Virtual *Drosophila* Project: Simulation of *Drosophila* Leg Formation

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1 Introduction

Historically, *Drosophila* has been an extremely popular animal for molecular and developmental biology. There is a substantial accumulation of genetic and cytological knowledge and detailed analysis for the organism. The formation of leg, wing, eye, and other structures from imaginal discs is particularly interesting as these discs undergo dramatic changes in structure. Leg formation in *Drosophila* is especially important not only for *Drosophila* research but also vertebrate development research, as they may share some common mechanisms in forming limb axes.

The goal of this paper is to reproduce the patterns of gene expressions observed in actual leg discs, and propose a biologically faithful model in the light of recent of molecular biology studies, involving gene regulation and axis determination in the *Drosophila* leg disc.

2 Modeling and Design

The leg disc of this simulation has more than 1,000 cells which are approximated as spheres and arranged as a circle. We have implemented eight major genes and their regulations involved in the formation of the *Drosophila* leg disc. In the simulation, we defined four processes: transcription, translation, protein diffusion and protein decay. We unify these processes with the following equation [1].

$$\frac{\partial U_i}{\partial t} = D_i \left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} \right) U_i + f(\mathbf{U}) - g \cdot U_i \tag{1}$$

U_i	:	concentration of protein i	D_i	:	diffusion constant
t	:	time	f	:	protein production function
x	:	position on x axis	$\mathbf{U}$	:	concentration vector
y	:	position on y axis	g	:	degradation rate ($g = 0.1$)

Currently we hand-optimize the binding affinity, protein diffusion constant value, etc. In the future we hope to use an optimization algorithm to determine ideal parameter setting for the simulator.

The system is composed of the *Leg, Cell, Gene* and *Protein* classes. Each cell in this system contains a list of proteins. First, the system checks whether a protein is secretable. If the protein secretable, the amount of diffusing protein is calculated in comparison with the protein concentration in the adjacent cells by the *Diffusion Engine*. Second, the *Reaction Engine* calculates the amount of protein which is produced from genes through transcription and translation in the presence of activator and repressor protein concentrations.

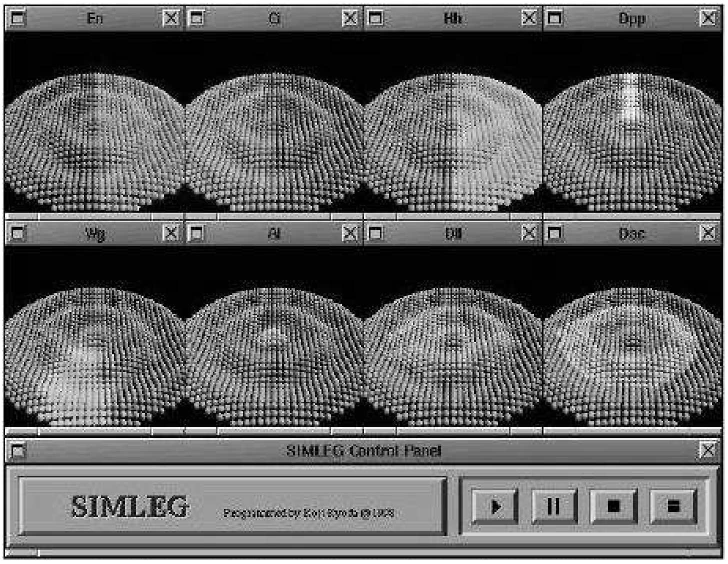

Figure 1: A Screen Dump of the Leg Simulator.

3 Results

The simulator successfully reproduces the expression patterns for the genes involved and the localization patterns of their products. Fig. 1 shows simulated patterns for the genes *ci, hh, en, wg, dpp, dll, dac, al*. These results agree well with experimental biological data.

4 Summary and Conclusions

In this paper, we present a simulation system for leg formation, simulating the genes interactions involved. We use this simulator to investigate a mathematical framework of leg formation which is otherwise well-founded from a molecular perspective. Particularly, we focus on the formation of the expression patterns of *dpp, wg, dll, dac, al, en, hh* and *ci* genes, which are involved in the development of the third instar *Drosophila* leg disc. Our results support the theory that the coaxial patterns of gene expressions of *al, dll* and *dac* in the leg disc are formed by two chemical gradients of *wg* and *dpp* products [2].

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