Selection of Catalysts through Cellular Reproduction

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Abstract

A series of simulation studies (Ono & Ikegami 1999; 2001) show that a proto cell spontaneously emerges from a chemical soup by acquiring membrane structures. In 2-dimensional space, the emergence of proto cells is followed by the reproduction of cells. A major unsolved problem is the evolution of proto cells; how the proto cells evolve into modern cells with higher functionalities. Here we examine, as the first step, the evolution of catalysts within the proto-cells. Catalytic chemicals have different catalytic activity in generating membrane chemicals. We show that cells with higher activity of membrane production evolve through cellular selection.

Introduction

It is widely accepted that the origin of life was a set of molecules that catalyzed the reproduction of each other. However, when we consider the evolution of such primitive chemical systems, the compartmentalization of molecules is indispensable for establishing the co-evolution of cooperative catalytic reactions and protecting them from parasites that would spoil the evolution (Szathmáry & Maynard Smith 1997). Though it is difficult to know about the structure of primitive cells because there remain few physical records of the earliest living cells, there have been various theoretical approaches to understanding the emergence and evolution of proto-cell systems.

Gánti proposed a minimal model of primitive self-maintaining cells named "chemoton" (Gánti 1975; 1997). It is composed of (1) a metabolic system of autocatalytic molecules, (2) self-replicating molecules that inherit genetic information and (3) a self-organizing membrane molecule to enclose the whole system. This system maintains itself by consuming resources and discharging waste into the environment. It can be easily imagined that if the reproduction of the cell is appended to this system, it would be a primitive unit of Darwinian selection and evolve into more stable structures.

It should be stressed that a cell defines itself as an individual by producing a membrane that distinguishes itself from the outside. Maturana and Varela pointed out that this is a unique feature of living organisms, and named it "autopoiesis" (Maturana & Varela 1980). To demonstrate the self-maintenance of an autopoietic structure, abstract computational models of an autopoietic cell based on a Cellular Automaton were proposed (originally by Varela (Varela, Maturana, & Uribe 1974), and re-implemented by Zeleny (Zeleny 1977) and by McMullin (McMullin & Varela 1997)). Breyer and McCaskill introduced the metabolism of a catalyst into this model (Breyer, Ackermann, & McCaskill 1998). It was also shown that an autopoietic proto-cell can reproduce itself automatically (Ono & Ikegami 1999; 2001). Speroni di Fenizio and Dittrich proposed another approach to represent proto-cells that are embedded in a triangular planar graph (Speroni di Fenizio, Dittrich, & Banzhaf 2001).

The remaining question is "How was the *first* cell organized?" Answering this question will give us the first step in understanding the emergence of higher order structures in life's evolution. This paper consists of two parts. The computational algorithm of the model is explained in detail in the first part. We introduce a Lattice Artificial Chemistry (LAC) model that simulates the chemical reactions and spatial interactions of abstract chemicals. In the second part, an emergence of a proto-cell from a non-organized initial state, its reproduction and the selection of inside catalysts through the cell reproduction are reported in order.

Lattice Artificial Chemistry

Our model is based on discrete and stochastic dynamics, which is extended from a lattice-gas model. Chemicals are represented by particles on reaction sites that are arranged as a two-dimensional triangular lattice. Note that any number of particles can be placed on a single site. The vector $\mathbf{n}(\mathbf{x}) = (n_1(\mathbf{x}), n_2(\mathbf{x}), \ldots, n_m(\mathbf{x}))$ gives the number of each type of particles on the site $\mathbf{x}$. N_i gives the total amount of i-th particles in the system.

Chemical reactions are expressed by the probabilistic transition of particle types. The diffusion of chemicals is expressed by random walks of particles on the sites. These transition probabilities are given as the products

of the associated rate coefficients and the following function of the potential change ΔE,

$$f(\Delta E) \quad = \quad \frac{\Delta E}{e^{\beta \Delta E} - 1}. \tag{1}$$

where β represents the inverse of the product of the Boltzmann constant and temperature (note that, $f(\Delta E)/f(-\Delta E) = e^{-\beta \Delta E}$). In the simulations reported hereafter, the value of β is normalized and fixed to 1.

Hydrophobic Interaction

The probabilities of random walks of particles are biased according to the gradient of the potential $\Psi(\mathbf{x})$ which is given by summing up the interaction from all particles in the same and adjacent sites. The probability p with which a particle i moves from a site $\mathbf{x}$ to $\mathbf{x}'$ is calculated as follows,

$$\Psi_i(\mathbf{x}) \quad = \quad \sum_{|\mathbf{x}' - \mathbf{x}| \leq 1} \sum_j \psi_{ij}(\mathbf{x}' - \mathbf{x}) n_i(\mathbf{x}) \tag{2}$$

$$p_i(\mathbf{x} \to \mathbf{x}') \quad = \quad Dif_i \, f(\Psi_i(\mathbf{x}') - \Psi_i(\mathbf{x})) \tag{3}$$

where $\Psi_i(\mathbf{x})$ denotes the potential of particle i in the site $\mathbf{x}$, Dif_i denotes the diffusion coefficient of particle i, and $\psi_{ij}(d\mathbf{x})$ denotes the interaction on particle i from particle j. Diffusion coefficients depend on the species of the particles. Autocatalytic and membrane particles are assumed to be larger molecules so that their diffusion coefficients are smaller than those of other particles ($Dif_{A_i} = Dif_M = 0.003$, $Dif_{\mathrm{others}} = 0.01$).

To simulate the formation of membranes, we introduce hydrophobic interactions between particles. First, the particles are grouped into three classes: hydrophilic, hydrophobic and neutral. In general, all particles repel each other, but repulsion between hydrophilic and hydrophobic particles is much stronger than that between other particles so that phase separation between different classes of particles takes place. On the other hand, neutral particles do not repel other particles very strongly so that they can diffuse more freely.

Next, we assume that hydrophobic particles $\mathbf{M}$ are anisotropic. Namely, the repulsion around a particle $\mathbf{M}$ depends on its orientation and the configuration of the particles as illustrated in Fig. 1. There are specific directions in which the repulsion becomes strong, while the repulsion becomes weak in the other directions Taking its symmetry into account, a particle $\mathbf{M}$ can rotate to six different orientations ($\mathbf{M}^0$, $\mathbf{M}^{\pm \pi/6}$, $\mathbf{M}^{\pm \pi/3}$, $\mathbf{M}^{\pi/2}$) stochastically according to the gradient of the potential as follows,

$$p_{\mathbf{M}^k \to k'}(\mathbf{x}) \quad = \quad Rot \, f(\Psi_{\mathbf{M}^{k'}}(\mathbf{x}) - \Psi_{\mathbf{M}^k}(\mathbf{x})) \tag{4}$$

where $Rot = 0.01$ denotes the rotation coefficient. The repulsion between two particles $\mathbf{M}$ becomes strong when their orientations are different, so that they tend to align

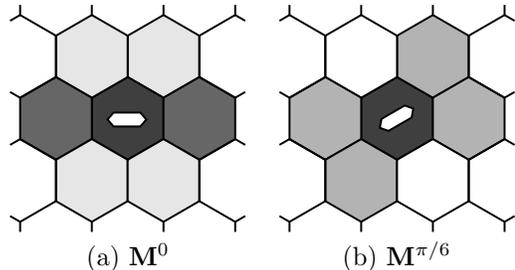(a) $\mathbf{M}^0$ (b) $\mathbf{M}^{\pi/6}$

Figure 1: Illustration of repulsion around a particle $\mathbf{M}$. The honeycomb cells represent the lattice sites. The depth of gray shade corresponds to the magnitude of repulsion against a hydrophilic particle on the site from the particle $\mathbf{M}$ on the center site. The repulsion becomes stronger on the dark gray sites than on the light gray sites.

in the same orientation. According to these interactions, particles $\mathbf{M}$ gather together to form stretched clusters. We call these stretched structures of particle $\mathbf{M}$ "membrane". Though the characters of membranes, such as flexibility, depends on these values, the formation of membranes can be observed in a wide range of parameters. The detail values of repulsion $\psi_{ij}(d\mathbf{x})$ which are arbitrary chosen for the following experiments are listed in Tables 1a and 1b.

Table 1: a. Repulsion between isotropic particles.

particles		position	
		$dr = 0$	$dr = 1$
hydrophilic	hydrophilic	0.0100	0.0033
	neutral	0.0010	0.0003
neutral	neutral	0.0010	0.0003

Chemical Reaction

We introduce a simple metabolic system of autocatalytic particles. Consider that there are various species of self-replicating particles, and some of them have the ability to catalyze the production of membrane particles. Resources of these particles are supplied from some external source homogeneously.

Figure 2 illustrates the reaction paths. The probabilities of chemical reactions depend on the enthalpy change along with the transition, as follows,

$$\Delta H_{ij} \quad = \quad \Delta H_j - \Delta H_i \tag{5}$$

$$p_{i \to j}(\mathbf{x}) \quad = \quad k_{ij}(\mathbf{x}) \, f(\Delta H_{ij} + \Psi_j(\mathbf{x}) - \Psi_i(\mathbf{x})) \tag{6}$$

where ΔH_{ij} denotes the enthalpy change that is given by the difference in the formation enthalpy listed in Table 2.

Table 1.b Repulsion between hydrophobic and other particles

particles		$dr = 0$	$dr = 1$		
			$\theta = 0, \pi$	$\theta = \pi/3, -2\pi/3$	$\theta = 2\pi/3, -\pi/3$
$\mathbf{M^0}$	hydrophilic	0.2000	0.1600	0.0200	0.0200
	neutral	0.0010	0.0008	0.0001	0.0001
	$\mathbf{M^0}$	0.0100	0.0033	0.0033	0.0033
	$\mathbf{M^{\pi/6}}$	0.0777	0.0259	0.0259	0.0259
	$\mathbf{M^{\pi/3}}$	0.1433	0.0477	0.0477	0.0477
	$\mathbf{M^{\pi/2}}$	0.2100	0.0700	0.0700	0.0700
$\mathbf{M^{\pi/6}}$	hydrophilic	0.2000	0.1000	0.1000	0.0000
	neutral	0.0010	0.0005	0.0005	0.0000
	$\mathbf{M^{\pi/6}}$	0.0100	0.0033	0.0033	0.0033
	$\mathbf{M^{-\pi/3}}$	0.2100	0.0700	0.0700	0.0700

$k_{ij}(\mathbf{x})$ denotes the coefficient of reaction $i \leftrightarrow j$ that may depend on the number of catalysts on the site. Note that the effects of the interactive potential, namely, the effects of hydrophilic/hydrophobic environments are also taken into account here, therefore, for example, it becomes more difficult to synthesize a hydrophilic particle in a hydrophobic environment.
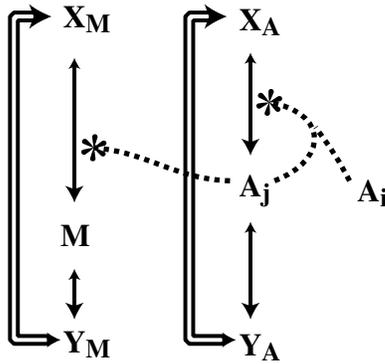

Figure 2: Schematic drawings of reaction paths. An autocatalyst ($\mathbf{A_i}$) catalyzes the reproduction of another particle $\mathbf{A_j}$ from a resource particle ($\mathbf{X_A}$) that has a higher chemical energy. It also catalyzes the production of a membrane particle ($\mathbf{M}$) from another resource particle ($\mathbf{X_M}$). All particles decay into waste particles ($\mathbf{Y_A}$ and $\mathbf{Y_M}$, respectively), spontaneously, however, an external energy supply recycles $\mathbf{Y_A}$ and $\mathbf{Y_M}$ into $\mathbf{X_A}$ and $\mathbf{X_M}$, respectively. The number of total particles is preserved.

Table 2: Formation enthalpy

particle	$\mathbf{X_A}, \mathbf{X_M}$	$\mathbf{A_i}$	$\mathbf{M}$	$\mathbf{Y_A}, \mathbf{Y_M}$
ΔH_i	12.0	6.0	4.0	0.0

There are ten species of autocatalytic particles ($\mathbf{A_0} \ldots \mathbf{A_9}$). An autocatalytic particle $\mathbf{A_i}$ catalyzes the replication of another particle $\mathbf{A_j}$ using it as a template and consuming a resource particle ($\mathbf{X_A}$).

$$\mathbf{A_i} + \mathbf{A_j} \quad \longleftrightarrow \quad \mathbf{A_i A_j} \qquad (7)$$
$$\mathbf{A_i A_j} + \mathbf{X_A} \quad \longleftrightarrow \quad \mathbf{A_i A_j} + \mathbf{A_j} \qquad (8)$$

There is a probability of mutation μ with which a particle $\mathbf{A_i}$ mutates to $\mathbf{A_{i\pm1}}$ when it is reproduced. Assuming that the rate of the first reaction is much faster than that of the second one, the rate coefficients between $\mathbf{X_A}$ and $\mathbf{A_j}$ can be given as follows,

$$n'_{A_i}(\mathbf{x}) = \mu n_{A_{j-1}}(\mathbf{x}) + (1 - 2\mu)n_{A_j}(\mathbf{x}) + \mu n_{A_{j+1}}(\mathbf{x}) \quad (9)$$

$$k_{X_A \leftrightarrow A_j}(\mathbf{x}) = k_A + C_A n'_{A_i}(\mathbf{x}) \sum_i n_{A_i}(\mathbf{x}) \quad (10)$$

where $n_{A_i}(\mathbf{x})$ denotes the number of particles $\mathbf{A_i}$ on the site $\mathbf{x}$, and k_A denotes the rate of spontaneous reaction. Note that all autocatalysts share a common catalytic activity C_A and catalyze the replication of each other equally.

An autocatalytic particle also catalyzes the production of a membrane particle ($\mathbf{M}$) from a resource ($\mathbf{X_M}$). The activity (C_{M_i}) depends on the species. The catalytic activity of each species $\mathbf{A_i}$ is given by the following equation, namely, the activity of particle $\mathbf{A_i}$ is i-th times larger than that of particle $\mathbf{A_1}$, so that the rate coefficients between $\mathbf{X_M}$ and $\mathbf{M}$ are given as follows,

$$C_{M_i} = C_M \times i \qquad (11)$$
$$k_{X_M \leftrightarrow M}(\mathbf{x}) = k_M + \sum_i C_{M_i} n_{A_i}(\mathbf{x}), \qquad (12)$$

where C_M is a given constant, and k_M denotes the rate of spontaneous reaction.

These particles naturally decay into waste particles ($\mathbf{Y_A}$ and $\mathbf{Y_M}$, respectively) at a constant rate k_Y. However, we introduce an external source that supplies resources. To preserve the total number of particles, the resource supply is expressed by the exchange from waste

to resource particles.Thus the transition coefficients are given as follows,

$$k_{A_j \leftrightarrow Y_A} = k_{M \leftrightarrow Y_M} \equiv k_Y \qquad (13)$$

$$k_{X_A \to Y_A} = k_{X_M \to Y_M} \equiv k_Y \qquad (14)$$

$$k_{Y_A \to X_A} = k_{Y_M \to X_M} \equiv k_Y + S_X. \qquad (15)$$

Due to the term S_X, the whole system is kept in a non-equilibrium state. The last particle ($\mathbf{W}$) represents water that does not change into other particles. We assume that water and autocatalytic particles are hydrophilic particles that are repelled by membranes, and resource and waste particles are neutral particles which can diffuse through membranes.

The rate coefficients of spontaneous reactions are $k_A = k_M = 1.0 \times 10^{-8}$, $k_Y = 1.0 \times 10^{-4}$. The coefficients of catalytic activity are $C_A = 1.0 \times 10^{-5}$ and $C_M = 1.0 \times 10^{-5}$. The mutation rate is $\mu = 1.0 \times 10^{-12}$. The rate of resource supply is given a constant $S_X = 16$.

The simulation is based on a Metropolis method. At each iteration, the following steps are repeated,

1. Calculate the potential of each particle.

2. Calculate the probabilities of diffusion, rotation and chemical transition according to the potential difference.

3. Change the state of particles according to the probabilities synchronously.

In the initial state, the particles are placed randomly. There are 30 particles on a site on average, and the mean numbers of particles on a site are listed in Table 3. There is a sufficient number of resource particles and supplies to sustain metabolism. The average production rate of membranes is set very low at first. Catalysts with higher activity only emerge through random mutations. The reaction sites are arranged as a 64×64 triangular lattice whose boundaries are periodic.

Table 3: Mean numbers on a site in the initial state

| particle	$\mathbf{A_0}$	$\mathbf{A_1}$	$\mathbf{A_2}$	$\mathbf{A_3}$	$\mathbf{A_4} \ldots \mathbf{A_9}$	
$\overline{n}_i$	1.6	1.2	0.8	0.4	0.0	
particle	$\mathbf{X_A}$	$\mathbf{Y_A}$	$\mathbf{M}$	$\mathbf{X_M}$	$\mathbf{Y_M}$	$\mathbf{W}$
$\overline{n}_i$	2.0	2.0	0.0	5.0	5.0	10.0

Simulation Results

The evolution of this system is roughly divided into three characteristic stages: (1) Chemical evolution, (2) Emergence of proto-cells, and (3) Cellular evolution.

Chemical Evolution

Fig. 3(1) shows the initial configuration. Before cellular selection starts, the chemical evolution simply depends on the reproduction rate of each species. In this model, because they share the same reproduction rate, the evolution is mostly driven by mutations and random fluctuation. At first, the largest part of the autocatalytic particles is $\mathbf{A_0}$ which does not produce membrane particles. Table 4 shows a profile of the population after 30,000 iterations for a single run. However, as the populations of other species increase, small pieces of membranes are gradually formed. (Fig. 3(2)).
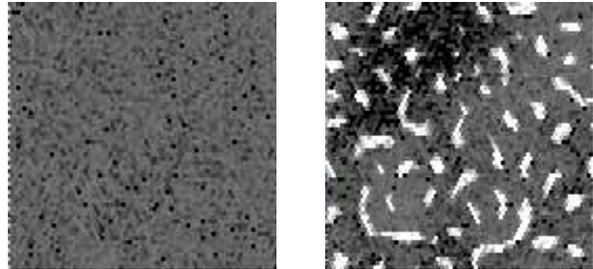
(1) Initial state   (2) After 30,000 iterations

Figure 3: Chemical evolution. The white regions are dominated by particle $\mathbf{M}$. The depth of gray shade represents the total population of the autocatalysts ($\sum \mathbf{A_i}$). The black regions are dominated by particle $\mathbf{W}$. Resource and waste particles are not displayed in the figures. Pieces of membranes are produced by the catalysts which emerged through mutations.

Table 4: A profile of the population of particles after 30,000 iterations.

particle	$\mathbf{A_0}$	$\mathbf{A_1}$	$\mathbf{A_2}$	$\mathbf{A_3}$	$\mathbf{A_4}$
$\overline{n}_i$	1.00	0.60	0.42	0.20	0.05
particle	$\mathbf{A_5}$	$\mathbf{A_6}$	$\mathbf{A_7}$	$\mathbf{A_8}$	$\mathbf{A_9}$
$\overline{n}_i$	0.07	0.08	0.05	0.04	0.06
particle	$\mathbf{X_A}$	$\mathbf{Y_A}$	$\mathbf{M}$	$\mathbf{X_M}$	$\mathbf{Y_M}$
$\overline{n}_i$	3.00	4.43	1.57	3.68	4.77

Emergence of Proto-cells

Once membranes are formed, they begin to restrict the diffusion of catalysts. Thus, membranes can keep the local population and also their reaction rate high. As resource particles are consumed faster in such regions, resource particles diffuse into these regions according to the gradient of the population. It increases their reaction rate more. Due to this osmotic competition for resources, a small difference in the population of autocatalysts between the two sides of the membrane becomes larger.

When the density of resources becomes too low in some regions, autocatalysts are no longer able to sustain their replication. Autocatalysts and membrane particles in these regions decay. At last, most regions become in-