383f Markov Chain Modeling of Pyelonephritis-Associated Pili Expression in Uropathogenic Escherichia Coli

Laura R. Jarboe, Baiyu Zhou, David Beckwith, and James C. Liao

Expression of pyelonephritis-associated pili (Pap) in uropathogenic Escherichia coli is regulated by a complex phase variation mechanism involving competition between leucine-responsive regulatory protein (Lrp) and DNA adenine methylase (Dam). The population dynamics of pap expression has been studied extensively and the detailed molecular mechanism has been largely elucidated, providing sufficient information for mathematical modeling. Although the Gillespie algorithm is suited for modeling of stochastic systems such as the pap operon, it becomes computationally expensive when detailed molecular steps are explicitly modeled in a population. We have developed a Markov Chain model that is analytically derived from the molecular mechanisms to simplify the computation. The model is able to reproduce results presented using the Gillespie method (Jarboe et al., 2004), but since the regulatory information is incorporated before simulation, the Markov Chain model runs more efficiently and allows investigation of additional regulatory features. The model predictions are consistent with experimental data obtained in this work and in the literature. The results show that pap expression in uropathogenic E. coli is initial state dependent, as previously reported. However, without environment stimuli, the pap-expressing fraction in a population will reach an equilibrium level after about 50-100 generations. The transient time before reaching equilibrium is determined by PapI stability and the number of Lrp and Dam per cell. This work demonstrates that the Markov Chain model captures the essence of the complex molecular mechanism and greatly simplifies the computation.