Determining the stability of genetic switches: Explicitly accounting for mRNA noise

MICHAEL ASSAF, ELIJAH ROBERTS, ZAN LUTHEY-SCHULTEN, University of Illinois at Urbana-Champaign — Cells use genetic switches to shift between alternate gene expression states, e.g. to adapt to new environments or to follow a developmental pathway. Here, we study the dynamics of switching in a generic-feedback on/off switch. Unlike protein-only models, we explicitly account for stochastic fluctuations of mRNA, which have a dramatic impact on the genetic switch dynamics. Employing a semi-classical theory to treat the underlying chemical master equations, we obtain accurate results for the quasi-stationary distributions of mRNA and protein copy numbers and for the mean switching time, starting from either state. Our analytical results agree well with extensive Monte Carlo simulations. Importantly, one can use the approach to study the effect of varying biological parameters, and of extrinsic noise, on the switch stability.