

# Simulation of cell-like self-replication phenomenon in a two-dimensional hybrid cellular automata model

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## Abstract

An understanding of the generalized mechanism of self-reproduction is fundamental to applications in various fields, such as the mass-production of molecular machines in nanotechnology. We have developed a model for the simulation of cellular self-reproduction in a two-dimensional cellular automaton, and we have demonstrated that the following three functions can be realized: (1) formation of a border similar to a cell membrane, (2) self-replication while maintaining carrier-containing information, and (3) division of the cell membrane while maintaining the total structure. Furthermore, we have constructed a hybrid cellular automaton model. To reduce the number of transition rules, we considered not only the state transition rules but also the concentration diffusion in the Gray Scott model, in which the self-reproduction phenomenon emerges under certain parameters.

## Introduction

An understanding of the generalized mechanism of self-reproduction is considered fundamental to applications in various fields, such as the mass-production of molecular machines in nanotechnology and artificial synthetics in biology (synthetic biology). Furthermore, it is difficult to construct large, complex machine systems that exceed a certain size, using a top-down approach. Therefore, such complex systems must be constructed using a bottom-up approach based on the phenomenon of biological self-organization. Thus, it is crucial to elucidate not only the details of real cellular reaction networks but also the conditions necessary for self-organized and self-replicating cells.

A system that can simulate the self-reproduction of a cell must fulfill the following requirements. 1) It can express phenomena of nanolevel molecular behavior such as the Brownian movement. 2) It can express a chemical reaction system. 3) It can express the shape (difference in reaction process according to the shape) of compounds such as proteins. 4) It can express the emergence of macro shape and function for a bottom-up approach. For such a calculation, a particle system model is a potentially superior option.

Fifty years ago, von Neumann (1966) initiated a study on self-reproduction models from a mathematical viewpoint. His study theoretically proved the possibility of constructing a self-reproducing machine using cell states and the transition rules of two-dimensional square cells. However, von Neumann's

self-reproducing machine was large; therefore, it is difficult to implement this machine perfectly in a computer system (Mange, 2004). In 2010, Hutton (2010) implemented and simulated over its entire replication cycles. Later, Langton (1989) developed a simple machine capable of self-reproduction, by abandoning the completeness of von Neumann's machine; although its shape was quite simple and it could reproduce specific shapes, the rules of transition were complicated. The derivation of transition rules using genetic algorithms has been investigated (Reggia, 1998)(Sipper, 1998); however, it is difficult to derive the generalized rules.

Historically, researchers have attempted to develop a mathematical model to simulate the morphosis of living matter. Studies on the reproductive models of a body surface design, namely, the Turing model (Turing, 1952), and those on the leaf vein pattern of a plant (Feugier, 2005) and mollusk shell patterns (Meinhardt, 2003) are examples of previous research. In addition, many researchers have used a cellular automaton model to study tissue or tumor growth. Although these models can simulate a number of features of biological self-reproduction on a computer, they cannot reproduce the entire body on the basis of unified equations and rules, such as cytodifferentiation by gene expression→morphosis of cells→organogenesis→emergence of function.

In our previous study (Ishida, 2010) we developed a model for the simulation of cellular self-reproduction in a two-dimensional cellular automaton. We demonstrated that the following three functions could be realized by the transition between two adjacent cells.

- (1) Formation of a border similar to a cell membrane.
- (2) Self-replication while maintaining carrier-containing information (information carrier).
- (3) Division of the cell membrane while maintaining the total structure of the cell.

In this study, we demonstrate the self-reproducing ability of a shape that is similar to that of a real living cell. Figure 1 shows the results of a cell-type self-reproducing two-dimensional cellular automaton. It is important to note that the objective of this study is not to clarify all the necessary and sufficient conditions for self-reproduction. Instead, we consider the possibility of simulating self-replication in a real dynamic chemical reaction environment by applying the transition rules determined in this study. A similar previous studies by Ono, Ikegami (2000), and Hutton (2007). Ono & Ikegami does not completely lead to the replication of the

same cell. Hutton's work involves self-reproduction that does not include information carriers such as genes. The latter point indicates the novelty of the present study.

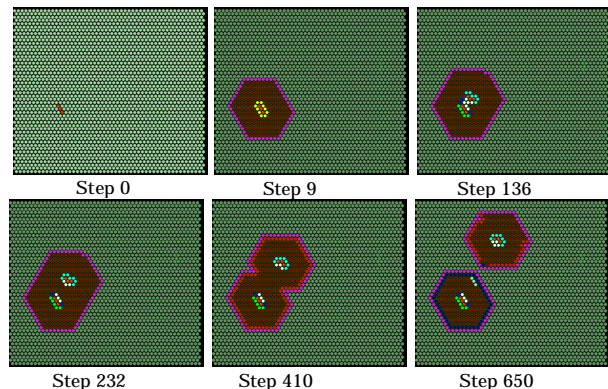


Figure 1 Results of a cell-type self-reproducing two-dimensional cellular automaton (Ishida, 2010)

## Objective

In this study, we constructed a hybrid cellular automaton (CA) model. Figure 2 shows the outline of the hybrid model. To reduce the number of transition rules, we considered not only the state transition rules but also the concentration diffusion of the field. We chose the Gray Scott model (GS model) (Gray, 1984), in which the self-reproduction phenomenon emerges with certain parameters. In this hybrid model, information carriers trigger the self-reproduction phenomenon of the GS model, and a cell membrane is formed by a part of the specific concentration of the GS model. If a single cell is being simulated, cell membrane formation is possible using a linear diffusion equation. This is difficult to accomplish using a simple linear model, and the GS model is necessary to fill the space while multiple cells are adjacent to one another and to maintain the distance between them.

This model is new, and it can be combined with existing models, such as the reaction diffusion equation models in the CA model. We express a macromolecule system in the CA model, and we express the small molecule-based reaction system that constitutes a reaction diffusion model, because the calculations become enormous when we calculate the reactions of all the molecules.

The simulation of a real living cell was considered difficult to express with only two phases, but it was based on future development. Furthermore, because a simple chemical reaction system can be substituted for the GS model, it is thought that we can simplify the model in the future.

As shown in Figure 3, we arranged the transition rules in the CA model and the GS equation parameters in two-dimensional space in order to simulate the duplication of hereditary information carriers, the encapsulation of information carriers by a cell membrane, and maintenance of the shape of the membrane.

Cellular automata possess characteristics that can help us understand the association between transition rules and results so that a state is determined solely by the rules governing the

transition between adjacent cells. In addition, the cellular automaton model has already been applied to discrete particle simulation, as in the case of fluids. For these reasons, it is theoretically possible to apply the transition rules to chemical or particle-collision systems.

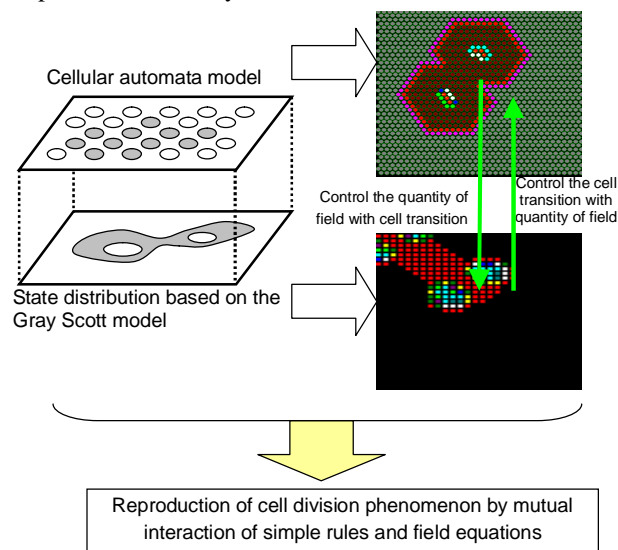


Figure 2 Outline of hybrid cellular automaton model

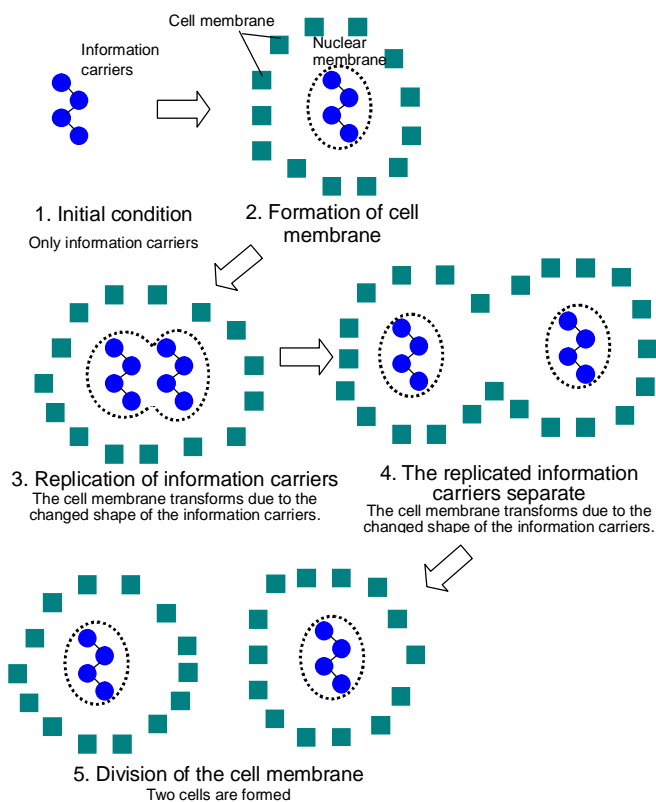


Figure 3 Conceptual diagram of cell-type self-reproduction in two-dimensional cellular automata

## Research Method

### Cellular automaton model

A two-dimensional hexagonal grid model was used in this study (Figure 4). Although square grids are typically used for two-dimensional cellular automata, a hexagonal grid model was used in this study for two reasons.

(1) In the case of a square grid, the state of an automaton in the next step is determined on the basis of the state of the cell itself and the states of the eight adjacent sites. This increases the number of transition rules, and consequently their complexity. In the case of a hexagonal grid, the state of the next step is determined by the state of the cell itself and the states of the six adjacent sites. This reduces the number of transition rules.

(2) Isotropy in the horizontal/vertical and diagonal directions is maintained in a hexagonal grid but not in a square grid.

The cell automaton was constructed according to the transition rules so that the state of the next step was determined by the state of the cell itself and the states of the six neighboring cells. Each cell had a state (0–19 states) and a direction (6 directions) as attributes.

0: State of non-being

1: States in which hereditary information carriers (Only states 1 and 2) have a directional attribute (any one of the 6 directions)). We can describe various types of information by creating subspecies (1-a, 1-b, etc.) for state 1.

2–10: States in which the nuclear membrane surrounds the hereditary information carriers

11–18: States that constitute space within the cell

19: States that consist of the cell membrane

In a hexagonal grid, the calculations start from a certain initial condition. As shown in Figure 5, the transition rules were divided into the following 4 phases: 1) state transition as regards cell membrane formation, 2) division of the information carriers, 3) movement of the information carriers, and 4) formation of a nuclear membrane surrounding the information carriers. In other words, we first applied the transition rules for cell membrane formation and settled the total states in all cells. Then, we applied the transition rules for the division of information carriers, after which we applied the transition rules for movement of the information carriers and formation of the nuclear membrane.

To induce objective state transitions of the cellular automata, we added transition rules to remove the unnecessary side effect reaction at the same time. We divided the

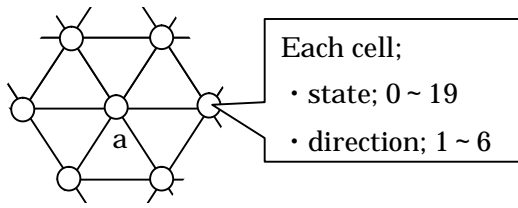


Figure 4 Hexagonal grid model used in this study

transitions into 4 phases to discover the transition rules, because discovery of the entire set of transition rules was difficult to achieve all at once.

### Gray Scott (GS) model

The cell transition patterns in this cellular automaton model resemble those of physical phenomena. Thus, we considered the possibility of replacing the transition rules with those of a non-linear quantity model such as the GS model. The equations for the GS model are given below. The self-replication patterns occur under certain conditions ( $D_u = 0.04$ ,  $D_v = 0.02$ ,  $F = 0.02$ , and  $k = 0.06$  in this study).

The initial concentrations of  $U$  and  $V$  assumed for the differential equation of the GS model were 1.0 and 0.0, respectively. This is a steady state in which there is no change in the concentration distribution. When there is a change in the concentration level in some spatial position, this triggers a dynamic change. When state 19 exists, the concentration distribution in the GS model in the same spatial position changes (from  $U = 1.0$  and  $V = 0.0$ , to  $U = 0.25$  and  $V = 0.35$ ). This unstable state leads to changes in the concentration distribution of the GS model.

On the other hand, as regards the action from the GS model to CA model, it is as follows. We calculated the ratio  $(500-U)/V$  of density  $U, V$  in the GS model and divided it into 10 parts between the minimums and the maximum of the value, and thus derived a potential level (1-10). A transition appeared in the CA model space when the condition appeared of a potential level shown in Table 4 on the GS model.

In addition, in the GS model, we can clarify the parameter set for when a self-reproduction design appears, but we cannot control the size of the self-reproduction design. Therefore, we adjusted the space scale of the CA model and the space scale of the GS model so that a cell membrane that encapsulated an information carrier was formed. The theoretical determination of the space scale method requires further investigation examination.

$$\frac{\partial V}{\partial t} = D_v \Delta V - U^2 V + F(1 - V) \quad (1)$$

$$\frac{\partial U}{\partial t} = D_u \Delta U + U^2 V - (F + k)U \quad (2)$$

### Transition rules

Each cell was renewed by the transition rules, and the state of the next step was determined by the state of the cell and the states of its 6 neighboring sites. The transition rules are presented in Tables 1–4. We have not yet discovered a method with which to derive transition rules automatically according to a uniform law. Therefore, we constructed transition rules step-by-step according to the movements of the automaton.

In this hybrid model, the information carriers first activate the GS model. Cell membrane states appear under certain concentrations of the GS fields. The movement of the nuclear membrane was controlled by the concentration of the GS fields.

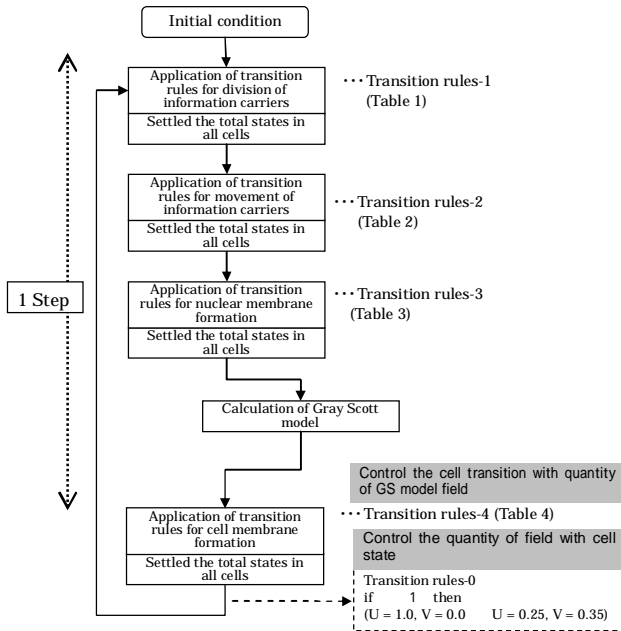


Figure 5 Calculation flow

### Initial conditions

Figure 6 shows the initial condition. The entire cell is in state 19. State 1 indicates the information carriers, three of which are arranged consecutively in the central part. The

intersection of state 19 and state 1 triggers the GS calculation. The purpose of this study is to find a minimum set of transition rules to achieve self-reproduction in a two-dimensional cellular automaton space. Our transition rule does not realize self-reproduction in any initial state.

## Results

Figure 7 shows the process of cell membrane formation and the process of the division of information carriers within the cell membrane. We carried out calculations for 101 steps; some of our results are shown in the figure. In each image in the figure, the upper part is the CA model and the lower part is the distribution of the potential level by the GS model. In this way, we were able to replicate the phenomenon of cell-like division.

Table 5 shows the number of transition rules for the cellular automaton model (Ishida, 2010) and the hybrid model. Using the hybrid model, we reduced the number of transition rules. In the case of the CA model, the transition rules to synchronize the cell-centered nuclear shape and the shape of the cell membrane were complicated. In the hybrid model, on the other hand, self-replication was possible with fewer rules, such that a cell membrane was formed on areas of a specific concentration. As compared with the CA model, the hybrid model is complicated in terms the calculation of the GS model; however, simpler rule description will be possible in the future because the GS model can replace the simple metabolism system.

Table 1 Transition Rule 1 (division of the information carriers)

	State	Direction	Transition of central cell (state)	Transition of central cell (direction)	Supplementary explanation	
1	3300311	11	2	5		
2	3300211	510	2	5		
3	3300211	511	2	5		
4	3303211	510	2	5		
5	3303211	511	2	5		
6	3003213	500	2	5		
7	3300322	55	1	6		
8	3303122	655	1	6		
9	3003123	650	1	6		
10	2213311	5560011	4	0		
11	2211411	5566011	4	0		
12	2211411	5566010	4	0		
13	2311413	5066000	4	0		
14	1133344	6600000	1	1		
15	1133144	6600100	1	1		
16	1333143	6000100	1	0		

Supplementary explanation of Table 1 and Table 2

State  
1 0 2 1 0 0 0  
Direction  
1 0 2 4 0 0 0

State and direction of each cell indicated by seven columns of progression in order of a - g from a central cell.

Table 2 Transition Rule 2 (movement of the information carriers)

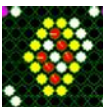
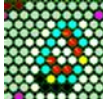
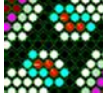
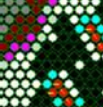
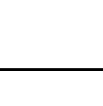
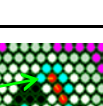
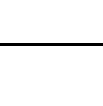
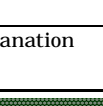
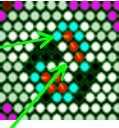
	State	Direction	Transition of central cell (state)	Transition of central cell (direction)	Supplementary explanation	
1	3300031	1	4	0	Control of DNA division	
2	8800041	1	4	0		
3	8800411	11	1	1		
4	1114844	1110000	4	0	movement of terminal	
5	1114444	1110000	4	0		
6	8808111	111	1	1		
7	1111444	1111000	4	0	Movement of middle cell	
8	8808111	110	1	1		
9	1111444	1011000	4	0		
10	8008116	100	1	0	Movement of middle cell ( in front of tip)	
11	1611445	1000	4	0		
12	8008118	100	1	0		
13	1811446	1000	4	0	Movement of tip	
14	1811448	1000	4	0		
15	1118844	1110000	4	0		
16	8611800	1000	1	0	continual movement of terminal	
17	1544116	100	4	0		
18	8811800	1000	1	0		
19	1644118	100	4	0	Movement of tip	
20	1844118	100	4	0		
21	8111808	11000	1	1		
22	1444111	1000110	4	0	Movement of middle cell	
23	8118008	110000	1	1		
24	1445811	1000011	4	0		
25	1448811	1000011	4	0	movement of terminal	

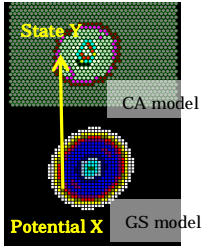
Table 3 Transition Rule 3 (formation of the nuclear membrane surrounding the information carriers)

	Central Cell	Conditions of six neighborhoods	Transition of central cell (state)	Supplementary explanation	
1	~	1		formation of the nuclear membrane	
2	~	1			
3	and (Potential Value = 7)	-			
4		1			
5	~	( < 1)and( 1)		nonessential removal between information	

·The circled number the state of the cell. (ex. indicates state 0, indicates state 1)

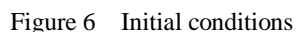
·Method of describing condition : e.g., " 1" indicates that there is more than one cell in state 1 among the six neighborhoods.

Table 4 Transition Rule 4 (formation of the cell membrane)

	Central Cell	Conditions of six neighborhoods	Transition of central cell (state)	Supplementary explanation	
1	Potential Value = 1or 2	-		formation of the cytoplasm	
2	Potential Value = 3or 4	-		formation of the cytoplasm	
3	Potential Value = 5	-		formation of the cell	
4	Potential Value = 6	-		formation of the cytoplasm	
5	Potential Value = 7	-		formation of the cytoplasm	
6	Potential Value = 8	-		formation of the constitutive space in the cell	
7	Potential Value = 9	-		formation of the constitutive space in the cell	
8	Potential Value = 10	-		formation of the cytoplasm	

·The circled number show the state of the cell. (ex. indicates state 0, indicates state 1)





CA model		Hybrid model	
Process	Number of transition rules	Alternate physical phenomenon	Number of transition rules
Application of transition rules for cell membrane formation	34	Gray Scott Model	8
Application of transition rules for division of information carriers	17	—	16
Application of transition rules for movement of information carriers	25	—	25
Application of transition rules for nuclear membrane formation	13	—	5
Total	89		54

In this study, we constructed a model of a hybrid cellular automaton model. Our model displayed self-reproduction in a cell-like shape with few state transition rules. To reduce the number of transition rules, we considered not only the state transition rules but also the concentration diffusion in the Gray Scott model, in which the self-reproduction phenomenon emerges with certain parameters.

Figure 8 shows the overall perspective of our artificial cell simulation. We believe that the transition rules of this model can be applied to the simulation of self-replication phenomena in a real dynamic chemical reaction environment. Initially, we plan to simulate cell division in a discrete particle reaction. It is relatively easy to replace state transition rules with collision/reaction rules of discrete particles. Next, we plan to simulate cell division in a continuous chemical reaction by converting discrete particles rules into chemical equations.

Ishida, T., (2011). Simulation of self-reproduction phenomenon of cells in two-dimensional hybrid-cellular automata model, The 16th International Symposium on Artificial Life and Robotics (AROB 16th '11), January 27-29, 2011, Beppu, Oita, JAPAN

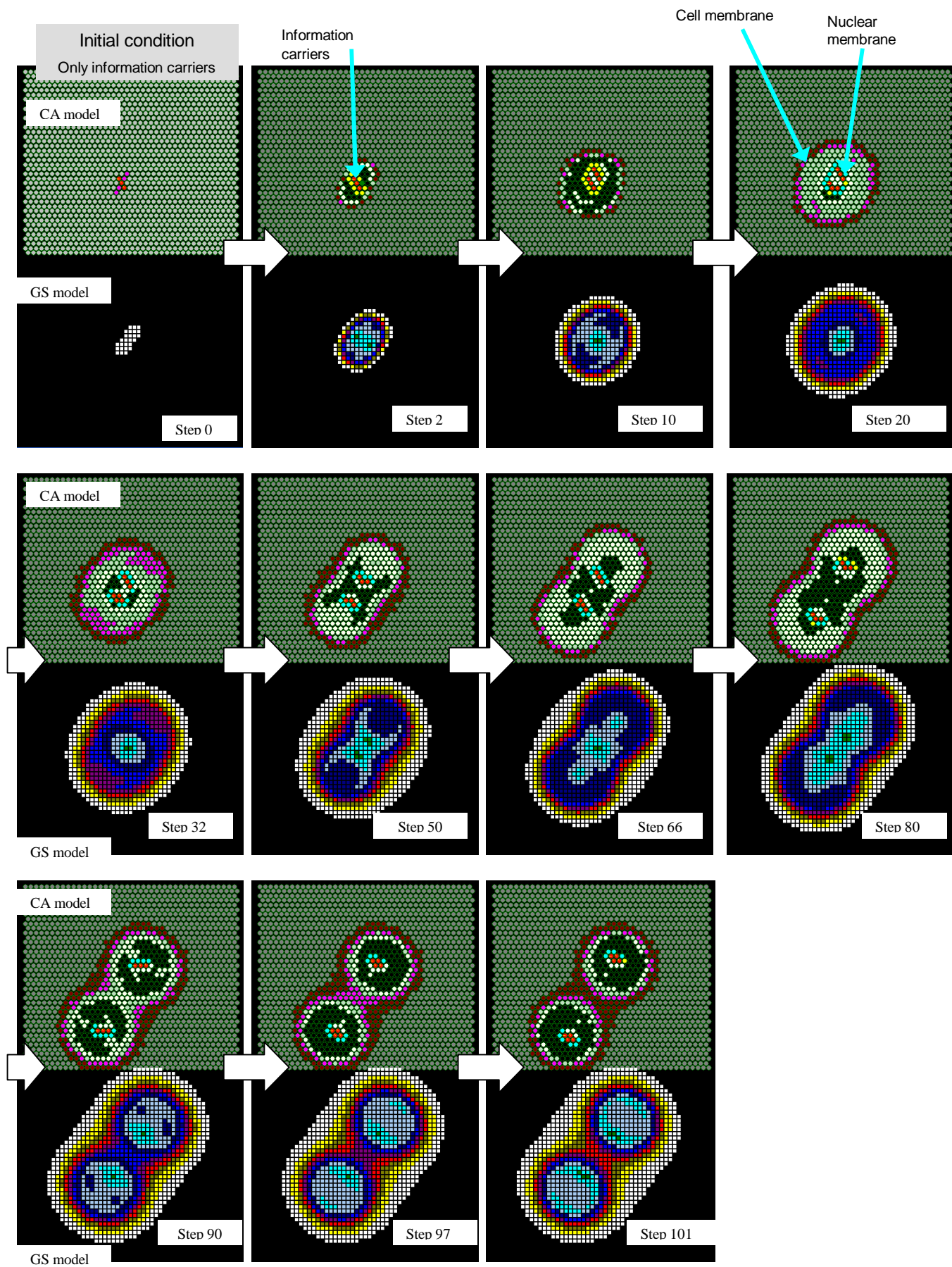


Figure 7 Results of hybrid cellular automaton model

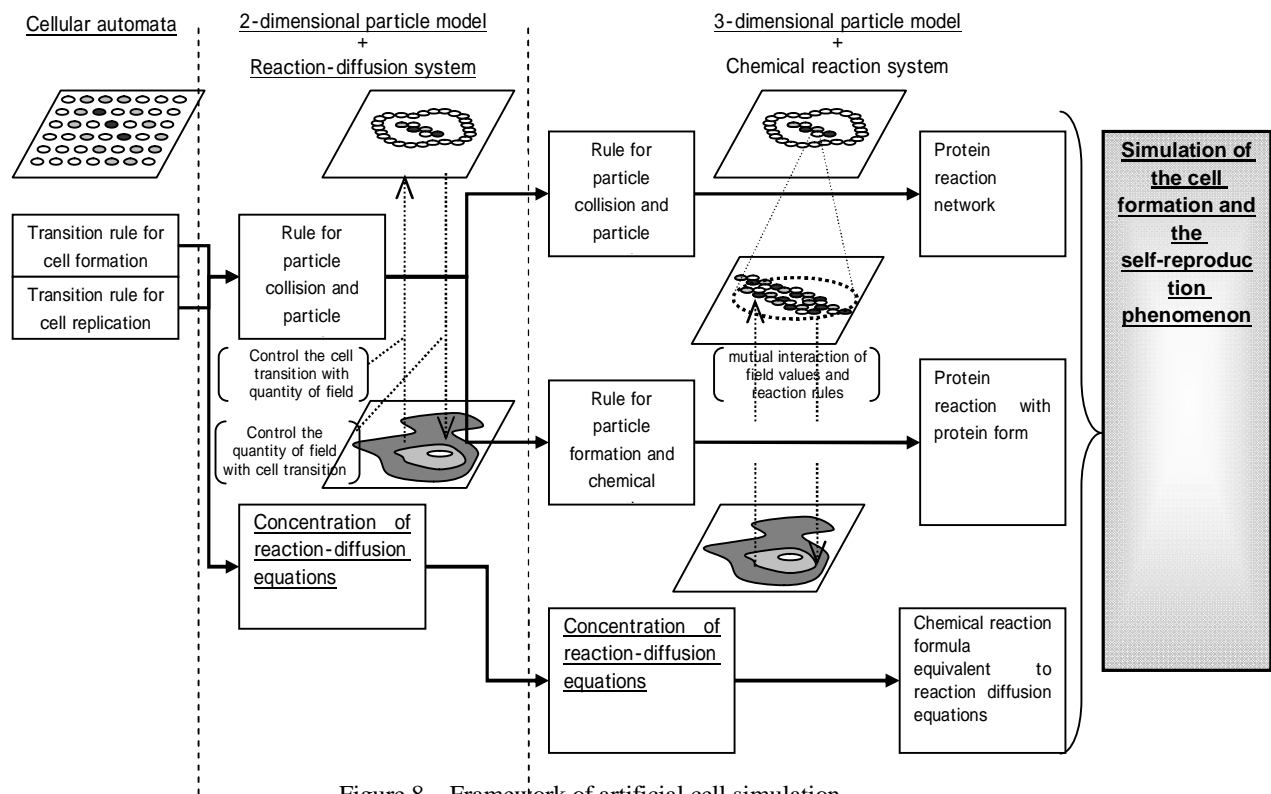


Figure 8 Framework of artificial cell simulation