Stochastic activation in a genetic switch model

John Hertz[*]   Joanna Tyrcha[†]   Alvaro Correales[‡]

August 2018

Abstract

We study a biological autoregulation process, involving a protein that enhances its own transcription, in a parameter region where bistability would be present in the absence of fluctuations. We calculate the rate of fluctuation-induced rare transitions between locally-stable states using a path integral formulation and Master and Chapman-Kolmogorov equations. As in simpler models for rare transitions, the rate has the form of the exponential of a quantity S_0 (a "barrier") multiplied by a prefactor η. We calculate S_0 and η first in the bursting limit (where the ratio γ of the protein and mRNA lifetimes is very large). In this limit, the calculation can be done almost entirely analytically, and the results are in good agreement with simulations. For finite γ numerical calculations are generally required. However, S_0 can be calculated analytically to first order in $1/\gamma$, and the result agrees well with the full numerical calculation for all $\gamma > 1$. Employing a method used previously on other problems, we find we can account qualitatively for the way the prefactor η varies with γ, but its value is 15-20% higher than that inferred from simulations.

[*]Nordita, Sweden; john.hertz@nordita.org
[†]Stockholm University, Sweden; joanna@math.su.se
[‡]Universitaria de Cantoblanco, Spain; alvaro.correales@estudiante.uam.es