Noise Sources and Accuracy of *Drosophila* Dorsoventral Patterning

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***Short Abstract* — Spatially-graded activation of the transcription factor Dorsal allows individual nuclei to estimate their dorsal-ventral location within the developing *Drosophila melanogaster* embryo. Noise in nuclear Dorsal concentrations places limits on the accuracy of patterning along the dorsoventral axis. To investigate these limits, we developed methods to measure extrinsic embryo-to-embryo and intrinsic within-embryo contributions to Dorsal noise, along with their sub-components. Total noise permits enough information to pattern the three primary dorsoventral domains whereas intrinsic noise alone permits enough information to pattern the six secondary subdomains. These results suggest that dorsoventral patterning is accurate in terms of relative, rather than absolute, positions.**

***Keywords* — information theory, Drosophila, Dorsal, noise**

I. Introduction

DURING the development of the fruit fly *Drosophila melanogaster*, morphogen gradients encode positional information that enables individual cells to determine their location within the embryo and adopt position-specific fates [1,2]. Information about position along the dorsal-ventral axis is relayed through the transcription factor Dorsal, which translocates to the nucleus in a spatially-graded manner. Dorsal regulates gene expression in a concentration dependent manner, directly defining the location and size of three primary tissues (mesoderm, neuroectoderm, dorsal ectoderm) and indirectly defining six secondary domains [3].

Dorsal is the only known source of dorsoventral positional information available to each nucleus, and due to the Data Processing Inequality, downstream processing cannot increase the amount of information available [4]. Thus, noise in Dorsal concentrations can limit the amount of available positional information, and thereby limit how accurately the *Drosophila* embryo can be patterned along its dorsoventral axis. Based upon the reported size of the domains, we estimate that the amount of positional information needed to precisely position the boundaries between the primary and secondary domains is ~1.6 and ~2.0 bits, respectively [3]. Both amounts are greater than the capacity reported for many biochemical signals [1,4], raising the question of whether noise prevents the Dorsal concentration gradient from providing enough information for accurate dorsoventral patterning.

II. Results

We examined variability in Dorsal gradients in stage 14 embryos using quantitative immunofluorescence. Nuclear Dorsal concentrations were determined using a novel, robust image processing technique based on adaptive thresholding and the watershed algorithm. Based upon these measurements, we determined that the channel capacity of Dorsal for position information is ~1.5 bits, which approaches but is insufficient to accurately pattern the absolute position of the primary domains.

To determine how noise limits the precision of primary and secondary domain patterning, we investigated the factors contributing to the overall noise. Analogous to noise analysis in dual reporter systems [5], we can decompose the total noise into embryo-to-embryo (extrinsic) and within-embryo (intrinsic) components. Examination of these components showed that most of the noise is extrinsic, and most of the extrinsic noise is due to differences in the width of the Dorsal gradient. By simulating embryos with only intrinsic noise, we find that the channel capacity of Dorsal increases to ~2.4 bits, indicating that Dorsal concentration may carry enough information to accurately position the secondary domains relative to width of the Dorsal gradient.

III. Conclusion

We developed a generalizable approach to analyzing how different noise sources affect information transduction capacity. This approach showed that the *Drosophila* Dorsal gradient contains enough information to accurately specify the absolute positions of the primary domains, or the relative positions of the secondary domains.

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References

[1] Tkacik G, et al. (2008) Information flow and optimization in transcriptional regulation. *Proc Natl Acad Sci* **105**, 12265-12270.

[2] Dubuis JO, et al. (2011) Positional information, in bits, arXiv:1201.0198v1 [q-bio.MN]

[3] Hong JW, et al. (2008) How the Dorsal gradient works: Insights from postgenome technologies. *Proc Natl Acad Sci* **105**, 20072-20076.

[4] Cheong R, et al. (2011) Information transduction capacity of noisy biochemical signaling networks. *Science* **334**, 354-358.

[5] Elowitz MB, et al. (2002) Stochastic gene expression in a single cell. *Science* **297**, 1183-1186.