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The effect of extrinsic noise on cellular decision making ELIJAH ROBERTS, Johns Hopkins University, MICHAEL ASSAF, Hebrew University of Jerusalem, ZAIDA LUTHEY-SCHULTEN, NIGEL GOLDENFELD, University of Illinois — Many cellular processes are not deterministic, i.e., genetically identical cells can display different phenotypic behavior even in identical environments. Such processes involve cellular decision making, in which individual cells randomly make choices determining their fate. One view is that the stochastic nature of cellular decision making is due to noise present in the biomolecular interaction networks. Most previous work has focused on the role of intrinsic noise of these networks. Yet, especially in the high copy-number regime, extrinsic noise may be much more significant, likely governing the overall dynamics. Here we develop a theoretical framework describing the combined effect of intrinsic and extrinsic noise on the stochastic dynamics of genetic switches responsible for cellular decision making. We do so by devising a semi-classical theory accounting for extrinsic noise as an effective species. Our theory, corroborated by extensive Monte-Carlo simulations, is tested on a simple bistable self-regulating gene model, and is then generalized to gain insight on the behavior of the lac genetic switch under extrinsic noise. We show that extrinsic noise not only significantly lowers the escape time from a phenotypic state, but can fundamentally change the actual escape process.

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