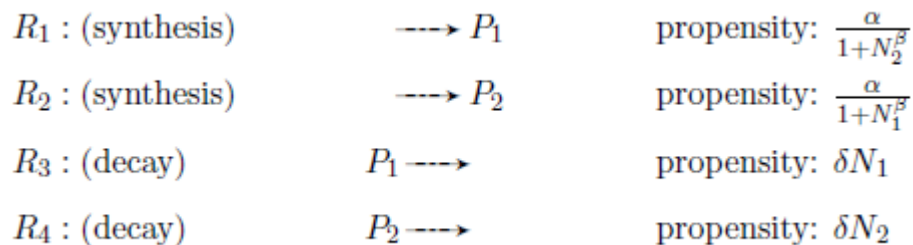


Mathematical Modeling in Systems Biology problem sets: 7.8.26 Noisy toggle switch

7.8.26 *Noisy toggle switch. Stochastic systems can exhibit a range of bistable-like behaviours, ranging from 'true' bistability to frequent noise-induced transitions between two nominally stable states. To explore this behaviour, consider a stochastic system that recapitulates the bistable toggle switch discussed in Section 7.2.3:



Here N_1 and N_2 are the molecular counts for the two repressors. The Hill-type propensities for the synthesis reactions are not well-justified at the molecular level, but these expressions nevertheless provide a simple formulation of a bistable stochastic system. Take parameter $\delta = 1$ and $\beta = 4$. The corresponding deterministic system (i.e. $dp_i/dt = \alpha_i/(1 + p_j^4) - p_i$) is bistable for any $\alpha_i > 1$. Run simulations of the stochastic system for $\alpha = 5, 50, 500$, and 5000 . Be sure to run the simulations sufficiently long so that the steady trend is clear (i.e. at least 10,000 reaction steps). Verify that for $\alpha = 5000$ the system exhibits bistability (with about 5000 molecules of the dominant species, in the long term). In contrast, verify that with $\alpha = 5$, noise dominates and the system shows no signs of bistability. What about at $\alpha = 50$ and 500 ? Comment on how the steady-state molecule abundance affects system behaviour. (Note: it may be necessary to run multiple simulations to confirm your findings.)

Agent-based modeling

Simulates viral spread in a population using a SIR model.

Please simulate a combination of three β_{\max} parameters = 0.05, 0.03, 0.01 (representing personal hygiene: e.g., Washing hands, wearing a mask) and three isolated parameters = 0.0, 0.5, 0.9. (Representing social distancing and/or lockdown measures) Therefore, there would be nine simulations. Plot the number of infected individuals over 5000 steps with three β_{\max} parameters, each isolated parameter on a different plot. (That is, plot #1 contains three curves: isolated = 0.0 for $\beta_{\max} = 0.05, 0.03, 0.01$, and plot #2 contains three curves: isolated = 0.5 for $\beta_{\max} = 0.05, 0.03, 0.01$, and plot #3 contains three curves: isolated = 0.9 for $\beta_{\max} = 0.05, 0.03, 0.01$) List the maxima (peaks) of infected individuals in the nine simulations. Which parameter set is the most effective in "flattening the curve" (having the lowest peak infected individuals)?

Compared to decreasing the transmission rate (the β_{\max} parameter), is increasing the "isolated" parameter more effective in flattening the curve?