A Simulation Tool for Regulatory Network of Gene Expressions in the Patterning of Multicellular Organisms

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1 Introduction

Detailed knowledge has rapidly been accumulating on the regulatory network of gene expression in patterning of multicellular animals. With the expansion of knowledge, it is getting more and more difficult to understand and predict the working of gene regulatory networks. Usage of some simulation tool would be inevitable to improve thinking of researchers of gene regulatory networks, though only a few simulation methods have been proposed for multicellular systems [1]. We constructed a simulation tool for gene regulatory network in developing multicellular animals. Intracellular regulatory network was constructed by the Petri net [2]. Working of the network in individual cells of multicellular system is coordinated by a modeling system for extracellular signalings, with visual interface whose operation and presentation are designed to be familiar and easy to biologists.

2 System Architecture

The system consists of two parts. One is the intracellular regulatory network module (Fig. 1A). This part of the system is constructed by the Petri net, which has successfully been exploited for modeling of gene regulatory network in single cells [2]. To coordinate working of the network of constituent cells of multicellular system, we constructed a modeling system for extracellular signalings, “multicellular signaling module (MSM)” . In MSM, various spatial distribution pattern of cells is defined. Extracellular outputs of signalling molecules from individual cells are collected and calculated, and values of signalling inputs are returned to each cell (Fig. 1B). Various calculation methods, ranging from precise reaction-diffusion equations to simple assignments of values from arbitrarily-delineated concentration gradient curve, could be applied to MSM.

3 Simulation of a Delta-Notch Patterning

In this paper, a simulation of Delta-Notch patterning is presented. An epithelial cell sheet composed of 100 cells is defined and analysed. Intracellular regulatory network is composed of five genes (Fig. 2A). Signaling of Delta protein is defined so as to make the protein act only on adjacent cells (Fig. 2B). Status of activity of each gene is represented by color intensity in each window. Stable spacing patterns of gene activation were obtained, but the pattern were always somewhat irregular (Fig. 2C). Although further optimization is necessary to refine the simulation, this system will be a powerful tool to help thinking of complicated networks of gene regulation in multicellular systems.
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References
