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Probabilistic and Flux Landscapes of the Phage λ Genetic Switch

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The phage λ infection of an \textit{E. coli} cell has become a paradigm for understanding the molecular processes involved in gene expression and cell signaling. This system provides an example of a genetic switch, as 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 rarely spontaneously flips, and external stressors or instantaneous cell conditions are required to induce flipping. In particular, the cell fate decision can depend on the populations of two proteins, cI and Cro, as well as their oligomerization and subsequent binding affinities to three DNA sites. These processes in turn govern the rates at which RNAp transcribes the cI and Cro genes to produce more of their respective proteins.

In this work, a dynamical model of the non-equilibrium statistical mechanics is revisited and generalized. 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 for advection-diffusion equations have been developed and numerically solved for a variety of mutants and assumptions about the state of the cells. These solutions quantify the probabilistic and flux landscapes of the ensembles' evolution in concentration space and are used to predict the populations of the cell states, 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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