Chemical fluctuation theorem for vibrant reaction networks in living cells

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An intracellular reaction network is often constituted by complex stochastic processes interacting with cell environments. To understand stochastic and dynamic biological processes occurring in living cells, it is essential to construct a rigorous mathematical description of intracellular reaction networks interacting with the complex cell environment, which is often hidden and beyond direct observation. In this presentation, we introduce a novel concept, which we term the vibrant reaction process, whose rate coefficient is a stochastic variable that differs from cell to cell and fluctuates over time due to its coupling to cell state variables. Additionally, we present a stochastic kinetic theory for vibrant, intracellular networks interacting with hidden cell environments, utilizing a formal, implicit description of cell environmental dynamics and its coupling to the system network and an explicit modeling of the system part of the network. By applying our stochastic kinetic theory to a general model of the intracellular birth-death processes, we obtain the chemical fluctuation theorem, which relates microscopic dynamics of the birth and death processes to cell-to-cell variation in product number. The chemical fluctuation theorem provides a unified, quantitative explanation of cell-to-cell variation in mRNA and protein levels for various recently investigated gene expression systems. Our analysis of gene expression variability in *Escherichia coli* shows that the transcription of an active gene is a strongly non-Poisson process whose rate coefficient is a dynamic stochastic variable with either an oscillatory or monotonically decaying time correlation function. The time correlation function of the rate coefficient has an important consequence for cellular control over transcriptional noise. This work demonstrates a promising, new approach in quantitative biology, making the complex dynamics of chemical reactions in living cells and its biological consequences accessible to a rigorous mathematical description.

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