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The stochastic spectral analysis of transcriptional regulatory cascades ANDREW MUGLER, Columbia University, Physics, ALEKSANDRA M. WALCZAK, Princeton University, PCTS, CHRIS H. WIGGINS, Columbia University, APAM, C2B2 — Modeling the dynamics of biological networks while respecting the intrinsic stochasticity requires accounting for intrinsic fluctuations arising from the low copy count of the constituent particles. Traditional simulation-based approaches to computing the probability distribution, rather than by direct solution of its master equation, are fundamentally limited by long runtimes and the need to estimate a the distribution from samples. We obviate both limitations by directly solving for the distribution using a fast and accurate method that exploits the natural basis of the uncoupled problem from the same class. We illustrate our method on a ubiquitous biological example: linear signaling cascades. The huge efficiency gains permit optimization of information transmission over input and regulatory parameters, revealing design properties of the most informative cascades. We find, for threshold regulation, that a cascade of strong regulations converts a unimodal input to a bimodal output, that multimodal inputs are no more informative than bimodal inputs, and that a chain of DC up-regulations outperforms a chain of AC down-regulations.

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