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Cellular volume is a global controller of mRNA abundance
OLIVIA PADOVAN-MERHAR, University of Pennsylvania, Department of Physics and Astronomy, ARJUN RAJ, University of Pennsylvania, Department of Bioengineering — Many researchers have observed large variability in the numbers of RNA and protein molecules from cell to cell, a phenomenon thought to result from random bursts of transcription. These findings hold even for genes involved in core cellular processes, raising questions as to how cells can function in the presence of such molecular noise. However, biochemical processes typically depend on concentrations of cellular constituents rather than absolute numbers, so we use RNA fluorescence in situ hybridization to measure mRNA counts and cellular volume in single cells. We find that while both mRNA numbers and volume vary widely between cells, mRNA density does not. Thus, for many genes, mRNA abundance is precisely controlled to match the volume of the cell, as though the genes know how big the cell is. We measure transcription on a global and single-gene scale, and find that transcriptional activity scales with volume, suggesting that density is regulated at a transcriptional level. We present a mathematical model explaining which transcriptional bursting parameters account for the presence or lack of density conservation. Our findings suggest that global properties of RNA dynamics require a reassessment of our understanding of cellular heterogeneity and stochastic gene expression.

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