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**Single-cell analysis of transcription kinetics across the cell cycle** SAMUEL SKINNER, HENG XU, Department of Biochemistry and Molecular Biology, Baylor College of Medicine; Center for Theoretical Biological Physics, Rice University, SONAL JAISWAL, PABLO FREIRE, Baylor College of Medicine, THOMAS ZWAKA, Department for Developmental and Regenerative Biology, Icahn School of Medicine at Mount Sinai, IDO GOLDING, Department of Physics and Center for the Physics of Living Cells, University of Illinois at Urbana-Champaign — Transcription is a highly stochastic process. A common way of inferring transcription kinetics is to measure mRNA abundance in individual cells and compare the observed copy-number statistics to the prediction of a theoretical stochastic model. However, the reliability of this procedure is hampered by the fact that the measured mRNA numbers represent integration over the finite lifetime of mRNA, over multiple copies of the same gene, and the mixing of cells from different phases of the cell cycle. Here we address these limitations by simultaneously quantifying nascent and mature mRNA in individual cells, and incorporating gene-copy and cell-cycle effects in the analysis of mRNA statistics. We demonstrate this approach on *Oct4* and *Nanog*, two key players in the mouse pluripotency network. We find that both genes are well described by a two-state stochastic model for transcription initiation. The difference in their expression characteristics is attributed to a 2.6-fold difference in the probability of switching to an active transcriptional state. Early in the cell cycle, the two copies of each gene exhibit independent activity. However, after gene replication, the probability of each gene copy to be active diminishes, resulting in dosage compensation.

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