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 (Szathmary & 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

\[ p_{ij}(\Delta t) = \begin{cases} 1 & \text{if } i = j \\ \sum_{k \neq j} p_{ik}(\Delta t) & \text{otherwise} \end{cases} \]
of the associated rate coefficients and the following function of the potential change $\Delta E$,

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

(1)

where $\beta$ 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 $\beta$ is normalized and fixed to 1.

### Hydrophobic Interaction

The probabilities of random walks of particles are biased according to the gradient of the potential $\Psi(x)$ 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 $x$ to $x'$ is calculated as follows,

$$\Psi_i(x) = \sum_{|x' - x| \leq 1} \sum_j \psi_{ij}(x' - x)p_i(x)$$

(2)

$$p_i(x \rightarrow x') = D_{ij} f(\Psi_i(x') - \Psi_i(x))$$

(3)

where $\Psi_i(x)$ denotes the potential of particle $i$ in the site $x$, $D_{ij}$ denotes the diffusion coefficient of particle $i$, and $\psi_{ij}(dx)$ 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 ($D_{ij \_ \_} = 0.003$, $D_{ij \_ \_} = 0.01$).

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 $M$ are anisotropic. Namely, the repulsion around a particle $M$ 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 $M$ can rotate to six different orientations ($M^0$, $M^\pm \pi/6$, $M^\pm \pi/3$, $M^\pm \pi/2$) stochastically according to the gradient of the potential as follows,

$$p_{M \rightarrow M'}(x) = Rot f(\Psi_{M}(x') - \Psi_{M'}(x))$$

(4)

where $Rot = 0.01$ denotes the rotation coefficient. The repulsion between two particles $M$ becomes strong when their orientations are different, so that they tend to align in the same orientation. According to these interactions, particles $M$ gather together to form stretched clusters. We call these stretched structures of particle $M$ “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 $\psi_{ij}(dx)$ which are arbitrary chosen for the following experiments are listed in Tables 1a and 1b.

### 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,

$$\Delta H_{ij} = \Delta H_i - \Delta H_j$$

$$p_{i \rightarrow j}(x) = k_{ij}(x) f(\Delta H_{ij} + \Psi_j(x) - \Psi_i(x))$$

(5)

(6)

where $\Delta H_{ij}$ 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

<table>
<thead>
<tr>
<th>particles</th>
<th>$dr = 0$</th>
<th>$dr = 1$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\theta = 0, \pi$</td>
<td>$\theta = \pi/2, -\pi/2$</td>
</tr>
<tr>
<td>$M^0$</td>
<td>0.2000</td>
<td>0.1600</td>
</tr>
<tr>
<td></td>
<td>0.0010</td>
<td>0.0008</td>
</tr>
<tr>
<td>$M^1$</td>
<td>0.0100</td>
<td>0.0033</td>
</tr>
<tr>
<td>$M^{7/6}$</td>
<td>0.0777</td>
<td>0.0259</td>
</tr>
<tr>
<td>$M^{7/3}$</td>
<td>0.1433</td>
<td>0.0477</td>
</tr>
<tr>
<td>$M^{7/2}$</td>
<td>0.2100</td>
<td>0.0700</td>
</tr>
<tr>
<td>$M^{-\pi/3}$</td>
<td>0.2100</td>
<td>0.0700</td>
</tr>
</tbody>
</table>

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

Table 2: Formation enthalpy

<table>
<thead>
<tr>
<th>particle</th>
<th>$\Delta H_i$</th>
<th>X_A, X_M</th>
<th>A_i</th>
<th>M</th>
<th>Y_A, Y_M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12.0</td>
<td>6.0</td>
<td>4.0</td>
<td>0.0</td>
<td></td>
</tr>
</tbody>
</table>

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

$$A_i + A_j \leftrightarrow A_i A_j \quad (7)$$

$$A_i A_j + X_A \leftrightarrow A_i A_j + A_j \quad (8)$$

There is a probability of mutation $\mu$ with which a particle $A_i$ mutates to $A_{i \pm 1}$ 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 X_A and A_j can be given as follows,

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

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

where $n_{A_i}(x)$ denotes the number of particles $A_i$ on the site $x$, 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 (M) from a resource (X_M). The activity ($C_{M_i}$) depends on the species. The catalytic activity of each species $A_i$ is given by the following equation, namely, the activity of particle $A_i$ is $i$-times larger than that of particle $A_1$, so that the rate coefficients between X_M and M are given as follows,

$$C_{M_i} = C_M \times i \quad (11)$$

$$k_{X_M\rightarrow M}(x) = k_M + \sum C_{M_i} n_{A_i}(x), \quad (12)$$

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

These particles naturally decay into waste particles (Y_A and 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

$k_{ij}(x)$ 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.
to resource particles. Thus the transition coefficients are
given as follows,

\[ k_{A \rightarrow Y} = k_{M \rightarrow Y} = k_Y \] (13)
\[ k_{X \rightarrow Y} = k_{X_M \rightarrow Y_M} = k_Y \] (14)
\[ k_{Y \rightarrow X} = k_{Y_M \rightarrow X_M} = k_Y + S_X. \] (15)

Due to the term \( S_X \), the whole system is kept in a non-
equilibrium state. The last particle (\( W \)) represents wa-
ter 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 dif-
cuse 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 \( C_A = 1.0 \times 10^{-8} \) 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 differ-
ence.
3. Change the state of particles according to the proba-
bilities 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 \( \times \) 64 triangular lattice
whose boundaries are periodic.

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

<table>
<thead>
<tr>
<th>particle</th>
<th>( A_0 )</th>
<th>( A_1 )</th>
<th>( A_2 )</th>
<th>( A_3 )</th>
<th>( A_4 \ldots A_9 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \pi_i )</td>
<td>1.6</td>
<td>1.2</td>
<td>0.8</td>
<td>0.4</td>
<td>0.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>particle</th>
<th>( X_A )</th>
<th>( Y_A )</th>
<th>M</th>
<th>( X_M )</th>
<th>( Y_M )</th>
<th>( W )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \pi_i )</td>
<td>2.0</td>
<td>2.0</td>
<td>0.0</td>
<td>5.0</td>
<td>5.0</td>
<td>10.0</td>
</tr>
</tbody>
</table>

Simulation Results

The evolution of this system is roughly divided into three
characteristic stages: (1) Chemical evolution, (2) Emer-
gence 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 evolu-
tion is mostly driven by mutations and random fluctua-
tion. At first, the largest part of the autocatalytic par-
icles is \( A_0 \) 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)).

Figure 3: Chemical evolution. The white regions are
dominated by particle \( M \). The depth of gray shade rep-
resents the total population of the autocatalysts (\( \sum A_i \)).
The black regions are dominated by particle \( W \). Re-
source and waste particles are not displayed in the fig-
ures. 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.

<table>
<thead>
<tr>
<th>particle</th>
<th>( A_0 )</th>
<th>( A_1 )</th>
<th>( A_2 )</th>
<th>( A_3 )</th>
<th>( A_4 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \pi_i )</td>
<td>1.00</td>
<td>0.60</td>
<td>0.42</td>
<td>0.20</td>
<td>0.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>particle</th>
<th>( A_5 )</th>
<th>( A_6 )</th>
<th>( A_7 )</th>
<th>( A_8 )</th>
<th>( A_9 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \pi_i )</td>
<td>0.07</td>
<td>0.08</td>
<td>0.05</td>
<td>0.04</td>
<td>0.00</td>
</tr>
</tbody>
</table>

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 be-
tween 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-