Bistable motif: 2kinase1substrate

Finding the condition of multistationarity

We consider the following reactions:

$K + S \to KS \to K + S_p$
$K_p + S \to K_p S \to K_p + S_p$
$K \to K_p$
$KS \leftarrow K_p S$
$E + S \to ES \to E + S_p$
$E_p + S \to E_p S \to E_p + S_p$
$E \to E_p$
$ES \leftarrow E_p S$
$S_p \to S$

The species of the system are:

$\{S, S_p, K, K_p, KS, K_p S, E, E_p, ES, E_p S\}$

In total, there are 13 reations and 10 species.

We firstly construct the ordinary differential equations based on mass-action kinetics. Then compute the determinant of Jacobian, using the solution at critical point (steady state) to calculate the determinant. The (necessary) condition for multistationarity is to make determinant equal to zero (non-zero determinant implys injectivity).

```
A = Table[0, {13}, {10}];
A[[1]][[1]] = -1; A[[1]][[3]] = -1; A[[1]][[5]] = 1;
A[[2]][[3]] = 1; A[[2]][[2]] = 1; A[[2]][[5]] = -1;
A[[3]][[1]] = -1; A[[3]][[4]] = -1; A[[3]][[6]] = 1;
A[[4]][[4]] = 1; A[[4]][[2]] = 1; A[[4]][[6]] = -1;
A[[5]][[3]] = -1;
A[[5]][[4]] = 1;
A[[6]][[5]] = 1;
A[[6]][[6]] = -1;
A[[13]][[2]] = -1; A[[13]][[1]] = 1;
A[[7]][[1]] = -1; A[[7]][[7]] = -1; A[[7]][[9]] = 1;
A[[8]][[7]] = 1; A[[8]][[2]] = 1; A[[8]][[9]] = -1;
A[[9]][[1]] = -1; A[[9]][[8]] = -1; A[[9]][[10]] = 1;
A[[10]][[8]] = 1; A[[10]][[2]] = 1; A[[10]][[10]] = -1;
A[[11]][[7]] = -1; A[[11]][[8]] = 1;
A[[12]][[9]] = 1;
A[[12]][[10]] = -1;
```

```
stoiM = Transpose[A]
```

```
{{-1, 0, -1, 0, 0, 0, -1, 0, -1, 0, 0, 0, 1}, {0, 1, 0, 1, 0, 0, 0, 1, 0, 1, 0, 0, -1},
 {-1, 1, 0, 0, -1, 0, 0, 0, 0, 0, 0, 0, 0}, {0, 0, -1, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0},
 {1, -1, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0}, {0, 0, 1, -1, 0, -1, 0, 0, 0, 0, 0, 0, 0},
 {0, 0, 0, 0, 0, 0, -1, 1, 0, 0, -1, 0, 0}, {0, 0, 0, 0, 0, 0, 0, 0, -1, 1, 1, 0, 0},
 {0, 0, 0, 0, 0, 0, 1, -1, 0, 0, 0, 1, 0}, {0, 0, 0, 0, 0, 0, 0, 0, 1, -1, 0, -1, 0}}
```

$$\mathbf{ks} = \{k_1 \times x_3 \times x_1,\ k_2 \times x_5,\ k_3 \times x_4 \times x_1,\ k_4 \times x_6,\ k_5 \times x_3,\ k_6 \times x_6,\ k_7 \times x_7 \times x_1,\ k_8 \times x_9,\ k_9 \times x_8 * x_1,\ k_{10} * x_{10},\ k_{11} * x_7,\ k_{12} \times x_{10},\ k_{13} * x_2\}$$

$$\{k_1\, x_1\, x_3,\ k_2\, x_5,\ k_3\, x_1\, x_4,\ k_4\, x_6,\ k_5\, x_3,\ k_6\, x_6,\ k_7\, x_1\, x_7,\ k_8\, x_9,\ k_9\, x_1\, x_8,\ k_{10}\, x_{10},\ k_{11}\, x_7,\ k_{12}\, x_{10},\ k_{13}\, x_2\}$$

```
ssEqns = stoiM.ks
```

$$\{k_{13}\, x_2 - k_1\, x_1\, x_3 - k_3\, x_1\, x_4 - k_7\, x_1\, x_7 - k_9\, x_1\, x_8,\ -k_{13}\, x_2 + k_2\, x_5 + k_4\, x_6 + k_8\, x_9 + k_{10}\, x_{10},\ -k_5\, x_3 - k_1\, x_1\, x_3 + k_2\, x_5,\ k_5\, x_3 - k_3\, x_1\, x_4 + k_4\, x_6,\ k_1\, x_1\, x_3 - k_2\, x_5 + k_6\, x_6,\ k_3\, x_1\, x_4 - k_4\, x_6 - k_6\, x_6,\ -k_{11}\, x_7 - k_7\, x_1\, x_7 + k_8\, x_9,\ k_{11}\, x_7 - k_9\, x_1\, x_8 + k_{10}\, x_{10},\ k_7\, x_1\, x_7 - k_8\, x_9 + k_{12}\, x_{10},\ k_9\, x_1\, x_8 - k_{10}\, x_{10} - k_{12}\, x_{10}\}$$

```
mC = RowReduce[NullSpace[A]]
```

$$\{\{1, 1, 0, 0, 1, 1, 0, 0, 1, 1\},\ \{0, 0, 1, 1, 1, 1, 0, 0, 0, 0\},\ \{0, 0, 0, 0, 0, 0, 1, 1, 1, 1\}\}$$

$$\mathbf{cons} = \{x_1 + x_2 + x_5 + x_6 + x_9 + x_{10} - T_1,\ x_3 + x_4 + x_5 + x_6 - T_2,\ x_7 + x_8 + x_9 + x_{10} - T_3\};$$

```
subsEqns = {ssEqns[[2]], ssEqns[[4]], ssEqns[[5]], ssEqns[[6]],
  ssEqns[[8]], ssEqns[[9]], cons[[1]], cons[[2]], cons[[3]]}
```

$$\{-k_{13}\, x_2 + k_2\, x_5 + k_4\, x_6 + k_8\, x_9 + k_{10}\, x_{10},\ k_5\, x_3 - k_3\, x_1\, x_4 + k_4\, x_6,\ k_1\, x_1\, x_3 - k_2\, x_5 + k_6\, x_6,\ k_3\, x_1\, x_4 - k_4\, x_6 - k_6\, x_6,\ k_{11}\, x_7 - k_9\, x_1\, x_8 + k_{10}\, x_{10},\ k_7\, x_1\, x_7 - k_8\, x_9 + k_{12}\, x_{10},\ -T_1 + x_1 + x_2 + x_5 + x_6 + x_9 + x_{10},\ -T_2 + x_3 + x_4 + x_5 + x_6,\ -T_3 + x_7 + x_8 + x_9 + x_{10}\}$$

$$\mathbf{sol1} = \mathbf{Solve}[\{\mathbf{ssEqns}[[4]],\ \mathbf{ssEqns}[[5]],\ \mathbf{ssEqns}[[6]],\ \mathbf{cons}[[2]]\} == 0,\ \{x_3, x_4, x_5, x_6\}]$$

$$\Big\{\Big\{x_3 \to \frac{k_2\, k_3\, k_6\, T_2\, x_1}{k_2\, k_4\, k_5 + k_2\, k_5\, k_6 + k_2\, k_3\, k_5\, x_1 + k_2\, k_3\, k_6\, x_1 + k_3\, k_5\, k_6\, x_1 + k_1\, k_3\, k_6\, x_1^2},$$
$$x_4 \to \frac{k_2\, k_5\, (k_4 + k_6)\, T_2}{k_2\, k_4\, k_5 + k_2\, k_5\, k_6 + k_2\, k_3\, k_5\, x_1 + k_2\, k_3\, k_6\, x_1 + k_3\, k_5\, k_6\, x_1 + k_1\, k_3\, k_6\, x_1^2},$$
$$x_5 \to \frac{k_3\, T_2\, \left(k_5\, k_6\, x_1 + k_1\, k_6\, x_1^2\right)}{k_2\, k_4\, k_5 + k_2\, k_5\, k_6 + k_2\, k_3\, k_5\, x_1 + k_2\, k_3\, k_6\, x_1 + k_3\, k_5\, k_6\, x_1 + k_1\, k_3\, k_6\, x_1^2},$$
$$x_6 \to \frac{k_2\, k_3\, k_5\, T_2\, x_1}{k_2\, k_4\, k_5 + k_2\, k_5\, k_6 + k_2\, k_3\, k_5\, x_1 + k_2\, k_3\, k_6\, x_1 + k_3\, k_5\, k_6\, x_1 + k_1\, k_3\, k_6\, x_1^2}\Big\}\Big\}$$

$$\mathbf{sol2} = \mathbf{Solve}[\{\mathbf{ssEqns}[[8]],\ \mathbf{ssEqns}[[9]],\ \mathbf{ssEqns}[[10]],\ \mathbf{cons}[[3]]\} == 0,\ \{x_7, x_8, x_9, x_{10}\}]$$

$$\Big\{\Big\{x_7 \to \frac{k_8\, k_9\, k_{12}\, T_3\, x_1}{k_8\, k_{10}\, k_{11} + k_8\, k_{11}\, k_{12} + k_8\, k_9\, k_{11}\, x_1 + k_8\, k_9\, k_{12}\, x_1 + k_9\, k_{11}\, k_{12}\, x_1 + k_7\, k_9\, k_{12}\, x_1^2},$$
$$x_8 \to \frac{k_8\, k_{11}\, (k_{10} + k_{12})\, T_3}{k_8\, k_{10}\, k_{11} + k_8\, k_{11}\, k_{12} + k_8\, k_9\, k_{11}\, x_1 + k_8\, k_9\, k_{12}\, x_1 + k_9\, k_{11}\, k_{12}\, x_1 + k_7\, k_9\, k_{12}\, x_1^2},$$
$$x_9 \to \frac{k_9\, T_3\, \left(k_{11}\, k_{12}\, x_1 + k_7\, k_{12}\, x_1^2\right)}{k_8\, k_{10}\, k_{11} + k_8\, k_{11}\, k_{12} + k_8\, k_9\, k_{11}\, x_1 + k_8\, k_9\, k_{12}\, x_1 + k_9\, k_{11}\, k_{12}\, x_1 + k_7\, k_9\, k_{12}\, x_1^2},$$
$$x_{10} \to \frac{k_8\, k_9\, k_{11}\, T_3\, x_1}{k_8\, k_{10}\, k_{11} + k_8\, k_{11}\, k_{12} + k_8\, k_9\, k_{11}\, x_1 + k_8\, k_9\, k_{12}\, x_1 + k_9\, k_{11}\, k_{12}\, x_1 + k_7\, k_9\, k_{12}\, x_1^2}\Big\}\Big\}$$

$$\mathbf{sol3} = x_2\ /.\ \mathbf{Solve}[\{\mathbf{ssEqns}[[2]] == 0\},\ \{x_2\}]$$

$$\left\{\frac{k_2\, x_5 + k_4\, x_6 + k_8\, x_9 + k_{10}\, x_{10}}{k_{13}}\right\}$$

```
sol4 = Solve[{x2 == sol3[[1]]} /. Join[sol1[[1]], sol2[[1]]], {x2}]
```

$$\left\{\left\{x_2 \to \frac{1}{k_{13}}\left(\frac{k_2 k_3 k_4 k_5 T_2 x_1}{k_2 k_4 k_5 + k_2 k_5 k_6 + k_2 k_3 k_5 x_1 + k_2 k_3 k_6 x_1 + k_3 k_5 k_6 x_1 + k_1 k_3 k_6 x_1^2} + \frac{k_2 k_3 T_2 \left(k_5 k_6 x_1 + k_1 k_6 x_1^2\right)}{k_2 k_4 k_5 + k_2 k_5 k_6 + k_2 k_3 k_5 x_1 + k_2 k_3 k_6 x_1 + k_3 k_5 k_6 x_1 + k_1 k_3 k_6 x_1^2} + \frac{k_8 k_9 k_{10} k_{11} T_3 x_1}{k_8 k_{10} k_{11} + k_8 k_{11} k_{12} + k_8 k_9 k_{11} x_1 + k_8 k_9 k_{12} x_1 + k_9 k_{11} k_{12} x_1 + k_7 k_9 k_{12} x_1^2} + \frac{k_8 k_9 T_3 \left(k_{11} k_{12} x_1 + k_7 k_{12} x_1^2\right)}{k_8 k_{10} k_{11} + k_8 k_{11} k_{12} + k_8 k_9 k_{11} x_1 + k_8 k_9 k_{12} x_1 + k_9 k_{11} k_{12} x_1 + k_7 k_9 k_{12} x_1^2}\right)\right\}\right\}$$

```
term =
 FullSimplify[x1 + x2 + x5 + x6 + x9 + x10 - T1 /. Join[sol1[[1]], sol2[[1]], sol4[[1]]]]
```

$$-T_1 + \frac{1}{k_{13}} x_1 \left(\frac{k_3 T_2 \left(k_5 \left(k_6 k_{13} + k_2 \left(k_4 + k_6 + k_{13}\right)\right) + k_1 k_6 \left(k_2 + k_{13}\right) x_1\right)}{k_3 k_6 x_1 \left(k_5 + k_1 x_1\right) + k_2 \left(k_5 \left(k_4 + k_6\right) + k_3 \left(k_5 + k_6\right) x_1\right)} + \left(k_9 k_{12} k_{13} \left(T_3 + x_1\right) \left(k_{11} + k_7 x_1\right) + k_8 \left(k_{11} \left(\left(k_{10} + k_{12}\right) k_{13} + k_9 \left(k_{10} + k_{12} + k_{13}\right) T_3\right) + k_9 \left(\left(k_{11} + k_{12}\right) k_{13} + k_7 k_{12} T_3\right) x_1\right)\right) / \left(k_9 k_{12} x_1 \left(k_{11} + k_7 x_1\right) + k_8 \left(k_{11} \left(k_{10} + k_{12}\right) + k_9 \left(k_{11} + k_{12}\right) x_1\right)\right)\right)$$

polynomial = Collect[Numerator[Together[term]], x_1]

$$
\begin{aligned}
&-k_2 k_4 k_5 k_8 k_{10} k_{11} k_{13} T_1 - k_2 k_5 k_6 k_8 k_{10} k_{11} k_{13} T_1 - \\
&k_2 k_4 k_5 k_8 k_{11} k_{12} k_{13} T_1 - k_2 k_5 k_6 k_8 k_{11} k_{12} k_{13} T_1 + \\
&(k_2 k_4 k_5 k_8 k_{10} k_{11} k_{13} + k_2 k_5 k_6 k_8 k_{10} k_{11} k_{13} + k_2 k_4 k_5 k_8 k_{11} k_{12} k_{13} + \\
&\quad k_2 k_5 k_6 k_8 k_{11} k_{12} k_{13} - k_2 k_4 k_5 k_8 k_9 k_{11} k_{13} T_1 - k_2 k_5 k_6 k_8 k_9 k_{11} k_{13} T_1 - \\
&\quad k_2 k_3 k_5 k_8 k_{10} k_{11} k_{13} T_1 - k_2 k_3 k_6 k_8 k_{10} k_{11} k_{13} T_1 - k_3 k_5 k_6 k_8 k_{10} k_{11} k_{13} T_1 - \\
&\quad k_2 k_4 k_5 k_8 k_9 k_{12} k_{13} T_1 - k_2 k_5 k_6 k_8 k_9 k_{12} k_{13} T_1 - k_2 k_3 k_5 k_8 k_{11} k_{12} k_{13} T_1 - \\
&\quad k_2 k_3 k_6 k_8 k_{11} k_{12} k_{13} T_1 - k_3 k_5 k_6 k_8 k_{11} k_{12} k_{13} T_1 - k_2 k_4 k_5 k_9 k_{11} k_{12} k_{13} T_1 - \\
&\quad k_2 k_5 k_6 k_9 k_{11} k_{12} k_{13} T_1 + k_2 k_3 k_4 k_5 k_8 k_{10} k_{11} T_2 + k_2 k_3 k_5 k_6 k_8 k_{10} k_{11} T_2 + \\
&\quad k_2 k_3 k_4 k_5 k_8 k_{11} k_{12} T_2 + k_2 k_3 k_5 k_6 k_8 k_{11} k_{12} T_2 + k_2 k_3 k_5 k_8 k_{10} k_{11} k_{13} T_2 + \\
&\quad k_3 k_5 k_6 k_8 k_{10} k_{11} k_{13} T_2 + k_2 k_3 k_5 k_8 k_{11} k_{12} k_{13} T_2 + k_3 k_5 k_6 k_8 k_{11} k_{12} k_{13} T_2 + \\
&\quad k_2 k_4 k_5 k_8 k_9 k_{10} k_{11} T_3 + k_2 k_5 k_6 k_8 k_9 k_{10} k_{11} T_3 + k_2 k_4 k_5 k_8 k_9 k_{11} k_{12} T_3 + \\
&\quad k_2 k_5 k_6 k_8 k_9 k_{11} k_{12} T_3 + k_2 k_4 k_5 k_8 k_9 k_{11} k_{13} T_3 + k_2 k_5 k_6 k_8 k_9 k_{11} k_{13} T_3 + \\
&\quad k_2 k_4 k_5 k_9 k_{11} k_{12} k_{13} T_3 + k_2 k_5 k_6 k_9 k_{11} k_{12} k_{13} T_3)\, x_1 + \\
&(k_2 k_4 k_5 k_8 k_9 k_{11} k_{13} + k_2 k_5 k_6 k_8 k_9 k_{11} k_{13} + k_2 k_3 k_5 k_8 k_{10} k_{11} k_{13} + \\
&\quad k_2 k_3 k_6 k_8 k_{10} k_{11} k_{13} + k_3 k_5 k_6 k_8 k_{10} k_{11} k_{13} + k_2 k_4 k_5 k_8 k_9 k_{12} k_{13} + \\
&\quad k_2 k_5 k_6 k_8 k_9 k_{12} k_{13} + k_2 k_3 k_5 k_8 k_{11} k_{12} k_{13} + k_2 k_3 k_6 k_8 k_{11} k_{12} k_{13} + \\
&\quad k_3 k_5 k_6 k_8 k_{11} k_{12} k_{13} + k_2 k_4 k_5 k_9 k_{11} k_{12} k_{13} + k_2 k_5 k_6 k_9 k_{11} k_{12} k_{13} - \\
&\quad k_2 k_3 k_5 k_8 k_9 k_{11} k_{13} T_1 - k_2 k_3 k_6 k_8 k_9 k_{11} k_{13} T_1 - k_3 k_5 k_6 k_8 k_9 k_{11} k_{13} T_1 - \\
&\quad k_1 k_3 k_6 k_8 k_{10} k_{11} k_{13} T_1 - k_2 k_4 k_5 k_7 k_9 k_{12} k_{13} T_1 - k_2 k_5 k_6 k_7 k_9 k_{12} k_{13} T_1 - \\
&\quad k_2 k_3 k_5 k_8 k_9 k_{12} k_{13} T_1 - k_2 k_3 k_6 k_8 k_9 k_{12} k_{13} T_1 - k_3 k_5 k_6 k_8 k_9 k_{12} k_{13} T_1 - \\
&\quad k_1 k_3 k_6 k_8 k_{11} k_{12} k_{13} T_1 - k_2 k_3 k_5 k_9 k_{11} k_{12} k_{13} T_1 - k_2 k_3 k_6 k_9 k_{11} k_{12} k_{13} T_1 - \\
&\quad k_3 k_5 k_6 k_9 k_{11} k_{12} k_{13} T_1 + k_2 k_3 k_4 k_5 k_8 k_9 k_{11} T_2 + k_2 k_3 k_5 k_6 k_8 k_9 k_{11} T_2 + \\
&\quad k_1 k_2 k_3 k_6 k_8 k_{10} k_{11} T_2 + k_2 k_3 k_4 k_5 k_8 k_9 k_{12} T_2 + k_2 k_3 k_5 k_6 k_8 k_9 k_{12} T_2 + \\
&\quad k_1 k_2 k_3 k_6 k_8 k_{11} k_{12} T_2 + k_2 k_3 k_4 k_5 k_9 k_{11} k_{12} T_2 + k_2 k_3 k_5 k_6 k_9 k_{11} k_{12} T_2 + \\
&\quad k_2 k_3 k_5 k_8 k_9 k_{11} k_{13} T_2 + k_3 k_5 k_6 k_8 k_9 k_{11} k_{13} T_2 + k_1 k_3 k_6 k_8 k_{10} k_{11} k_{13} T_2 + \\
&\quad k_2 k_3 k_5 k_8 k_9 k_{12} k_{13} T_2 + k_3 k_5 k_6 k_8 k_9 k_{12} k_{13} T_2 + k_1 k_3 k_6 k_8 k_{11} k_{12} k_{13} T_2 + \\
&\quad k_2 k_3 k_5 k_9 k_{11} k_{12} k_{13} T_2 + k_3 k_5 k_6 k_9 k_{11} k_{12} k_{13} T_2 + k_2 k_3 k_5 k_8 k_9 k_{10} k_{11} T_3 + \\
&\quad k_2 k_3 k_6 k_8 k_9 k_{10} k_{11} T_3 + k_3 k_5 k_6 k_8 k_9 k_{10} k_{11} T_3 + k_2 k_4 k_5 k_7 k_8 k_9 k_{12} T_3 + \\
&\quad k_2 k_5 k_6 k_7 k_8 k_9 k_{12} T_3 + k_2 k_3 k_5 k_8 k_9 k_{11} k_{12} T_3 + k_2 k_3 k_6 k_8 k_9 k_{11} k_{12} T_3 + \\
&\quad k_3 k_5 k_6 k_8 k_9 k_{11} k_{12} T_3 + k_2 k_3 k_5 k_8 k_9 k_{11} k_{13} T_3 + k_2 k_3 k_6 k_8 k_9 k_{11} k_{13} T_3 + \\
&\quad k_3 k_5 k_6 k_8 k_9 k_{11} k_{13} T_3 + k_2 k_4 k_5 k_7 k_9 k_{12} k_{13} T_3 + k_2 k_5 k_6 k_7 k_9 k_{12} k_{13} T_3 + \\
&\quad k_2 k_3 k_5 k_9 k_{11} k_{12} k_{13} T_3 + k_2 k_3 k_6 k_9 k_{11} k_{12} k_{13} T_3 + k_3 k_5 k_6 k_9 k_{11} k_{12} k_{13} T_3)\, x_1^2 + \\
&(k_2 k_3 k_5 k_8 k_9 k_{11} k_{13} + k_2 k_3 k_6 k_8 k_9 k_{11} k_{13} + k_3 k_5 k_6 k_8 k_9 k_{11} k_{13} + k_1 k_3 k_6 k_8 k_{10} k_{11} k_{13} + \\
&\quad k_2 k_4 k_5 k_7 k_9 k_{12} k_{13} + k_2 k_5 k_6 k_7 k_9 k_{12} k_{13} + k_2 k_3 k_5 k_8 k_9 k_{12} k_{13} + k_2 k_3 k_6 k_8 k_9 k_{12} k_{13} + \\
&\quad k_3 k_5 k_6 k_8 k_9 k_{12} k_{13} + k_1 k_3 k_6 k_8 k_{11} k_{12} k_{13} + k_2 k_3 k_5 k_9 k_{11} k_{12} k_{13} + k_2 k_3 k_6 k_9 k_{11} k_{12} k_{13} + \\
&\quad k_3 k_5 k_6 k_9 k_{11} k_{12} k_{13} - k_1 k_3 k_6 k_8 k_9 k_{11} k_{13} T_1 - k_2 k_3 k_5 k_7 k_9 k_{12} k_{13} T_1 - \\
&\quad k_2 k_3 k_6 k_7 k_9 k_{12} k_{13} T_1 - k_3 k_5 k_6 k_7 k_9 k_{12} k_{13} T_1 - k_1 k_3 k_6 k_8 k_9 k_{12} k_{13} T_1 - \\
&\quad k_1 k_3 k_6 k_9 k_{11} k_{12} k_{13} T_1 + k_1 k_2 k_3 k_6 k_8 k_9 k_{11} T_2 + k_2 k_3 k_4 k_5 k_7 k_9 k_{12} T_2 + \\
&\quad k_2 k_3 k_5 k_6 k_7 k_9 k_{12} T_2 + k_1 k_2 k_3 k_6 k_8 k_9 k_{12} T_2 + k_1 k_2 k_3 k_6 k_9 k_{11} k_{12} T_2 + \\
&\quad k_1 k_3 k_6 k_8 k_9 k_{11} k_{13} T_2 + k_2 k_3 k_5 k_7 k_9 k_{12} k_{13} T_2 + k_3 k_5 k_6 k_7 k_9 k_{12} k_{13} T_2 + \\
&\quad k_1 k_3 k_6 k_8 k_9 k_{12} k_{13} T_2 + k_1 k_3 k_6 k_9 k_{11} k_{12} k_{13} T_2 + k_1 k_3 k_6 k_8 k_9 k_{10} k_{11} T_3 + \\
&\quad k_2 k_3 k_5 k_7 k_8 k_9 k_{12} T_3 + k_2 k_3 k_6 k_7 k_8 k_9 k_{12} T_3 + k_3 k_5 k_6 k_7 k_8 k_9 k_{12} T_3 + \\
&\quad k_1 k_3 k_6 k_8 k_9 k_{11} k_{12} T_3 + k_1 k_3 k_6 k_8 k_9 k_{11} k_{13} T_3 + k_2 k_3 k_5 k_7 k_9 k_{12} k_{13} T_3 + \\
&\quad k_2 k_3 k_6 k_7 k_9 k_{12} k_{13} T_3 + k_3 k_5 k_6 k_7 k_9 k_{12} k_{13} T_3 + k_1 k_3 k_6 k_9 k_{11} k_{12} k_{13} T_3)\, x_1^3 + \\
&(k_1 k_3 k_6 k_8 k_9 k_{11} k_{13} + k_2 k_3 k_5 k_7 k_9 k_{12} k_{13} + k_2 k_3 k_6 k_7 k_9 k_{12} k_{13} + \\
&\quad k_3 k_5 k_6 k_7 k_9 k_{12} k_{13} + k_1 k_3 k_6 k_8 k_9 k_{12} k_{13} + k_1 k_3 k_6 k_9 k_{11} k_{12} k_{13} - \\
&\quad k_1 k_3 k_6 k_7 k_9 k_{12} k_{13} T_1 + k_1 k_2 k_3 k_6 k_7 k_9 k_{12} T_2 + k_1 k_3 k_6 k_7 k_9 k_{12} k_{13} T_2 + \\
&\quad k_1 k_3 k_6 k_7 k_8 k_9 k_{12} T_3 + k_1 k_3 k_6 k_7 k_9 k_{12} k_{13} T_3)\, x_1^4 + k_1 k_3 k_6 k_7 k_9 k_{12} k_{13} x_1^5
\end{aligned}
$$

This is a degree 5 polynomial which presumably admits 5 positive real roots. Any real root of this polynomial leads to a steady state for the fixed rate constants and total amounts. The values of the other variables at steady states are found by plugging the value of x1 (the root of the polynomial) into the expressions in sol1, sol2, and sol3 above.

A necessary condition for 5 positive roots is that the signs of the coefficient of the polynomial (in x1) alternate.

This is a pre-check when you do the sampling: you need to impose the coefficient of x1^4 to be negative , the coefficient of x1^3 to be positive, the coefficient of x1^2 to be negative and the coefficient of x1 to be positive. The coefficients of x1^5 and the independent term always have the right sign.

Sampling the parameters to make the term has 5 roots

```
ClearAll["Global`*"];
pol = -k2 k4 k5 k8 k10 k11 k13 T1 -
   k2 k5 k6 k8 k10 k11 k13 T1 - k2 k4 k5 k8 k11 k12 k13 T1 - k2 k5 k6 k8 k11 k12 k13 T1 +
   (k2 k4 k5 k8 k10 k11 k13 + k2 k5 k6 k8 k10 k11 k13 + k2 k4 k5 k8 k11 k12 k13 +
      k2 k5 k6 k8 k11 k12 k13 - k2 k4 k5 k8 k9 k11 k13 T1 - k2 k5 k6 k8 k9 k11 k13 T1 -
      k2 k3 k5 k8 k10 k11 k13 T1 - k2 k3 k6 k8 k10 k11 k13 T1 - k3 k5 k6 k8 k10 k11 k13 T1 -
      k2 k4 k5 k8 k9 k12 k13 T1 - k2 k5 k6 k8 k9 k12 k13 T1 - k2 k3 k5 k8 k11 k12 k13 T1 -
      k2 k3 k6 k8 k11 k12 k13 T1 - k3 k5 k6 k8 k11 k12 k13 T1 - k2 k4 k5 k9 k11 k12 k13 T1 -
      k2 k5 k6 k9 k11 k12 k13 T1 + k2 k3 k4 k5 k8 k10 k11 T2 + k2 k3 k5 k6 k8 k10 k11 T2 +
      k2 k3 k4 k5 k8 k11 k12 T2 + k2 k3 k5 k6 k8 k11 k12 T2 + k2 k3 k5 k8 k10 k11 k13 T2 +
      k3 k5 k6 k8 k10 k11 k13 T2 + k2 k3 k5 k8 k11 k12 k13 T2 + k3 k5 k6 k8 k11 k12 k13 T2 +
      k2 k4 k5 k8 k9 k10 k11 T3 + k2 k5 k6 k8 k9 k10 k11 T3 + k2 k4 k5 k8 k9 k11 k12 T3 +
      k2 k5 k6 k8 k9 k11 k12 T3 + k2 k4 k5 k8 k9 k11 k13 T3 + k2 k5 k6 k8 k9 k11 k13 T3 +
      k2 k4 k5 k9 k11 k12 k13 T3 + k2 k5 k6 k9 k11 k12 k13 T3) x1 +
   (k2 k4 k5 k8 k9 k11 k13 + k2 k5 k6 k8 k9 k11 k13 + k2 k3 k5 k8 k10 k11 k13 +
      k2 k3 k6 k8 k10 k11 k13 + k3 k5 k6 k8 k10 k11 k13 + k2 k4 k5 k8 k9 k12 k13 +
      k2 k5 k6 k8 k9 k12 k13 + k2 k3 k5 k8 k11 k12 k13 + k2 k3 k6 k8 k11 k12 k13 +
      k3 k5 k6 k8 k11 k12 k13 + k2 k4 k5 k9 k11 k12 k13 + k2 k5 k6 k9 k11 k12 k13 -
      k2 k3 k5 k8 k9 k11 k13 T1 - k2 k3 k6 k8 k9 k11 k13 T1 - k3 k5 k6 k8 k9 k11 k13 T1 -
      k1 k3 k6 k8 k10 k11 k13 T1 - k2 k4 k5 k7 k9 k12 k13 T1 - k2 k5 k6 k7 k9 k12 k13 T1 -
      k2 k3 k5 k8 k9 k12 k13 T1 - k2 k3 k6 k8 k9 k12 k13 T1 - k3 k5 k6 k8 k9 k12 k13 T1 -
      k1 k3 k6 k8 k11 k12 k13 T1 - k2 k3 k5 k9 k11 k12 k13 T1 - k2 k3 k6 k9 k11 k12 k13 T1 -
      k3 k5 k6 k9 k11 k12 k13 T1 + k2 k3 k4 k5 k8 k9 k11 T2 + k2 k3 k5 k6 k8 k9 k11 T2 +
      k1 k2 k3 k6 k8 k10 k11 T2 + k2 k3 k4 k5 k8 k9 k12 T2 + k2 k3 k5 k6 k8 k9 k12 T2 +
      k1 k2 k3 k6 k8 k11 k12 T2 + k2 k3 k4 k5 k9 k11 k12 T2 + k2 k3 k5 k6 k9 k11 k12 T2 +
      k2 k3 k5 k8 k9 k11 k13 T2 + k3 k5 k6 k8 k9 k11 k13 T2 + k1 k3 k6 k8 k10 k11 k13 T2 +
      k2 k3 k5 k8 k9 k12 k13 T2 + k3 k5 k6 k8 k9 k12 k13 T2 + k1 k3 k6 k8 k11 k12 k13 T2 +
      k2 k3 k5 k9 k11 k12 k13 T2 + k3 k5 k6 k9 k11 k12 k13 T2 + k2 k3 k5 k8 k9 k10 k11 T3 +
      k2 k3 k6 k8 k9 k10 k11 T3 + k3 k5 k6 k8 k9 k10 k11 T3 + k2 k4 k5 k7 k8 k9 k12 T3 +
      k2 k5 k6 k7 k8 k9 k12 T3 + k2 k3 k5 k8 k9 k11 k12 T3 + k2 k3 k6 k8 k9 k11 k12 T3 +
      k3 k5 k6 k8 k9 k11 k12 T3 + k2 k3 k5 k8 k9 k11 k13 T3 + k2 k3 k6 k8 k9 k11 k13 T3 +
      k3 k5 k6 k8 k9 k11 k13 T3 + k2 k4 k5 k7 k9 k12 k13 T3 + k2 k5 k6 k7 k9 k12 k13 T3 +
      k2 k3 k5 k9 k11 k12 k13 T3 + k2 k3 k6 k9 k11 k12 k13 T3 + k3 k5 k6 k9 k11 k12 k13 T3) x1^2 +
   (k2 k3 k5 k8 k9 k11 k13 + k2 k3 k6 k8 k9 k11 k13 + k3 k5 k6 k8 k9 k11 k13 +
      k1 k3 k6 k8 k10 k11 k13 + k2 k4 k5 k7 k9 k12 k13 + k2 k5 k6 k7 k9 k12 k13 +
      k2 k3 k5 k8 k9 k12 k13 + k2 k3 k6 k8 k9 k12 k13 + k3 k5 k6 k8 k9 k12 k13 +
      k1 k3 k6 k8 k11 k12 k13 + k2 k3 k5 k9 k11 k12 k13 + k2 k3 k6 k9 k11 k12 k13 +
      k3 k5 k6 k9 k11 k12 k13 - k1 k3 k6 k8 k9 k11 k13 T1 - k2 k3 k5 k7 k9 k12 k13 T1 -
      k2 k3 k6 k7 k9 k12 k13 T1 - k3 k5 k6 k7 k9 k12 k13 T1 - k1 k3 k6 k8 k9 k12 k13 T1 -
      k1 k3 k6 k9 k11 k12 k13 T1 + k1 k2 k3 k6 k8 k9 k11 T2 + k2 k3 k4 k5 k7 k9 k12 T2 +
      k2 k3 k5 k6 k7 k9 k12 T2 + k1 k2 k3 k6 k8 k9 k12 T2 + k1 k2 k3 k6 k9 k11 k12 T2 +
      k1 k3 k6 k8 k9 k11 k13 T2 + k2 k3 k5 k7 k9 k12 k13 T2 + k3 k5 k6 k7 k9 k12 k13 T2 +
      k1 k3 k6 k8 k9 k12 k13 T2 + k1 k3 k6 k9 k11 k12 k13 T2 + k1 k3 k6 k8 k9 k10 k11 T3 +
      k2 k3 k5 k7 k8 k9 k12 T3 + k2 k3 k6 k7 k8 k9 k12 T3 + k3 k5 k6 k7 k8 k9 k12 T3 +
      k1 k3 k6 k8 k9 k11 k12 T3 + k1 k3 k6 k8 k9 k11 k13 T3 + k2 k3 k5 k7 k9 k12 k13 T3 +
      k2 k3 k6 k7 k9 k12 k13 T3 + k3 k5 k6 k7 k9 k12 k13 T3 + k1 k3 k6 k9 k11 k12 k13 T3) x1^3 +
   (k1 k3 k6 k8 k9 k11 k13 + k2 k3 k5 k7 k9 k12 k13 + k2 k3 k6 k7 k9 k12 k13 +
      k3 k5 k6 k7 k9 k12 k13 + k1 k3 k6 k8 k9 k12 k13 + k1 k3 k6 k9 k11 k12 k13 -
      k1 k3 k6 k7 k9 k12 k13 T1 + k1 k2 k3 k6 k7 k9 k12 T2 + k1 k3 k6 k7 k9 k12 k13 T2 +
      k1 k3 k6 k7 k8 k9 k12 T3 + k1 k3 k6 k7 k9 k12 k13 T3) x1^4 + k1 k3 k6 k7 k9 k12 k13 x1^5;
```

Coeffs

Sampling

```
multistableParSets = {};
multistablePolSets = {};
multistableSolSets = {};
bistableParSets = {};
bistablePolSets = {};
bistableSolSets = {};
biCount = 0;
multiCount = 0;
termCount = 0;
Timing[
 Do[{
    pars = Exp[-RandomVariate[
         ExponentialDistribution[Log[2] / (-Log[0.001])], 13]] * 1000;
    tots = Exp[-RandomVariate[ExponentialDistribution[
          Log[2] / (-Log[0.001])], 3]] * 1000;
    (*pars=Exp[RandomReal[{Log[0.001],Log[1000.]},13]];*)
    (*tots=Exp[RandomReal[{Log[0.001],Log[10.]},3]];*)
    subs = {k1 → pars[[1]], k2 → pars[[2]], k3 → pars[[3]], k4 → pars[[4]],
      k5 → pars[[5]], k6 → pars[[6]], k7 → pars[[7]], k8 → pars[[8]],
      k9 → pars[[9]], k10 → pars[[10]], k11 → pars[[11]], k12 → pars[[12]],
      k13 → pars[[13]], T1 → tots[[1]], T2 → tots[[2]], T3 → tots[[3]]};
    (*term4=coeff4/.subs;
    term3=coeff3/.subs;
    term2=coeff2/.subs;
    term1=coeff1/.subs;
    If[term4<0&&term3>0&&term2<0&&term1>0,{*)
    solution = NSolve[{pol == 0 && x1 > 0} /. subs, x1, Reals];
    (*termCount++;*)
    If[Length[Flatten[solution]] > 1, {
      AppendTo[bistableParSets, Flatten[Join[pars, tots]]];
      AppendTo[bistablePolSets, pol /. subs];
      AppendTo[bistableSolSets, Flatten[solution]];
      biCount++;
      If[Length[Flatten[solution]] > 3, {
        AppendTo[multistableParSets, Flatten[Join[pars, tots]]];
        AppendTo[multistablePolSets, pol /. subs];
        AppendTo[multistableSolSets, Flatten[solution]];
        multiCount++;
       }];
     }];
    (*}];*)
   }, {i, 1 000 000}];
]
{2294.45, Null}
```

```
Length[bistableParSets]
```

```
701
```

```
Length[multistableParSets]
```

```
0
```

```
InputForm[bistableParSets[[1 ;; 50]]]
```

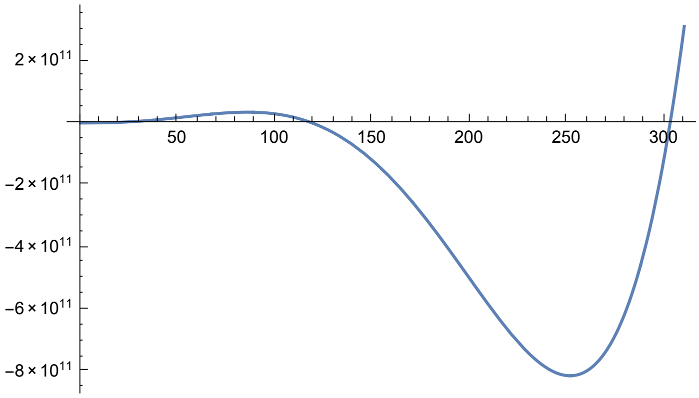
```
bistableSolSets[[1 ;; 50]]
```

```
{{x1 → 0.00275821, x1 → 4.47861, x1 → 14.0472},
 {x1 → 0.000281256, x1 → 0.204154, x1 → 2.98431},
 {x1 → 0.0358597, x1 → 0.143274, x1 → 782.206},
 {x1 → 5.7227 × 10^-7, x1 → 0.0000834245, x1 → 725.452},
 {x1 → 1.20477 × 10^-6, x1 → 0.00321882, x1 → 61.7904},
 {x1 → 0.0263379, x1 → 29.1998, x1 → 102.667},
 {x1 → 2.23995 × 10^-6, x1 → 0.390836, x1 → 4.48494},
 {x1 → 1.08418 × 10^-14, x1 → 0.00668897, x1 → 260.404},
 {x1 → 7.70987 × 10^-6, x1 → 22.668, x1 → 171.73},
 {x1 → 0.625486, x1 → 2.44407, x1 → 165.798},
 {x1 → 0.0000224073, x1 → 0.0000701277, x1 → 0.723713},
 {x1 → 5.97223 × 10^-8, x1 → 0.00214513, x1 → 781.638},
 {x1 → 7.25378 × 10^-8, x1 → 0.0000446211, x1 → 0.00175757},
 {x1 → 9.00434, x1 → 44.2176, x1 → 67.7837},
 {x1 → 0.00642932, x1 → 1.21019, x1 → 19.4252},
 {x1 → 0.217426, x1 → 102.641, x1 → 562.132},
 {x1 → 0.000118194, x1 → 0.872202, x1 → 266.415},
 {x1 → 0.00419153, x1 → 0.172909, x1 → 89.9307},
 {x1 → 3.15635, x1 → 4.5011, x1 → 39.0505},
 {x1 → 4.66659 × 10^-6, x1 → 0.00320223, x1 → 408.028},
 {x1 → 0.0924295, x1 → 0.37375, x1 → 250.431},
 {x1 → 4.52792 × 10^-6, x1 → 0.00128723, x1 → 0.0329867},
 {x1 → 0.0938524, x1 → 0.552778, x1 → 688.816},
 {x1 → 2.66262 × 10^-7, x1 → 0.191586, x1 → 17.1547},
 {x1 → 0.0330878, x1 → 0.174425, x1 → 375.352},
 {x1 → 0.000788716, x1 → 0.00627802, x1 → 0.79084},
 {x1 → 0.0153617, x1 → 0.061438, x1 → 95.079},
 {x1 → 7.34605 × 10^-6, x1 → 0.000156223, x1 → 0.02106},
 {x1 → 2.92156, x1 → 4.01718, x1 → 208.318},
 {x1 → 0.107459, x1 → 4.09316, x1 → 433.066},
 {x1 → 0.0000198778, x1 → 0.0216719, x1 → 18.5379},
 {x1 → 0.00831671, x1 → 1.83148, x1 → 61.9437},
 {x1 → 0.0252228, x1 → 2.35283, x1 → 181.456},
 {x1 → 0.00356962, x1 → 0.147133, x1 → 176.507},
 {x1 → 0.000181545, x1 → 0.226576, x1 → 0.815798},
 {x1 → 0.0178888, x1 → 58.368, x1 → 431.63},
 {x1 → 2.99332, x1 → 65.5889, x1 → 131.292},
 {x1 → 0.000817703, x1 → 0.0253721, x1 → 0.67715},
 {x1 → 0.13928, x1 → 15.6635, x1 → 75.2222},
 {x1 → 5.01776, x1 → 35.6684, x1 → 184.249},
 {x1 → 1.6696 × 10^-6, x1 → 0.00527399, x1 → 0.0431478},
 {x1 → 0.118118, x1 → 0.712658, x1 → 15.9451},
 {x1 → 0.000273715, x1 → 6.02954, x1 → 470.976},
 {x1 → 0.0700232, x1 → 4.22994, x1 → 621.588},
 {x1 → 0.0157948, x1 → 7.99914, x1 → 884.458},
 {x1 → 0.000121473, x1 → 0.287795, x1 → 227.411},
 {x1 → 0.0000983331, x1 → 0.903753, x1 → 103.688},
 {x1 → 0.0103199, x1 → 0.804873, x1 → 40.9821},
 {x1 → 1.31798 × 10^-7, x1 → 0.0119621, x1 → 6.38003},
 {x1 → 0.0705423, x1 → 59.1696, x1 → 338.86}}
```

```
Solve[bistablePolSets[[14]] == 0, x1]
```

```
{{x1 → -0.384066 - 10.0926 i}, {x1 → -0.384066 + 10.0926 i},
 {x1 → 0.0105899}, {x1 → 118.909}, {x1 → 302.746}}
```

```
Plot[bistablePolSets[[14]], {x1, 0, 310}, PlotRange → Full]
```



Test