Emerging Cell Array based on Reaction-Diffusion

Shuhei Miyashita
Department of Informatics
University of Zurich
Andreasstrasse 15
CH8050 Zurich, Switzerland

Satoshi Murata

Tokyo Institute of Technology
4259 Nagatsuta, Midori
Yokohama, 226–8502 Japan

Abstract

This paper demonstrates self-replication and self-organization phenomenon based on reaction-diffusion mechanism by computer simulation. The simulation model consists of one dimensional cell array. Each cell contains two kinds of chemical substances - activator u and inhibitor v - that can generate reaction-diffusion wave, which is a spatial concentration pattern. The cells are supposed to be divided or be deleted depending on its concentrations of chemical substances. As we tried several kinds of diffusion coefficients to the model, in some simulations, self-replication process and generating cell array with metabolic process were observed. By applying division rule and apoptosis rule, cell arrays duplicate itself oscillating two states, that is, self-replication process were observed. And by applying division rule and annihilation rule, a cell array that has stable length is generated changing its cell components, that is, generating cell array with metabolic process were observed. Surprisingly, these two phenomena are realized independently of the initial number of cells.

1 Introduction

Self-replication and self-organization abilities of multicellular organisms are one of the most fundamental characteristics that discriminate creatures from non-creatures. As each cell contains the same genome, this feat is realized in a distributed and autonomous way with the absence of centralized control. However, no matter how big progress has been made in molecular biology over the past few decades, overall picture of principles behind the spatiotemporal dynamics of these processes is still lacking.

In 1952, A.M.Turing advocated a reaction-diffusion mechanism and suggested that the reaction-diffusion mechanism, which is a kind of spatial concentration pattern, plays a key role in forming a periodic shape on a small creature called hydra [1]. L.Wolpert suggested a concept of positional information when he thought that all identical cells should recognize their own position in order for the cells that had identical gene [2]. C.G.Langton built a cellular automata model of self-replication (SRloops) on a two dimensional cell array [3]. As the model consists of discrete internal state with finite state automata, it is not easy to relate this models to the biological cell. K.Tomita et al. created graph automata, which enable description of dynamic topological change of cell network, [4]. They extended the concept of cellular automata to certain graphs of cells. This model is able to describe morphological change such as cell division or cell death. But little attention has been given to a relation between morphogenetic process and reaction-diffusion mechanism.

2 Model

2.1 Reaction-diffusion

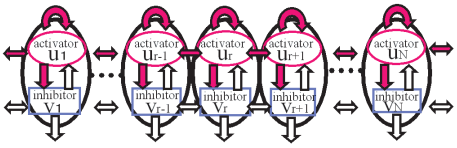

Figure 1: One dimensional cell array.

In this research, one dimensional cell array model was chosen for simplification. Fig.1 is a schema of the model. These nodes represent cells containing two kinds of chemical substances - activator u and inhibitor v - that can generate reaction-diffusion wave. These two chemicals react each other and diffuse to neighboring cells according to its concentration gradient.

$$\begin{aligned} du_r/dt &= +5u_r(t) - 6v_r(t) + 1 \\ &\quad + D_u\{u_{r-1}(t) + u_{r+1}(t) - 2u_r(t)\} \quad (1) \\ dv_r/dt &= +6u_r(t) - 7v_r + 1 \\ &\quad + D_v\{v_{r-1}(t) + v_{r+1}(t) - 2v_r(t)\} \quad (2) \end{aligned}$$

The reaction-diffusion model that we use is the same as Turing's, which is expressed as partial differential equations (1), (2). Where, u_r and v_r represents the concentration of activator and inhibitor, respectively with subscript r as an identification number. D_u and D_v represent diffusion constants of activator and inhibitor, respectively ($D_u = 0.7, D_v = 1.2$). To the system, Dirichlet boundary conditions were applied, which set the chemical concentration at the boundary to zero. The initial concentrations are set as equilibrium point $(u, v) = (1.0, 1.0)$.

2.2 Cell cycle and cell differenciation

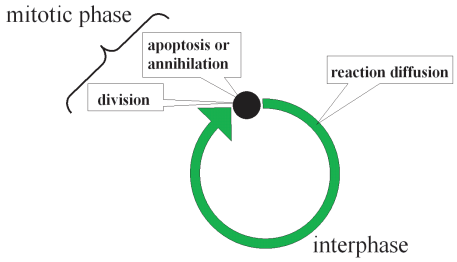

Figure 2: Cell cycle.

Since cell cycle is determined by various factors, in this paper, cell cycle is supposed to be generated synchronously. Fig.2 represents the cell cycle of the model. Every cell has interphase and mitotic phase in the cell cycle. In mitotic phase, reaction and diffusion of the chemical substances take place. In interphase, cells are differentiated depending on the concentrations (see below).

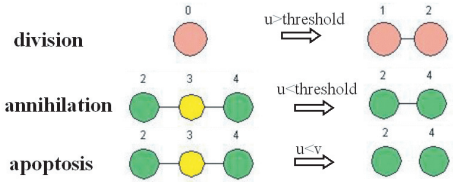

Figure 3: Cell differenciation.

Fig.3 shows cell differentiation rules. Cell division (top) is took place when the concentration of activator becomes larger than specific threshold (division threshold set as 1.5) in mitotic phase. The cell is divided into two cells, and the concentration of each chemical substance right before division is applied to the concentration of the cell divided. Contrary, annihilation rule (middle) is activated when the concentration of activator becomes smaller than another specific threshold (annihilation threshold set as 1.0) in mitotic phase. In this rule, the cell is deleted but the cell connections of both sides are kept connected. Apoptosis rule (bottom) is similar to the annihilation rule, which is activated when the concentration of activator becomes smaller than that of inhibitor in the same phase. The system is divided into two separate groups by the cell deletion. Every differential equation is integrated by the Runge-Kutta method ($\delta t = 0.01$, 1step=$100\delta t$, 1 interphase corresponds to 150 steps).

3 Simulations and Results

In the computer simulations, equations (1), (2) and cell differentiation rules are simulated synchronously according to the cell cycle.

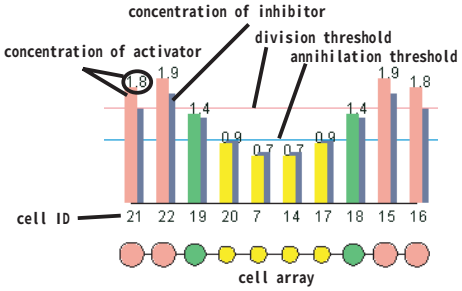

Figure 4: Simulation model.

Figure 4 shows the simulation model. Bars above each cell represent the concentrations of activator and inhibitor. The concentrations of activator is displayed front and that of inhibitor is displayed behind. Values of the concentrations of activator is presented on each shoulder of bar. division threshold, annihilation threshold and identification numbers of cells are also listed.

3.1 Self-replication process

In this model, division rule and apoptosis rule are applied in mitotic phase. Fig.5 shows self-replication process when we settled one cell as an initial condition. In the first stage, cell divisions are repeated two times in mitotic phase and the initial cell grows into 8 (#1 - #4). Then apoptosis rule is activated and four cells positioned at the center (cell 8,13 at #4) are deleted and four cells at the side (cell 9,10,11,12 at #4) are divided. Consequently, the system duplicates itself oscillating between state #5 and #6.

Fig.6 shows the case that the number of initial cells is larger than the oscillating number 10 (#7). The phenomenon that final state converges to the state #5 and #6 are observed.

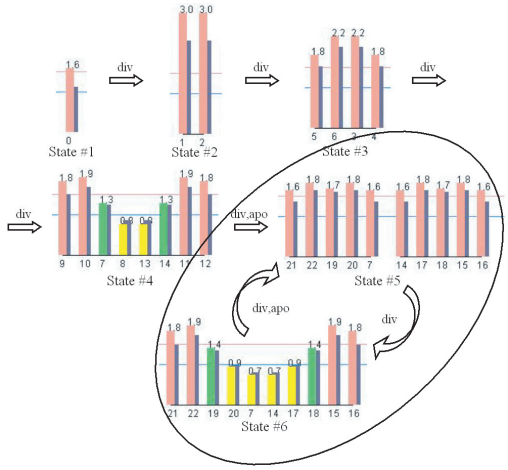

Figure 5: A self-replication process from one cell.

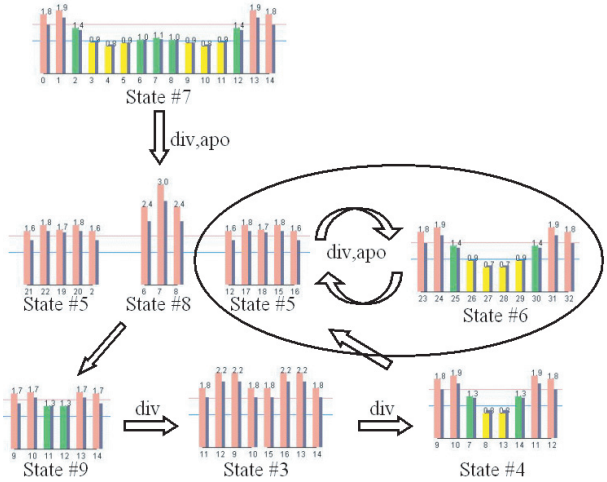

Figure 6: A self-replication process from 15 cells.

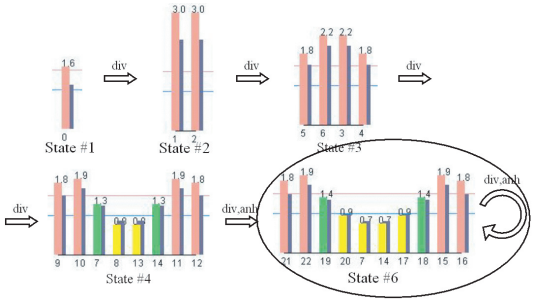

Figure 7: A generating cell array with metabolic process from one cell.

3.2 Generating cell array with Metabolic process

Division rule and annihilation rule are applied in mitotic phase. Fig.7 shows that the number of cells increases and the number finally becomes to 10 according to the cell division rule. In the mitotic phase at state #6, four cells positioning at the center (cell 20,7,14,17 at #6) are annihilated. And other four cells (21,22,15,16) at the sides are divided. At the end, the number of cells is kept stable to the fixed number, 10. The system perpetually produces new cells replacing some old cells.

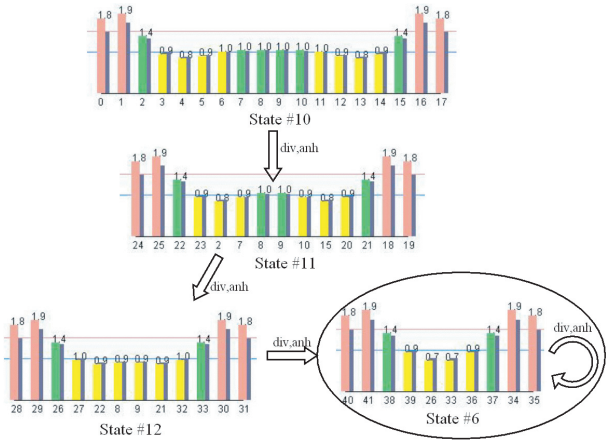

Figure 8: Generating cell array from 18 cells.

In order to investigate stability of the process, 18 cells are set for a initial state. Fig.8 shows the number of cells finally converges to the same pattern (#6).

4 Discussions

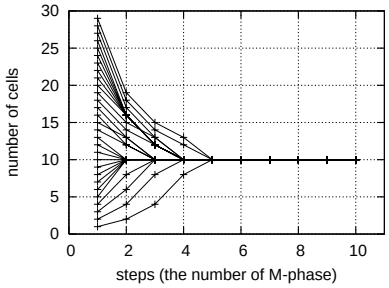

Figure 9: The number of cells transition graph.

In addition to the simulation 3.2, we settled different number of cells as a initial condition and showed

the results in Fig.9. The X-axis represents the number of passed mitotic phases and Y-axis represents the number of cells. The figure shows that the length of all cell arrays which start from 1 cell to 30 cells finally converge to 10. This suggests not only that we can settle variable numbers of cells for a initial condition (at least 1 to 30) but also we can cut any cell connections as we want which leads to generate two cell arrays consisting of same size, 10.

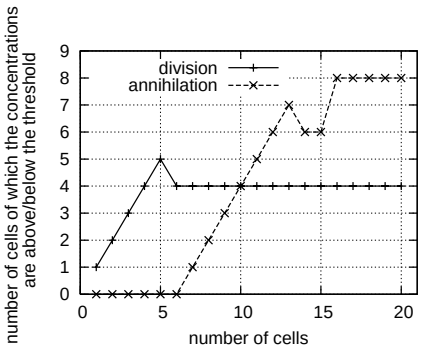

Figure 10: Exceed threshold graph.

Since patterns of reaction-diffusion waves are seem to be unique to the length of cell arrays especially the length is short, we counted the number of cells which exceed division threshold and which are below annihilation threshold in the first mitotic phase. The X-axis in Fig.10 represents the number of cells, and Y-axis represents the number of cells of which the concentrations are above (or below) the threshold. As the figure indicates, When the number of cells is less than 9, the number of cells that the concentration exceed division threshold is larger than that the concentration are below annihilation threshold. That is, the length becomes short in the next mitotic phase. And when we settle the number of cells more than 11, the other way round. This figure clearly shows that the length of the system converges to 10.

Fig.11 represents the number of cells when mitotic phase passed ten times in different diffusion coefficients. Initial number of cells were settled from 1 to 30 for each parameter sets. X and Y axis represent diffusion coefficients Du and Dv, respectively and Z axis represents the number of cells. As it can be seen, the system doesn't always converge to one state and though the system shows its robustness for external disturbances in adequate diffusion coefficients, the ranges of these parameters are narrow.

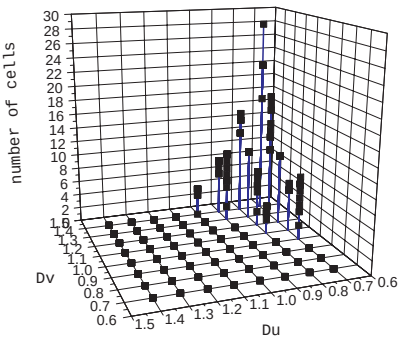

Figure 11: The number of cells in each parameter sets.

5 Conclusion

In conclusion, two fundamental organic behaviors, that is, self-replication process and generating cell array with metabolic process were observed by applying reaction-diffusion mechanism on distributed space. In self-replicaion process, a phenomenon that cell arrays duplicate itself oscillating two states were observed. And in generating cell array with metabolic process, a phenomenon that a cell array which has stable length is generated changing its cell components were observed. This research shows posibilities that reaction-diffusion system plays some roles in controlling these vital activities of living things.

Acknowledgment Many thanks to Peter Eggenberger Hotz for helpful suggestions. This research is supported by the Swiss National Science Foundation, project #200021-105634/1.

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