Life as Complex Systems: Viewpoint from Intra-Inter Dynamics

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Basic problems in complex systems are surveyed in connection with life. As a key issue for complex systems, complementarity between syntax/rule/parts and semantics/behavior/whole is stressed. To address the issue, a constructive approach for a biological system is proposed. As a construction in a computer, intra-inter dynamics is presented for cell biology, where the following five general features are drawn from our model experiments: intrinsic diversification, recursive type formation, rule generation, formation of internal representation, and macroscopic robustness. Significance of the constructed logic to the biology of existing organisms is also discussed.

COMPLEX SYSTEMS

In the recent trend, complex systems have often been studied as a problem of self-organization or adaptation. It is typically seen in the term "complex adaptive systems," while the long-term studies for self-organization have been pursued in the Brussels group as "dissipative structures" [1] and at the Stuttgart group as "synergetics" [2]. As is discussed in this paper, "complex system" studies should be distinguished from such self-organization or adaptation. (Complex system studies in Japan, started around mid-80s, are aimed at the understanding of life by going beyond "chaos" or "self-organization" [3,4].)

To discuss the problem of "complexity," one should carefully distinguish "complex" from "complicated." The latter is a system composed of a variety of elements, which requires hard efforts to disintegrate it into parts, but in principle it is possible. On the other hand, in complex systems, one has to face the circular situation in which the parts are understood only through the whole, although the whole, of course, consists of parts. We call such a structure "complementarity" [5] between the whole and parts.

Indeed, such complementarity is extended to that between a group of *symbol, rule, syntax* and that of *image, behavior, semantics.* (see Table 1) [6]. The former group is given by discrete representation, while the latter uses continuum. For most so-called complex systems, people still focus on the studies from the former to the latter. For example, chaos and cellular automata studies have shown how complex behavior emerges from a simple rule, while the rule formation from dynamic behavior is not well discussed. In complex system studies, we also have to study how the former set (syntax, etc.) emerges from the latter (semantics, etc.).

There are very few studies toward this direction, although in chaos studies there are some germs for it. In Crutchfield's "ϵ-machine," he tries to construct an automaton rule from data [7]. In several high-dimensional dynamical systems, chaotic itinerancy [8–10] over ordered states have been found, where the transition from one ordered state to another is not random but is constrained with some rule generated from lower-level dynamics. Indeed, the frequent appearance of chaotic itinerancy in biologically oriented problems gives us a hope

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that the formation of a syntactic rule from complex behavior may be associated with it.

Let us take an example in molecular biology. It is now generally believed that genes switch on and off, according to signals. The mechanism of on-off switching has been studied in detail [11]. As a combination of such local switching process, the body plan is described. The question remains whether this mechanism is complete as explanation. In spite of such "mechanical" explanation there, biological processes in cells occur in a thermodynamic fluctuation, and explanation on the robustness against fluctuations is required. Even if some errors such as somatic mutations occur, the total body often remains robust against such errors. If one assumes that cells change their fates passively under externally given signals, instability in the developmental process remains, since tiny perturbations can change their cells' fates according to the switching mechanism with a given threshold. Then we need another mechanism to modify local rules so that global developmental process is robust. (Such mechanism to correct error, however, is under molecular fluctuation again. Hence, a logic leading to global robustness is postulated [12].) One might describe such mechanism in terms of molecules and add a new complicated rule. This process of searching for and adding a new local process can continue forever so that the molecular biology looks complete. Still one may wonder if this is the ultimate explanation.

TABLE 1

parts	whole
efficiency of parts	macroscopic robustness
digital logic	analogue pattern dynamics
syntax	semantics
symbol	image
rule of gene switch	body plan (pattern)

Complementarity between the whole and parts.

One has to note that organisms are not designed by somebody but have evolved spontaneously. In man-made machines, parts, chosen to have efficient function, are combined to work as designed so that no serious damage is given by the interaction among the parts. The principle of organisms can be different from such machines. The function of each part changes in relationship with other parts. Rules that each part obeys are neither designed nor given in advance. They are context-dependent and are variable according to the information on the whole. We need some logic why such rules appear generically for a class of biological systems.

OUR APPROACH

Constructive Biology

If a biological system were just a machine with a complicated combination of parts, our possible study would be just to describe the details of elementary processes in the present organisms by abandoning the attempt to find any universal logic therein. On the contrary, we believe that organisms are complex systems and that there exists universal logic leading to their common nature.

Note that approaches for complex and complicated systems should be distinguished. Since the latter are essentially understood as a combination of simple processes, what should be done here is to search for minimal sets of local processes that can fit real data. On the other hand, for complex systems (in the sense of complementarity discussed above), such an approach is not effective. One has to search for a general logic why such a complex system is of necessity and universal.

Here it should be noted that the logic that organisms necessarily should obey is not revealed as long as we study only the present organisms (or slight modification to them by mutations). The approach that should be taken will be constructive [3,4] in nature. We combine several basic processes, and construct a class of models, to find universal logic underlying therein. With this logic, biological systems are classified into some universality classes. The present organisms, then, are understood as one representative for a universal class, to which the "life as it could be" also belongs.

Our "constructive biology" consists of the following steps: 1) construct a model by combining procedures, 2) clarify universal class of phenomena through the constructed model(s), 3) reveal the universal logic underlying the class of phenomena and extract logic that the life process should obey, 4) provide a new look at data on the present organisms from our discovered logic. There are two possible ways to perform these steps.

The first one is the construction of an artificial world in a computer by combining well-defined simple procedures and extraction of a general logic therein [13–16]. It should be noted that we do not intend to imitate the life. Instead, we search for a universal class of behaviors and reconstruct the present life as an example of such class. Strategy of such construction will be discussed in later subsections.

The second approach is experimental. In this case again, one constructs a possible biology world in a laboratory by combining several procedures. For example, this experimental constructive biology has been pursued by Yomo et al. [17] at the biochemical reaction level, the organism level, and the level of ensembles of cells.

In this respect, our constructive biology has something common with the so-called artificial life [18]. Still, there are

two differences. First, we are strongly motivated to search for universal logic underlying the constructed world. The second difference is our emphasis on the complementarity structure. The so-called artificial life focuses on the emergence of complex behavior from syntactic structure. In our approach for complex systems, the other direction (i.e., the emergence of syntactic rule from complex behavior) is pursued as mentioned. It should also be emphasized that we intend to reconstruct the present organisms as a class of constructed world and propose novel viewpoints to the "real" biology.

Dynamical Systems

Since we aim at constructing a scenario from image/pattern to symbol/rule, we need some system to describe the change in analog pattern. For this we adopt a dynamical system approach (in its broadest sense). A dynamical system consists of time, a set of states, an evolution rule, an initial condition of the states, and boundary conditions. The state is represented by a set of k variables, the "degrees of freedom." Thus the state at an instant is represented by a point in the k-dimensional space called "phase space."

It is generally assumed in a dynamical system that a set of state variables, an evolution rule, and initial and boundary conditions of the states are given independently of each other. The states evolve according to the rule, but the set of states itself (e.g., the number of variables) is fixed. The states cannot change the evolution rule itself. Choice of initial and boundary conditions are independent of the state and of the rule.

In biological problems, however, such separation between all these elements of the model may not be valid from the beginning [19]. The evolution rule itself is formed and changes in connection with the temporal evolution of the states. A simple example is the change of the number of variables with time: In the development of a cell society, when each cell state is represented by a set of variables, an extra set is demanded by cell division, unless the two cells remain identical. This change in degrees of freedom is dependent on the state, since the cell divides or dies according to its state. Hence we have to study open dynamical systems, in the sense that the phase space dimension changes according to the state. Some mechanism for the dynamics of dynamics has to be introduced to incorporate with the interference between the evolution rule and states.

Among the open dynamical systems, we have coined the term "open chaos" to discuss the change of the dimension associated with chaotic instability [20]. Indeed, in a model of cell differentiation to be discussed, difference between cells is amplified by orbital instability. If two cells remained identical, we would not need another set of variables. Thus, the increase in the number of variables is tightly connected with the orbital instability, as in chaos. It should also be noted that in the developmental process, in general, initial and boundary conditions of states are chosen so that reproduction continues from their mothers' states.

Intra-Inter Dynamics

What type of dynamical systems should one construct to capture the basic features outlined above? First, we assume there is a unit separated from the outside. This is not trivial, since in nonlinear systems, tiny change in one element may be amplified to other elements, and they are not separated from each other. As long as we take the importance of interactions for granted, the formation of a unit itself is nontrivial. In other words, the separation of the unit from surroundings cannot be complete in a nonlinear system, and holds only approximately. It is made possible only by forming an interface between the outside and internal structure, by which some information on external states is embedded inside. In terms of cell biology, this corresponds to the origin of cell, an important step to life, that is made possible by the existence of a membrane. It makes a boundary between the inside and the outside, but in a rather flexible way.

A biological unit thus formed must always have internal structure. Furthermore, these units strongly interact with each other due to incomplete separation. Hence, we need a model consisting of the interplay between inter-unit and intra-unit dynamics [8,12]. For example, complex chemical reaction dynamics in each unit (cell) is affected by the interaction among cells, which provides an interesting example of "intra-inter dynamics."

As a specific example of the scheme of intra-inter dynamics, we mainly discuss the development process of a cell society accompanied by cell differentiation [21]. Here the intra-inter dynamics consists of several biochemical reaction processes, while the interaction is inter-cellular through diffusion of chemicals, other signal transmission, and so forth. The change of dynamics itself is brought about by cell division and death, depending on the cellular state, by which the degree of freedom varies.

Our Model

Now the remaining questions are choice of 1) the internal variables and their dynamics, 2) interaction, and 3) a rule to change the degrees of freedom (e.g., cell division). There is a variety of possibilities of models according to these choices, and we have studied several of them.

Although the details of our model are given in previous publications [13–15,19,22,23], it may be helpful to explain the basic structure of our modeling briefly.

As a set of variables, we take concentration of a set of chemicals. For the internal dynamics, autocatalytic chemical reaction among these chemicals is chosen. This autocatalytic reaction mechanism is necessary to produce some chemicals in a cell (see also [24]). Note that such autocatalytic reaction dynamics often leads to nonlinear oscillation in chemicals.

As for the interaction, diffusion of chemicals between a cell and its surroundings is considered. The surrounding medium is assumed to be spatially homogeneous in most simulations

to avoid the complication by spatial pattern. In other words, all cells couple to all others. For some models, we assume a nutrition chemical, and its active transport into a cell, whose rate depends on the concentration of some chemicals within the cell.

The condition of cell division is written as an integral form. In one class of model, we assume that some products are accumulated through the chemical reaction. When the accumulated product concentration goes beyond some threshold, the cell divides into two. In another class of model, cell volume is computed according to the chemicals within, and a cell divides into two when the volume becomes twice the original.

Of course, there can be a variety of choices on the chemical reaction network. Indeed, the observed results do not depend on the details of the choice, as long as the network allows for growth in cell numbers. Note that we have not constructed our network based on some data on biochemical network. Rather, we try to demonstrate that important features in a biological system are a consequence of a system with internal dynamics, interaction, and reproduction. From the study we have found a universal logic underlying this class of models. Later we will survey the logic in connection with cell biology, although the scenario itself is believed to hold generally in a biological system.

Remarks

Note that our approach for development is intended to make a connection from "pattern" to "rule" in Table 1. As for the study of the development at the pattern level (right-hand side of Table 1), there is Turing's pioneering study, while the study from a digital rule (from the left-hand side of Table 1) is pioneered by Kauffman [25] and Lindenmeyer [26]. Before discussing our scenario and logic of the development of a cell society, it may be relevant to comment on the previous theoretical studies on differentiation and development.

Turing proposed a pattern-formation mechanism according to the instability in a reaction-diffusion system. In this sense, Turing's study aims at understanding the morphogenesis at the right side of Table 1. On the other hand, we aim at reaching the rule formation starting from the right side. Note also that inclusion of threshold mechanism on the diffusion mechanism [27], which may be regarded as a variant of Turing's idea, is not sufficient to form a process from the right to the left side in Table 1. See also [28] for a connection from Turing pattern to a genetic rule.

In contrast with these "cell-to-cell interaction"–based studies, differented cell types are attributed to different attractors in an intra-cellular dynamics in some other studies. For example, in Kauffman's study [25], coexistence of many attractors in a Boolean network is corresponded to a different cell type. Attraction to different states is found in a coupled system of Boolean-network–type differential equations [29], while a CML corresponding to such Boolean networks is studied by Bignone [30] (see also [31]). As will be seen later, our cell type is not represented by an attractor but by a state stabilized through cell-to-cell interaction.

In our approach, we assume temporal oscillations of intra-cellular chemical dynamics. The importance of oscillations was pioneered by Goodwin [32], and the existence of oscillatory dynamics for cell division processes has been discussed both experimentally and theoretically. In connection with the development process, Goodwin and Cohen [33] proposed a mechanism of positional information through the phase difference of intra-cellular oscillations.

As will be seen, our scenario is distinguished from previous studies by the importance of instability, stability at an ensemble level, change of cell numbers in conjunction with dynamics, formation of recursive types, and differentiation rules.

Clustering generally appears in a coupled system as long as there is both orbital instability to amplify small differences and a tendency to keep the synchronization. The differentiation at the second stage, with the separation in the phase space, is expected if the instability is related also to the amplitude of oscillations and some internal degrees of freedom exist to support the difference in the phase-space position.

LOGIC FOR DIVERSIFICATION, MEMORY, AND ROBUSTNESS

From several simulations of the models starting from a single-cell initial condition, Yomo and the author proposed the "isologous diversification theory" as a general mechanism of spontaneous differentiation of replicating biological units [13–15]. From the differentiation process of the models, we extract the following basic features: 1) intrinsic diversification, 2) type formation, 3) recursivity, 4) rule formation, and 5) macroscopic robustness. Here we will discuss these features from the viewpoints of model results, the logic that supports them, and their significance to biology. (For other related issues, see [16]).

Intrinsic Diversification

Observation from our model—Up to some number of cells, all cells are identical as to the chemical concentration, which oscillate coherently. Accordingly, the cells divide almost simultaneously, and the number of cells is a power of two. When the number of cells exceeds some threshold, they lose identical and coherent dynamics. Cells separate into several groups whose phases of oscillations are close. At this first stage, only the phases of oscillations are different by cells. Cells are not differentiated yet, since the temporal averages of chemicals, measured over periods of oscillations, are almost identical. After further divisions of cells, chemical compositions start to be different by

cells, and the differences remain. At this second stage, the chemical concentrations differ by cells, even after taking the temporal average over periods. Thus the behavior of states is differentiated. Here the orbits of chemical dynamics lie in a different region by groups within the phase space.

Logic—The change of phases at the first stage is due to clustering, studied in coupled nonlinear oscillators [8]. Clustering generally appears in a coupled system as long as there is both orbital instability to amplify small differences and a tendency to keep the synchronization. The differentiation at the second stage, with the separation in the phase space, is expected if the instability is related also to the amplitude of oscillations and some internal degrees of freedom exist to support the difference in the phase space position. We should note that the diversification is a general consequence of coupled nonlinear systems.

Biology—Note that the cell has an intrinsic trend for diversification. Indeed, it is hard to imagine that a complete replication machinery existed at the early stage of life. Furthermore, all cells are different in our body, strictly speaking. Cells tend to diversify at the early stage of a developmental process.

The diversification is relevant to the effective use of finite resources. As has been discussed [13,23], phase clustering provides time sharing for resources: Cells can get a chemical resource successively in order, according to the difference in phase of oscillations. The differentiation of chemical compositions supports the differentiation of roles. Such differentiation is seen at a rather primitive stage of multicellular organisms, such as the Volvox [34].

Recursive Type Formation

Observation from our model—After fixed differentiation, the chemical composition of each group is inherited by its daughter cells. The determination of a cell has occurred at this stage. The cell state represented by average chemical composition remains identical by division, and thus the cells keep the "recursivity" by divisions. The chemical characters are "inherited" just through the initial conditions of chemical concentrations after the division, although we have not explicitly imposed any specific mechanisms to keep the type. In other words, a kind of memory is formed.

Logic—The cellular memory at the above stage is formed as a result of the selection of initial conditions for a cellular state. In our model all cells are coupled and form a single dynamical system. Each cellular state does not constitute an independent dynamical system. Still, it is effective to define an initial condition of each cell state forming a "partial dynamical system" out of the whole. The recursivity is attained through the selection of initial conditions of such a partial system, so that it is rather robust against change of interaction terms also. This mechanism for recursivity is possible only in an open dynamical systems that allows for change of degrees of freedom.

Biology—In spite of the first diversification trend, biological units (e.g., cells) tend to be classified into several types, whose number is much smaller than the number of units. With growth in numbers, newborn units (cells) themselves are not identical with their ancestors, as mentioned, but after some generations, they tend to belong to the same type. Although cells of the same type are not completely identical with each other, the difference among them is much smaller than that between cells of different types. In the developmental course, cells are initially undifferentiated, and change their states with time. Later, fixed cell types appear, called determination [11].

Indeed, such a tendency to form discrete types is not limited to cells. Organisms seem to be classified into types, which may often be called "species." Currently, "species" are defined through the sterility of hybrids, leading to sexual isolation. However, we should note that such species-like types also exist in asexual organisms, and even in unicellular organism. Hence, we need some logic that supports the type formation beyond sexual isolation.

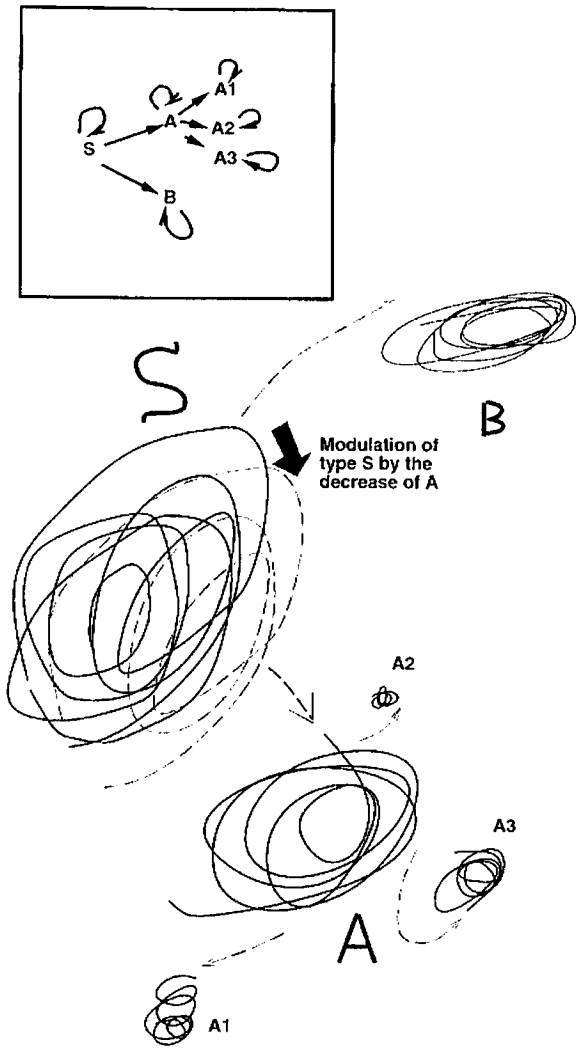
Rule Generation

Observation from our model—As the cell number increases, further differentiation proceeds. Each group of cells further differentiates into two or more subgroups. Some cell types continue to switch to others besides replication of the same type. Here, the switching follows some rule, by which hierarchical differentiation proceeds.

For example, six types (S, A, B, $A1$, $A2$, $A3$) are formed successively in a model [22]. The orbits of each type are clearly separated from each other in the phase space of chemical concentrations. Chronologically speaking, the type S first appears and replicates. When the number goes beyond some threshold, switching from S to A or to B starts to occur at some rate. With further divisions, switching from A to three types $A1$, $A2$, and $A3$ occurs. The chemical compositions of these three types are not much different from A, as compared with the differences to B or S. The differentiation rule here is found to obey the rule shown in Figure 1. ($S \rightarrow S, A, B \mid A \rightarrow A, A1, A2, A3 \mid B \rightarrow B \mid A1 \rightarrow A1 \mid A2 \rightarrow A2 \mid$ and $A3$–$A3$), in the normal course of differentiation starting from a single cell. A hierarchical rule of differentiation is thus generated. Formation of this kind of rule is generally observed in a class of chemical networks.

Logic—This differentiation rule that the cells obey is given in their internal state and interaction. In the above case, the orbits corresponding to the S state has paths to the states A and B, in the presence of sufficient number of other cells. The rule

FIGURE 1



Schematic representation of hierarchical differentiation.

is given in the orbits in the internal dynamics, which is modulated by the interaction. This rule is a higher-level one than the original dynamical systems (i.e., chemical reaction rule). Formation of such higher-level rules reminds us of chaotic itinerancy, where switches among several ordered states (with lower degrees of freedom) emerge out of high-dimensional chaotic dynamics [8-10].

Biology—Stem cells either replicate or differentiate into different cell type(s). This differentiation rule is often hierarchical, as in Figure 1 [11,35]. Such rule is expected to be not solely determined by internal cell states. Otherwise, it is hard to explain why the development process is robust. For example, when the number of some terminal cells is decreased, there should be some regulation to increase the rate of the differentiation from the stem cell to the terminal cells. This suggests the importance of interaction, as in our model results.

Internal Representation

Observation and logic—As for cell types, one might think that this selection is nothing but a choice of basin of attractions for a multiple attractor system. If the interaction were neglected, this would be basically correct. In our case, this is not true. Indeed, most dynamical states of each cell type do not exist as an attractor but are stabilized through interaction. The observed memory lies not solely in the internal states but also in the interactions among the units.

To see the intra-inter nature of this memory explicitly, one effective method is a transplantation experiment. Numerically, transplantation experiments are carried out by choosing determined cells (obtained from the normal differentiation process) and putting them among a different set of surrounding cells, to make a cell society that could not appear through the normal course of development.

When a determined cell is transplanted to another cell society, the offspring of the cell remain the same type, unless the cell-type distribution of the society is strongly biased (e.g., the ensemble consisting only of the same type of the cell as transplanted). The cell memory is preserved mainly in each cell, but suitable cellular interactions are also necessary to keep it. The achieved recursivity is understood as the choice of internal dynamics through cellular interactions.

Depending on the distribution of other cell types, the orbit of internal cell state is deformed and leads to a switch to other cell types if the deformation is large. Such modulation is possible, due to our "dual" memory system: A cell's state is mainly characterized by its discrete types, while there remains analog modulation even among the same cell types, which reflects on the global information on cell distributions. Internal representation of other cells is formed with the modulation of each cell.

Such continuous deformation (modulation) is also seen in the model for a stem cell, where cell types switch to further subgroups with some rate [22]. The rate of the differentiation or the replication (e.g., the rate to select an arrow among $S \to S$, A, B) depends on the cell-type distribution. For example, when the number of A-type cells is reduced, the orbit of an S-type cell is shifted toward the orbits of A, with which the rate of switch to A is enhanced. In this case, again, the information on cell number distribution is represented by the internal dynamics of S-type cells.

Macroscopic Robustness

Observation from our model—Since our differentiation mechanism includes instability in internal dynamics triggered by cell-to-cell interactions, one might then suspect that such a developmental process would not be robust against pertur-

bations. This is not the case. With the above modulation mechanism, a kind of robustness at the ensemble level is generated. The switch of types is regulated so that the distribution of diverse cell types is restored to the original one. The global stability of the whole system is thus obtained by spontaneous regulation of the rates of the differentiation.

Logic—In the present case, macroscopic stability is sustained by the change of the rate of differentiation. But why is the regulation oriented to keep the stability, instead of the other direction? As an example, consider the branch in Figure 1. As mentioned, the differentiation from S to A is enhanced when the type-A cell is removed. If the regulation worked in the other way (i.e., the decrease of the rate $S \rightarrow A$ by the removal of A), then the type-A cell would hardly exist from the beginning. Consider the developmental process: In the initial stage of the appearance of type-A cells, their numbers are small. If the regulation worked to decrease the rate to type-A in the environment with fewer type-A cells, then the number of type-A cells would be decreased to zero. If this were the case, the type-A cell would not appear from the beginning. In other words, only the cell types that have a regulation mechanism to stabilize their coexistence can appear in our dynamical system. Note that this logic is possible since, in our theory, types and rules of switches are not given in advance but appear as a consequence of dynamics.

In general, stability at the ensemble level is a rather general consequence of coupled dynamical systems.

Biology—It should be noticed that global robustness has higher priority than local rule. For example, by a mutation to triploidy in the newt, the cell becomes three times large. In this case, the total cell number is reduced to one third, and the final body remains not much affected by the mutation. In other words, the local rule of cell divisions (e.g., the number of divisions) is modified so that the global body pattern remains undamaged [11].

In general, the developmental course is rather stable against possible somatic mutations, while in the hemopoietic system [35], existence of regulation mechanism to keep suitable distribution of cell types is expected. In the hierarchical structure represented in Figure 1, the cells at an upper node behave like stem cells and regulate the number of cells at a lower node. This type of regulation system is expected in real multicellular organisms.

It should be stressed that our dynamical differentiation process is always accompanied by this kind of regulation process, without any sophisticated programs implemented in advance. This autonomous robustness provides a novel viewpoint to the stability of the cell society in multicellular organisms.

DISCUSSION

At the next step in the constructive biology, we have to provide a new look at present organisms from our standpoint. Note that our model experiments show correspondence to tumor cell formation, stem cells, relevance of chemicals with low concentrations, germ-line segregation, and so forth. However, our goal in this constructive biology is not limited to seeking for such correspondence. Rather, we aim at recapturing existing organisms from our constructed classes of intra-inter dynamics. So far, we have found the following classes for each unit behavior:

- *Undifferentiated cell class*—Cells are not recursive, and their states change with time, through several switching-type behaviors.
- *Stem cell class*—Cells either reproduce the same type or switch to different types with some rate.
- *Germ-line cell class*—After division, one of the cells keeps the recursivity and high activity, while the other loses activity and division is suppressed.
- *Determined cell class*—Cell types are kept by the division. Note, however, this determination is relative. When a cell is determined in the course of development, it can be dedifferentiated and switched to other types by a "radical" change of interaction.
- *Tumor-type cell class*—These cells destroy the cooperativity attained in the cell society and grow in numbers in a selfish way. In simulations with a larger diffusion coupling, this type of cell which is an extreme limit of a differentiated cell with specialization in chemical compositions, is observed. Its chemical configuration loses diversity, and the ongoing chemical pathway there is simpler than other cell types. These cells replicate faster. Since the emergence of this cell type destroys the order allowing for diversity in cells, we have called it tumor cell [14]. Note also that the recursivity by cell division is partially destroyed, in the sense that the bias in chemical concentrations is preserved to daughter cells, but the concentrations themselves differ by cells [14,15].

It is hoped that the present cells can be classified according to such classes, and general features extracted. For example, we have proposed that the tumor cells lose chemical diversity and also suggested a possible way to redifferentiate the cells to normal course by restoring the diversity [14,15].

There are also several possible classes for an ensemble of cells. In this case, behavior is classified according to the spatiotemporal dynamics of the distribution of cells. From this viewpoint, it is again expected that stages of multicellular organisms are classified, starting from the primitive stage by Dictyostellum discoideum, Volvox, Anabena, ···, and higher organisms. It should also be noted that detailed process to form a cell society is not required in our model study. This implies that the origin of a multicellular organism is a rather natural consequence when cells increase in number and are concentrated to have strong interaction with each other.

We believe that the current approach is not limited to cell biology. One may have noted that our logic for the formation (and collapse [19]) of the cell society may be extended to human society. Indeed, temporal switching of roles and class differentiations are generally seen in sociodynamics. An example of the formation of a complex society through such differentiations is studied in the evolutionary dynamics of iterated games [36].

Of course, the complementarity structure between syntax and semantics is most important in human cognition processes. Internal images are formed so that the emergent rules have context dependence. In this sense, our scenario for the cell society will be relevant to the problem of cognition.

In neural dynamics, we often adopt the concept of a module and then try to combine modules to make a total image of the world. It is a typical approach from the left to right in Table 1. However, the modules are not separated with each other and work only as an approximate separation from dynamically connected elements. In this sense, the approach from the right to left in Table 1 has to be pursued, as has been demonstrated in this article. Extension of our approach to neural dynamics and to the logic formation from pattern dynamics will be discussed elsewhere.

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