

Publication

Protein Dimerization Generates Bistability in Positive Feedback Loops

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Bistability plays an important role in cellular memory and cell-fate determination. A positive feedback loop can generate bistability if it contains ultrasensitive molecular reactions. It is often difficult to detect bistability based on such molecular mechanisms due to its intricate interaction with cellular growth. We constructed transcriptional feedback loops in yeast. To eliminate growth alterations, we reduced the protein levels of the transcription factors by tuning the translation rates over two orders of magnitude with designed RNA stem loops. We modulated two ultrasensitive reactions, homodimerization and the cooperative binding of the transcription factor to the promoter. Either of them is sufficient to generate bistability on its own, and when acting together, a particularly robust bistability emerges. This bistability persists even in the presence of a negative feedback loop. Given that protein homodimerization is ubiquitous, it is likely to play a major role in the behavior of regulatory networks.

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