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Threshold response and bimodality in non-cooperative auto-activation circuits[1] RUTGER HERMSEN, DAVID ERICKSON, TERENCE HWA, Center for Theoretical Biological Physics, UC San Diego — In prokaryotes as well as in eukaryotes, many transcription factors (TFs) activate their own gene. For that reason the benefits of auto-activation have been studied extensively. However, little attention is paid to the fact that many TFs are modified by a signal, usually through phosphorylation or binding of a ligand. Typically only one version of the TF—the modified or the unmodified one—can activate transcription. Consequently the TF's expression level responds to changes in the signal. Here, we use stochastic models to study the response properties of such circuits. In real examples the auto-activation is often mediated by a single binding site. Surprisingly, in that case we find that an arbitrarily sensitive threshold response can be obtained, while the bistability and hysteresis associated with multiple cooperative binding sites are avoided. Also, we find that the steady-state probability distributions of the TF expression level can be bimodal even though the system is not bistable. This is not caused by slow TF–DNA binding kinetics or bursty protein production, as in earlier studies, but by strongly reduced production and degradation rates at low expression levels.

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