Appendix

Ordinary differential equation(ODE)-based model for the bistable switch:

Based on a deterministic model, we describe the transcription and translation of *cI* and *cI434* genes using a set of differential equations listed below[1]. According to Lou et al.(2009), we quantify the respective effects of CI and CI434 proteins on the P_{RM} and P_R promoters with a Hill function.

Transcription:

$$\frac{d[mRNA_{CI}]}{dt} = \alpha_{PRM} \times \frac{\alpha_{CI} \times (\frac{CI}{K_{CI}})^{n1} + 1}{1 + (\frac{CI}{K_{CI}})^{n1} + (\frac{CI434}{K_{CI434}})^{n2} + (\frac{CI}{K_{CI}})^{n1}(\frac{CI434}{K_{CI434}})^{n2}} - r_0 \times [mRNA_{CI}] \quad (1)$$

$$\frac{d[mRNA_{CI434}]}{dt} = \alpha_{PR} \times \frac{1}{1 + (\frac{CI}{K_{CI}})^{n1}} - r_0 \times [mRNA_{CI434}] \quad (2)$$

in which:

α_{CI} is the activation factor of CI on promoter P_{RM}, α_{PR} is the maximal rate of *cI434* gene transcription, K_{CI} is the binding affinity of CI to its operator, K_{CI434} is the binding affinity of CI434 to its operator, and n_1(set to 4) and n_2(set to 2) are the Hill coefficients to describe the cooperativity of CI and CI434 effects respectively[1]. r_0 is the mRNA degradation rate(assumed to be equal for all genes in this model).

Translation:

$$\frac{d[CI]}{dt} = \beta_{SDA} \times [mRNA_{CI}] - \gamma_0 \times [CI] \quad (3)$$

$$\frac{d[CI434]}{dt} = \beta_{SDcro} \times [mRNA_{CI434}] - \gamma_0 \times [CI434] \quad (4)$$

in which:

β_{SDA} is the translation rate constant for CI, and β_{SDcro} is that for CI434. Protein degradation rate, γ_0, is assumed to be the same for both proteins.

When simulating the distribution of CI434 in an assembly of cells, a stochastic differential equation(SDE)-based algorithm was used to simulate the steady-state distribution of the number of CI434 molecules in 1000 cells. For more details, please contact us for the Matlab code.

Reference

1. Lou, C., Liu, X., Ni, M., et al. (2009). Synthesizing a novel genetic sequential logic circuit: a push-on push-off switch-Supplementary Information. Nature Molecular Systems Biology *6*, 350.