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Effects of coarse-graining on fluctuations in gene expression JUAN PEDRAZA, JOHAN PAULSSON, Department of Systems Biology, Harvard University — Many cellular components are present in such low numbers per cell that random births and deaths of individual molecules can cause significant 'noise' in concentrations. But biochemical events do not necessarily occur in steps of individual molecules. Some processes are greatly randomized when synthesis or degradation occurs in large bursts of many molecules in a short time interval. Conversely, each birth or death of a macromolecule could involve several small steps, creating a memory between individual events. Here we present generalized theory for stochastic gene expression, formulating the variance in protein abundance in terms of the randomness of the individual events, and discuss the effective coarse-graining of the molecular hardware. We show that common molecular mechanisms produce gestation and senescence periods that can reduce noise without changing average abundances, lifetimes, or any concentration-dependent control loops. We also show that single-cell experimental methods that are now commonplace in cell biology do not discriminate between qualitatively different stochastic principles, but that this in turn makes them better suited for identifying which components introduce fluctuations.

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