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Self-maintenance and Self-reproduction in an Abstract Cell Model

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Living cells must maintain their membranes by active metabolism. The membrane is not static but a dynamic structure that has evolved along with its internal reactions. When we reflect on the emergence and evolution of primitive cells, we should not forget the mutual dependency between membranes and metabolic cycles inside the cell. In this paper, we present a simple abstract model of the self-maintaining cell. A metabolic cycle will produce a self-assembling membrane that will enclose the metabolic cycle. We show that a self-maintaining cell has the potential to reproduce itself spontaneously. Further, we have demonstrated two different ways of cellular reproduction depending on the mobility of chemicals. In the first case, a cell releases autocatalytic chemicals that create new cells outside the mother cell. In the second case, a cell grows larger and divides itself into daughter cells by creating a new internal dividing membrane.

1. Introduction

The acquisition of a membrane and the emergence of a cellular structure were major transitions in the early stages of life. Cell membranes have been studied as material structures, both experimentally and theoretically. For example, spontaneous formation of vesicles is known to exist for ensembles of simple molecules (e.g. long-chain fatty acids). It has also been demonstrated that vesicles of oleic acid/oleate can grow and replicate by autocatalytic hydrolyzation of the anhydride (Oberholzer *et al*., 1995). Theoretically, Rasmussen's cell model shows that the aggregation of amphiphilic trimers will result in the formation of micelles in water (Mayer *et al*., 1997). These may be a candidate for a primitive cellular structure.

The prerequisite of having membranes for autonomy of self-reproducing cell has been stressed from various aspects, but only a few theoretical studies treat the self-organizing aspect of cell membranes. For example, self-reproducing patterns has generally been analysed as a reaction–diffusion system, since Turing (1953) and recent development of this direction is seen in the Gray–Scott model (Pearson, 1993; Lee *et al*., 1994; Cronhjort & Blomberg, 1997). These series of studies show that a small spot of reactants will grow and divide into two. Other complicated spatial patterns are also discussed.

However, the essential property of the membrane may not be captured by simple dynamical systems approach, as stressed by Fontana & Buss (1994, 1996). They claim that changes and construction of the objects themselves (e.g. cell or membranes or any biological substances) are never treated in conventional dynamical systems. Only quantitative properties of fixed objects (e.g. cell numbers) are treated. But the quantitative

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properties are not equivalent to the objects themselves. A mathematical formalism which describes a motion of objects and the organization is required, which Fontana and Buss tried to build by using λ-calculus. In practice, they simulated a "λ-calculus flow reactor" (reactions of abstract molecules of some λ-expressions) to study an organization and maintenance of a certain set of λ-expressions; which gives invariant syntactical and algebraic structures. Those organizations are cell-like entities maintained not by physical but syntactic structures.

There are a few other approaches trying to handle the object concept in less-abstract models than λ-calculus to capture more self-organization aspect of membranes. Gánti (1975, 1997) has proposed an abstract model of primitive cells, in which self-maintenance of cell membranes is considered. Initiated by Maturana & Varela (1980), and recently improved by McMullin & Varela (1997) is a theoretical study of the self-organization of cell membranes. They model the capture and enclosure of catalysts by membranes. In turn, the membranes are activated by the catalysts they enclose. We here propose another model, based on spatially extended chemical reactions and focus on self-organization of membranes, to study how a cell divides and reproduces through the enclosure of catalysing particles by membrane elements.

An internal chemical network is maintained with stable cell membranes that can protect the network from environments. Cell membranes are internally generated by the inside network rather than provided externally. The internally generated cell membrane can feed back on the internal network to maintain its ongoing reaction. We discuss two different classes of self-reproduction mechanisms.

2. A Simple Model Approach

2.1. CHEMICAL REACTION

We consider a minimal autocatalytic cycle where molecules reproduce themselves and also catalyse membrane molecules. However, the cycle must contain nonlinear reactions to have more than two attractors. In practice, the system should have at least two attractors which correspond to "dead" and "alive" state, respectively. Since our purpose here is to see how such alive state is maintained by some spatial structures (i.e. membranes) and how it dissolves into dead states without having them.

Figure 1 provides our nearly minimal autocatalytic cycles studied in this paper. There are five types of particles (A, E, M, R and W). An autocatalytic (A) particle becomes an active enzyme (E) particle with the existence of another (A) at the rate P_E. An E particles catalyses the reaction which produces an A from a resource (R) particle at the rate P_A. It also catalyses the production of a membrane (M) particle from an R at the rate P_M. An A particle can be spontaneously produced from an R particle, but this rate $P_{A'}$ is smaller than that of the catalysed reaction. These particles spontaneously disintegrate into waste (W) particle at a common rate P_W. An R is produced from a W at a constant rate P_R (this represents a supply of some energy or resource). These reactions are described by the following stoichiometric equations:

$$A + A \xrightarrow{P_E} A + E, \tag{1}$$

$$E + R \xrightarrow{P_A} E + A, \tag{2}$$

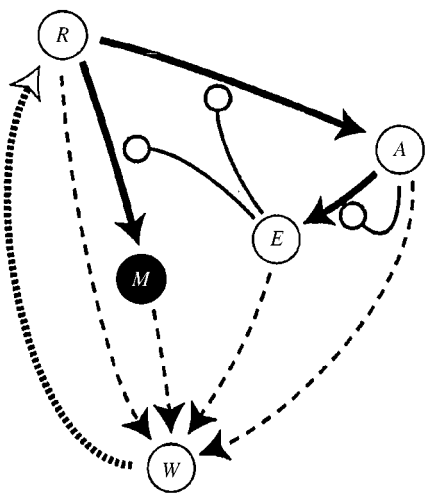

FIG. 1. The autocatalytic cycle considered in the paper. (⟶) production; (—○) catalysis; (⋯⋯▸) decomposition; (⋯⋯▸) synthesis. An autocatalyst (A) produces an active enzyme (E) from another A particle. An enzyme E produces an A particle or a membrane (M) particle from a resource (R) particle. All particles decompose into waste (W) particle. R particles are synthesized from W.

$$E + R \overset{P_M}{\rightarrow} E + M, \tag{3}$$

$$R \overset{P_A}{\rightarrow} A, \tag{4}$$

$$\{A, E, R, M\} \overset{P_W}{\rightarrow} W, \tag{5}$$

$$W \overset{P_R}{\rightarrow} R. \tag{6}$$

See the practical computation of the reaction rates in Appendix A [eqns (A.1)–(A.5)].

2.2. SPATIAL INTERACTION

The above chemical reactions occur in a one-dimensional space. The reaction space was coarse-grained into discrete reaction sites which carries 100 particles each. Spatial kinetics consists of two processes: diffusion and repulsion processes. First, in the diffusion process, each particle moves to its neighbouring sites with a constant probability P_D [Fig. 2(a)].

Next, we assume there are hydrophobic (M) and hydrophilic (A, E and R) particles which repel each other. In this process, a particle moves to neighbouring sites at a certain rate due to repulsion between particles on the same [Fig. 2(b)] or neighbouring sites [Fig. 2(c)]. Therefore, an M particle on the i-th site repelled into the $(i \pm 1)$-th site at the rate which is in proportion to the number of these three types of particles on the same site and the counter-neighbouring $(i \mp 1)$-th site. On the contrary, the three types of particles move to the neighbouring $(i \pm 1)$-th site at the rate which is proportional to the number of M particles on the i-th and the $(i \mp 1)$-th sites. In practice, when a particle on the i-th site moves to the adjacent j-th site, a counter-particle on the j-th site is randomly selected and moved to the i-th site to keep the total number of particles on the site constant. The detail description is written in Appendix A [eqns (A.6)–(A.9)]. We study two cases below. In the first case, every particle has equal mobility rates (i.e. diffusion and repulsion rate). In the second case, the mobility rates of autocatalytic particles differ from those of other particles.

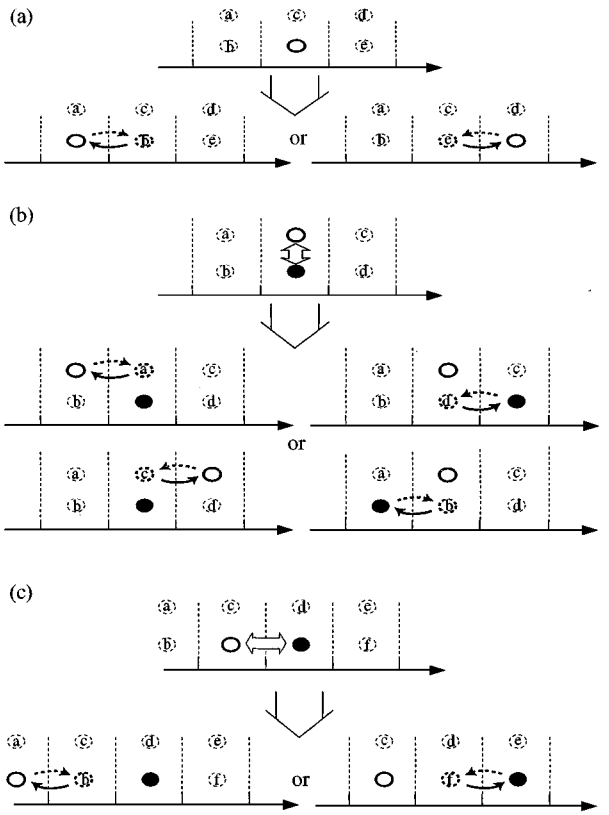

FIG. 2. Schematic drawings of spatial kinetics. The X-axis represents sites of course-grained reaction space. (a) Diffusion. A particle can diffuse into neighbouring sites. (b) Repulsion between particles in the same site. When hydrophobic (M: ●) and hydrophilic particles ($\{A, E \text{ and } R\}$: ○) are on the same site, repulsion take place with the probability P_{R0} and one moves into the neighbouring site. (c) Repulsion between particles in the neighbouring sites. Repulsion also take place between particles on the adjacent sites (with the probability P_{R1}). The repelled particle moves one step aside. In any case, a counter-particle is randomly chosen from the destination site, and this replaces the moved particle to keep the total number of particles on the site constant.

2.3. MEMBRANE FORMATION

The M particles tend to cluster around each other because of repulsion, when the density of M particles are high. In the case of one-dimensional space, each M cluster is like a wall which occupies a few sites (see Fig. 3). In the case of two-dimensional space, a potential membrane will form chains or stripes. It is relatively easy to trap catalysts in the one-dimensional case, as the two-sided walls are sufficient to trap catalytic particles inside. In the present model, a membrane cannot be sustained just by having some

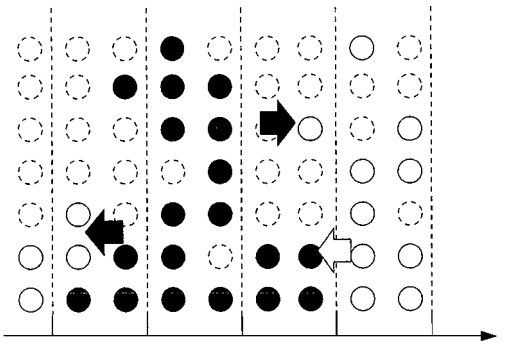

FIG. 3. A schematic drawing of membrane formation. The probability with which the repulsion take place is proportional to the number of repelling particles in neighbouring site (illustrated black and white arrows). Therefore, if there is a site which contains many hydrophobic particles (M: ●), they expel hydrophilic particles ($\{A, E \text{ and } R\}$: ○) from the adjacent site and vice versa.

catalyst particles. Rather, it needs an active and dynamic state of the chemical network. In other words, a mechanical aspect of self-reproduction, such as catalyst trapping will be investigated from a spatially extended reaction–diffusion system. Therefore, as Turing (1953) did, we start from a one-dimensional case and successively extend it to two- and three-dimensional cases. Simulations in the two-dimensional case will be reported elsewhere (Ono & Ikegami, 1999).

3. Results

We have conducted a series of three experiments. The first one is from a homogeneous initial configuration. The second one is from a cell-like initial structure, and the last one is an experiment with giving different diffusion and repulsion parameters allocated to A and E particles.

We introduce two important controlling parameters, namely, the A particle reproduction rate (P_A) and the membrane production rate (P_M) as for controlling parameters.

3.1. AN EXPERIMENT FROM A HOMOGENEOUS INITIAL STATE

A final stage derived from a homogeneous initial configuration [Fig. 4(a)] will be categorized into three regions with respect to the concentration of A particles. When sufficient A particles are produced, the membrane M particles are generated under the enzymatic E particles which also catalyse A particles. Therefore, the high-density state of A particle indicates an ongoing reaction cycle as shown in Fig. 1. The M particles build periodic membranes automatically [Fig. 4(b)].

Figure 5 shows the phase diagram against parameters P_A and P_M. Also, a numerical analysis of the case $P_M \equiv 0$ in the homogeneous case is explained in Appendix B.

In region 0, A particles cannot sustain their own replication. Because the reproduction rate is set too low, A particles will be removed either by a spontaneous or diffusing process before they catalyses themselves.

In region I, a final steady state can have either high or low concentrations of A particles.

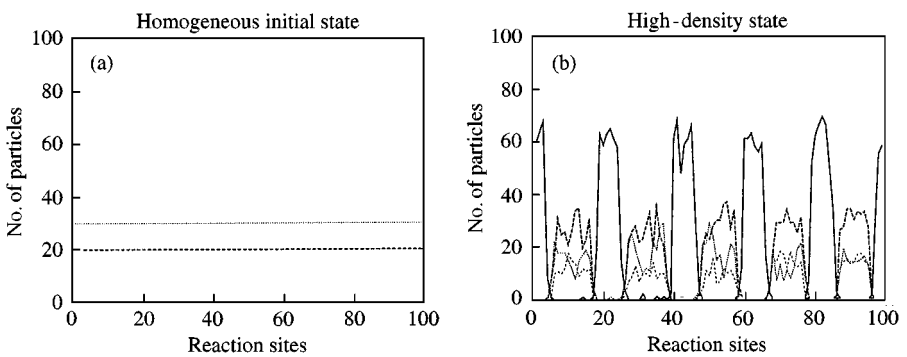

FIG. 4. Snapshots of the dynamics in the spatially extended reaction diffusion system. The X-axis denotes the reaction sites and the Y-axis denotes the number of particles on each site. Each line shows the distribution of particles (——) R; (·····) A; (·····) E; (——) M. (a) The homogeneous initial state. (b) A state after 500 000 iteration. When A particles can produce enough E particles, they reproduce A and M, and M particles form the periodic clusters of about 20 sites ($P_A = 9 \times 10^{-6}$, $P_M = 7 \times 10^{-6}$).

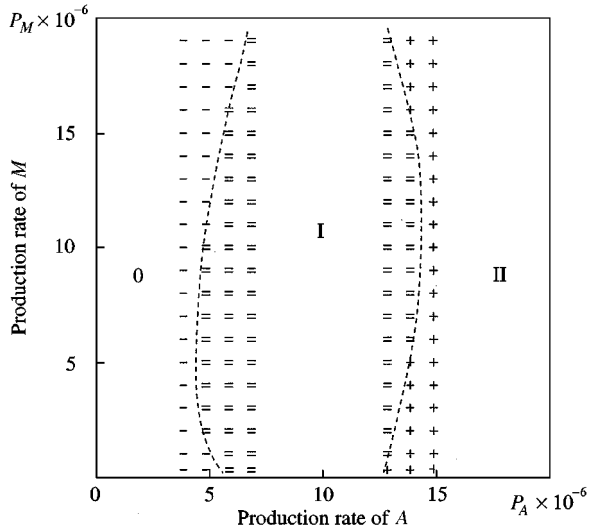

FIG. 5. The phase diagram with respect to the final density of A particles from a homogeneous initial configuration. The X- and Y-axis represent the production rate of A and of M (i.e. P_A and P_M). Each mark represents a run of 1 000 000 iteration from the initial configuration shown in Fig. 4(a). Region 0: a mark (−) denotes the region where the density of A becomes very low though it started from a high-density state. Region I: a mark (=) denotes the region where the final state depends on the initial density. Region II: a mark (+) denotes the region where the density of A particles becomes high, even evolving from the low initial density state.

Spatially homogeneous but low-density state will evolve to a low-density final state. On the other hand, a high-density state can keep a high-density state. There is a threshold with respect to an initial A particle density.

In region II, a final state is always high-density with respect to A particles even from a low-density initial state.

We are especially interested in region I, where the final state is not determined by a mere parameter tuning. Self-reproduction is, of course, not equivalent to just a high-density state of A particles. However, we assume that the maintenance of the high-density state is a necessary condition of self-reproduction process. Therefore, we study the time evolution of an inhomogeneous initial configuration in region I.

3.2. AN EXPERIMENT FROM AN INITIAL CELL-LIKE STATE

First, we briefly discuss on the time evolution from an initial localized state under the condition $P_M = 0$ where no membrane particles are produced. The fate of this state depends on the initial amount of A particles. If its amount is sufficiently high, A particles are replicated gradually and spreading over the whole space [Fig. 6(a)]. If it is lower, A particle will diffuse away [Fig. 6(b)].

However, if A particles can produce membrane particles, the time evolution becomes very different ones. The initial configuration of this experiment is illustrated in Fig. 7(a). Between the clusters of M particles, there is a domain containing high density of A particles. We simply call this configuration "cell" and the adjacent M particles are called the "membrane" of the cell.

A rough diagram is computed from the final states evolving from this initial cell-like configuration as in Fig. 8. It is found that region I is sensitive to the cell initial condition. Region I in Fig. 5 is now categorized into three subregions according to their temporal behaviour.

In region Ia, the supply of M particle catalysed by E particles is too low to sustain the initial membranes. When the membranes degenerate, A particles diffuse away quickly. The more A particles escape from the cell, the less likely that the membrane can be re-organized. Thus, the initial cell disappears rather quickly [Fig. 7(b)]. This behaviour is compared to the case where the initial membranes fail to enclose the inside catalyst, described by McMullin & Varela (1997), although their model assumes a two-dimensional cell pattern.

In region Ib, the production and degeneration rate of A particles is balanced, depending on the production rate of membranes. The size of the cell is held constant stably [Fig. 7(c)].

In region Ic, when the production rate of M is low and the reproduction rate of A is high, a cell can produce only thin membranes which allow more A particles to permeate through them and those particles increase their density outside the cell due to the autocatalytic cycle. This region differs from the regions Ia and Ib, with new membranes being generated outside the cell [Fig. 7(d)]. We then have new cells. The above process is repeated to successively create new cells. Finally, the whole space is filled with the cells of a typical size. This is the *cell-reproducing* dynamics of this model.

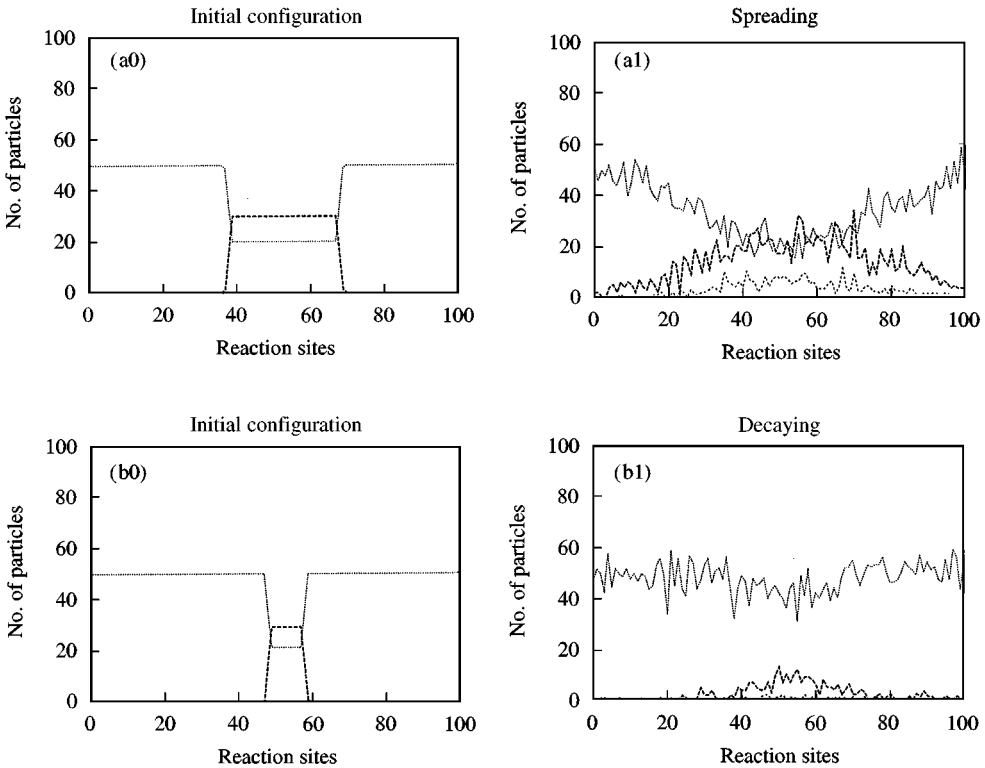

FIG. 6. A time evolution of an inhomogeneous initial state without membranes. (a0) The initial configuration without membranes but contains a large amount of A particles. The parameters are chosen from the region Ic ($P_A = 8 \times 10^{-6}$, $P_M = 0$). (a1) A state after 50 000 iteration. A particles increase their number and spread to fill the space finally. (b0) The smaller initial configuration. (b1) A state after 10 000 iteration. A particles diffuse away before they begin to replicate themselves stably. The parameters are as same as that of (a) ($P_A = 8 \times 10^{-6}$, $P_M = 0$). (——) R; (·····) A; (·····) E; (——) M.

We call the process which is observed in region Ic as "open reproduction". Because, in this process, the enclosed particles of the daughter cell are not only transferred directly from the mother cell, rather, the permeated particles that react with the outside particles will create a new membrane to enclose the new catalytic particles. If we assume that particles are easy to mutate, this self-reproduction will be inaccurate due to the contamination. The internal content is updated for the new cells, which is why we also call this reproduction "open reproduction". However, "closed reproduction" is also made possible by introducing mobility differences. We study this alternate reproduction process in the future experiment.

3.3. AN EXPERIMENT WITH DIFFERENT MOBILITIES

In general, a stable size of cell is determined both by the reaction and mobility parameters. For example, the initial large cell [Fig. 9(a)] will break into two, by creating a new membrane in the middle of the first cell [Fig. 9(b)], because the larger cell can produce surplus M particles. Finally, the new cells arrive at a stable cell size.

We found another dynamic aspect of cell reproduction. In the following experiment, we give different mobility rates to particles, assuming that A and E particles have lower diffusion and repulsion rates than M and R [see Appendix A]. In this case, inside A and E particles repel membrane more than outside R particles do. Therefore, the membranes move outwards. When the cell reaches a critical size, it divides itself spontaneously. This process can take place recursively (Fig. 10). Compared with the previous open reproduction dynamics, we call this "closed reproduction" dynamics, because the internal particles are kept from outside through the reproduction process.

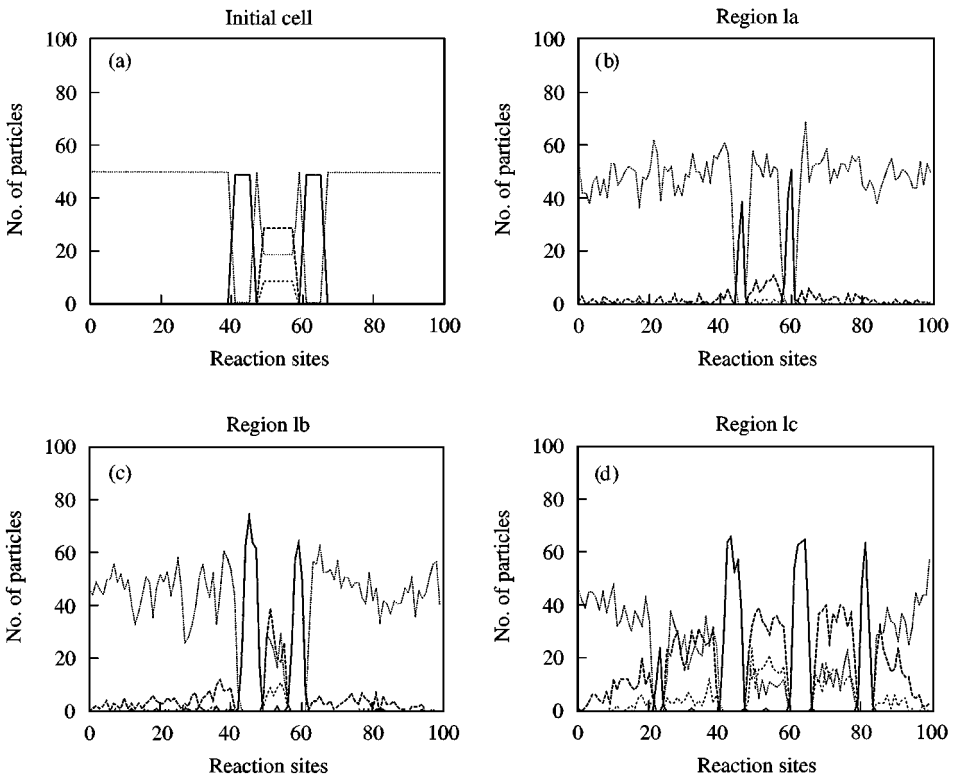

FIG. 7. Snapshots of the dynamics of cells. (a) The initial "cell" configuration. There is a region containing A particles [as same size as that of Fig. 6(b)] between the "membranes" (i.e. clusters of M). (b)–(d) Snapshots after 100 000 iteration. (b) When P_A and P_M are set low, the production of M is too small so that the membranes cannot keep particles inside the cell ($P_A = 5 \times 10^{-6}$, $P_M = 3 \times 10^{-6}$). By losing A particles by diffusion and decomposition, this cell is going to disappear. (c) When P_A and P_M are balanced, a cell can sustain itself stably ($P_A = 7 \times 10^{-6}$, $P_M = 9 \times 10^{-6}$). (d) When P_M is low or P_A is high, A particles can increase in the outside of the membrane. They construct new membranes and new cells ($P_A = 11 \times 10^{-6}$, $P_M = 5 \times 10^{-6}$). (·····) R; (·····) A; (·····) E; (——) M.

4. Discussion

In existing living organisms, cell membranes have various functions, such as recognizing other cells, bonding to each other, maintaining an electric potential, etc. However, for our primary concern is that a membrane is a boundary that separates a cell from the environment. Maturana & Varela (1980) have stressed that self-maintenance of this boundary is an indispensable feature for living cells. This idea of boundary is known as *autopoiesis*. In a sense, most of the previous theoretical studies of self-replicators are not adequate for the models of living cells, except for those originally proposed by Varela, and recently re-examined by McMullin & Varela (1997) and Breyer *et al.* (1998). These models try to implement the thrust of autopoiesis in a simple two-dimensional cellular automata model. Yet the model described here is simple, it also characterizes the complementary features of a catalyst and the boundary particles.

Our purpose here is to study more dynamic features of cell reproduction between membranes and their internal catalysts. We focus on two properties:

1. Self-organization of membranes.
2. Self-maintenance of both membranes and catalysts.

We have also introduced the self-assembling effects of membrane molecules into our model, based on the abstract hydrophobic effects. Self-assembling allows for dynamic maintenance of membrane. It shows naturally how the membranes restrict the diffusion of molecules.

Then the restriction maintains autocatalytic reaction.

As an outcome, the cell was shown to divide itself recursively by creating new boundary when it divides. It should be noted that cell division process takes place without any *ad-hoc* rules and it shows two different ways of reproduction. Reproduction by making a new boundary within the cell has greater potential to inherit internal information than the other way of reproduction. It is, of course, more difficult to trap molecules in the higher dimensions. We have already shown that membrane self-maintenance and reproduction of the cell is also possible in the two-dimensional space (Ono & Ikegami, 1999), a natural extension of the present model into two-dimensional case. We further report that it is possible to have a spontaneous formation of self-reproducing cell from random initial states for the two-dimensional case (Ono & Ikegami, in preparation).

What we have not discussed here is the further evolution of membrane structures and functions.

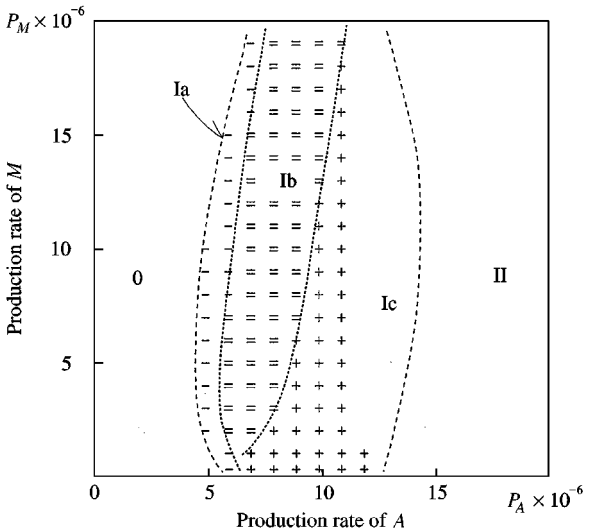

FIG. 8. The phase diagram with respect to the time evolution of the initial cell state. There are three sub-classifications in region I. Each mark represents a run of 1 000 000 iteration starting from the initial cell state [Fig. 7(a)]. Region Ia: a mark (−) denotes where cells cannot sustain membranes. Region Ib: a mark (=) denotes where cells can maintain themselves in a stable manner. Region Ic: a mark (+) denotes where cells can reproduce.

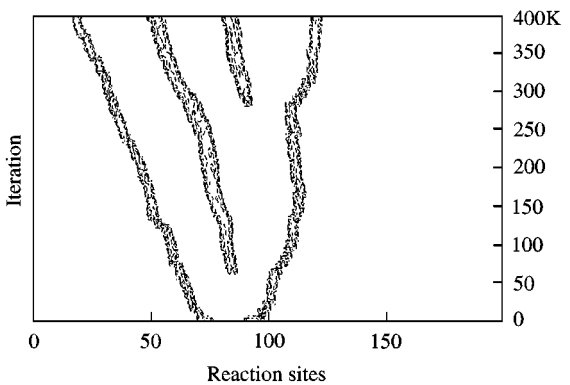

FIG. 10. An example of recursive cell division. The X-axis denotes the reaction sites and the Y-axis denotes the time axis A and E particles have lower diffusion and repulsion rates than M and R ($m = 5$). Though the distribution of M particles is only displayed in this figure, there are A and E particles between the membranes of M. Starting from a cell configuration [the same configuration as Fig. 7(a)], membranes move outwards because the mobilities of particles inside the cell is smaller than that of outside the cell. When the cell reaches a critical size, new membranes are created in the middle of the mother cell. This division takes place recursively ($P_A = 7 \times 10^{-6}$, $P_M = 5 \times 10^{-6}$).

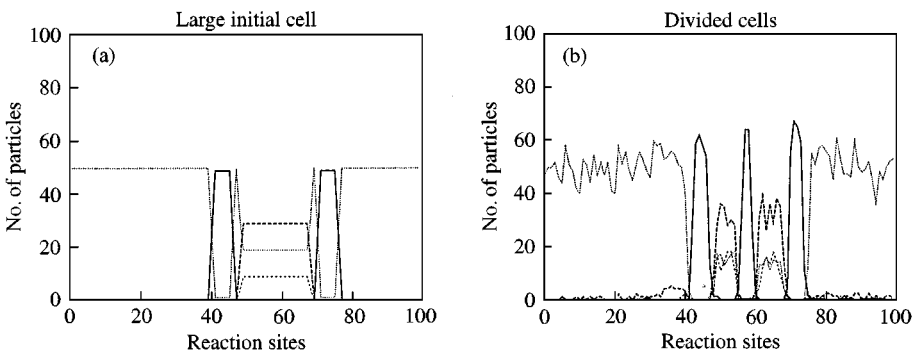

FIG. 9. An example of cell division. (a) The initial large cell configuration. A cell larger than its stable size is prepared. (b) After 100 000 iteration, larger cell produces surplus M particles and a new membrane is created in the middle of the initial cell at the reaction site 60 ($P_A = 7 \times 10^{-6}$, $P_M = 9 \times 10^{-6}$, $m = 1$). (——) R; (- - - - -) A; (·····) E; (——) M.

A cell does not simply show a precise replication. It only reproduces itself, and the new cells and their membranes should emerge through interactions between the cells. It has been recently reported that simple replicating loops evolve via interaction in the improved Langton's cell automaton system (Sayama, 1999). Using an approach from reaction–diffusion system, Kaneko, Yomo and Furusawa have shown that interaction of chemical networks can show differentiation of "cell types", when those networks are captured in cells (Kaneko & Yomo, 1997; Furusawa & Kaneko, 1998). In addition, Ikegami & Hashimoto (1996) have shown that assembly of Turing machines and tapes with cell system show differentiation of replicating assembly. In particular, it is shown that unstable replicators can be held in the system when there are stable replicators (Ikegami, 1999). While they do not simulate the self-organization of membranes themselves, how replicators can evolve should be worth investigating and we will study these evolutionary aspects in the present scheme in the near future.

Present-day living cell membrane molecules seem to be highly adopted, and are difficult to synthesis automatically in the non-living environment. However, molecules of primitive membranes may have been much simpler. Yanagawa *et al.* (1988) have shown an example of such early membrane formations. The minimal complexity of primitive cell system should be argued further. The model described here assumes one set of intermediate catalytic E particles and not the higher-order catalysts. A cell reproduction with a minimal membranes requires at least this complexity. We postulate that the emergence of proto membranes is not an independent event of that of self-replication, but rather a simultaneous process from their earliest stage. We still do not know the role of that higher-order catalysts (i.e. catalysts of catalysts of catalysts, etc.) played in primitive cell system, nor how to model them. We hope to reveal some dynamic patterns of this possible early co-evolution within the present model approach. The further evolutions of cell reproduction to the present form may then remain an important subject of future study.

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REFERENCES

Breyer, J., Ackermann, J. & McCaskill, J. (1998). Evolving reaction-diffusion ecosystems with self-assembling structures in thin films. *Artif. Life* **4,** 25–40.

Cronhjort, M. B. & Blomberg, C. (1997). Cluster compartmentalization may provide resistance to parasites for catalytic networks. *Physica D* **101,** 289–298.

Fontana, W. & Buss, L. W. (1994). The arrival of the fittest: toward a theory of biological organization. *Bull. Math. Biol.* **56,** 1–64.

Fontana, W. & Buss, L. W. (1996). The barrier of objects: from dynamical systems to bounded organizations. In: *Boundaries and Barriers* (Casti, J. & Karlqvist, A., eds), pp. 56–116. Reading MA: Addison-Wesley.

Furusawa, C. & Kaneko, K. (1998). Emergence of multicellular organisms with dynamic differentiation and spatial pattern. *Artif. Life* **4,** 79–93.

Gánti, T. (1975). Organization of chemical reactions into dividing and metabolizing units: the chemotons. *BioSystems* **7,** 15–21.

Gánti, T. (1997). Biogenesis itself. *J. theor. Biol.* **187,** 583–593.

Ikegami, T. (1999). Evolvability of machines and tapes. *Artif. Life Robotics* **3,** 242–245.

Ikegami, T. & Hashimoto, T. (1996). Replication and diversity in machine-tape coevolutionary systems. *Artif. Life V*, 426–433.

Kaneko, K. & Yomo, T. (1997). Isologous diversification: a theory of cell differentiation. *Bull. Math. Biol.* **59,** 139–196.

Lee, K. J., McCormick, W. D., Pearson, J. E. & Swinney, H. L. (1994). Experimental observation of self-replication spots in a reaction-diffusion system. *Nature* **369,** 215–218.

Maturana, H. R. & Varela, F. J. (1980). Autopoiesis and Cognition: the Realization of the Living. Dordrecht: D. Reidel Publishing.

Mayer, B., Köhler, G. & Rasmussen, S. (1997). Simulation and dynamics of entropy-driven, molecular self-assembly processes. *Phys. Rev. E* **55,** 4489–4499.

McMullin, B. & Varela, F. J. (1997). Rediscovering computational autopoiesis. *Proc. ECAL97*, Brighton, U.K., 1997 (Husbands, P. & Harvey, I., eds). pp. 38–47. MIT Press.

Oberholzer, T., Wick, R., Luisi, P. L. & Biebricher, C. K. (1995). Enzymatic RNA replication in self-reproducing vesicles: an approach to a minimal cell. *Biochem. Biophys. Res. Commun.* **207,** 250–257.

Ono, N. & Ikegami, T. (1999). Model of self-replicating cell capable of self-maintenance. *Proc. ECAL99*, Lausanne, Switzerland, 1999 (Floreano, D., Nicoud, J.-D. & Mondana, F., eds). Springer. pp. 399–406.

Pearson, J. E. (1993). Complex patterns in a simple system. *Science* **261,** 189–192.

Sayama, H. (1999). Toward the realization of an evolving ecosystem on cellular automata. *Proc. 4th AROB '99*, pp. 254–257.

Turing, A. M. (1953). The chemical basis of morphogenesis. *Philos. Trans. Roy. Soc.* (*Part B*) **237,** 32–72 (Reprinted from *Bull. Math. Biol.* **52,** 153–197, 1990).

Yanagawa, H., Ogawa, Y., Kojima, K. & Ito, M. (1988). Construction of protocellular structures under simulated primitive earth conditions. *Origins Life Evol. Biosphere* **18,** 179–207.

APPENDIX A

The transition probabilities of chemical reaction are calculated by the following formula:

$$P^i_{A\to E} = P_E \times [A](i), \tag{A.1}$$

$$P^i_{R\to A} = P_A \times [E](i) + P_{A'}, \tag{A.2}$$

$$P^i_{R\to M} = P_M \times [E](i), \tag{A.3}$$

$$P^i_{X\to W} = P_W \quad (X \in \{R, A, E, M\}), \tag{A.4}$$

$$P^i_{W\to R} = P_R. \tag{A.5}$$

Here $P^i_{A\to E}$ denotes the transition probability from particle A to E on the i-th site and $[A](i)$ denotes the number of particle A on the i-th site.

The values of the reaction rate fixed through the present simulations are $P_E = 0.5\times10^{-6}$, $P_{A'} = 2\times10^{-6}$, $P_R = 100\times10^{-6}$ and $P_W = 100\times10^{-6}$.

The mobility probabilities of the particles are

$$P_R^{i\to i\pm1} = P_D + P_{R0}\times[M](i) + P_{R1}\times[M](i\mp1), \tag{A.6}$$

$$P_{\{A,E\}}^{i\to i\pm1} = (P_D + P_{R0}\times[M](i) + P_{R1}\times[M](i\mp1))/m, \tag{A.7}$$

$$P_M^{i\to i\pm1} = \left(P_D + P_{R0}\sum_X^{R,A,E}[X](i) + P_{R1}\sum_X^{R,A,E}[X](i\mp1)\right)\Big/m, \tag{A.8}$$

$$P_W^{i\to i\pm1} = P_D. \tag{A.9}$$

Here $P_R^{i\to i\pm1}$ denotes the mobility probability of particle R from the i-th site to the $(i\pm1)$-th site. The rates are $P_D = 7\times10^{-3}$, $P_{R0} = 5\times10^{-3}$ and $P_{R1} = P_{R0}$ 0.5. Another mobility parameter m is different in Sections 3.1, 3.2 ($m = 1$) and 3.3 ($m = 5$).

Using the variables and parameter given above, execute the below algorithm on one-dimensional distributed particle system. There are 100 sites each containing always 100 particles. The boundary of reaction space is periodic. The algorithm is as follows

1. Calculate the transition probabilities for every particle. Then, change the chemical state of the particles according to the probabilities.
2. Particles diffuse on sites by the following steps.
   (a) Choose a site in a random order.
   (b) Calculate the probabilities of mobility of the particles on the site.
   (c) Let particles move to the adjacent site according to the evaluated probabilities. In order to conserve the number of the particles on the site, when a particle on the i-th site moves to the adjacent j-th site, a randomly chosen particle on the j-th site will in turn occupy the i-th site.
   (d) Repeat these steps until all sites are processed.

These procedures complete a unit simulation iteration.

APPENDIX B

Before considering the role of membrane and spatial configuration, we analyse the behaviours of the system without spatial structures. Starting from homogeneous initial configuration, this system stays in a homogeneous state, when we set $P_M = 0$. The behaviours can be described by three variables, i.e. the mean number of R, A and E on a site [the mean number of W trivially falls into a stable fixed value $(W_0 = 100/(1 + P_R/P_W)]$. Concerning these conditions, we study the mean-field-type equations in order to investigate the phase diagram of Fig. 5:

$$\dot{\bar{R}} = P_R W_0 - (P_A\bar{E} + P_W)\bar{R}, \tag{B.1}$$

$$\dot{\bar{A}} = P_{A'}W_0 + P_A\bar{E}\bar{R} - (P_E\bar{A} + P_W)\bar{A}, \tag{B.2}$$

$$\dot{\bar{E}} = P_E\bar{A}^2 - P_W\bar{E}. \tag{B.3}$$

Numerically solving the equations and analysing the stability of the solutions, we obtain the phase diagram Fig. B1 which corresponds to the line $P_M \equiv 0$ (i.e. no membrane particles are produced) in Fig. 5. Below the critical value P_{A_1}, the

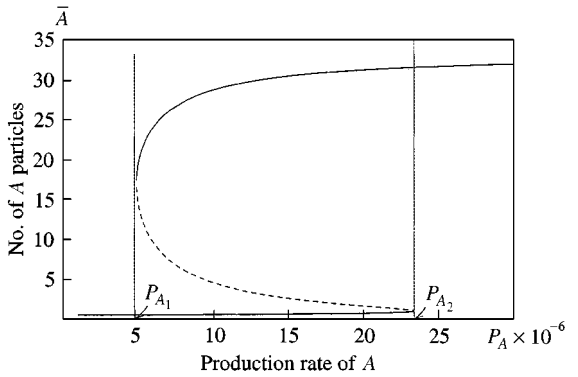

FIG. B1. The bifurcation diagram of the expected number of A ($\bar{A}$) against their reproduction (P_A). Solid line denotes stable and a dashed line denotes unstable fixed point branch of $\bar{A}$, respectively. On the value $P_A = P_{A_1}$ and P_{A_2}, there occur saddle-node bifurcations. In the region below P_{A_1}, $\bar{A}$ has only a lower fixed point branch. Between P_{A_1} and P_{A_2}, there are two stable and one unstable fixed point branches. Beyond P_{A_2}, $\bar{A}$ has only an upper fixed point branch. Each region corresponds to the region 0, I and II in Fig. 5, respectively.

steady state of A particle is suppressed. This region corresponds to the region 0 in Fig. 5. On this value, a saddle-node bifurcation generates two stable states and one unstable state. This region corresponds to region I in Fig. 5 where two different steady states are possible depending on the initial state pattern. Above the second critical point P_{A_2}, the upper steady state becomes a unique equilibrium state through the inverse saddle-node bifurcation. This region corresponds to region II in Fig. 5. The boundary between regions 0 and I is well estimated by the mean-field approximation. However, the boundary between regions I and II is overestimated. Since the simulation is based on stochastic dynamics, the system can leap into the upper steady state from the lower due to the fluctuation of the number of particles, which is not assumed in the mean-field-type equation.