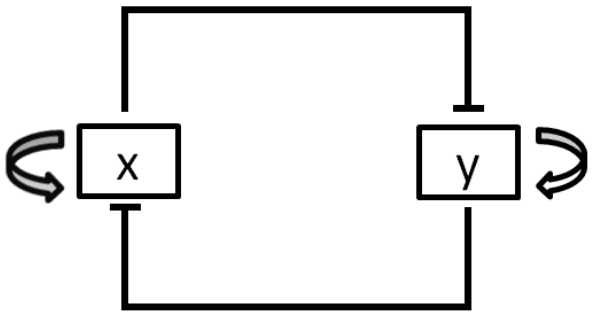
Stability



You want to test the stability of a circuit you designed with the following properties:

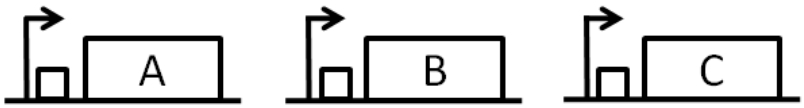
- x activates further production of x at a rate of $k_1*x^n/(k_2+x^n)$
- y activates further production of y at a rate of $k_4*y^m/(k_5+y^m)$
- x and y bind each other in a bimolecular interaction to form a dead end complex with rate constant k_3.

Write differential equations for x and y.
Sketch nullclines for x and y if n=m=4
Graph the nullclines and velocity plots using the following sets of parameters

- k_1 = 5 nM/s, k_2 = 1 nM^4, k_3 = 1/(nM*s), k_4 = 5 nM/s, k_5 = 1 nM^4, n=4, m = 4
- k_1 = 5 nM/s, k_2 = 1 nM^2, k_3 = 1/(nM*s), k_4 = 5 nM/s, k_5 = 1 nM^2, n=2, m = 2
- k_1 = 1 nM/s, k_2 = 1 nM^2, k_3 = 1/(nM*s), k_4 = 1 nM/s, k_5 = 1 nM^2, n=2, m = 2

Does the circuit perform like a toggle switch in any of the simulated parameter sets? Why or why not?
What values for which parameters promote multiple steady-states? Why? Which steady-states are stable?

Feedforward and feedback



Hook up the above transcription units into a feedforward pulse generator that responds to step increases in A. Write differential equations for rate changes in proteins A, B, and C and in other relevant species. Justify your choice of rate forms for reactions with order 2 or greater. Do you think you can speed up the response rate by adding negative feedback? Explain or use simulations to prove your point. What other modifications will you have to make to make sure the amplitude of C is the same as without negative feedback?

Is the process reversible (ie. if you take the high A, low C state and remove A will you reset to the low A, low C state)? Is there anything peculiar about the dynamics of the reverse process (or lack therof)?

Is there a way to hook up the above transcription units to give a transient decrease in C below a high basal level when A goes from off to on, without adding additional elements?