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Stochastic expression and epigenetic memory of the HO promoter

LUCY BAI, Pennsylvania State University

Eukaryotic gene regulation usually involves sequence-specific transcription factors and sequence-nonspecific cofactors. Large effort has been made to understand how these factors affect the average gene expression level among a population. However, little is known about how they regulate gene expression in individual cells. In this work, we address this question by mutating multiple factors in the regulation pathway of the yeast HO promoter and probing the corresponding promoter activity in single cells using time-lapse fluorescence microscopy. We show that the HO promoter fires in a stochastic, "on or off" fashion in wild type cells as well as in different genetic backgrounds. Many chromatin-related co-factors that affect the average level of HO expression do not actually affect the firing amplitude of the HO promoter; instead they affect the firing frequency among individual cell cycles. With certain mutations, the bimodal expression exhibits short-term epigenetic memory across the mitotic boundary. The memory is propagated in "cis" and caused by enhanced activator binding after a previous "on" cycle. Finally, we proposed a novel model that the short transcriptional memory is a result of slow turnover of the histone acetylation marks.