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**Recursiveness and Evolvability in a
Mutually Catalytic Reaction System**

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RECURSIVENESS AND EVOLVABILITY IN A MUTUALLY CATALYTIC REACTION SYSTEM

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We discuss how recursive production of a proto-cell consisting of a mutually catalytic reaction network is possible. It is shown that a minority molecule species plays an essential role in carrying heredity, in the sense that the molecule is preserved well and controls replication of the cell. The cell state controlled by such a minority molecule is shown to have evolvability. Successive switches over quasi-recursive states are found, caused by extinction of minority molecules. Experimental demonstration of the theory is also discussed.

Keywords: Minority control; hypercycle; origin of life.

1. Question on Recursive Production of a Cell and Heredity

A cell consists of several replicating molecules that mutually help the synthesis. These synthesis processes must maintain some synchronization. For example, a membrane that partly separates a cell from the outside has to be synthesized, maintain some degree of synchronization with the replication of other internal chemicals. Molecules to catalyze other molecules must also be synthesized. How is such recursive production maintained while keeping a diversity of chemicals? In addition, this recursive production is not complete, and changes in chemicals or their composition occurs over generations, giving a basis for evolution. How is such evolvability compatible with recursive production?

In a cell, among many chemicals, only some chemicals (e.g. DNA) are regarded as carrying genetic information. Why do only specific molecules play this role? How has such separation of roles in molecules between genetic information and metabolism progressed? Is this the necessary course of a system with internal degrees and reproduction?

Our motivation here is to propose a general logic to answer the above questions, but not to unveil 'what happened in past.' Still, these questions have been addressed in the study of the origin of life. Hence, it is relevant to review previous theoretical studies on the origin of life briefly.

Eigen, following the experimental study of Spiegelman on replication of RNA [13], considered how recursive production of catalytic molecules is possible [4]. For replication, catalysts are necessary, and information to produce them must be preserved in RNA. However, error rates in replication must have been high at a primitive stage of life, and accordingly, it is recognized that the information to carry catalytic activity will be lost within few generations. To resolve this problem of inevitable loss of catalytic activities through replication errors, Eigen and Schuster proposed the hypercycle [4], where replicating chemicals catalyze one another forming a cycle, as *A* catalyzes *B*, *B* catalyzes *C*, *C* catalyzes *D*, and *D* catalyzes *A*. With this hypercycle, the original problem of error accumulation is avoided. However, the hypercycle itself turns out to be weak against parasitic molecules, i.e. those which are catalyzed by a molecule in the cycle, but do not catalyze those in the cycle. Later, it was discussed that compartmentalization by a cell structure may suppress the invasion of parasitic molecules [5, 15], or that the use of spatially reaction-diffusion system may resolve this parasite problem [1, 2].

On the other hand, Dyson [3] discussed a possibility that a set of a large number of chemical species may continue reproduction, sustaining catalytic activity. Although accurate replication of such a variety of chemicals is not possible, chemicals, as a set, may continue reproducing themselves loosely, while maintaining catalytic activity. Indeed, he proposed an abstract model to demonstrate such a possibility.

It is important to study if such loose reproduction as a set is possible in a mutually catalytic reaction network. If this is possible, and if these chemicals also include molecules forming a membrane for compartmentalization, reproduction of a primitive cell will become possible. In fact, from the chemical nature of lipid molecules, it is not so surprising that a compartment structure is formed from lipids.

Still, in this reproduction system, any particular molecules carrying information for reproduction do not exist, in contrast to the present cell which has specific molecules (DNA) for it. As for a transition from early loose reproduction to later accurate replication with genetic information, Dyson only referred to 'genetic takeover', while its mechanism is not discussed.

Considering these theoretical studies so far, it is important to study how recursive production of a cell is possible, with the appearance of some molecules to play a specific role for heredity. For this study, let us consider a simple prototype cell that consists of mutually catalyzing molecule species whose growth in number leads to cell reproduction [9]. In this protocell, the molecules that carry the genetic information are not initially specified. The first question we discuss here is whether some specific molecules start to carry information for heredity in order to realize continual reproduction of such a protocell.

In the present cells, it is generally believed that information is encoded in DNA, which controls the behavior of a cell. Still, even in these cells, proteins and DNA both influence the replication process of each other. In spite of this mutual dependence, the DNA molecule is usually regarded as the carrier of heredity.

Now, we need to first clarify what 'heredity' really means. Here, one might point out that DNA molecules would be suited to encode many bits of information, and hence would be selected as an information carrier. Although this 'combinatorial' capacity of DNA molecules as an information carrier is important, what we are interested in here is a basic property that has to be satisfied prior to that, i.e. the origin of heredity. Heredity causes a strong correlation in phenotype between ancestor and offspring. For a molecule to carry heredity, the following two features are necessary:

- (1) Such molecules are preserved well over generations. The number of such molecules exhibits smaller fluctuations than that of other molecules, and their chemical structure (such as polymer sequence) is preserved over a long time span. We refer to this as the '**preservation property**.'
- (2) If this molecule is replaced by some other type of molecule, there is a much stronger influence on the behavior of the cell than the case when other molecules are changed. We refer to this as the '**control property**.'

The question we address in the next section is as follows. Consider a protocell with mutually catalyzing molecules. Then, under what conditions does recursive production continue to maintain catalytic activities? How are recursiveness and diversity in chemicals compatible? How is evolvability of such protocells possible? To answer these questions, are molecules carrying heredity necessary? Under what conditions, does one molecule species begin to satisfy the conditions (1) and (2) so that the molecule carries heredity?

2. Minority Controlled State

A theoretical study to answer the question in Sec. 1 was presented in Ref. 9. By setting up a condition for prototype of a cell consisting of mutually catalyzing molecules, it was shown, under rather general conditions, that symmetry breaking between two kinds of molecules takes place. Through replication and selection, one kind of molecule comes to satisfy conditions (1) and (2) in Sec. 1. In this section, we summarize the logic of the study, without going into the details.

Recall that a present cell has several chemicals, whose functions are differentiated. The molecules carrying heredity (DNA) are rather stable, and synthesized slowly compared with proteins or other molecules for metabolism. In a cell, the number of DNA molecules is much smaller than the proteins. Here, without assuming the detailed biochemical properties of DNA, we seek a general condition for the differentiation of the roles of molecules in a cell and study the origin of the controlling behavior of some molecules.

First, assume a prototype of cell, consisting of molecules that catalyze each other (see Fig. 1). As the reaction progresses, the number of molecules will increase. Then, considering the physical nature of the membrane, this cell will divide when its volume (the total number of molecules) is beyond some threshold. Then, the

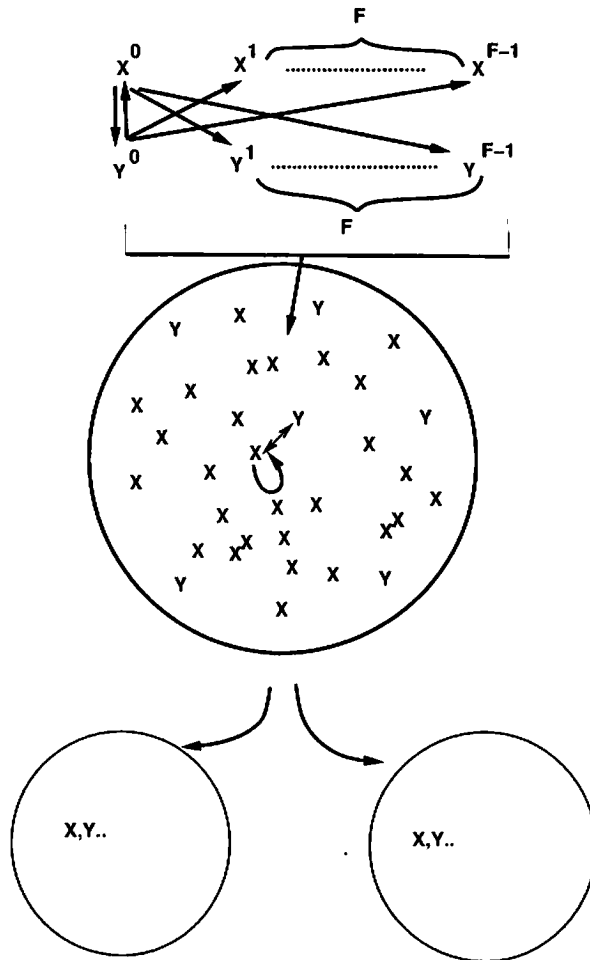


Fig. 1. Schematic representation of our model.

molecules split into two 'daughter cells.' The question here is how the compositions are transferred and if there appear some specific molecules carrying heredity. To clarify the logic of the theory, we consider the simplest case: Only two kinds of molecules, X and Y , exist in this protocell, and they catalyze each other for the synthesis of the molecules. Without losing generality, one can assume that the synthesis speed of X is faster than that of Y (or in other words, one can say that the catalytic activity of Y is much stronger than that of X .)

In the chemical replication process of complex polymers, some structural changes in molecules can occur, which may be termed 'replication error.' These structural changes in each kind of molecule may result in the loss of catalytic activity. Indeed, the molecules with catalytic activity are not so common. Still, molecules without catalytic activity can grow in number, as long as they are catalyzed by

other catalytic molecules. Then, this protocell is taken over by such non-catalytic molecules, as discussed in the parasite problem for the hypercycle. Hence, the maintenance of reproduction of this protocell is not so easy.

As a simple 'gendaken experiment' consider the case that each kind of X and Y has several types $0, 1, \dots, F-1$, and only the type 0 has catalytic activity. (For example X and Y are different kinds of molecules, while the index j for X^j or Y^j represents a different sequence of each polymer). Then, the question is how the active form 0 is maintained through reproduction, even if F is large.

Here, recall that due to the difference in the speed of synthesis, the number of X molecules will get larger than that of Y in each protocell. As long as the number of molecules in a cell is not large, eventually, there comes a point when the catalytically active Y molecule (i.e. Y^0) is extinct. Then, X molecules are no longer synthesized. Inactive Y molecules ($Y^j; j > 0$) may still be synthesized as long as X^0 molecules remain. However, after each division, the number of X^0 molecules halves, and sooner or later, the cell stops division. Hence, once the number of Y^0 becomes 0, the reproductivity of the cell will be lost.

As long as the total number of molecules N is not very large, there are fluctuations in the number of each molecule species. Then, some cells, due to fluctuations in molecule numbers, may keep active Y molecules. Since there is little room for Y molecules in protocells, due to its slow synthesis, the number of Y^j molecules (for all $j = 0, 1, \dots, F-1$) should be small. Hence, typically, to keep the active Y molecules, the number of all the other Y molecules should be suppressed, probably to zero. Once the inactive Y molecules are extinct, they do not reappear so often, since the expectation value for it is given by the product of the number of Y molecules and the error rate in replication. Since the former is very few, the expectation value is less than 1. Hence a cell state with very few Y^0 molecules and almost zero Y^j ($j > 0$) molecules can maintain reproduction.

Note that such a state does not exist if the total number of molecules is very large. Indeed, as a solution of a continuous differential equation (rate equation) for chemical concentrations, obtained by the limit $N \rightarrow \infty$, such a state does not exist. Due to the finiteness in molecule numbers, fluctuations for such special initial conditions can occur, and such rare fluctuations, once they occur, are preserved, since the cell with such compositions can continue reproduction.

Indeed, the above argument was numerically confirmed by stochastic simulations of the above model. (In the simulation, we fix a total number of such protocells, and when a protocell divides, one randomly chosen protocell is removed, so that the number is fixed. This process provides competition for the survival of such protocells, arising from competition for chemical resources for reproduction.) Note that the state with few active Y molecules (Y^0) and almost zero inactive Y molecules ($Y^j; j > 0$) is established, under the following conditions: (i) the number of molecules in a cell is not too large, (ii) the number of types of inactive molecules (F) is large, and (iii) there is sufficient difference between the growth speeds of the two kinds of molecules (X and Y).

In this state with few Y^0 molecules, the active Y molecule is a carrier for heredity, in the sense that the molecule has the following properties.

- **‘Preservation property’**: First, these active Y molecules are well preserved over generations, since otherwise the corresponding cell cannot replicate. Indeed, from numerical simulations, selected and preserved is a state with the number of active Y molecules $2 \sim 6$, and with almost zero inactive Y molecules. The realization of such a state is very rare when we consider the rate equation obtained in the continuum limit. Hence, the preservation is satisfied.
- **‘Control property’**: Next, consider a structural change in the Y molecule that may occur as a replication error and causes a change of catalytic activity. Since the number of active Y molecules is low, and all the X molecules are catalyzed by them, this influence is enormous. The synthesis speed of a protocell should drastically change. On the other hand, a change to X molecules has a weaker influence, since there are many active X molecules, and the influence of change in each molecule is averaged out. Unless almost all molecules change in the same way simultaneously, the average catalytic activity of X molecules would not change much, but such coherent change is not possible, as deduced from the law of large numbers. Hence, the change of the Y molecule has a crucial influence on the cell behavior, compared with that of X molecules.

Summing up the argument in this section, the molecule species with slower replication speed and (accordingly) with minor population, comes to possess the properties for the heredity. Indeed, this argument is confirmed in numerical simulations. The state controlled by the minority molecule species is termed the minority controlled state (MCS).

3. Biological Significance

Here, we discuss the possible biological significance of the minority controlled state (MCS).

Since the change of the minority molecules is not smeared out by the law of large numbers, an important characteristic of the MCS is evolvability. Let us discuss this point by considering the case that there are several types of catalytic molecules for X and Y , with different degrees of catalytic activities.

Since the replication process is entirely facilitated by catalytic activity, growth speed of the protocell depends on catalytic activities of molecules in it. With some change to molecules, the protocells including greater catalytic activities will be selected through evolution, leading to the selection of molecules with higher catalytic activities.

Because only a few Y^0 molecules exist in the MCS, a change to one of them strongly influences the catalytic activity of the protocell, as supported by the control property. On the other hand, a change to X molecules has a weaker influence, on average, as can be deduced from the law of large numbers. Hence, the MCS is important for evolvability of a protocell.

This MCS has a positive feedback process to stabilize the state itself, by opening a route to the evolution of genetic information [9]. Since the preservation of minority molecules is essential to a cell of MCS, a new selection pressure emerges to further ensure the preservation of the minority molecule into the offspring cells. (Otherwise the reproduction of the cell is seriously damaged.) A machinery to guarantee the faithful transmission of the minority molecule should evolve, which further strengthens the preservation of the minority molecule. Hence, heredity evolves only as a result of kinetic phenomenon in a reproducing protocell consisting of mutually catalytic molecules.

Once this faithful transmission of a minority molecule is evolved, it is probable that other chemicals that are synthesized in connection with it are transmitted. Then, more molecules are transmitted, and more information will be encoded on the minority molecule. With this evolution having more molecules catalyzed by the minority molecule, the machinery to better take care of minority molecules will also evolve, since this minority molecule is involved in reactions for the synthesis of many other molecules. Hence, the MCS allows for co-evolution for better transmission of minority molecules and for the coding of more information. At this point, genetic information is separated from other molecules carrying metabolism.

4. Experiment

Is it possible to experimentally verify the argument so far? In a possible relationship with the present theory, Matsuura *et al.* (Yomo's group) constructed an *in vitro* replication system. The system consists of enzymes, DNA and RNA [12]. It includes DNA polymerase, synthesized by the corresponding gene, which catalyzes the synthesis of the DNA. In contrast to PCR, where enzymes have to be added from outside, enzymes are also synthesized from the amino acid. Only by supplying amino acids and ATP, and some other material molecules, is a set of chemicals including DNA, RNA, and proteins, synthesized autonomously.

Through a mutual catalytic process, the chemicals replicate themselves. A gene facilitates the production of a DNA polymerase, and the DNA polymerase catalyzes the synthesis of the DNA with that gene. Roughly speaking, the polymerase (enzyme) in their experiment corresponds to X^0 in our model, while the polymerase gene corresponds to Y^0 .

In this experiment, the compartment structure of a cell with autonomous replication of the membrane has not yet been synthesized. Instead, one can split the solution including the chemicals by external manipulation. To be specific, they adopted the following procedure. After the replication of chemicals progressed, the system was split into several tubes containing a given number of DNA. In each tube, the synthesis to amplify DNA and enzymes was carried out. After this replication stage, the contents of tubes were put together into a container. From this container, contents are extracted and split into several tubes. This procedure is repeated.

The catalytic activity of the corresponding polymerase may change, when the structure is changed, according to the error in DNA. Hence, the multiplication of DNA differs in each tube. In some tubes, genes for a polymerase with a higher catalytic activity are preserved, resulting in a higher rate of replication, while in other tubes, the synthesis does not progress much. Since the next generation is selected from the contents of all the tubes, a gene corresponding to a DNA polymerase with a higher catalytic activity will be selected with a higher probability. Hence, the present experimental system constitutes a Darwinian system, in the sense that replicators with some error compete for the number of offspring.

If the catalytic activity of DNA is maintained through the above procedure, by allowing the synthesis of the corresponding polymerase to synthesize itself, the above replication continues. However, this is not necessarily easy, since most errors in replication lead to enzymes with low or null catalytic activity. Then, it is probable that the catalytic activity in a tube may decrease by generation. Eventually, the polymerase for the synthesis of the DNA may no longer be synthesized and the reproduction may stop. Indeed, this was discussed as the 'parasite problem' in Sec. 1. Then, can the replication continue over generations?

Note that in this experiment, one can control the number of DNA molecules in each tube. One can start from a single DNA molecule and choose a single DNA after multiplication, or a larger number of DNA molecules. Matsuura *et al.* carried out the above experiment starting from a single DNA molecule and also, separately, starting from 100 DNA molecules. In the former case with a single DNA, it was found that replication is maintained over generations, even under deleterious mutations (that correspond to structural changes from active to inactive molecules in our theory). On the other hand, for the latter case with 100 DNA molecules, the catalytic activity is lost within a few generations, and self-replication is no longer maintained.

This experimental result is consistent with the theory presented in Sec. 2. Note that DNA molecules in the experiment correspond to Y molecules in the theory. A change in the molecules, if their number is small, drastically influences the synthesis speed in a tube (protocell). Indeed, in the single-DNA experiment, the catalytic activity differs much in each tube. In many of the tubes, molecules may have lower catalytic activities, but in a few of them the activity remains high or becomes higher. Since in the latter tubes, the number of DNA is multiplied to a large degree, it is more probable that such DNA molecules are selected for the next generation. Hence, the tube in the next generation maintains high catalytic activity, or may even gain a higher activity. Although genes for polymerases with a high catalytic activity are rare, such rare molecules are preserved, as found in the theory.

On the other hand, when the number of DNA molecules in a tube is 100, the catalytic activity is given by the average from 100 types of the genes. Since the types with high catalytic activity are rare, the average catalytic activity, after some replication errors, will be lower. This is true for all tubes. Hence, it is not possible to select rare fluctuations. Indeed, the catalytic activity decreases about $2/3$ in each generation, and the replication does not continue over five generations.

Now, it is shown that the system has evolvability only if the number of DNA in the system is only few. Otherwise, the system gradually loses its activity to replicate itself. These experimental results are consistent with the minority control theory described already. (Still, the correspondence between the theory and experiment is incomplete as yet. The preservation property is not discussed in the experiment, and a mutual catalytic relationship is not fully considered.)

5. Recursive Production and Switching of a Catalytic Reaction Network System

In the discussion in Sec. 2, we considered a system consisting of two kinds of molecules. To study the general features of a system with mutually catalyzing molecules, it is also important to consider a system with a variety of chemicals (k molecule species), forming a mutually catalyzing network. The molecules replicate through catalytic reactions, so that their numbers within a cell increase. Again, when the total number of molecules exceeds a given threshold (here, we used $2N$), the cell divides into two, with each daughter cell inheriting half of the molecules of the mother cell, chosen randomly. Here, we consider the following model [10]. We choose a random catalytic network, i.e. a chemical species catalyzes the synthesis of some other randomly chosen chemical as



with $i, j = 1, \dots, k$. The connection rate of the catalytic paths is given by p per each chemical. Again, replication is accompanied by some 'error,' and instead of the replication of the molecule i , one of other k molecule species is synthesized with an error rate μ .

In our model, there are four basic parameters: the total number of molecules N , the total number of molecule species k , the mutation rate μ , and the reaction path rate p . Catalytic activity depends on each molecule, which gives the rate of the above reaction (1). We assume that the catalytic activity $c(j)$ is chosen again from a random number over $[0, 1]$, which depends on the molecule species j , but is fixed. By carrying out simulations of this model, choosing a variety of parameter values N , k , μ and p , also by taking various random networks, we have found that the behaviors are classified into the following three types:

- (1) Fast switching states without recursiveness,
- (2) Achievement of recursive production with similar chemical compositions,
- (3) Switch over several quasi-recursive states.

In the first phase, there is no clear recursive production and the dominant molecule species changes frequently. At one time step, some chemical species are dominant but only a few generations later, this information is lost, and the number of the molecules in this species goes to zero (see Fig. 2(a)). No stable set of catalytic networks is formed. Here, the time required for the reproduction of a cell is much larger than in case (2).

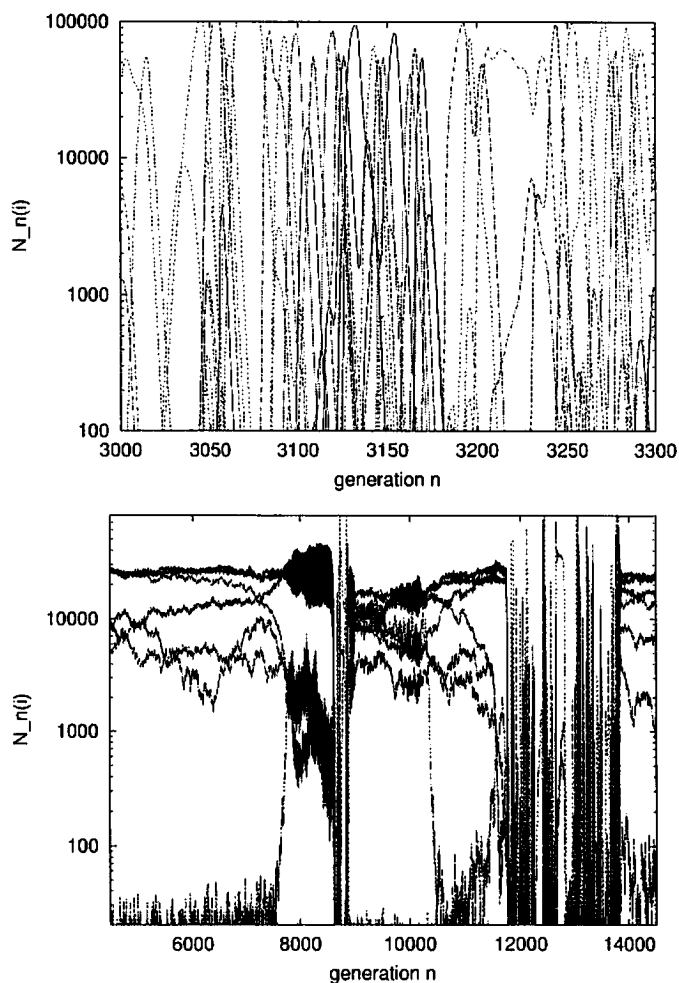


Fig. 2. The number of molecules $N_n(i)$ for the species i is plotted as a function of generation n of cells, i.e. at each successive division event n . In (a) a random network with $k = 500$ and $p = 0.2$, and in (b) that with $k = 200$ and $p = 0.2$ was adopted, with $N = 64,000$ and $\mu = 0.01$. Only some species (whose population gets large in some generations) are plotted. In (a) dominant species change successively in generation, while in (b) three quasi-recursive states are observed.

In the second phase, on the other hand, a recursive state is established, and the chemical composition is stabilized such that it is not altered much by the division process. Generally, all the observed recursive states consist of 5–10 species, except for those species with one or two molecule numbers, which exist only as a result of replication errors. These 5–10 chemicals mutually catalyze, by forming a catalytic network as will be discussed later. The members of these 5–10 species do not change by generation, and the chemical compositions are transferred to the offspring cells. Once reached, this state is preserved throughout the whole simulation, lasting more than 10,000 generations.

The recursive state observed here is not necessarily a fixed point with regard to the population dynamics of the chemical concentrations. In some cases, the chemical concentrations oscillate in time, but the nature of the oscillation is not altered by the process of cell division. In all of these cases, the number of each molecule shows relatively large fluctuations, since the total number of molecules N is not large (typically we choose $N \sim (10^2 \sim 10^5)$ in our simulations).

In the third phase, after one recursive state lasts over many generations (typically a thousand generations), a fast switching state appears until a new (quasi-)recursive state appears. As shown in Fig. 2(b), for example, each (quasi-)recursive state is similar to that in phase (2), but in this case, its lifetime is finite, and it is replaced by the fast switching state as in phase (1). Then, the same or different (quasi-)recursive state is reached again, which lasts until the next switching occurs.

Although the behavior of the system depends on the choice of the network, there is a general trend with regard to the phase change, from (1) to (2), and then to (3) with the increase of N , or with the decrease of k .

Now we study how recursive states are sustained in phase (2). Here, one might wonder why the species with higher catalytic activities are not taken over by parasitic molecule species that have lower catalytic activities and are catalyzed by molecules with higher catalytic activities. By examining several reaction networks, we came to understand itinerancy and the stability of recursive states as follows.

The 5–10 species in the recursive state form a mutually catalytic network, for example, as in Fig. 3. This network has a *core hypercycle network*, as shown by thick arrows in Fig. 3, i.e. A catalyzes B , B catalyzes C , and C catalyzes A . Here, the number of molecules N_j of molecule species j , is in the inverse order of their catalytic activity $c(j)$, i.e. $N_A > N_B > N_C$ for $c_A < c_B < c_C$. In fact, because a molecule with higher catalytic activity helps the synthesis of others more, this inverse relationship is derived. (The population of the molecule C is usually larger than D , E , etc., though.)

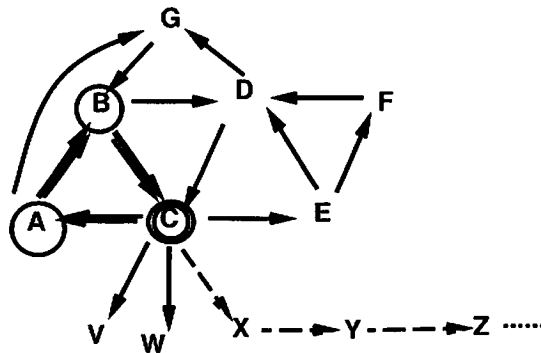


Fig. 3. An example of a mutually catalytic network in our model. The core network for the recursive state is shown by circles, while parasitic molecules (X, Y, \dots) connected by broken arrows, are suppressed at the (quasi-)recursive state.

This recursive state may be destabilized if the population of parasitic molecules (e.g. X, Y, \dots) increases, which are catalyzed by the molecule C , but do not catalyze any member of the catalytic network. In our model, the molecule with a higher catalytic activity (C) is catalyzed by a molecule species with lower activities but larger populations (A). Hence, the parasitic molecule species cannot easily invade to disrupt this mutually catalytic network. Since the minority molecule (C) and majority molecule (A) form a mutual catalytic network (with the aid of another molecule (B)), a large fluctuation in molecule numbers is required to destroy this network.

Next, we discuss the mechanism of switching. When the total population of molecules in a cell is not so large, the fluctuations are relatively large, especially with regard to the minority molecule C . The number of the molecule C may decrease due to fluctuations, while the number of some parasitic molecules (X) that are not originally in the catalytic network, but are catalyzed by C , may increase. Since the total number of molecules in a cell is limited, the number of minority molecules (C) may decrease, then, and the molecule C may be taken over by the new parasitic molecule species X . If this happens, the other molecule species in the original network loses the main source that catalyzes their synthesis, successively. Then the new parasitic molecule X occupies a large portion of populations. However, the molecule's main catalyst (C) soon disappears, and this species X is taken over by some molecules Y that are catalyzed by X (see the broken arrows in Fig. 3). Then, within a few generations, dominant species changes, and recursive production does not occur. Indeed, this is what occurred in phase (1). After the system has been in a fast switching state for a while, another (or possibly the same) catalytic network is formed, where the existence of a minority molecule species with a higher catalytic activity stabilizes this (quasi-)recursive state. Hence, the fluctuation in the minority molecule in the core network is relevant to the switching process.

Note that phase (3) gives a basis for evolvability, since a novel, (quasi-)recursive state with different chemical compositions is visited successively. To see this point, we have also studied a model with two modifications from the original. First, the catalytic activity is set as $c(i) = i/k$, i.e. the activity is monotonically increasing with the species index. Second, instead of a global change to any molecule species by replication error, we modify the rule so that the change occurs only within a given range $i_0 (\ll k)$ (i.e. when the molecule species j is synthesized, with the error rate μ , the molecule $j + j'$ with j' a random number over $[-i_0, i_0]$ is synthesized). Starting from species with $i < i_{ini}$, one can examine if the evolution to a network with higher catalytic activities progresses or not, i.e. if the indices i in the network increase successively or not. As is expected, for phase (3), after one (quasi-)recursive state (consisting of species within the width of the order $2i_0$) lasts for some time, switching occurs. With the pressure for selection of the protocells, those with a new (quasi-)recursive state are selected that consist of molecules with higher catalytic activities (i.e. with larger indices of species). Here, the species with the highest catalytic activity in the network is a minority in population. Once the population

of such species is decreased by fluctuations, there occurs a switch to a new state that has higher catalytic activities, and the species indices successively increase. Hence, evolution from a rather primitive cell consisting of low catalytic activities to that with higher activities is possible, by taking advantage of minority molecules.

6. Summary and Discussion

In the present paper, we have discussed how recursive production and evolvability are achieved in a cell consisting of mutually catalytic molecules. The importance of minority molecules is stressed. First, it is shown that molecule species, a minority in number, carry the heredity, in the sense that the molecule is preserved well over generations, and it controls the behavior of a cell strongly. How genetic information evolves from this minority controlled state is discussed, noting a positive feedback to enhance the preservation of such a minority molecule and controllability of the molecule. An experiment with an artificial replication system is discussed, from the viewpoint of this minority control theory.

Then, a recursive production of a system with catalytic reaction network is studied. A recursive production consisting of 5 ~ 10 molecules forming a mutually catalytic network is shown, while the switching to a new quasi-recursive state (that achieves almost recursive reproduction over many generations) is also pointed out.

A recursive state in a mutually catalytic system was also discussed by Sergre, Ben-Eli and Lancet [14] as a 'compositional genome.' In the present paper, the relevance of minority molecules is stressed, which leads to successive switches over several quasi-recursive states. The evolvability of such a state is also stressed.

It is also interesting to study statistical properties of such a catalytic reaction network, as recently has been discussed [7, 11] Also, introduction of cell-cell interaction with such a chemical reaction network model is important for the study of cell differentiation and development. Recursive states with differentiation has been discussed as isologous diversification [6, 8], where the chemical composition of a cell is transferred to its offspring.

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