Simulation of the Pattern Formation in Multicellular Organism by Genomic Object Net

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1 Introduction

Genomic Object Net (GON) is a powerful simulation tool for representing biopathways [2, 4]. In this study, by using GON, we constructed Delta-Notch mechanism [1], which is working in a pattern formation of multicellular organism. In the simulation, the number of the neural precursor cells increases when the value of Notch signal decreases, which is thought to represent the situation of Notch mutation. Thus, GON was proved to be useful for representing gene regulatory network of the pattern formation of multicellular system.

2 Delta-Notch Lateral Inhibition Mechanism

Delta protein is a transmembrane protein and works as a ligand for Notch receptor of adjacent cells. Binding of Delta ligand to the Notch receptor activates Notch signaling cascade, resulting in repression of Delta in the Notch-active cells. Conversely, Notch cascade is suppressed in Delta-expressing cells by Delta protein. This intricate cell-to-cell interaction is called "lateral inhibition", and is essential for segregating a small number of neural precursor cells from equipotent ectodermal cells.

3 GON Modeling

In wild-type embryos, about four neural precursor cells are detected per one hemisegment (Figure 1 (a)), whereas more than ten neural precursor cells differentiated in Notch mutant embryos (Fig. 1 (b)), as a consequence of low activity of Notch.

We have constructed a gene regulatory network (Figure 2(a)) of Delta-Notch lateral inhibition system by using GON Assembler [2], and analyzed the differentiation of neural precursor cells in wild-type and Notch mutant embryos of *Drosophila* by observing behavior of Notch concentration through GON Visualizer (Figure 2(b)) [3].

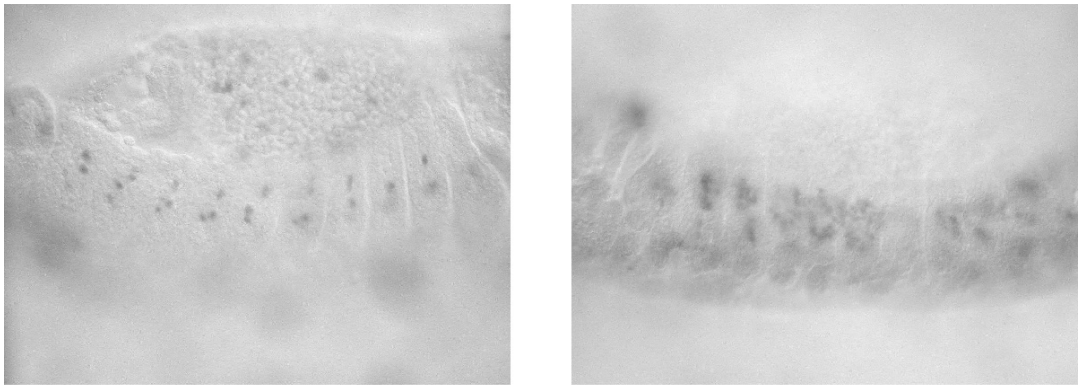

Figure 1: Lateral inhibition in *Drosophila*.

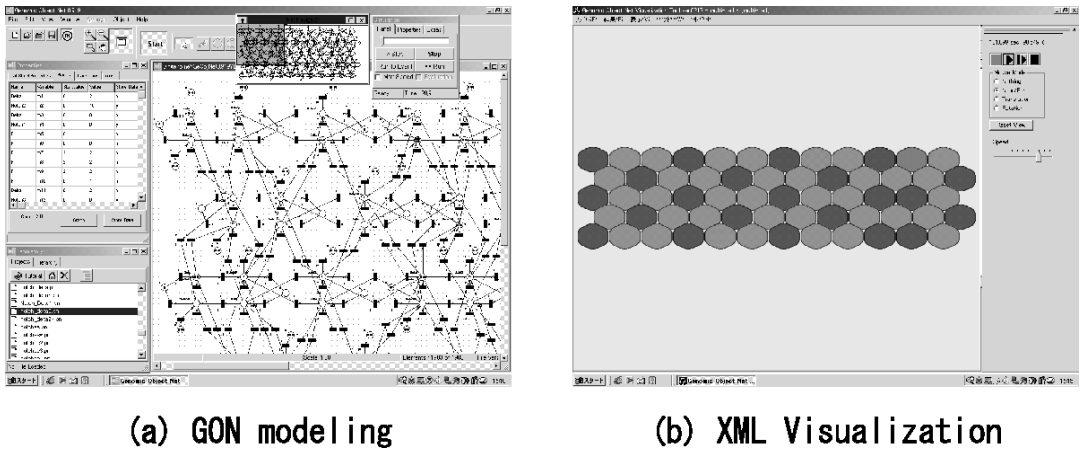

Figure 2: GON Assembler and GON Visualizer.

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[3] Matsuno, H, Doi, A., Hirata, Y., and Miyano, S., XML documentation of biopathways and their simulations in Genomic Object Net, *Genome Informatics*, 12, 2001.

[4] http://GenomicObject.Net/