# Bistable motif: parameter sampling

## Finding the condition of multistationarity

We consider the following reactions:

$K + S \to KS \to K + S_p$
$K_p + S \to K_p\,S \to K_p + S_p$
$S_p \to S$
$K + E \to EK \to K_p + E$
$KS + E \to EKS \to K_p\,S + E$
$K_p \to K$
$K_p\,S \to KS$

The species of the system are:

$\{S,\ S_p,\ K,\ K_p,\ KS,\ K_p\,S,\ E,\ EK,\ EKS\}$

In total, there are 11 reations and 9 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, {11}, {9}];
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]][[2]] = -1;
A[[5]][[1]] = 1;
A[[6]][[3]] = -1; A[[6]][[7]] = -1; A[[6]][[8]] = 1;
A[[7]][[8]] = -1; A[[7]][[4]] = 1; A[[7]][[7]] = 1;
A[[8]][[5]] = -1; A[[8]][[7]] = -1; A[[8]][[9]] = 1;
A[[9]][[9]] = -1; A[[9]][[6]] = 1; A[[9]][[7]] = 1;
A[[10]][[4]] = -1; A[[10]][[3]] = 1;
A[[11]][[6]] = -1;
A[[11]][[5]] = 1;
```

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

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

```
ks = {k1 × x3 × x1, k2 × x5, k3 × x4 × x1, k4 × x6,
   k5 × x2, k6 × x3 * x7, k7 * x8, k8 × x5 * x7, k9 * x9, k10 * x4, k11 * x6}
```

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

```
ssEqns = stoiM.ks
```

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

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

{{1, 1, 0, 0, 1, 1, 0, 0, 1}, {0, 0, 1, 1, 1, 1, 0, 1, 1}, {0, 0, 0, 0, 0, 0, 1, 1, 1}}

```
cons = {x1 + x2 + x5 + x6 + x9 - T1, x3 + x4 + x5 + x6 + x8 + x9 - T2, x7 + x8 + x9 - T3};
```

```
subsEqns = {ssEqns[[2]], ssEqns[[4]], ssEqns[[5]], ssEqns[[6]], ssEqns[[8]],
   ssEqns[[9]], x1 + x2 + x5 + x6 + x9 - T1, x3 + x4 + x5 + x6 + x8 + x9 - T2, x7 + x8 + x9 - T3}
```

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

```
sol1 = Solve[{ssEqns[[8]], ssEqns[[9]], cons[[3]]} == 0, {x7, x8, x9}]
```

$$\left\{\left\{x_7 \to \frac{k_7\,k_9\,T_3}{k_7\,k_9 + k_6\,k_9\,x_3 + k_7\,k_8\,x_5},\; x_8 \to \frac{k_6\,k_9\,T_3\,x_3}{k_7\,k_9 + k_6\,k_9\,x_3 + k_7\,k_8\,x_5},\; x_9 \to \frac{k_7\,k_8\,T_3\,x_5}{k_7\,k_9 + k_6\,k_9\,x_3 + k_7\,k_8\,x_5}\right\}\right\}$$

```
sol2 =
 Solve[{ssEqns[[3]], ssEqns[[4]], ssEqns[[6]], cons[[2]]} == 0, {x3, x4, x5, x6}]
```

$$\Big\{\Big\{x_3 \to -\big((-k_2\,k_4\,k_{10}\,T_2 - k_2\,k_{10}\,k_{11}\,T_2 - k_2\,k_3\,k_{11}\,T_2\,x_1 + k_2\,k_4\,k_7\,x_8 + k_2\,k_4\,k_{10}\,x_8 - k_4\,k_7\,k_{10}\,x_8 + k_2\,k_7\,k_{11}\,x_8 + k_2\,k_{10}\,k_{11}\,x_8 - k_7\,k_{10}\,k_{11}\,x_8 + k_2\,k_3\,k_7\,x_1\,x_8 + k_2\,k_3\,k_{11}\,x_1\,x_8 + k_2\,k_4\,k_9\,x_9 + k_2\,k_4\,k_{10}\,x_9 + k_2\,k_9\,k_{10}\,x_9 - k_4\,k_9\,k_{10}\,x_9 + k_2\,k_{10}\,k_{11}\,x_9 + k_2\,k_3\,k_9\,x_1\,x_9 + k_2\,k_3\,k_{11}\,x_1\,x_9) \,/\, ((k_4\,k_{10} + k_{10}\,k_{11} + k_3\,k_{11}\,x_1)\,(k_2 + k_1\,x_1 + k_6\,x_7))\big),$$

$$x_4 \to -\frac{-k_4\,k_7\,x_8 - k_7\,k_{11}\,x_8 - k_4\,k_9\,x_9}{k_4\,k_{10} + k_{10}\,k_{11} + k_3\,k_{11}\,x_1},$$

$$x_5 \to -\Big(\Big(-k_1\,k_4\,k_{10}\,T_2\,x_1 - k_1\,k_{10}\,k_{11}\,T_2\,x_1 - k_1\,k_3\,k_{11}\,T_2\,x_1^2 - k_4\,k_6\,k_{10}\,T_2\,x_7 - k_6\,k_{10}\,k_{11}\,T_2\,x_7 - k_3\,k_6\,k_{11}\,T_2\,x_1\,x_7 + k_4\,k_7\,k_{10}\,x_8 + k_7\,k_{10}\,k_{11}\,x_8 + k_1\,k_4\,k_7\,x_1\,x_8 + k_1\,k_4\,k_{10}\,x_1\,x_8 + k_1\,k_7\,k_{11}\,x_1\,x_8 + k_1\,k_{10}\,k_{11}\,x_1\,x_8 + k_1\,k_3\,k_7\,x_1^2\,x_8 + k_1\,k_3\,k_{11}\,x_1^2\,x_8 + k_4\,k_6\,k_7\,x_7\,x_8 + k_4\,k_6\,k_{10}\,x_7\,x_8 + k_6\,k_7\,k_{11}\,x_7\,x_8 + k_6\,k_{10}\,k_{11}\,x_7\,x_8 + k_3\,k_6\,k_7\,x_1\,x_7\,x_8 + k_3\,k_6\,k_{11}\,x_1\,x_7\,x_8 + k_4\,k_9\,k_{10}\,x_9 + k_1\,k_4\,k_9\,x_1\,x_9 + k_1\,k_4\,k_{10}\,x_1\,x_9 + k_1\,k_9\,k_{10}\,x_1\,x_9 + k_1\,k_{10}\,k_{11}\,x_1\,x_9 + k_1\,k_3\,k_9\,x_1^2\,x_9 + k_1\,k_3\,k_{11}\,x_1^2\,x_9 + k_4\,k_6\,k_9\,x_7\,x_9 + k_4\,k_6\,k_{10}\,x_7\,x_9 + k_6\,k_9\,k_{10}\,x_7\,x_9 + k_6\,k_{10}\,k_{11}\,x_7\,x_9 + k_3\,k_6\,k_9\,x_1\,x_7\,x_9 + k_3\,k_6\,k_{11}\,x_1\,x_7\,x_9\Big) \Big/ ((k_4\,k_{10} + k_{10}\,k_{11} + k_3\,k_{11}\,x_1)\,(k_2 + k_1\,x_1 + k_6\,x_7))\Big),$$

$$x_6 \to -\frac{-k_3\,k_7\,x_1\,x_8 - k_9\,k_{10}\,x_9 - k_3\,k_9\,x_1\,x_9}{k_4\,k_{10} + k_{10}\,k_{11} + k_3\,k_{11}\,x_1}\Big\}\Big\}$$

```
sol3 = Solve[{ssEqns[[2]], ssEqns[[5]], ssEqns[[6]], ssEqns[[9]], cons[[1]]} == 0,
  {x1, x2, x5, x6, x9}]
```

$$\{\{x_1 \to (k_5\,k_9\,T_1\,(k_2\,k_4 + k_2\,k_{11} + k_4\,k_8\,x_7)) / (k_2\,k_4\,k_5\,k_9 + k_2\,k_5\,k_9\,k_{11} + k_1\,k_2\,k_4\,k_9\,x_3 + k_1\,k_4\,k_5\,k_9\,x_3 + k_1\,k_2\,k_9\,k_{11}\,x_3 + k_1\,k_5\,k_9\,k_{11}\,x_3 + k_2\,k_3\,k_4\,k_9\,x_4 + k_2\,k_3\,k_5\,k_9\,x_4 + k_2\,k_3\,k_9\,k_{11}\,x_4 + k_3\,k_5\,k_9\,k_{11}\,x_4 + k_4\,k_5\,k_8\,k_9\,x_7 + k_1\,k_4\,k_5\,k_8\,x_3\,x_7 + k_1\,k_4\,k_8\,k_9\,x_3\,x_7 + k_1\,k_5\,k_8\,k_9\,x_3\,x_7 + k_1\,k_5\,k_8\,k_{11}\,x_3\,x_7 + k_3\,k_4\,k_8\,k_9\,x_4\,x_7 + k_3\,k_5\,k_8\,k_9\,x_4\,x_7 + k_3\,k_5\,k_8\,k_{11}\,x_4\,x_7),$$

$$x_2 \to (k_9\,T_1\,(k_1\,k_2\,k_4\,x_3 + k_1\,k_2\,k_{11}\,x_3 + k_2\,k_3\,k_4\,x_4 + k_2\,k_3\,k_{11}\,x_4 + k_1\,k_4\,k_8\,x_3\,x_7 + k_3\,k_4\,k_8\,x_4\,x_7)) / (k_2\,k_4\,k_5\,k_9 + k_2\,k_5\,k_9\,k_{11} + k_1\,k_2\,k_4\,k_9\,x_3 + k_1\,k_4\,k_5\,k_9\,x_3 + k_1\,k_2\,k_9\,k_{11}\,x_3 + k_1\,k_5\,k_9\,k_{11}\,x_3 + k_2\,k_3\,k_4\,k_9\,x_4 + k_2\,k_3\,k_5\,k_9\,x_4 + k_2\,k_3\,k_9\,k_{11}\,x_4 + k_3\,k_5\,k_9\,k_{11}\,x_4 + k_4\,k_5\,k_8\,k_9\,x_7 + k_1\,k_4\,k_5\,k_8\,x_3\,x_7 + k_1\,k_4\,k_8\,k_9\,x_3\,x_7 + k_1\,k_5\,k_8\,k_9\,x_3\,x_7 + k_1\,k_5\,k_8\,k_{11}\,x_3\,x_7 + k_3\,k_4\,k_8\,k_9\,x_4\,x_7 + k_3\,k_5\,k_8\,k_9\,x_4\,x_7 + k_3\,k_5\,k_8\,k_{11}\,x_4\,x_7),$$

$$x_5 \to (k_1\,k_5\,k_9\,T_1\,x_3\,(k_1\,(-k_4 - k_{11})\,x_3 - k_3\,k_{11}\,x_4)) / (-k_8\,(-k_1\,k_9\,x_3\,(k_5\,k_{11} + k_1\,(-k_4 - k_5)\,x_3) - k_1\,k_5\,x_3\,(k_1\,(-k_4 - k_{11})\,x_3 - k_3\,k_{11}\,x_4))\,x_7 - k_9\,(-(k_5\,k_{11} + k_1\,(-k_4 - k_5)\,x_3)\,(k_2\,k_3\,x_4 + k_3\,k_8\,x_4\,x_7) + (k_1\,(-k_4 - k_{11})\,x_3 - k_3\,k_{11}\,x_4)\,(k_1\,(-k_2 - k_5)\,x_3 + k_5\,(-k_2 - k_8\,x_7)))),$$

$$x_6 \to (k_5\,k_9\,T_1\,(k_2\,k_3\,x_4 + k_1\,k_8\,x_3\,x_7 + k_3\,k_8\,x_4\,x_7)) / (k_2\,k_4\,k_5\,k_9 + k_2\,k_5\,k_9\,k_{11} + k_1\,k_2\,k_4\,k_9\,x_3 + k_1\,k_4\,k_5\,k_9\,x_3 + k_1\,k_2\,k_9\,k_{11}\,x_3 + k_1\,k_5\,k_9\,k_{11}\,x_3 + k_2\,k_3\,k_4\,k_9\,x_4 + k_2\,k_3\,k_5\,k_9\,x_4 + k_2\,k_3\,k_9\,k_{11}\,x_4 + k_3\,k_5\,k_9\,k_{11}\,x_4 + k_4\,k_5\,k_8\,k_9\,x_7 + k_1\,k_4\,k_5\,k_8\,x_3\,x_7 + k_1\,k_4\,k_8\,k_9\,x_3\,x_7 + k_1\,k_5\,k_8\,k_9\,x_3\,x_7 + k_1\,k_5\,k_8\,k_{11}\,x_3\,x_7 + k_3\,k_4\,k_8\,k_9\,x_4\,x_7 + k_3\,k_5\,k_8\,k_9\,x_4\,x_7 + k_3\,k_5\,k_8\,k_{11}\,x_4\,x_7),$$

$$x_9 \to (k_5\,k_8\,T_1\,(k_1\,k_4\,x_3 + k_1\,k_{11}\,x_3 + k_3\,k_{11}\,x_4)\,x_7) / (k_2\,k_4\,k_5\,k_9 + k_2\,k_5\,k_9\,k_{11} + k_1\,k_2\,k_4\,k_9\,x_3 + k_1\,k_4\,k_5\,k_9\,x_3 + k_1\,k_2\,k_9\,k_{11}\,x_3 + k_1\,k_5\,k_9\,k_{11}\,x_3 + k_2\,k_3\,k_4\,k_9\,x_4 + k_2\,k_3\,k_5\,k_9\,x_4 + k_2\,k_3\,k_9\,k_{11}\,x_4 + k_3\,k_5\,k_9\,k_{11}\,x_4 + k_4\,k_5\,k_8\,k_9\,x_7 + k_1\,k_4\,k_5\,k_8\,x_3\,x_7 + k_1\,k_4\,k_8\,k_9\,x_3\,x_7 + k_1\,k_5\,k_8\,k_9\,x_3\,x_7 + k_1\,k_5\,k_8\,k_{11}\,x_3\,x_7 + k_3\,k_4\,k_8\,k_9\,x_4\,x_7 + k_3\,k_5\,k_8\,k_9\,x_4\,x_7 + k_3\,k_5\,k_8\,k_{11}\,x_4\,x_7)\}\}$$

The difficulty here is that the solution of each x is a function of more than two other x, makes the solution very complicated.