewpoint. Besides, when we would like to see the effect of hypothetical elements or functions, we can observe how it goes, immediately, by embedding them into the simulation. As a part of Virtual *Drosophila* Project [2], our aim is to develop the powerful computer simulation which synthesizes all knowledge acquired from biological experiments, and from which new prediction or mechanism can be denoted.

2 Development of *Drosophila*'s Eye

The structure of the compound eye is highly organized, and composed of 800 units referred to as ommatidia. Each of these ommatidia consists of 20 cells, namely, photoreceptor cells(R1–R8) and other accessory cells(pigment cells, and cone cells) [4].

Neuronal differentiation in the eyes starts during the third instar larval stage in retinal epithelium, i.e. eye imaginal disc. The morphogenetic furrow, a dorso-ventral indentation, sweeps from the posterior part toward anterior side. In the posterior part of the furrow, cells begin to differentiate and assemble into preclusters and express neuron-specific antigens [3]. During differentiation, communication between cells is mediated by various kinds of signals. One of them can be referred as lateral inhibition mediated by Notch and its ligand Delta.

3 Modeling

Our modeling is based on cell-cell interaction model. Modeling is on the gene cascade, during differentiation of the eye. As an initial phase, we simulate the interaction between about 10 genes, i.e. atonal,

argos, spitz, notch, delta, DER, E(spl)-C, seven-up, BarH1/H2, rhomboid, etc. When activators and repressors compete for one gene Z, the further amount of the Z product is determined by an inequality below:

$$\frac{\sum_i R_A(\text{gene}_i) \times \text{amount}(\text{gene}_i)}{\sum_i R_A(\text{gene}_i) \times \text{amount}(\text{gene}_i) + \sum_j R_R(Y) \times \text{amount}(\text{gene}_j)} > \text{Threshold}(\text{gene}_Z) \quad (1)$$

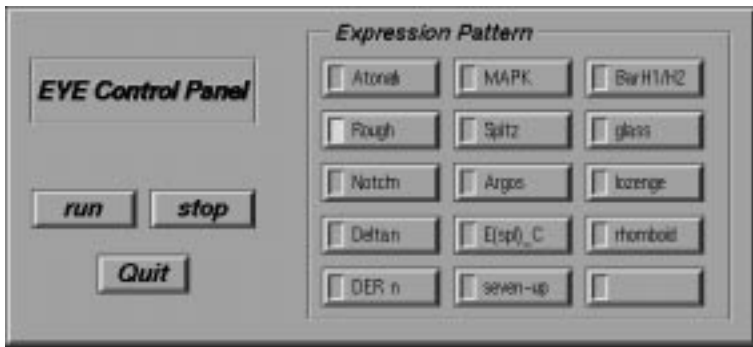
```

if (1) is true then add_amount(gene_Z)
else nothing

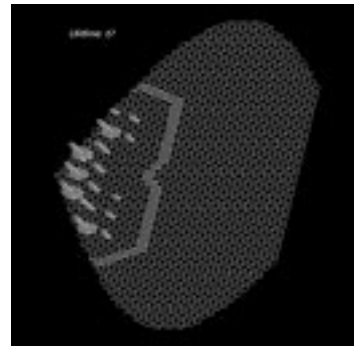
```

where $R_A(X)$ and $R_R(Y)$ the activate and inhibit rate of gene X and Y, and $\text{amount}(X)$ and $\text{amount}(Y)$ is the amount of X, Y gene product, respectively.

Each of cell's shape is simulated as hexagon, thus it has 6 cells surrounded. In order to observe the expression pattern of genes, we arranged about 2,500 cells. Since the regulation in transcription/translate level has not quantitatively analyzed yet, currently we focus on how the genes, involved in development of *Drosophila's* eye, interact each other inside the cell or among cells.



(a) Control Panel



(b) Expression pattern

Fig.1: Simulation image¹

4 Summary

We designed a computer simulation system, which simulates dynamics of gene cascade during development of *Drosophila's* eye. So far, we have implemented the simulation which involves the interaction among 10 genes cascade. As a next phase, we have a plan to integrate a system so that we would make sure whether a certain hypothetical cascade or element, which we assume, is relevant or not.

References

- [1] Gilbert, S.F., *Developmental Biology*, (Fourth Edition), Sinauer Associates, Inc., 1994.
- [2] Kitano, H., Hamahashi, S., Kitazawa, J., Takao, K., and Imai, S., *Virtual Biology Laboratories: A New Approach of Computational Biology*, *Proc. of Fourth European Conference on Artificial Life*, 274–283, 1997.
- [3] Tomlinson, A. and Ready, D.F., *Neuronal Differentiation in the Drosophila Ommatidium*, *Developmental Biology*, 120:366-376, 1987.
- [4] Yamamoto, D., *Molecular Dynamics in the Developing Drosophila Eye*, Springer-Verlag, 1996.

¹Computer graphics image of the simulation. We have been developing it on UNIX system, using C++ with OpenGL library. As current version of the simulation, we can look on expression pattern of each gene of wild-type.