

Title	In cut tail reproduction model, its reformation according to Homeotic genes, tumor production and its detection by immune system (Theory of Biomathematics and its Applications XIII : Modeling and Analysis for Discrete and Continuous Models)
Author(s)	Takase, Mitsuo
Citation	数理解析研究所講究録 = RIMS Kokyuroku (2017), 2043: 20-24
Issue Date	2017-09
URL	<a href="http://hdl.handle.net/2433/236951">http://hdl.handle.net/2433/236951</a>
Right	
Type	Departmental Bulletin Paper
Textversion	publisher

## In cut tail reproduction model, its reformation according to Homeotic genes, tumor production and its detection by immune system

Mitsuo Takase

LINFOPS Inc.

6-21-1-503 OukurayamaKouhoku-ku Yokohama 222-0037 Japan

GZL03154@nifty.com

Abstract. I already made a cut tail reproduction model where the tail cut can be not only reproduced, but also each cell in the tail has its own positional value. It is known that the distribution order of Homeotic genes tends to be the same with that of the parts of the organ like the tail here each of which is expressed by some of the genes. So the model is reformed to be able to meet this condition. Then through this modification, the model seems to approach to a more realistic situation.

When a solid tumor begins to form in the model, their tumor cells are thought to proliferate losing their stability beyond a few conditions which make the stability for healthy cells. In this case, it is seen more clearly that the tumor cells will be inhibited by the shape violation in the model.

Moreover, the separation of the information in the tail formation into the shape and the scale can be seen like in the memorization of the brain.

### 1. Introduction

(1) I already made a cut tail reproduction model where the tail cut can be not only reproduced, but also each cell in the tail has its own positional value [2]. This is shown in [1] in detail. Here, this is shown briefly in section 2.1.

It is known that the distribution order of Homeotic genes [2] tends to be the same with that of the parts of the organ like the tail here each of which is expressed by some of the genes [2]. So the model is reformed to be able to meet this condition. Then through this modification, the model seems to approach to a more realistic situation. This is shown in section 2.2.

(2) When a solid tumor begins to form in the model, their tumor cells are thought to proliferate losing their stability beyond a few conditions which make the stability for healthy cells [3]. In this case, it seems to be clearer in multiple sine expression that the tumor cells will be inhibited by the shape violation in the model. Moreover, the separation of the information in the tail formation into the shape and the scale can be seen.

These are shown in section 3.

### 2. Cut tail reproduction model and its modification

#### 2.1 A short explanation of cut tail reproduction model

The cut tail reproduction model is explained briefly. The detailed explanation is shown in [1].

The main idea of sine expression comes from that the body shapes expressed by Homeotic genes or morphogens [2] seem to be concerned with that of sine curves intuitively.

##### 2.1.1 The case where a body can be expressed by only a sine curve.

If a body can be expressed by a sine curve, the body can be expressed by genes and the cells with the expressions of some of the genes as shown in Fig. 1 and its explanation, making the total affinity of the cells in the body biggest.

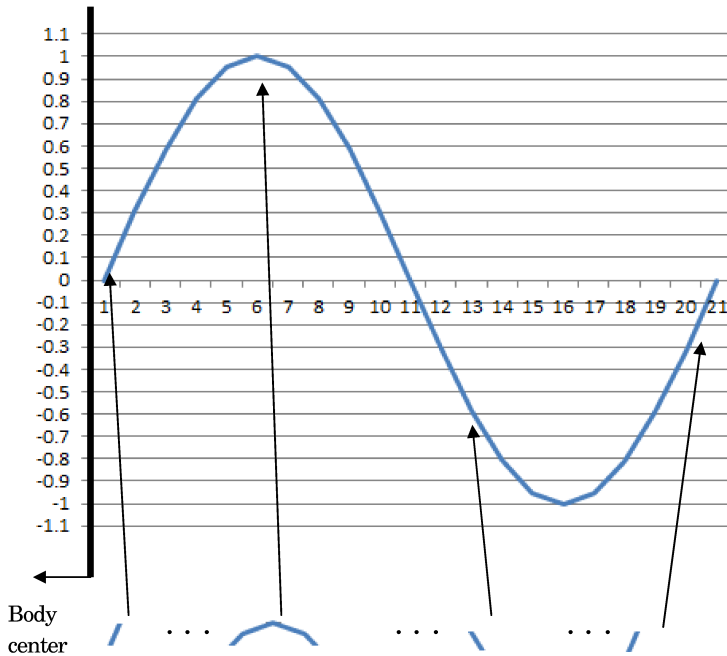


Fig. 1 A shape or a character distribution of a partial system of a body is expressed by a set of genes making the the partial system connecting the parts and their cells with the cells connection conditions shown in this section. At the bottom of the graph some of the parts of the curve are shown.

The meanings of Fig. 1 are shown as follows.

- (1) It is assumed that a gene or a set of genes make the parts of a partial system of the body along the longer axis or the shorter axis of the system. Each part consists of cells with similar expressed characters and the cells connection conditions shown below. The longer part consists of more cells.
- (2) So as to meet the following cells connection conditions and align the parts with similar values keeping slope continuity, the set of genes put the next part at the terminal of the last part making the system grow.
- (3) When the system is made according to the following cells connection conditions, the system is thought to have the biggest affinity and the stability which makes the connection among the cells of the system strong. Because all the parts and the cells of the parts can be joined making the total affinity the highest. Here, it is assumed that to put two cells with similar gene expressions together increases the affinity between the two cells.

[Cells connection conditions to unify cells]

- (1) The most similar two parts where the expressed character value of the cells of one part is nearest to that of the other part are put adjacently.
- (2) The character values must have slope continuity.

This means that when three parts are connected and the character values are A, B and C where  $A > B > C$ , the order A·B·C must be kept. A·B·A makes distortion.

### 2.1.2 The case where the body is expressed by two or more sine curves

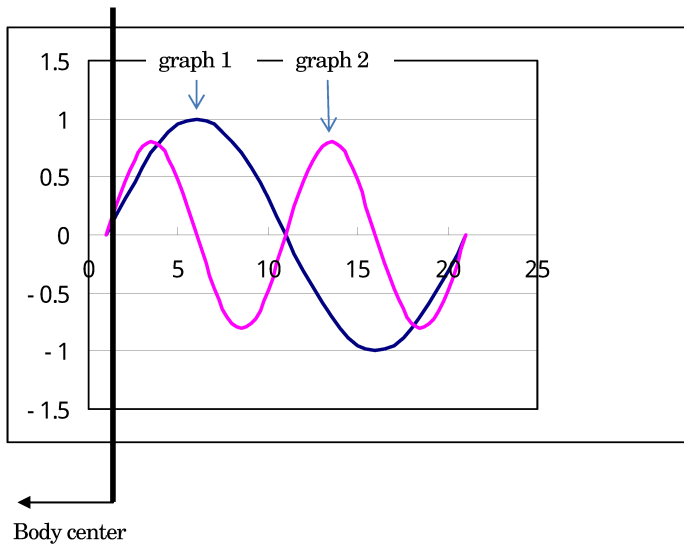


Fig. 2.1 Case with two characters and two sets of genes for them

As shown in Fig. 2.1 the two sine curves make the curve shown in Fig. 2.2. So genes can express any curve under the cells connection conditions and the mechanism using multiple sine curves (and multiple set of genes) making the affinity between adjacent two parts more and more strong and specific than the case with one sine curve and its genes.

Formation of a partial system of the body is shown.

Here the orthogonal width at each point along the axial length is expressed as a function by a set of sine curves.

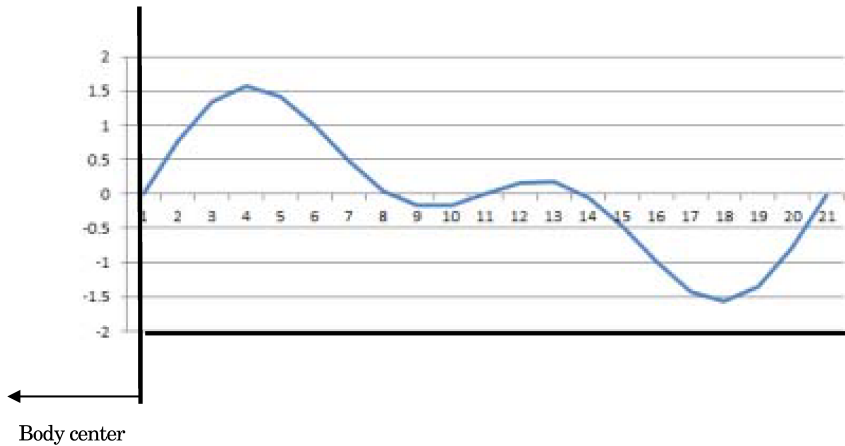


Fig. 2.2 The shape obtained from the two sine curves in Fig. 2.1 by algebraic sum

The curve of Fig. 2.2 can express the distribution of any value. So if the genes have the thecells connectionconditions and the mechanism, genes can not only express any curve but alsohave the possibility to express the whole body.

The examples which the genes can express are shown.

[Examples of the meanings which the curve in Fig. 2.2 can have.]

- (1) Width distribution along the longer axis of a partial system of the body like a tail
- (2) The distribution of some material in an interstitial tissue
- (3) The distribution of secretion ability of an enzyme

## 2.2 The order of genes is rearranged to meet the actual situation.

### 2.2.1 Rearrangement of genes

We consider the case of two groups of genes shown in Fig. 2.1. The genes of the group 1 in Fig. 2.1 and the genes of the graph 2 in Fig. 2.1 are rearranged where the gene at  $x_i$  in the graph 1 and that at  $x_i$  in graph 2 are put together at the place which expresses the situation at  $x_i$  of the body like in (3) of Fig. 3. There it is assumed that the information of the gene at  $x_i$  in the graph 1 and that of the gene at  $x_i$  of the graph 2 are kept at  $x_i$  like in (3) in Fig. 3 after the rearrangement.

The situation of (3) in Fig. 3 can meet the condition shown in section 1 (1) that the distribution order of Homeotic genes tends to be the same with that of the parts of the organ like the tail here each of which is expressed by some of the genes.

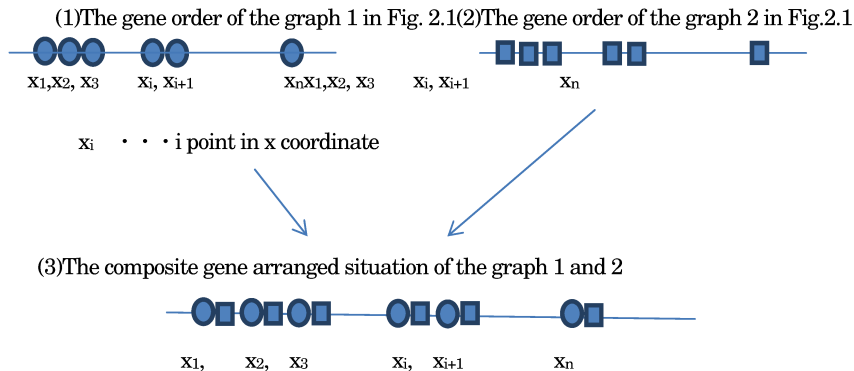


Fig. 3 Expression on genes

### 2.2.2 Effect and characteristics of the composite gene situation

- (1) The form of the body does not deform much by a point mutation of a gene as the case of the morphogens. This may be coherent to what we know about the effect of a point mutation.
- (2) The separation between shape and its scale must be and can be seen in the memorized information in genes from shown in section 2.1.1. But here it is thought for the growth hormone to increase the scale.

This means that many bodies can be made by changing the scale with the same shape. The

separation is necessary when the growth after the birth to an adult is considered.

- (3) When there are multiple distributions like a shape, the distribution of an enzyme secretion, etc., the distributions can give a coordinate to each cell which means a positional value [1].
- (4) When the order of genes in DNA is the same with the order of the cells in the tissue each of which expresses the corresponding genes like in Homeotic genes, it seems that the genes have the information to recover the cut tail. But the expression by multiple sine curves makes the space coordinates clearer and makes the formation of the body more stable with the increase of total affinity among all the cells, making the affinity between each pair of adjacent two cells more specific, the meaning of which is that the deformation and its violation of a local shape like by a small tumor lead to a clear detection by the local cells themselves and the inhibition of the growth by themselves from the characteristics of healthy body cells [3].

3. Discussion about the behavior of the cell or the group of cells when a mutation or a tumor is made in the assumption of the gene expression in the composite case of Fig. 2.

(1) About the case where a gene which expresses the shape of the body mutated

When a gene which expresses the shape of the body mutated, the cell will decrease its affinity with the cells around it as explained in section 2.2.2 (4). So the cell tends to do apoptosis.

(2) About the case where a gene which makes a cell proliferate is activated by a mutation.

In the case where the information processing for the proliferation of the cell in it is always activated by a mutation, a tumor can be made around the cell. This process is different from the case in (1). Then the deformation of a sine curve and the increase of the number of such deformed sine curves have a possibility to weaken the existence of the cell toward their apoptosis or the inhibition of the growth by themselves more clearly than the case without the multiple sine expressions as explained in section 2.2.2 (4).

#### 4. Discussion

The body expression through sine curves by genes seems to give us some more concrete and clearer frame structure. Using the frame structure, the elements shown in section 2.2.1 and 3 can be obtained. Some of them like the positional value in section 2.2.1 (3) can be explained more clearly.

On the other hand, as explained at the beginning of section 2 the sine expression comes from some intuition felt from the body formation by the genes, so to find more information for the relation between the expression and actual biological situation will be necessary.

#### References

1. Takase, M. (2010) An information processing and body formation mechanism with its condition in development. Theory of Biomathematics and its applications X. RISM 1917, 78-85 Kyoto University.
2. Alberts, B et al. (1994) Molecular biology of the cell. Garland publishing Inc.
3. Takase, M. (2012) Definition of tumor by the loss of stability and functional analytic approach with scale changes for tumor behaviors based on genes. Theory of Biomathematics and its applications VIII. RISM 1796, 158-166 Kyoto University.