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Talk 1:

The effects of extrinsic noise on cellular decision making

Analysis of complex gene regulation networks gives rise to a landscape of metastable phenotypic states for cells. Heterogeneity within a population arises due to infrequent noise-driven transitions of individual cells between nearby metastable states. While most previous work has focused on the role of intrinsic fluctuations in driving such transitions, in this work we investigate the role of extrinsic fluctuations. We develop an analytical framework to study the combined effect of intrinsic and extrinsic noise on the dynamics of simple network motifs that comprise more complex genetic networks. In particular, we quantify the effects of extrinsic noise on the steady state distribution of protein copy numbers. We then investigate simple genetic switches and their stability when applying extrinsic noise. We show that extrinsic noise can significantly alter the lifetimes of the phenotypic states, and may fundamentally change the escape mechanism compared to intrinsic-noise-driven escape. All our analytical results are corroborated by extensive Monte-Carlo simulations, which are also used to study more complex higher-dimensional decision-making networks in biology.