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Type of noise defines the most stable attractor in bistable gene expression model

We consider simplified stochastic model of gene expression with the nonlinear positive feedback. It is assumed that the gene may be in one of the two states: active or inactive. Protein molecules are produced directly from the active gene. We focus on the case in which in the deterministic approximation the system has two stable steady state solutions. Two types of noise are considered; transcriptional (characteristic for bacteria) - due to the limited number of protein molecules, and gene switching noise (important in Eukaryotes) - due to gene activation and inactivation transitions. We explore the correspondence between the stochastic system and its deterministic approximation in the limit of low noise. Analytical analysis of two approximations of the stochastic system, each with only one type of noise included, showed that when noise decreases to zero (I) the stationary probability density (SPD) converges to Dirac delta in one of two stable steady states, (II) in a broad range of parameters the SPD of the system with transcriptional noise converges to Dirac delta in a different steady state than the SPD of the system with gene switching noise. This suggest that the ratio of the transcriptional to the gene-switching noise dictates in which state the SPD concentrates. We verified this hypothesis by Monte Carlo simulations of the exact model. This finding has the following thermodynamic interpretation. The non interacting molecules diffusing in the uniform temperature field settle in the lowest potential well as temperature tends to zero. However when the temperature field is not uniform temperature profile dictates in which well molecules concentrate. Apparently, the two types of noise specific for gene expression are connected with two different temperature fields and thus favors the different attractors.

Our study demonstrates that in systems with the underlying bistability, like genetic switches, the noise characteristic controls in which of the epigenetic attractors cell population will settle.