Morphogenesis of 3D Sheets Exploiting a Spatial Condition

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Abstract

This paper reports on the morphogenesis of three-dimensional folding sheets in computer simulation. In order to exploit the topology of these cellular sheets, we introduced cell connection map, which can prescript cell connections regardless of changing the number of cells. We show that morphogenetic patterns such as exponential growth, self-replication process and annihilation process can be easily realized just by observing the number of neighbors of each cell. That means this feat is achieved in a distributed and autonomous way.

1 Introduction

Multicellular organisms usually consist of large numbers of cells, which are able to shape an organism by an intricate web of cell-cell interactions, a process called morphogenesis. As each cell contains the same genome, morphogenesis relies on autonomous and distributed processes with no centralized control. Although the elucidation of the molecular details of morphogenesis has made big progress in biology, an overall picture is still lacking. We hypothesize that morphogenesis depends on the following two conditions:

1. Morphogenesis is an autonomous, distributed process without any centralized control for all cells.

2. In essence, morphogenesis of living things is basically understood as expanding and folding sheets.

We used these two conditions as guidelines to screen the existing literature of morphogenetic models. Alan Turing's reaction-diffusion model [1] uses two chemical substances that are able to produce spatial patterns in space. The point of this mechanism is that in essence, reaction-diffusion mechanisms are means of breaking the symmetry among homogeneous cells in autonomous and distributed way. Focusing on the form of gastrointestinal tract, H.Honda advocates that in general the form of multi cellular system is realized as two-dimensional sheets rather than three-dimensional solids [3]. There exist many approaches for morphogenesis that can be divided into several types: Lindenmayer grammars [4], cellular automata [5], [9], concentration gradient[2], mechanical approaches [6], recurrent diagram networks to express the bodies of simulated creatures [7], and extended grid space into graph model [8]. However, little attention has been given to the characteristics of form - the topology of the cellular network.

2 Model

In our model, we choose the cell as the level of abstraction. System consists of cells connecting each other.

Cells differentiate depending on the number of neighbors.

Cells divide and die (cell differentiation) depending on the number of neighbors. This is according to the fact that one of the possible biological mechanism assumed to code the behavior of morphogenesis would be the concentration of chemical substances that diffuse into neighboring cells through channels. In other words, its concentration could reflect the number of neighbors.

Differentiation rules are applied synchronously.

These cell behavior rules are applied synchronously in specific order. After specific time passes (100 steps), all cells count its neighbors and take actions. (The definition of step is prescripted below.) Once cell division is took place, the cell is divided into four cells. This is in order to sustain the symmetry of the cell network. In cell deletion, the cell is deleted by cutting connection to its neighbors.

Cell-cell mechanical interaction

Cells are expressed as mass points. Links between them are represented as mechanical connections. The mechanical interactions are expressed as spring and damper model. Although it takes time to converge to the form, the form of cell network topology is unique to each sequence. We show the parameters of the system in Table.1. The equation of motion for the cell i is expressed in eq.1. Where subscript i, j is an identification number of the cell.

Table 1: Sets of parameters.

Symbol	Definition	Value
k	spring coefficient	50
l	spring natural length	50
m	mass	10
c	damper coefficient	30
g	gravity	50
a	cross product	2000

$$m\ddot{\mathbf{q}}_\mathbf{i} + c\sum_j(\dot{\mathbf{q}}_\mathbf{i} - \dot{\mathbf{q}}_\mathbf{j}) + k\sum_j\left(1 - \frac{l}{|\mathbf{q}_\mathbf{i} - \mathbf{q}_\mathbf{j}|}\right)(\mathbf{q}_\mathbf{i} - \mathbf{q}_\mathbf{j}) + a\frac{\sum_j\big((\mathbf{q}_\mathbf{j} - \mathbf{q}_\mathbf{i}) \times (\mathbf{q}_\mathbf{j+1} - \mathbf{q}_\mathbf{i})\big)}{|\sum_j\big((\mathbf{q}_\mathbf{j} - \mathbf{q}_\mathbf{i}) \times (\mathbf{q}_\mathbf{j+1} - \mathbf{q}_\mathbf{i})\big)|} + g\mathbf{q}_\mathbf{i} = 0 \quad (1)$$

The position of the cell q_i is defined as a vector. The cell that exists in neighbor of cell i is denoted as j. Gravity is added to the system for z-axis direction and cross-product force is also added in order to swell the form of the sheet. The differential equation is integrated by the Euler method ($\delta t = 0.01$, 1step=$30\delta t$).

Cell connection map is introduced to constrain the form in "a sheet"

Since cell reconnection after cell division sustaining adequate topology is tricky, we introduced cell connection map, which prescripts relation of cell connection. Fig.1 shows the example of cell connection map. When cell is divided, the square corresponding to the cell is also divided into four small squares. ("a)" and "c)" corresponds to "d)" and "e)", respectively). Links are connected if squares touches other squares through the edge. As we are interested in how the two-dimensional sheets expand, the most external cells, which exist at edge of the connection map, are fixed in the same position. Due to this settling, the system grows like an expanding balloon. Although many parameters are decided arbitrarily, the most important thing here is that once the feature of the model is decided, the form converges to unique form.

Form can be evaluated using cell connection map

Form of living things always relates to its function, and it plays an important role in the evolutionary process. But evaluating form is quite difficult and sometimes tends to be arbitrary. However, if we evaluate the form by analyzing cell connection map, the whole cell relations can be detected and estimated easily. We

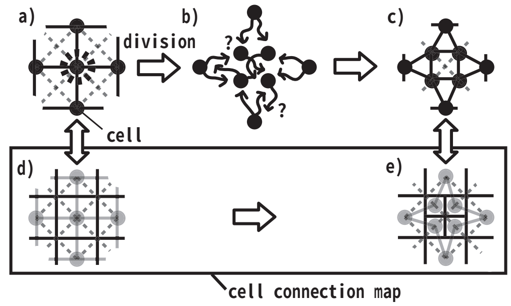

Figure 1: Cell reconnection.

introduced fitness value (F), -kind of entropy- which is prescribed as the follow equation (2), where S_i denotes the area of each cell in cell connection map with subscript i as an identification number of the cell.

$$F = -\frac{1}{N}\sum_i log\frac{S_i}{S_T} \quad (2)$$

We set the area of the whole map 1.0. S_T represents sum of all areas of the cell. We generalized the value by dividing a number of cells, N. The characteristics of this fitness value is as follows:

1. The fitness value gets larger when the distribution of area sizes gets larger.
2. If the sum of areas are same, the larger the number of cells is, the bigger the value becomes.
3. If cell distribution is same, it doesn't depend on its scale. That means that the value doesn't depend on order of morphogenesis.

3 Simulations and Results

By applying several parameter sets, some fundamental morphogenetic process were observed.

Exponential growth

Figure 2 shows the examples of exponential growth of the system. X-Z side view, X-Y top view, Cell connection map in left to right order. (The magnifier is changed in each view.) In the left model(seq.A), we set rule that if the number of neighbor cells is 0,2,4,6, or 8, the cell is divided, and if the number is more than 10, the cell is deleted. And these rules are applied one after the other starting with division rule. The figure shows by only counting the neighbors, the system can generate bended "two dimensional" morphological form from one single cell. In the right model(seq.B), if the number of neighbor cells is 0,2,4,6, or 8, the cell is divided, and if the number is 1,3,5,7, or 9, the cell is deleted. This time division rule is applied twice then cell deletion rule is applied once starting with division rule. Judging from the X-Y and X-Z view, the form generated by the rule seems completely different from that of seq.A.

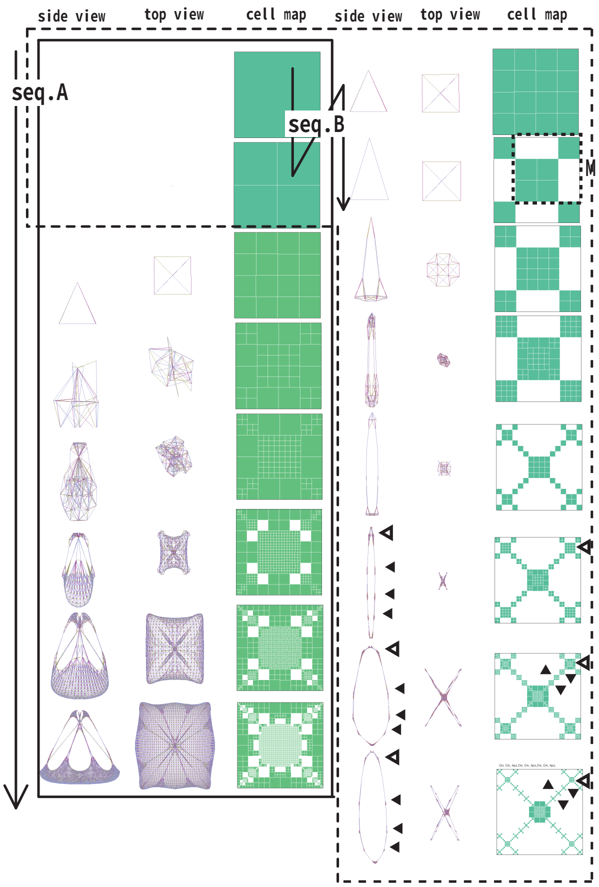

Figure 2: Exponential growth sequences A(left) and B(two left blocks and right).

Self-replication, Annihilation, Stop Growth

Fig.3 shows self-replication process. In this model, if the number of neighbor cells is 0,2,5,7, or 9, the cell is divided. And if the number of neighbors is 1,3,4,6, or 8, the cell is deleted. Each group keeps changing the number of cells which consist its network one and four generating new groups. Several model in other parameters showed annihilation and stop growth behaviors. The simplest model of annihilation behavior can be observed when we set the number of neighbors 0 for cell division and 2 for cell deletion applying division rule and deletion rule one after another. And the simplest growth saturation model can be observed by settling 0 for cell division and any numbers except for 2 for cell deletion.

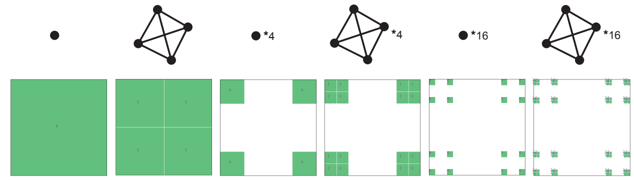

Figure 3: Self-replication.

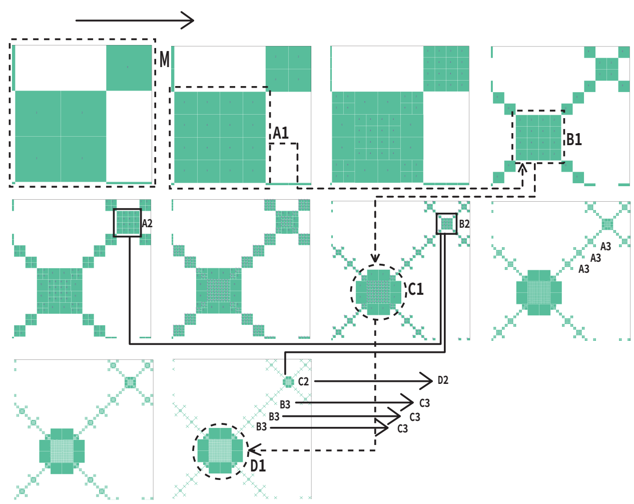

Figure 4: Detail of exponential growth sequences B.

4 Discussions

Figure 4 represents the magnification of the part of cell connection map in Figure 2 (as marked "M"). After 16 cells, which are arrayed in square grid appears (A1 and B1), this part gets rounded (C1). Once this form is created, all internal cells have four-neighbors thus keep dividing. And "big" eight cells surrounding the cells have more than at least 10cells. Therefore these cells won't be divided any more. This is a kind of "expanding bag". And this bag can be seen at other part of the body (A2,B2,C2, and A3,B3,C3 and so on). This shows that the system is growing creating many expanding bags around the body.

Figure 5 represents the same part of cell connection map under the different condition of cell division and cell deletion. This time, cell is divided if the number of neighbor cells is 0,2,6, or 8. Cell is deleted if it is 1,3,5,7, or 9. Although most of the condition are the same between seq.A and seq.B, the morphogenetic processes are essentially different. See the part marked "A". Once this shape is created, the shape doesn't change any more. That means that the number of cells included in this part doesn't change. (This

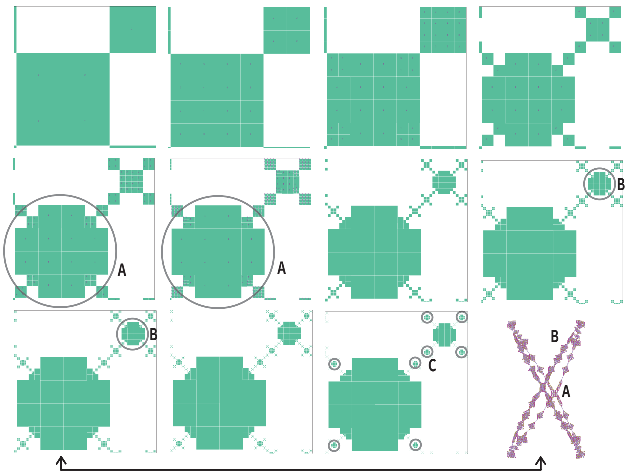

Figure 5: Detail of exponential growth sequence C.

is seen in other parts of sequences B and C and so on.) This system keeps generating many "gnarls" in different positions. The X-Y view is shown in the same figure. It can be seen that many gnarls are created in the form. Sizes of each gnarl are the same.

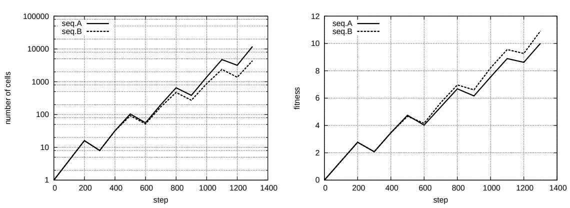

Figure 6: Left: Fitness value transition graph. Right: Number of cells transition graph.

We show the number of cells and fitness value transition graph in Fig.6 in order to quantify the difference of the characteristics of these forms between sequence B and C. In Fig.6 left, the X-axis and Y-axis represents steps and the number of cells, respectively, comparing sequence B and C. As the figure shows, the fitness in seq. B is smaller than that in seq. C although the number of cells in seq. B is larger than that of seq. C in each time. This means uniformity of the whole system of seq.C par cell is larger than that of seq.B. Hence, it suggests that many kinds of differentiation rules are not needed in order to get complicated forms. In other words, sustaining an adequate cell differentiation rule is necessary for the morphogenesis of the model.

5 Conclusion

These results lead to the following conclusion.

1. Several types of morphogenetic behaviors of three-dimensional sheets can be realized in autonomous and distributed way - just by counting the number of neighbors.
2. The form can be quantified easily by evaluating cell connection map.

Some fundamental morphogenetic behaviors are observed; two types of exponential growth, self-replication, stop growth and annihilation process. Those models were sensitive to the cell differentiation rules, to put it another way, sensitive to the topology of cell connections. What we intended to show in this paper is the abundant power of morphogenetic expression supported by the condition of spatial constraint, and the possibility that we can evaluate complicate forms by mapping it into other method, cell connection map.

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