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Nonlinear degradation and the function of genetic circuits NICOLAS BUCHLER, Rockefeller University, ULRICH GERLAND, Ludwig-Maximilians University, TERENCE HWA, University of California, San Diego — The functions of most genetic circuits require a sufficient degree of cooperativity in the circuit components. We examine a simple source of cooperativity that stems from the nonlinear degradation of multimeric proteins. Ample experimental evidence suggests that protein subunits can degrade less rapidly when associated in multimeric complexes, an effect we refer to as "cooperative stabilization," For homodimers, this effect leads to a concentration dependence in the protein degradation rate because monomers which are predominant at low protein concentrations will be more rapidly degraded. Theoretical analysis of two model gene circuits in bacteria, i.e. genetic switch and oscillator, demonstrates that a few-fold difference between the degradation rate of monomers and dimers can substantially enhance the function of these circuits. Our results suggest that cooperative stabilization needs to be considered explicitly and characterized quantitatively in any systematic experimental or theoretical study of gene circuits.

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