Mathematical Methods and Models in Biosciences
June 15–20, 2025, Sofia, Bulgaria
https://biomath.math.bas.bg/biomath/index.php/bmcs

Mixed positive and negative feedback loops drive diverse single-cell gene expression dynamics

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Genetic circuits with only a few components can generate complex gene regulatory dynamics. Here, we combine stochastic modelling and single-cell time-lapse microscopy to reveal the possible behaviours generated by a key gene circuit motif: the mixed positive/negative feedback loop. Our minimal stochastic model of this motif reveals ten distinct classes of output, including stochastic pulsing, oscillations, and bistability. Using an automatic classifier we map these behaviours across parameter space, showing how the behaviours are influenced by a few important biological parameters, such as the strength of the positive and negative feedbacks. Experimental validation in two different mixed feedback circuits in the bacterium *Bacillus subtilis*, σ^B and σ^V, confirms our model's predictive power. Guided by our simulations, we are able to transition between dynamic behaviours by modulating in vivo parameters. Together, these results demonstrate how mixed feedback loops generate diverse single-cell behaviours, improving our understanding of this common biological network motif and informing our efforts to engineer them for synthetic biology applications.