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Emergence of Pattern Formation Mechanisms in *Drosophila* Embryogenesis

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1 Purpose

In the embryo of the insect *Drosophila melanogaster*, many gene regulatory proteins work as *positional information* that distinguishes one part of the embryo from another. And they establish a detailed spatial pattern that will be segments. It is well known that the process tolerates the variances of positional signal concentrations. How *Drosophila* equips a robust mechanism of phased pattern formation in the evolution process? This paper proposes a hypothesis that the complicated and robust mechanism can be emerged from a series of small changes in evolutionary process. To prove this, we simulated the evolution process using an evolutionary computation model such as genetic programming, and checked whether a robust mechanism of spatial pattern formation emerges on a computer or not.

2 Backgrounds

We focus on *even-skipped* (*eve*) gene, because the *eve* gene expression pattern is the first direct manifestation of a periodic pattern of segments. The transcription pattern

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of *eve* gene gives a striped pattern of seven vertical bands perpendicular to the anterior-posterior axis. Some gene products already exist before fertilization, and form lenient concentration gradients. Under the supervision of concentration gradients, various gene regulatory proteins are expressed one after another, and make various distributions. In these gene regulatory proteins at early embryogenesis, firstly *eve* gene products establish a periodic pattern. For this reason, on this paper we particularly focus on emergence of the *eve* gene expression pattern.

It would not be appropriate to think that the above-mentioned complex mechanism of *eve* gene expression was made all at once in the natural world. We should think that it had been gradually built up from a simple mechanism on the evolution process. In other words, we should think that the mechanism results from a series of simple evolutionary operations such as "mutation" or "cross-over". This is *emergence*, that is, the complex result made through repetitive recombination of simple elements. This is similar that *building blocks* in genetic algorithms¹ are recombined by *crossover* and form an optimum solution. For this analogous, we use genetic programming² for an emergence mechanism.

3 Experiments and Results

To emerge a mechanism of *eve* stripe formation, we express activation and repression of gene regulatory proteins as an *if-then* rule. In our model, an *if-then* rule is composed of simple symbols. A set of rules was treated as an individual, and was optimized to form four stripes at center of embryo with genetic programming. As a result, we got a set of rules that can form four stripes under the specific conditions. The specific conditions are careful restriction of symbols occurring in *if-then* rules and stabilization of initial distributions. The obtained rule formed four stripes under the different initial distribution ranged from 12% to -5% of the positional signal concentration. That is, the rule is robust enough to deal with the variances of the initial distribution.

This paper mainly focuses on the following:

- Evaluation of genetic programming in order to form *eve* gene expression emergence.
- Observation of complex expression dynamics of regulatory gene proteins with a computer simulation.
- Robustness of the obtained rules with respect to initial distribution variation.

¹Genetic algorithms are a class of algorithms for optimization and learning based on the principles of natural evolution.

²Genetic programming is a extension of genetic algorithms to treat structure expression.

- Analysis of evolutionary simulation, with respect to the family lineage of excellent mutants and evolutionary operators effectively worked.

4 System Environments

We developed a distributed computation system on personal computers called "Mugyu". Mugyu greatly accelerates evolutionary simulation for emerging a stripe formation mechanism which needs enormous computation power. The system achieved the following:

- Temporary clients starting up with two boot floppy disks and accessing no local hard disk drive.
- Network file access and remote job control facilities.

These features makes it possible for us to use dozens of personal computers without accessing local file systems. Mugyu is a fault-tolerance system in the sense that it can continue a computation, even if any client process is killed or any client personal computer is turned off. Actually, we carried out large-scale computation over a period of five weeks with dozens of personal computers that includes personal computers installed at the knowledge science training room.