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The addition of a coarse-grained looping state enhances bistability in a gene expression model of lac TYLER EARNEST, Department of Physics, University of Illinois at Urbana-Champaign, Urbana, IL, ELIJAH ROBERTS, Department of Biophysics, Johns Hopkins University, Baltimore, MD, MICHAEL ASSAF, KARIN DAHMEN, Department of Physics, University of Illinois at Urbana-Champaign, Urbana, IL, ZAIDA LUTHEY-SCHULTEN, Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, IL —

Bistability of the *lac* genetic switch in *Escherichia coli* is known to depend on its ability to form DNA loops with the *lac* repressor. Here we present a stochastic gene–mRNA–protein model of the *lac* switch that includes a third transcriptional state describing the DNA loop. We introduce a novel geometric burst extension to the finite state projection method, which allows us to eliminate mRNA as an independent species and rapidly search the parameter space of the model. We evaluate how the addition of the third state changes the model's bistability properties and find a region of parameter space where the system behaves in a way consistent to that seen experimentally for *lac*. Induction in the looping model is preceded by a rare complete dissociation of the loop followed by an immediate burst of mRNA rather than a slower build up of mRNA as in the two-state model. The overall effect of the looped state is to allow for faster switching times while at the same time further separating the uninduced and induced phenotypes from each other. These properties of loop regulatory elements give them intriguing implications for use in synthetic biology.

Tyler Earnest
Dept of Physics, University of Illinois at Urbana-Champaign, Urbana, IL

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