Assignment 3

Help

The **due date** for this quiz is **Fri 23 May 2014 8:59 PM PDT**.

☐ **In accordance with the Coursera Honor Code, I (Gene Cho) certify that the answers here are my own work.**

Question 1

At noted in the lectures, in single-variable systems, rate-balance plots can be used to determine whether bistability is present.

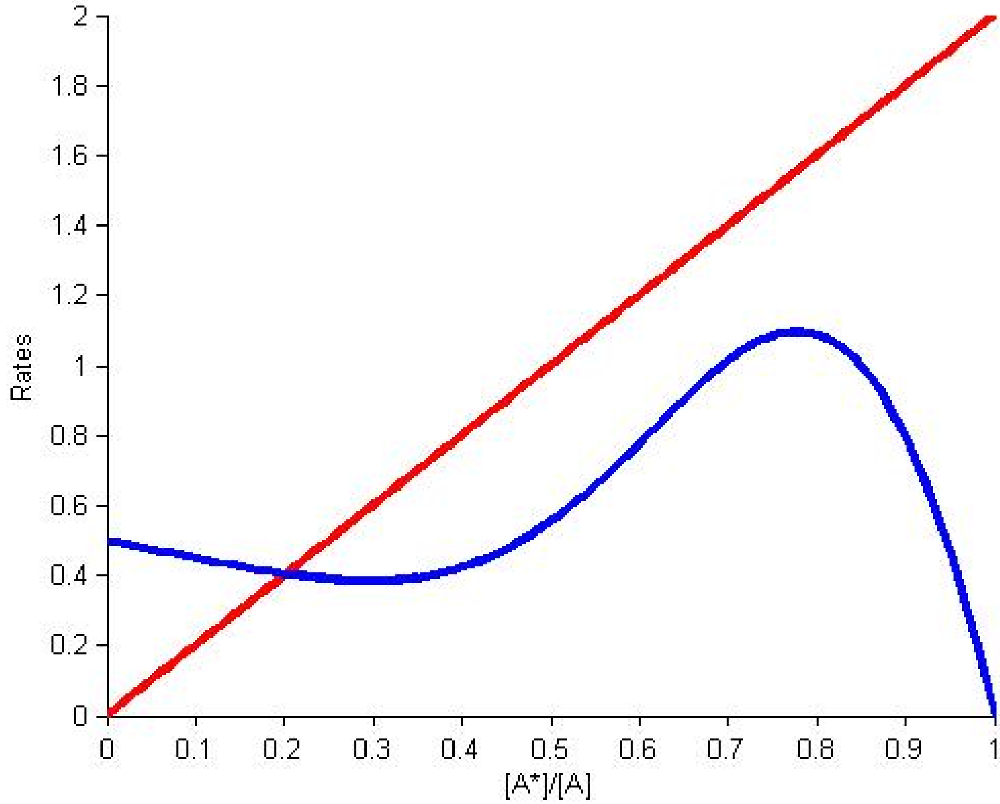
Several examples are given in the lecture notes. Download the Matlab script ratebalance.m from here . This script plots these curves for two simple cases:

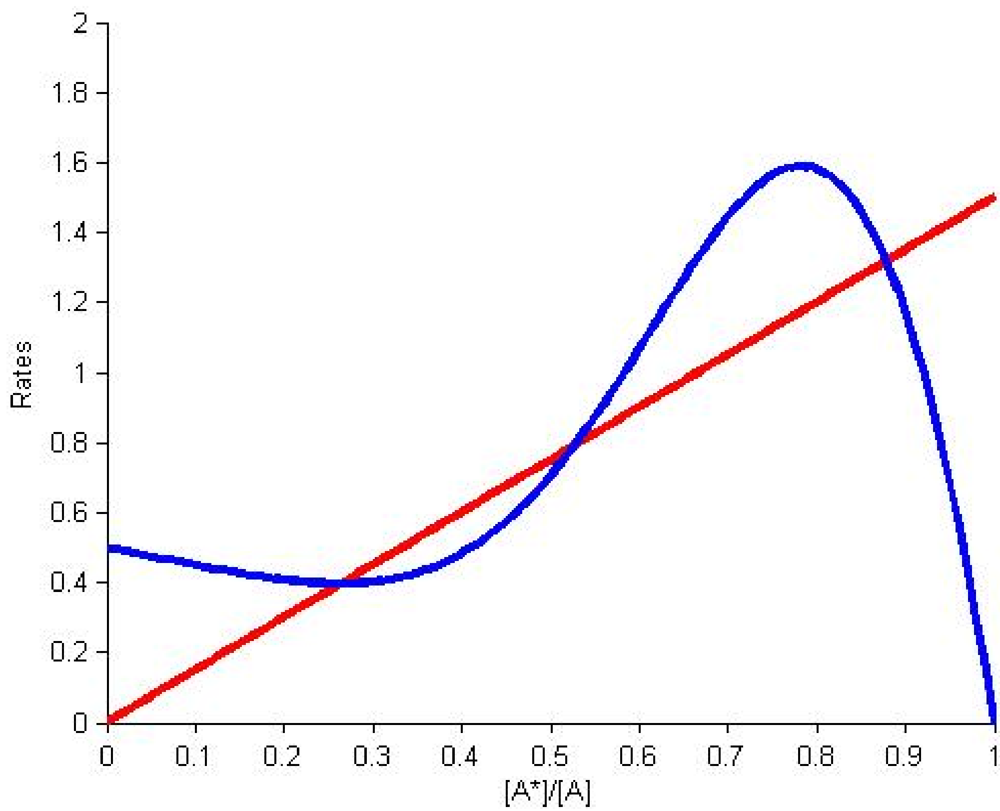
1) A constant forward rate

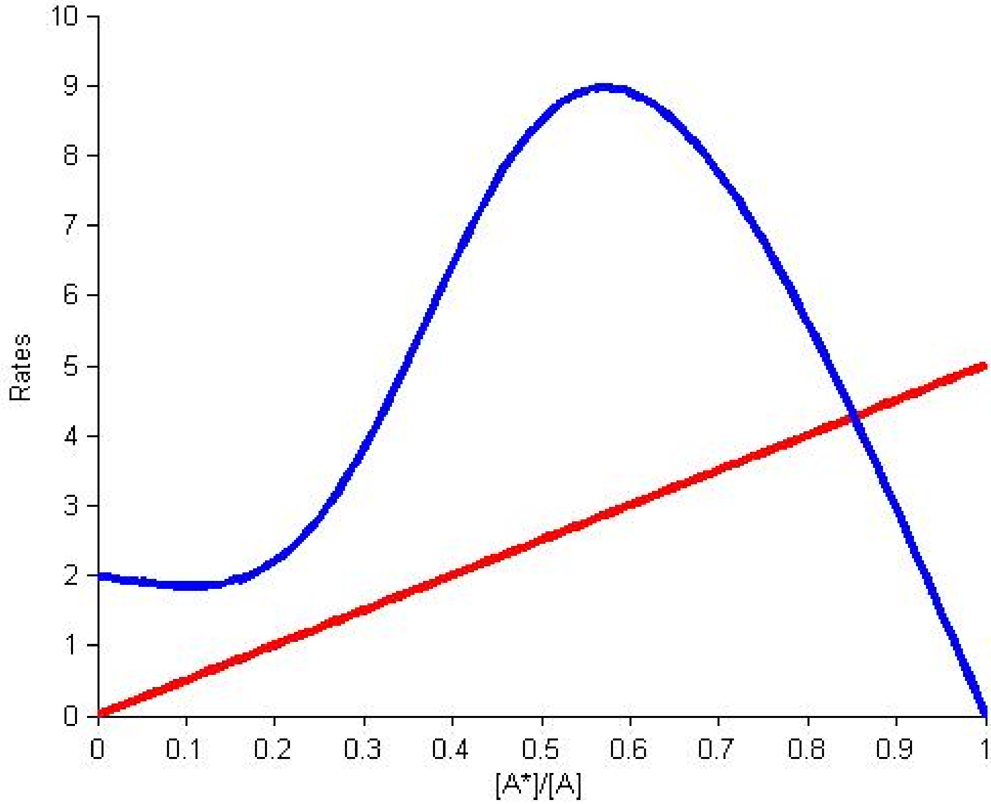
2) An ultrasensitive autocatalytic feedback that causes the forward rate to be highly nonlinear.

The variable of interest A* (Astar in the code) is assumed to be normalized to the quantity $[A]_{TOTAL}$, so this ranges from 0 to 1. For several values of the stimulus S, the program plots forward and backward rates, as well as the steady-states where the forward and backward rates cross.

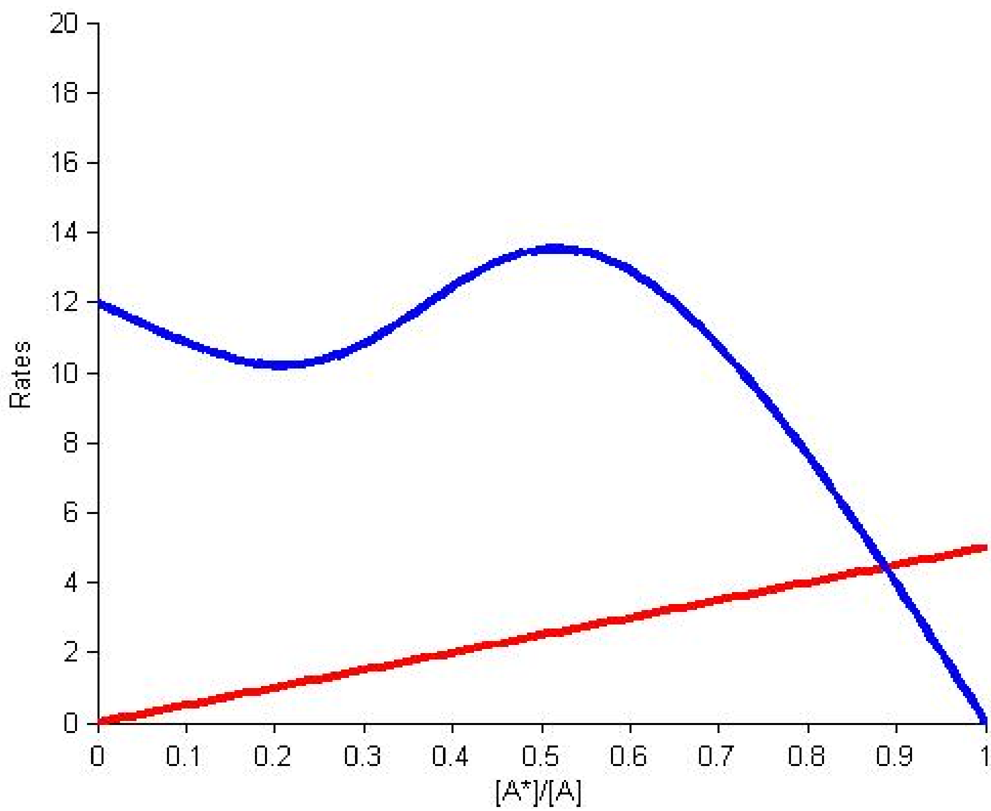
Based on what you have learnt about autocatalytic feedback loops , which of the following plots represents a case where bistability presents? (Red line shows the backward rate and blue line shows the forward rate)


2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Rates
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
[A*]/[A]


2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Rates
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
[A*]/[A]



Rates
[A*]/[A]
0
1
2
3
4
5
6
7
8
9
10
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9

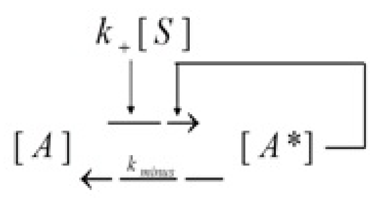


Rates
[A*]/[A]
0
2
4
6
8
10
12
14
16
18
20
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1

Question 2

Bistability can be produced with ultrasensitive feedback as in the example. It is not possible with linear feedback and a first order reverse rate. However, bistability can be produced if linear autocatalytic feedback is combined with a "back reaction" that becomes partially saturated when the level of product (A* in this case) increases.

Consider the linear feedback plus saturating back reaction:



$$FR = \left(k_+[S] + k_f[A^*]\right)\left([A]_{TOTAL} - [A^*]\right)$$

$$BR = k_{minus}\left(\frac{[A^*]}{[A^*]+K_{mb}}\right)$$

Modify ratebalance.m to simulate this condition. You can assume that the stimulus S is zero. Use the following constants: kminus = 5; K_{mb} = 0.1, kplus=2, kf=30.

Test several different values of K_{mb} and determine which values of K_{mb} produce bistability. You will have to determine the "interesting" range of K_{mb} values to examine. Plot your results as a bifurcation diagram: K_{mb} on the abscissa, steady-state values of [A*] on the ordinate. Lines 61-69 in the program are written to be able to accommodate the situation in which one or multiple steady-states are possible.

Which of the following statements is correct about K_{mb} and bistability in this system? (Assume: kminus = 5, kplus=2, kf=30, S=1)

- The only condition in which bistability present is when K_{mb} >1.
- When K_{mb} >0.1 bistability is present.
- When K_{mb} >3 , there is no bistability in the system.
- There is no bistability in the system when 0.1> K_{mb} .

Question 3

In the above case assume that K_{mb} is fixed and equals to 1 , which of the following statements is correct? (kminus = 5, kplus=2, kf=30) (Remeber that S can not be a negative number)

- The system shows bistability when S>1.
- The system is always mono-stable regardless of value of S.
- The system shows bistability when $0.1 < S < 1$.
- The system shows bistability when S>3.

Question 4

What if a system has both ultrasensitive autocatalytic feedback and a back reaction that becomes saturated? Is bistability in such a system likely to be less robust or more robust compared with a system that contains only one of these features? You do not have to explicitly simulate this condition, but you should be able to make an argument based on the shapes of the forward and backwards reaction rates. If you do choose to simulate this, it is probably easiest to modify the code so that it simulates several values of stimulus [S] but only single values of other parameters.

Using the following parameter sets which statement is correct when comparing a system with ultrasensitive autocatalytic feedback loop, a system with linear feedback plus saturating back reaction and a system which has both of this conditions? (kminus = 5; K_{mb} = 0.5, kplus=0.5, kf=30, Kmf = 0.5, h = 4)

- Ultrasensitive autocatalytic feedback loop, linear feedback loop plus saturating back reaction, and a system with both of them show bistability in the same range of values of parameter S.
- Ultrasensitive autocatalytic feedback loop with a back reaction that becomes saturated shows bistability in a longer range of values of parameter S.
- Ultrasensitive autocatalytic feedback loop shows bistability in a longer range of values of parameter S.
- Linear feedback plus saturating back reaction shows bistability in a longer range of values of parameter S.

Question 5

We now implement a simple two-variable model of the E. coli lac operon. The differential equations governing this system are as follows:

$$\frac{dl}{dt} = \beta l_{ext} LacY - \gamma l$$

$$\frac{dLacY}{dt} = \delta + p\frac{l^4}{l^4 + l_0^4} - \sigma LacY$$

β =1, γ =1, δ =0.2, l_0=4, p=4, σ =1

The variable l_{ext} , representing extracellular lactose, is the variable that can vary and potentially cause the bacteria to change states. Plot the nullclines of this model for l_{ext} =2.5. Because of the l^4 term appearing in the second equation, it is easiest to treat LacY as the dependent variable (ordinate) and l as the independent variable (abscissa). Which of the following statements is correct?

- ◯ Nullclines intersect in three points which all of them are stable steady states.
- ◯ Above the LacY nullcline, LacY and l are increasing.
- ◯ Nullclines intersect in three points which one of them is an unstable steady states.
- ◯ Nullclines intersect in two points which both of them are unstable steady states.

Question 6

Modify the program repression.m (You can download it from here) so that this model now simulates the temporal evolution of l and LacY. To reach steady-state, a total simulation time of 20 seconds is reasonable, and the solution converges with a time step of 0.01 if Euler's method is used. For l_{ext} = 2.5, plot the time evolution of LacY and l for the following initial conditions:

1) l =8, LacY=3;

2) I =3, LacY=1.3;

3) I =3, LacY=1.2;

4) I =2, LacY=1;

Which of the following statements is correct?

- Initial values of LacY and I determine if they will reach their lower or higher stable steady state levels.
- Changing the initial condition of LacY and I can remove the bistability from the system.
- I has always lower stable steady state levels compared to LacY.
- LacY has two stable steady states and I has one stable steady state.

Question 7

Vary I_{ext} over the range 1 to 7 and compute the temporal evolution of I and LacY. For each simulation, store the final value of LacY. Run two sets of simulations: one in which the initial conditions are I =8, LacY=3, and a second in which the initial conditions are I =2, LacY=1. Generate a bifurcation diagram of how the final value of LacY varies as a function of I_{ext} . Plot the results of the two sets of simulations in different colors.

Which of the following statements is correct?

- For $I_{ext} > 6$ the system is bistable.
- When extracellular lactose is less than 1, the system is bistable.
- Changing the initial conditions of I and LacY can change the bifurcation points.
- When $2 < I_{ext} < 4$, the system is bistable.

- [ ] **In accordance with the Coursera Honor Code, I (Gene Cho) certify that the answers here are my own work.**

Submit Answers | Save Answers

You cannot submit your work until you agree to the Honor Code. Thanks!