Precision in a rush: hunchback pattern formation in a limited time

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Fly development amazes us by the precision and reproducibility of gene expression, especially since the initial expression patterns are established during very short nuclear cycles. Recent live imaging of hunchback promoter dynamics shows a stable sharp binary expression pattern established within the 3 minute interphase of nuclear cycle 11. Considering expression models of different complexity we show how a limited readout time imposed by short developmental cycles affects the ability of the gene to read positional information and express reliably. Comparing our theoretical results to real-time monitoring of the hunchback transcription dynamics in live flies we discuss possible regulatory strategies.

Keywords — Drosophila melanogaster, hunchback, gene expression regulation, positional sensing

I. INTRODUCTION

The hunchback pattern formation in Drosophila melanogaster has been extensively studied as a model to understand how cell identity is established reliably at the correct time, correct location in space [1-2]. In this system, the hunchback gene extracts the positional information from transcription factor gradients, including Bicoid, and forms a sharp binary-like expression pattern that is key for the development of properly proportioned individuals. Driven by recent real-time monitoring of the hunchback transcription activity in live fly embryos [3-4] using the MCP-GFP system [5], we explore the constraints that a limited readout time coming from the short developmental nuclear cycles (3-10 mins in cycle 11-13) imposes on the ability of the gene network to readout positional information.

II. RESULTS

Using a theoretical model of gene expression regulation at the molecular level [6], we show that the steep expression pattern can emerge from the cooperative interactions between transcription factors and the operator sites of the hunchback promoter. However, this cooperativity comes at the cost of a long pattern formation time and an increased heterogeneity of gene expression at the pattern boundary. The identified trade-off has an impact on the system’s “positional resolution”, which corresponds to the minimum morphogen concentration difference at the expression boundary that neighboring nuclei are able to detect. We find that the kinetic parameters controlling gene expression yielding the highest positional resolution depend on the nuclear cycle duration (Fig. 1).

Our results show that if transcription regulation is done by a single transcription factor (e.g. Bicoid) via the operator sites of the hunchback promoter alone, the hunchback readout is likely to adopt a pattern of moderate steepness, much less than the experimentally observed steepness in flies [7]. We hypothesize that multiple transcription factors are required to cooperate with one another to achieve such high steepness while ensuring that future cell identity can be correctly encoded in the hunchback readout.

Finally, we present our first attempts to validate the hypothesis experimentally using synthetic promoters derived from the hunchback promoter, where the operator sites of known transcription factors (Bicoid, Hunchback, Caudal, Zelda) are present/absent.

REFERENCES