Molecular Mechanisms of Precise Timing in Cell Lysis

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Abstract

Many biological systems exhibit precise timing of events, and one of the most known examples is cell lysis, which is a process of breaking bacterial host cells in the virus infection cycle. However, the underlying microscopic picture of precise timing remains not well understood. We present a novel theoretical approach to explain the molecular mechanisms of effectively deterministic dynamics in biological systems. Our hypothesis is based on the idea of stochastic coupling between relevant underlying biophysical and biochemical processes that lead to noise cancellation. To test this hypothesis, we introduced a minimal discrete-state stochastic model to investigate how holin proteins produced by bacteriophages break the inner membranes of Gram-negative bacteria. By explicitly solving this model, the dynamic properties of cell lysis are fully evaluated, and theoretical predictions quantitatively agree with available experimental data for both wild-type and holin mutants. It is found that the observed threshold-like behavior is a result of the balance between holin proteins entering the membrane and leaving the membrane during the lysis. Theoretical analysis suggests that the cell lysis achieves precise timing for wild-type species by maximizing the number of holins in the membrane and narrowing their spatial distribution. In contrast, for mutated species, these conditions are not satisfied. Our theoretical approach presents a possible molecular picture of precise dynamic regulation in intrinsically random biological processes.