

Abstract Submitted
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Multi-Scale Modeling to Improve Single-Molecule, Single-Cell Experiments BRIAN MUNSKY, Colorado State University, Fort Collins, DOUGLAS SHEPHERD, University of Colorado, Denver — Single-cell, single-molecule experiments are producing an unprecedented amount of data to capture the dynamics of biological systems. When integrated with computational models, observations of spatial, temporal and stochastic fluctuations can yield powerful quantitative insight. We concentrate on experiments that localize and count individual molecules of mRNA. These high precision experiments have large imaging and computational processing costs, and we explore how improved computational analyses can dramatically reduce overall data requirements. In particular, we show how analyses of spatial, temporal and stochastic fluctuations can significantly enhance parameter estimation results for small, noisy data sets. We also show how full probability distribution analyses can constrain parameters with far less data than bulk analyses or statistical moment closures. Finally, we discuss how a systematic modeling progression from simple to more complex analyses can reduce total computational costs by orders of magnitude. We illustrate our approach using single-molecule, spatial mRNA measurements of Interleukin 1-alpha mRNA induction in human THP1 cells following stimulation. Our approach could improve the effectiveness of single-molecule gene regulation analyses for many other process.

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