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Direct Quantification of Transcriptional Regulation at an Endogenous Gene Locus HENG XU, Department of Biochemistry and Molecular Biology, Baylor College of Medicine; Center for Theoretical Biological Physics, Rice University, ANNA SOKAC, Department of Biochemistry and Molecular Biology, Baylor College of Medicine, IDO GOLDING, Department of Physics and Center for the Physics of Living Cells, University of Illinois at Urbana-Champaign — The stochastic kinetics of gene activity in individual cells has been well characterized, but how this kinetics is modulated by the transcription factors that regulate expression remains largely unknown. We address this question using the Bicoid (Bcd) transcription factor and *hunchback* (*hb*) gene in early *Drosophila* embryos. We measure, simultaneously, the number of nascent *hb* mRNAs, nuclear Bcd concentration, and number of bound Bcd proteins, at individual gene loci. Using stochastic theoretical analysis, we find that Bcd modulates the probability of *hb* switching to an active transcriptional state, while not affecting the probabilities of transcription initiation or gene inactivation. Gene activation is achieved through the cooperative binding of 6 Bcd copies. Our data also reveals additional Bcd binding states of unknown function. In contrast to Bcd, binding of the Hunchback transcription factor represses *hb* transcription. Our approach can be used to elucidate the combinatorial activity of multiple transcription factors without the need for genetic perturbation.

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