

## SEVERAL SELF-ORGANIZED MORPHOGENESES IN TISSUES

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I will show several self-organized processes in tissues that I have been studying. Based on these example, a general scheme for the morphogenesis is proposed that dynamic units, which are determined by genes, are spontaneously assemble into a characteristic shape. Shapes being under construction may be affected by environmental and stochastic effects. A set of genes thereby does not produce homogeneous shapes. Some of these shapes may not be not adaptive (neutral or harmful) to their life. However, if these shapes are adaptive in average, the set of genes is transferred to descendants. Therefore, I would like to point out that every shape of living organisms may not be adaptive in the evolutionary process.

Genes do not instruct directly an egg in the final body shape, but how to make a shape. The genes determine proteins, and the proteins (as enzymes) catalyze material syntheses. These materials are organized into a complex, and these complexes are further organized into a more complicated complex. These processes are autonomous. Such an autonomous process is not exclusive for construction of molecules. In a similar way, cells are also organized into a tissue autonomously. For example, adhesive cells aggregate into a cell mass. A cell aggregate consisting of two cell types sometimes shows a sorting-out phenomenon, i.e. cells of one type which are strongly adhesive with each other are sorted to a cell mass, which is centered in the aggregate and surrounded with cells of the other type. The autonomous system of cells could be extended to tissues and higher organizations. Generally, genes produce dynamic units, which are spontaneously organized into a shape. I will show several self-organized processes in tissues that I have been studying. These processes are not reaction-diffusion systems, but reaction-diffusion systems belong to self-organized processes in general. The processes I present here and discussions on their meanings in evolution may be interested to investigators of reaction-diffusion systems

### SELF-ORGANIZED MORPHOGENESES

#### (1) *Colony patterns of the green algae Pediastrum (HONDA, 1973)*

*Pediastrum biwae* is a coenobial green algae in freshwater, and consists of  $2^n$  cells (e.g., 32 cells), and shows characteristic cell patterns, a few concentric circular strings (Fig. 1), a spiral string and so on. These patterns form through random swimming of small cells (zoospores). The zoospore is approximated as a sphere which has two C-sites (presumptive connection sites) and one H-site (presumptive site for horn formation), and undergoes a series of changes in its properties. The C-sites become connection sites then the zoospores form strings leading to the characteristic pattern. The H-site determines its fate, a horn or the third connection site according to absence or presence of

other cells which limit its growth.

Genes produce zoospores (units) and units are spontaneously organized into one of *Pediastrum* patterns. Stochastic process produces variation of final patterns, e.g., three-cell centered, four-cell centered, five-cell centered concentric circular pattern, or spiral pattern. The theory was confirmed by the observation that a single clone of *Pediastrum* shows all of these various patterns (HONDA, 1973).

**(2) Cell differentiation under the lateral inhibition control (HONDA et al., 1990)**

Cells in the neurogenic region of an insect ectoderm have two alternative fates: either neuroblasts or epidermis. The fate is determined through a laterally inhibitory interaction among cells. Initially homogeneous cells are all competent to differentiate into neuroblasts. However, once a cell has differentiated as a neuroblast, it inhibits its immediate neighbors from following this pathway. Initiation of the cell differentiation is by chance. The process is a discrete cell system, but essentially the same as the reaction-diffusion system. A distribution pattern of differentiated cells in the neurogenic region (Fig. 2) is a result of fluctuation of the initiation of individual cell differentiation. Genes determine only homogeneous (but competent) cells, but do not determine cell fates individually.

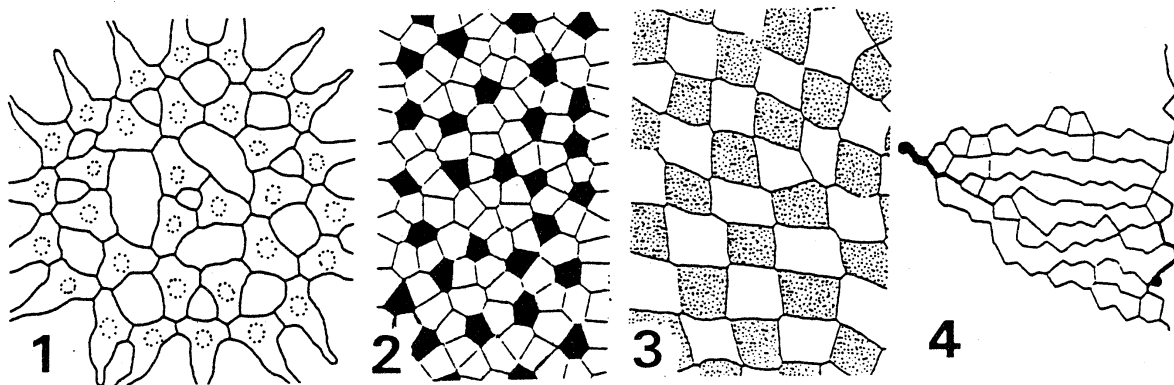


Fig. 1. A pattern of green algae *Pediastrum biwae* with three-cell centered concentric circles. [based on HONDA, 1973].

Fig. 2. Cells in the neurogenic region of an insect (*Drosophila*) ectoderm have two alternative fates, making neurons (solid polygon) or epidermis (open polygon). The fate is determined through the laterally inhibitory interaction among cells. A result of computer simulations. [HONDA et al., 1990].

Fig. 3. An avian oviduct epithelial sheet consists of two types of cells, ciliated cells and gland cells assembled in alternating blocks. The cell pattern is considered to form being based on the differential affinity between cells. [HONDA et al., 1986].

Fig. 4. Blood vessels in a blood branching system are formed by the selection of capillaries in the network. A result of computer simulations under the positive feedback control. [HONDA & YOSHIKATO, 1997].

**(3) Checkerboard cellular pattern of the oviduct epithelium (HONDA et al., 1986)**

A peculiar cellular pattern resembling a checkerboard has been observed on the luminal surface of the oviduct epithelium of a quail (Fig. 3). The epithelium is a monolayer cell sheet and consists of two types of columnar cells, ciliated cells and gland cells assembled in alternating blocks. The two cell types form a checkerboard pattern. It was assumed that adhesion is stronger between unlike cells than between like cells because all cell boundaries in the checkerboard are edges along which unlike cells meet. The assumption was supported by a computer simulation (HONDA et al., 1986). Genes produce two types of cells, and these cells are spontaneously organized into the checkerboard pattern.

**(4) Branching pattern formation of blood vessels (HONDA and YOSHIZATO, 1997)**

Blood vessels in a blood branching system are formed by the selection of capillaries in the network. A positive feedback system participates in the formation of a branching structure. Much used vessels are enlarged, whereas less used vessels are reduced in their size and finally extinguished (Fig. 4). The enlarged vessels become major components of the branching system. Genes produce capillary vessels consisting of endothelial cells. The endothelial cells detect signals of the shearing force by blood flow and the blood pressure, and reform the vessels according to degree of detected signals. The vessels are dynamic units of the self-organization.

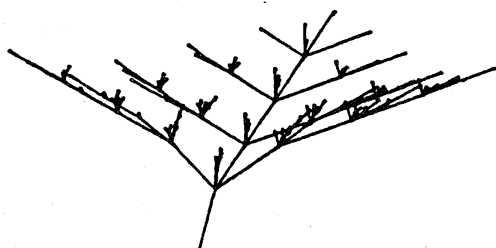


Fig. 5. A geometrical branching model is made that has parameters influenced by the direction of gravity. A tree made by a computer simulation using the model successfully make realistic *Cornus* tree shapes. [HONDA et al, 1997]

**(5) Branching structure of the Japanese strawberry tree Yamaboushi, *Cornus kousa* (HONDA et al, 1997)**

A crown of *Cornus kousa* consists of five-forked branchings showing various branching types. The branching type is determined by position within the crown and by the direction of the shoot with respect to gravity. A geometrical branching model is made that has parameters influenced by the direction of gravity. Computer simulations using the model successfully make realistic *Cornus* tree shapes (Fig. 5), and suggest that genes produce dynamic units having an ability of a physiological mechanism that responds to gravity and determines the orientation of themselves.

## DISCUSSION

I proposed genes produce dynamic structural units that are assembled into a characteristic shape spontaneously. The proposal leads to two important points. First,

biological shapes are not determined solely by genes. They are determined by characteristics of the units (gene products) and the environment around the units. The environment sometimes varies by chance. Horn cells, one of the two fates of *Pediastrum* cells are determined by their peripheral position in a colony. The fate of cells in the neuroblast generating region is determined by fluctuating properties of surrounding cells. Transformation of branching blood vessels from capillary vessels is carried out through random positioning and functioning of capillary vessels and the positive feedback system. The branching type is determined by the interaction between the intrinsic branching rule and the gravity direction.

The second important point is that biological shapes are not always adaptive: they sometimes may be neutral or harmful. Biological shapes are produced by self-organization. Shapes being under construction may be affected by environmental and stochastic effects. The set of genes produces variation in shape. Some of the shapes may not be adaptive (neutral or harmful) to their life. However, if these shapes are adaptive in average, the set of genes is transferred to descendants. *Pediastrum* shows various colony patterns, e.g. patterns having three, four and five centered cells (Fig. 2a - d). The variation of the patterns is due to the variables during the process of self-organization. These colonies having various patterns are considered to have a similar adaptive value with each other. The epithelium of hen oviducts shows a checkerboard pattern consisting of two types of cells. Even distribution of ciliary cells and gland cells on the inner surface of the oviduct tube seems to be convenient for egg transportation, but the complete intermixing of individual cells may be not necessary for smooth transportation. The checkerboard pattern may be simply a consequence of the process of self-organization.

Every shape of living organisms may not be adaptive in the evolutionary process. Living organisms do not follow rigidly an evolutionary path where they are adaptive throughout, but a path where they are sometimes neutral or harmful. A region that living organisms can reach in the evolutionary process is thereby considered to be remarkably larger than what we imagined by the rigid path of evolution.

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