

Emergence of mosaic and regulative developmental mode by a gene regulatory network model with interacting cells

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Short Abstract — In animal development, there exist two distinct modes, known as mosaic and regulative. How do these different modes emerge from underlining gene network and intercellular interaction? We answer this question by simulating a gene regulatory network model of interacting cells for development, and evolving the network via genetic algorithm to have a given number of cell types. We find that the two developmental modes emerge as a result of evolution, where regulative (mosaic) mode is characterized by higher (lower) diversity in the developmental paths to reach each cell type, and larger (smaller) robustness of development to noise, respectively.

Keywords — genotype-phenotype relationship, developmental mode, cell differentiation, mosaic development, regulative development, gene regulatory network model

I. INTRODUCTION

Animals develop from an egg to an adult to generate many different cell types, where each cell fate is successively determined through the developmental course. Concerning the cell fate determination process, two distinct modes are known to exist in animal development. One is mosaic development in which cell fates are mainly determined cell-autonomously, and the other is regulative development in which intercellular communication is essential to the cell fate determination. How these modes emerged in the course of evolution and how the differences of these modes are characterized in gene expression dynamics, however, remain to be an open problem. These differences should come from the architecture of underlining genetic network and intercellular interactions that organize the development. By use of computer modeling, we study these problems through evolutionary simulations of a gene regulatory network with cell-to-cell interaction, in particular from the standpoint of genotype-phenotype relationship.

II. RESULTS AND DISCUSSION

We construct and analyze a gene regulatory network model of interacting cells. The model consists of M cells that each

cell has N genes, which are represented by their expression patterns $\mathbf{X}^{(k)}(t) = (x_1^{(k)}(t), x_2^{(k)}(t), \dots, x_N^{(k)}(t))$, ($k = 1, 2, \dots, M$) at time t . Each gene $x_i^{(k)}(t)$ takes a discrete value, 1 if the gene is expressed, or 0 if not. Temporal change in gene expression follows a gene regulatory dynamics with stochasticity: The probability that a gene i is expressed at the next time step is given by the equation

$$P(x_i^{(k)}(t+1) = 1) = f\left(\sum_j^N J_{ij} x_j^{(k)}(t) + c \sum_m^M \sum_j^N J'_{ij} x_j^{(m)}(t)\right),$$

where the matrix J and J' represent an intracellular gene regulatory network and an intercellular signaling network, respectively. For all of M cells, identical matrices J and J' are used, while c gives a parameter controlling the strength of intercellular coupling. The matrix J and J' determined the gene expression dynamics and the final developmental state.

We are here concerned with the evolution of networks (J and J') to have many different cell types coexist at a final stage of developmental, where the cell type is defined by its gene expression pattern. Here we evolve the networks by adopting the genetic algorithm with a fitness to have a given number of cell types at the end of development.

Analysis of evolved network in the model demonstrates the successive cell differentiation process as in the present animal development. We characterize the process in terms of the diversity of gene expression trajectories that ended the same cell type. Accordingly, developmental modes are classified into mosaic-like and regulative-like development, by low and high diversity respectively.

Next, we investigate the difference in robustness in the developmental dynamics between the two modes. By randomizing the initial condition of the model and examining if the final state is disturbed or not, we analyze the robustness against the perturbation to initial condition. It is shown that networks with the regulative-like mode have robustness of the final state against the change in the initial gene expression pattern, while those with the mosaic-like mode are more sensitive to the initial state.

To sum up, we have shown that the two developmental modes emerge as a result of evolution in our model, which correspond to regulative and mosaic modes observed in the present animal development. We also hope to discuss evolutionary change in these developmental modes and robustness against mutation, as well as the evolutionary landscape.

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