Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

Probability and Flux Landscape of the Phage λ Genetic Switch

By

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The phage λ infection of an E. Coli cell has become a paradigm for understanding the molecular processes involved in gene expression and signaling within a cell. The bacteria cells when irradiated in the UV stopped growing and some time later burst into a crop of viruses. This was understood to be an example of a genetic switch; cells with identical DNA choose either of two cell cycles, a lysogenic cycle, in which the phage genome is incorporated into the host and copied by the host, or a lytic cycle, resulting in the death of the cell and a burst of viruses. The robustness of this switch is remarkable; although the first stages of the lysogenic and lytic cycles are identical, a lysogen virtually never spontaneously flips, and external stressors or instantaneous cell conditions are required to induce flipping. In particular the cell fate decision is regulated by the populations of two proteins, Ci and Cro, and their binding affinities to three DNA sites. This in turn governs the rates which RNAp transcribe the Ci and Cro genes to produce more of their respective proteins.

Although the biology in this case is well understood, the fundamental chemistry and physics underlying the bistability is still elusive. A dynamical model of the non-equilibrium statistical mechanics is revisited, generalized, and explored. The low number of proteins and other sources of noise are non-negligble and corrections to the kinetics are essential to understanding the stability. To this end, general integral forms, appropriate for finite element methods of advection-diffusion equations in concentration space have been developed and numerically solved for a variety of mutants and cellular assumptions. These solutions quantify the probability and flux landscapes of the ensembles evolution in concentration space and are used to predict the splitting of a cell population into the two states cell states, as well as the entropy production, passage times, and potential barriers of wild type and mutant bacteria to illuminate some structure of the configuration space from which Nature naturally selects.

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