Binary Transcriptional Control of Pattern Formation in Development

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During embryonic development, tightly choreographed patterns of gene expression specify cell fate. Output transcriptional activity is characterized by bursts of gene expression, where promoters stochastically transition between transcriptional ON and OFF states. Here, we quantitatively test the hypothesis that transcriptional bursts are the main drivers of pattern formation. We quantify the transcriptional activity that leads to the formation of the widely studied stripe 2 of the *even-skipped* gene in living embryos of the fruit fly at the single cell level. We develop a novel memory-adjusted hidden Markov model to extract the parameters governing transcriptional bursting and show that that promoter switching dynamics cannot quantitatively explain pattern formation in the embryo. We discover that, in addition to bursting, the window of time over which genes engage in transcription is also regulated along the embryo, and that this digital regulation of when promoters become competent for transcription is the main driver of pattern formation. Thus, in order to reveal the molecular rules behind the transcriptional control of pattern formation and reach a predictive understanding of development, a non-steady-state and quantitative description of both the regulation of promoter bursting and the transcriptional time window needs to be adopted.

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