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Emergence of a primitive cellular structure in a catalytic reaction network

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Abstract—It is essential to explain the emergence of primitive cellular structure from a set of chemical reactions to unveil the origin of life and to experimentally synthesize protocells. Recently, we considered a hypercycle with two mutually-catalyzing chemicals to demonstrate that the reproduction of a protocell with a growth-division process occurs when the replication and degradation speeds of one chemical are slower than those of the other chemical respectively, and molecules are crowded as a result of replication. In this paper, we discuss the effects of the crowding molecule on the formation of primitive structure by simulating a cellular automaton model, and also apply the model to a hypercycle with three molecular species.

1. Introduction

Understanding how cellular basic components are integrated into a reproducing cell is essential to unveil the origin of life, to give a comprehensive insight of cellular life, and to experimentally synthesize an artificial cell from its basic elements[1]. Several theoretical studies have been made to link a set of catalytic reactions with a reproducing cell[2, 3, 4, 5, 6]. In particular, a hypercycle model, in which different molecular species mutually catalyze the replication of each other, was proposed to give stable replications of informative polymers[7, 8]. Further, compartments of the catalytic reactions enhance the robustness of the growth[9, 10, 11, 12]. Thus, it is important to develop a simple mechanism to produce a compartmentalized structure of a protocell. Also, in the study of synthesizing an artificial cell, it is an important question how to synchronize division of a cell with replication of molecules inside, particularly, that of DNA[13].

Discreteness[14, 15, 16, 17] and crowding[18] of molecules have been suggested as two important aspects of biological systems while these have been neglected in the conventional reaction-diffusion equations. The discreteness of molecules attributes its relevance to the fact that the number of some specific molecules in the cell is very small, and the crowding of molecules is due to the fact that the cellular environment is under high concentrations of molecules with exclusion volumes. It is noticeable that a minority molecule in the hypercycle is suggested to play the role of DNA, i.e., heredity-carrier and also to its relevance for evolvability[19]. Here again, the catalytic reactions in a compartment and its division are assumed.

Recently, we have considered a hypercycle with two mutually-catalyzing chemicals to demonstrate that the reproduction of a protocell with a growth-division process occurs when the replication and degradation rates of one chemical are, respectively, slower than those of the other chemical, and molecules are crowded as a result of replication[20]. In addition, the protocell divides after the minority molecule is replicated at the slow synthesis rate, thus, a synchrony between divisions of a cell and molecule replications is achieved. While the model studied in [20] deals with Langevin dynamics in a continuous space, studying a lattice model will also be helpful to clarify the effect of exclusion volumes.

In this paper, we simulate a cellular automaton model with two mutually-catalyzing chemicals to show that the synergy effect of discreteness and crowding of molecules is essential to demonstrate the primitive cellular structure. In addition, we apply our model to a hypercycle with three molecular species.

2. Model and simulations

2.1. General setup

We consider a two-dimensional square lattice $L_x \times L_y$ with periodic boundary conditions. Each site is empty or occupied by one molecule to ensure the exclusion volume of molecules. The species of the molecule is represented by a "color" of the molecule, and replications of molecules occur based on catalytic relations between the species as described below. We introduce discrete simulation steps, and in each step, we update the system by applying following processes to each molecule in a random order.

The first process is replication of molecules. Figure 1 (a) outlines the process. When a molecule is located in the nearest neighboring site of its catalyzing molecule, a replication reaction can occur with a replication probability, and a new molecule is added at a randomly-chosen empty site of the six neighboring ones of the reaction pair. The example shown in the figure is the case in which the replication of a green molecule is catalyzed by the red one. If all of the six neighboring sites are occupied, the new molecule is not replicated.

The second process is degradation of molecules. In each step, degradation occurs by removing each molecule with a degradation probability from the system (see Fig. 1 (b)).

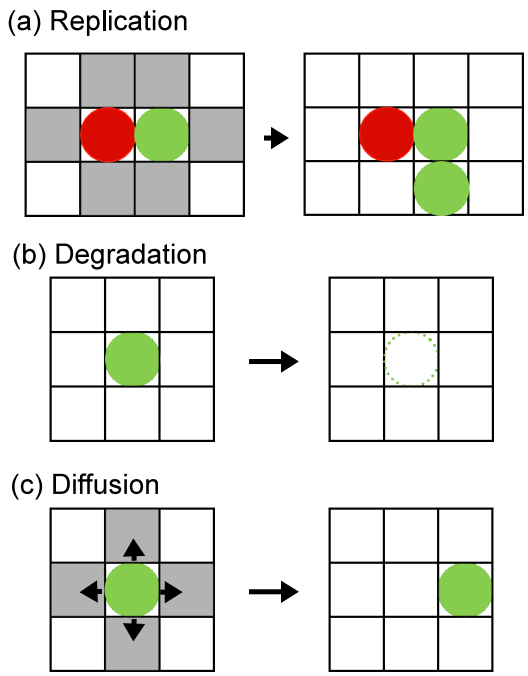


Figure 1: Three update processes of our model. In the right, examples of realizations for each process are shown. (a) Replication: If a pair of molecules with the catalytic relation is located next to each other, a replication can occur and the product molecule is added in one of the six neighboring sites(grey-shaded) if there is an empty one. (b) Degradation: In each step, a molecule is removed from the system with a fixed probability. (c) Diffusion: In each step, every molecule chooses one of the four nearest neighboring sites (grey-shaded) and hops to the site if it is empty.

The third process is diffusion of molecules. In each step, every molecule hops to one of its four nearest neighboring sites if the destination site is empty (see Fig.1 (c)). The destination site is chosen randomly from the four sites and, if the site is occupied, the molecule remains at the original site.

2.2. Mutually-catalytic replicating molecules

The simplest is the case of two molecular species X and Y. They mutually catalyze the replications as

$$X + Y \xrightarrow{p\gamma_x} 2X + Y, \quad X + Y \xrightarrow{p\gamma_y} 2Y + X.$$

When X and Y molecules are located next to each other, replication can occur with a probability p. If there is an empty site available, a new molecule is added and a species of the molecule is assigned as X and Y, respectively, with probabilities γ_x and $\gamma_y = 1-\gamma_x$. Degradations occur as $X \to 0$, and $Y \to 0$, respectively with degradation probabilities a_x and a_y.

Simulations are carried out from the initial condition in which a single Y is located in a group of X of sizes $L_{ini} \times L_{ini}$. Here, the value of L_{ini} is fixed to 10, however, it is not important if it is sufficiently large.

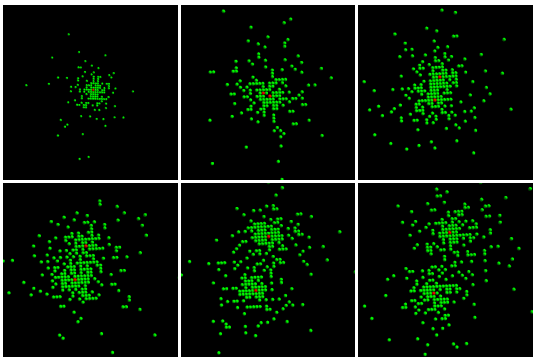
As shown in [20], the mutually-catalytic replicating molecules results in the emergence of a primitive spatial structure when the replication and degradation of Y are considerably slower than those of X. In fact, this lattice model also exhibit the structure of a protocell in which a single Y is surrounded by a group of X, shown in the left top of Fig. 2(a).

In addition, a division process of the structure is observed synchronously with the replication of Y. As the Y replicates at the slow replication rate, the two Ys start to diffuse apart (Fig. 2(a)). As each Y catalyzes the replications of X, a group of X surrounds each of Y. The X molecules between the two Ys degradate and, as a result, the two structures divide. By the division after the replication of Y, the number of X also doubles (Fig. 2(b)), and recursive growth by successive replications of Y can be possible. Here, we note that, in this lattice model, there is a case the two Ys get closer again by diffusion, which leads to a decrease in the total number of X as the effective replication rate of X is decreased.

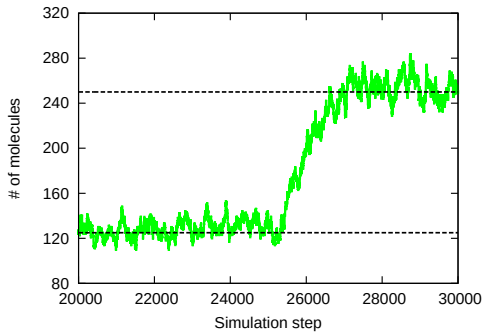
Emergence of the division process is possible both by the effects of the discreteness and the crowding of molecules. On the effect of the discreteness, Shnerb et.al. investigated a system with a reaction $X + Y \to 2X + Y$. They showed that the discreteness of Y molecule number leads to localized subpopulations and results in proliferating phase, in which the number of X diverges to infinity, even in the parameter ranges with which a continuous reaction-diffusion approach leads to extinction of X[14, 15].

By considering in our model the exclusion volume effect of molecules, being in reality present, the localized structure achieves a "quasi" stationary state, in which the number of X fluctuates around an average value unless the molecule Y replicates or degradates. In other words, the effect avoids the divergence of X observed in [14, 15]. As the Y replicates, the number of X shows the step-like increase(Fig. 2).

To further clarify the crowding effect, we investigate how dense the X molecules are distributed in the neighboring sites of the single Y. In Fig. 3, we show the average number of X, n_x, in the four nearest-neighboring sites of the single Y, as functions of p and a_x. Here, we suppress the number change of Y molecules so that replication/degradation of Y are absent, i.e., $\gamma_y = a_y = 0$. The plane of p and a_x is covered by two distinct region, $n_x = 0$ and $n_x > 3.5$. In the region $n_x = 0$, no replication of X occurs and degradation of X leads to extinction. In the region $n_x > 3.5$, the localized structure appears. We note that, in the simulations with the set of parameters near the boundary between the two regions, behavior of the system depends on samples: the localized stationary structure or extinction. As long as the system maintains the structure, the value of n_x is near to the fully-occupied value 4. These results suggest that the exclusion volume effect introduces the upper limit of ef-



(a) Snapshots of the system. The green and red molecules, respectively, denote X and Y. From left top to right one, left bottom to right one, snapshots for every 500 steps from 25000 to 27500 are shown.



(b) Time evolution of the number of X. The dotted lines, respectively, show the average number of X in the single structure and its doubled value.

Figure 2: Division of the structure in the two mutually-catalytic molecules. Replication of the Y occurs at simulation step 25329. Parameters are $p = 1, \gamma_y = 5 \times 10^{-6}, a_x = 0.01, L_x = L_y = 1000$.

fective replication rate of X. If the degradation rate of X is smaller than the replication rate, the replication of X results in the crowding of X around the single Y. If the degradation rate of X is greater than the replication one, the system goes to extinction.

2.3. Three-species hypercycle

The next simplest case will be the case of three molecular species X, Y and Z, and they catalyze the replications of other species cyclically as

$$X + Y \rightarrow 2X + Y\ ,\ \ Y + Z \rightarrow 2Y + Z\ , Z + X \rightarrow 2Z + X.$$

Here we denote replication probabilities of the species, respectively, by p_x, p_y, and p_z. Degradations also occur as $X \rightarrow 0$, $Y \rightarrow 0$ and $Z \rightarrow 0$, respectively with degradation probabilities a_x, a_y and a_z.

Simulations are carried out from the initial condition in which a single Y is located within a box of the sizes $L_{ini} \times L_{ini}$ where X or Z molecules are located.

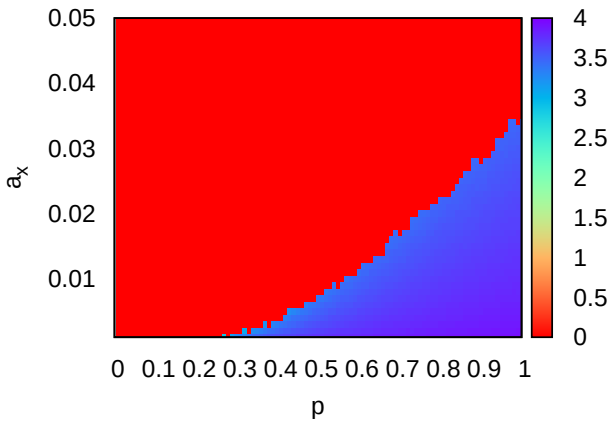


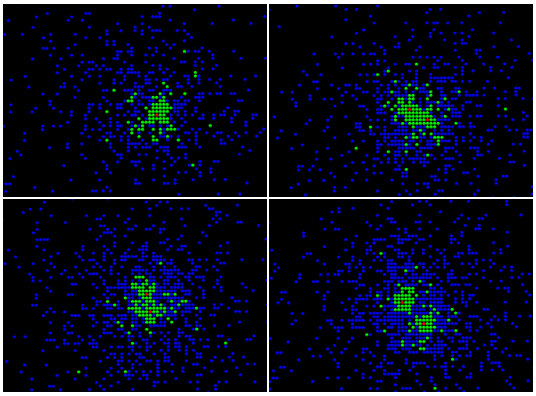
Figure 3: Average number of X in the four nearest-neighboring sites of the single Y as functions of p and a_x. Here, $\gamma_y = a_y = 0$.

For a set of parameters, the system organizes a localized nested structure in which a single Y is surrounded by numbers of X, which are surrounded by numbers of Z, as shown in Fig. 4(a) (See left top panel). When the replication rate of Y is small, the number of X distributes around the Y because the replication of X is catalyzed by Y. The replication of Z is catalyzed by X so that the number of Z distributes around the group of X. The replication of Y also occurs as a molecule of Z, although rarely, diffuses into the group of X occupying near the Y. When the Z is located next to the Y, a new Y molecule can be replicated. Once a new Y molecule is replicated, the two Y molecules diffuse apart, and the structure can gradually divide as shown in Fig. 4. After the replication of Y, the numbers of X and Z also double (Fig. 4(b)).

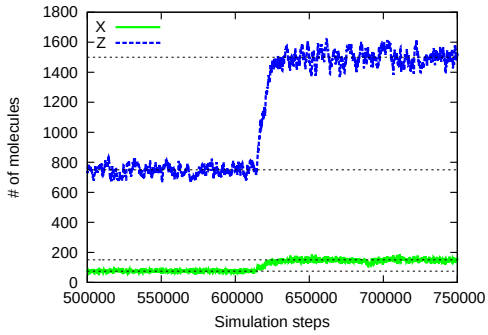
3. Summary

In this paper, we have demonstrated, using a cellular automaton model, that the primitive cellular structure appears when one molecular species is minority in mutually-catalytic replicating reactions with the exclusion volume of molecules. Both the lattice model with cellular automaton dynamics studied in this paper and the continuous space model with Langevin dynamics studied in [20] clarify that the synergy effect of discreteness and crowding of molecules is essential to the behavior.

In addition, we show in the lattice model that a nested structure appears when there is a minority molecule in a hypercycle consisting of three molecular species, and also the structure divides with the replication of the minority.



(a) Snapshots of the system. X, Y, and Z molecules are respectively denoted by green, red, and blue molecules. From left top to right one, left bottom to right one, snapshots for every 1000 steps from 614000 to 617000 steps are shown.



(b) Time evolution of the number of X and Z. The dotted lines, respectively, show the average number of X and Z in the single structure and their doubled values.

Figure 4: Division in the three-species hypercycle. Replication of the Y occurs at simulation step 614421. Parameters are $p_x = 1, p_y = 0.0001, p_z = 0.01, a_x = 0.01, a_y = 0, a_z = 0.001$.

Acknowledgments

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