Marking the Midpoint: Models for Robust Protein Gradients in the *Drosophila* Embryo

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***Short Abstract* — In early *Drosophila* development, one of the first specifications made in determining cell location is the formation of the anterior-posterior axis. Two of the first proteins involved in this process are bicoid and hunchback. Results have shown that the hunchback gradient scales with embryo length and drops sharply at the midpoint of the embryo, despite receiving noisy information from the already formed bicoid gradient. Even still, this process is robust to a wide array of mutations and changes in initial conditions [1]. Through numeric and analytic experiments, we present mathematical models that mimic the robustness of this phenomenon seen in nature.**

***Keywords* — robust, mathematical model, hunchback, bicoid.**

I. Purpose

THE purpose of this project was to find mathematical models that exhibit the same precision in scaling and robustness to initial conditions as the bicoid-hunchback system in early *Drosophila* development.

II. Methods

We used a system of partial differential equations to model the change in protein concentration in the developing embryo. We assumed, as in [2], proteins undergo changes due to diffusion, decay, and interaction.

A. Numeric Approach

.In this system of equations, there are many unknown parameters describing rates of decay, diffusion, maximal production, etc. We developed a program to search for these free parameters so that the solutions to the equations matched our desired output. In our case, the desired output was a robust gradient for one protein that dropped sharply at the midpoint.

We developed a genetic algorithm that moves through the parameter space, making changes to the coefficients to better match the desired function. When a local minimum is reached, the algorithm saves the set and then continues searching after randomizing the coefficients. After a sufficient amount of time, the local minimums are evaluated further to see if they indeed meet the requirements we were searching for.

We searched the parameter space for two protein systems, but where the gradient representing bicoid is fixed in time. Many systems were found, but none were robust to variations in the slope of the initial, fixed gradient.

Next, we added in a third protein. The results were that many types of networks were found that give a robust, precise gradient that marks the midpoint. We hope to review biological literature or propose new biological experiments to help identify the exact network type. However, our mathematical conclusion is that many network types exist that give a precise, robust gradient marking the midpoint.

B. Analytic Approach

When analyzing the system of two partial differential equations, it can be shown when the ratio of diffusion rates is sufficiently small, bifurcation occurs. The constant, stable solution loses stability and inhomogeneous spatial patterns emerge. As proposed by Alan Turing [3], patterns formed by this diffusion-driven instability could be the mechanism by which gradients are formed. Exploring this idea, we analyzed the behavior of solutions very close, but right after the first bifurcation point. Long term behavior resembles a cosine with wavelength half the interval length and is independent of initial conditions. This simple system exhibits some of the key properties of the bicoid-hunchback system, namely a drop at the midpoint that is robust to changes in initial conditions.

The numeric algorithm produced a lot of data and led us to conjecture that if one gradient is fixed in time, it is not possible to have a solution that is robust to variations in the slope of the fixed gradient. At this time, we are trying to prove this conjecture as well as others that came from the numeric data.

III. Conclusion

We have identified and studied several different systems of partial differential equations modeling the bicoid-hunchback system that exhibit some of the key features. We hope through this study, and new ones as more data becomes available, we can better understand the mechanism behind this anomalous precision seen in nature.

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