Stony Brook University
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Doctoral Defense Announcement

Abstract

Canalization of Gap Gene Expression During Early Development in *Drosophila melanogaster*

By

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The process of animal development is stable with respect to genotypic and environmental variation. This stability property was first described by C. H. Waddington, who characterized it in terms of a metaphor of canalized flow on the epigenetic landscape of an animal. Recent quantitative studies permit the analysis of canalization at the molecular level in certain systems, where it manifests itself as a reduction in the variation of gene expression over time. In particular, canalization is evident during the segment determination process of *Drosophila melanogaster*, during which gap genes form precisely positioned expression domains controlled by maternal factors and gap gene cross regulation. These studies have shown that besides reduction in variation over time, gap gene expression patterns also have much lower positional variance than Bicoid, a morphogenetic gradient active in the embryo.

This dissertation presents a theoretical and experimental analysis of the origin of canalization in the gap gene system. The theoretical analysis was performed using the method of gene circuits, which permits the representation of gene networks as dynamical systems which reproduce gene expression data with high fidelity. Despite biophysical evidence of the importance of protein synthesis delay in gene expression, I establish that ordinary differential equations are sufficient for implementing a gene circuit that describes the dynamics of the gap gene system.

I further demonstrate that such circuits correctly predict the observed variance of the gap gene borders in the presence of the much larger variance of the Bicoid gradient. Analysis of the regulation of the gap genes in these circuits leads to the prediction that the canalization of Bicoid variation results from gap gene cross-regulation. This prediction was confirmed experimentally.

These circuits also reproduce the reduction in variance of gap gene expression over time. This property of the gene circuit is characterized further by studying the qualitative dynamics of the phase space of the gap gene dynamical system. The dynamical analysis demonstrated that the embryo can be divided into two regions with very different qualitative properties. In the anterior, gap gene expression states are determined and canalized by point attractors. In the posterior, states are determined and canalized by a one-dimensional attracting manifold. Gap gene borders can form by one of the following mechanisms: 1) the movement of an attractor through the phase space; 2) an initial state crossing a boundary between basins of attraction; or 3) reaching different regions of the attracting one-dimensional manifold.

These results imply that stable steady states are not necessary to provide canalization, and furthermore that descriptions which only involve stable steady states are insufficient for capturing the dynamical behavior that occurs in actual developmental systems. These results provide a precise mathematical description of canalization in a specific biological system which is fully supported by quantitative molecular data

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