Bistable motif: parameter sampling

Finding the condition of multistationarity

We consider the following reactions:

$K + S \leftrightharpoons KS \to K + S_p$
$K^* + S \leftrightharpoons K^* S \to K^* + S_p$
$S_p \to S$
$K \leftrightharpoons K^*$
$KS \leftrightharpoons K^* S$

The species of the system are:

$\{S, S_p, K, K^*, KS, K^* S\}$

In total, there are 11 reations and 6 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).

In[6]:=
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A = Table[0, {11}, {6}];
A[[1]][[1]] = -1;
A[[1]][[3]] = -1;
A[[1]][[5]] = 1;
A[[2]] = -A[[1]];
A[[3]][[3]] = 1; A[[3]][[2]] = 1; A[[3]][[5]] = -1;
A[[4]][[1]] = -1;
A[[4]][[4]] = -1;
A[[4]][[6]] = 1;
A[[5]] = -A[[4]];
A[[6]][[4]] = 1;
A[[6]][[2]] = 1;
A[[6]][[6]] = -1;
A[[7]][[2]] = -1;
A[[7]][[1]] = 1;
A[[8]][[3]] = -1; A[[8]][[4]] = 1; A[[9]] = -A[[8]];
A[[10]][[5]] = -1; A[[10]][[6]] = 1; A[[11]] = -A[[10]];
stoiM = Transpose[A];
(* Now we construct the rate vector *)
ks = {k1 × x3 × x1, k2 × x5, k3 × x5, k4 × x4 × x1,
   k5 × x6, k6 × x6, k7 × x2, k8 × x3, k9 × x4, k10 × x5, k11 × x6};
ssEqns = stoiM.ks;
mC = RowReduce[NullSpace[A]];
subsEqns = {ssEqns[[2]], ssEqns[[4]],
   ssEqns[[5]], ssEqns[[6]], x1 + x2 + x5 + x6 - T1, x3 + x4 + x5 + x6 - T2};
jacobian = D[subsEqns, {{x1, x2, x3, x4, x5, x6}}];
detJ = Collect[Distribute[Det[jacobian]], {x1, x2, x3, x4, x5, x6}];
solution =
  Solve[{{subsEqns[[1]], subsEqns[[2]], subsEqns[[3]], subsEqns[[4]]} == 0},
   {x2, x4, x5, x6}];
detSubs = Replace[detJ, solution[[1]], {0, Infinity}];
(* Equivilant to detSubs=detJ/.solution[[1]]; *)
polSubs = Numerator[Together[detSubs]];
finalSubs = Collect[Distribute[polSubs], x_, FactorTerms]
```

Out[23]= $-k_2^2 k_5^2 k_7 k_8 k_9 - 2 k_2 k_3 k_5^2 k_7 k_8 k_9 - k_3^2 k_5^2 k_7 k_8 k_9 - 2 k_2^2 k_5 k_6 k_7 k_8 k_9 - 4 k_2 k_3 k_5 k_6 k_7 k_8 k_9 -$

$2 k_3^2 k_5 k_6 k_7 k_8 k_9 - k_2^2 k_6^2 k_7 k_8 k_9 - 2 k_2 k_3 k_6^2 k_7 k_8 k_9 - k_3^2 k_6^2 k_7 k_8 k_9 - k_2^2 k_5^2 k_7 k_9^2 -$

$2 k_2 k_3 k_5^2 k_7 k_9^2 - k_3^2 k_5^2 k_7 k_9^2 - 2 k_2^2 k_5 k_6 k_7 k_9^2 - 4 k_2 k_3 k_5 k_6 k_7 k_9^2 - 2 k_3^2 k_5 k_6 k_7 k_9^2 -$

$k_2^2 k_6^2 k_7 k_9^2 - 2 k_2 k_3 k_6^2 k_7 k_9^2 - k_3^2 k_6^2 k_7 k_9^2 - 2 k_2 k_5^2 k_7 k_8 k_9 k_{10} - 2 k_3 k_5^2 k_7 k_8 k_9 k_{10} -$

$4 k_2 k_5 k_6 k_7 k_8 k_9 k_{10} - 4 k_3 k_5 k_6 k_7 k_8 k_9 k_{10} - 2 k_2 k_6^2 k_7 k_8 k_9 k_{10} - 2 k_3 k_6^2 k_7 k_8 k_9 k_{10} -$

$2 k_2 k_5^2 k_7 k_9^2 k_{10} - 2 k_3 k_5^2 k_7 k_9^2 k_{10} - 4 k_2 k_5 k_6 k_7 k_9^2 k_{10} - 4 k_3 k_5 k_6 k_7 k_9^2 k_{10} - 2 k_2 k_6^2 k_7 k_9^2 k_{10} -$

$2 k_3 k_6^2 k_7 k_9^2 k_{10} - k_5^2 k_7 k_8 k_9 k_{10}^2 - 2 k_5 k_6 k_7 k_8 k_9 k_{10}^2 - k_6^2 k_7 k_8 k_9 k_{10}^2 - k_5^2 k_7 k_9^2 k_{10}^2 -$

$2 k_5 k_6 k_7 k_9^2 k_{10}^2 - k_6^2 k_7 k_9^2 k_{10}^2 - 2 k_2^2 k_5 k_7 k_8 k_9 k_{11} - 4 k_2 k_3 k_5 k_7 k_8 k_9 k_{11} - 2 k_3^2 k_5 k_7 k_8 k_9 k_{11} -$

$2 k_2^2 k_6 k_7 k_8 k_9 k_{11} - 4 k_2 k_3 k_6 k_7 k_8 k_9 k_{11} - 2 k_3^2 k_6 k_7 k_8 k_9 k_{11} - 2 k_2^2 k_5 k_7 k_9^2 k_{11} -$

$4 k_2 k_3 k_5 k_7 k_9^2 k_{11} - 2 k_3^2 k_5 k_7 k_9^2 k_{11} - 2 k_2^2 k_6 k_7 k_9^2 k_{11} - 4 k_2 k_3 k_6 k_7 k_9^2 k_{11} - 2 k_3^2 k_6 k_7 k_9^2 k_{11} -$

$2 k_2 k_5 k_7 k_8 k_9 k_{10} k_{11} - 2 k_3 k_5 k_7 k_8 k_9 k_{10} k_{11} - 2 k_2 k_6 k_7 k_8 k_9 k_{10} k_{11} - 2 k_3 k_6 k_7 k_8 k_9 k_{10} k_{11} -$

$2 k_2 k_5 k_7 k_9^2 k_{10} k_{11} - 2 k_3 k_5 k_7 k_9^2 k_{10} k_{11} - 2 k_2 k_6 k_7 k_9^2 k_{10} k_{11} - 2 k_3 k_6 k_7 k_9^2 k_{10} k_{11} -$

$k_2^2 k_7 k_8 k_9 k_{11}^2 - 2 k_2 k_3 k_7 k_8 k_9 k_{11}^2 - k_3^2 k_7 k_8 k_9 k_{11}^2 - k_2^2 k_7 k_9^2 k_{11}^2 - 2 k_2 k_3 k_7 k_9^2 k_{11}^2 -$

$k_3^2 k_7 k_9^2 k_{11}^2 + \left(-k_1 k_2 k_4^2 k_7 k_{10} k_{11} - k_1 k_3 k_4^2 k_7 k_{10} k_{11} - k_1 k_2 k_4^2 k_7 k_{11}^2 - k_1 k_3 k_4^2 k_7 k_{11}^2\right) x_1^3 +$

$\Big(-k_2^2 k_4 k_5 k_6 k_8^2 - 2 k_2 k_3 k_4 k_5 k_6 k_8^2 - k_3^2 k_4 k_5 k_6 k_8^2 - k_2^2 k_4 k_6^2 k_8^2 - 2 k_2 k_3 k_4 k_6^2 k_8^2 - k_3^2 k_4 k_6^2 k_8^2 -$

$k_2^2 k_4 k_5 k_7 k_8^2 - 2 k_2 k_3 k_4 k_5 k_7 k_8^2 - k_3^2 k_4 k_5 k_7 k_8^2 - k_2^2 k_4 k_6 k_7 k_8^2 - 2 k_2 k_3 k_4 k_6 k_7 k_8^2 -$

$k_3^2 k_4 k_6 k_7 k_8^2 - k_1 k_2 k_3 k_5^2 k_8 k_9 - k_1 k_3^2 k_5^2 k_8 k_9 - 2 k_1 k_2 k_3 k_5 k_6 k_8 k_9 - 2 k_1 k_3^2 k_5 k_6 k_8 k_9 -$

$k_2^2 k_4 k_5 k_6 k_8 k_9 - 2 k_2 k_3 k_4 k_5 k_6 k_8 k_9 - k_3^2 k_4 k_5 k_6 k_8 k_9 - k_1 k_2 k_3 k_6^2 k_8 k_9 -$

$k_1 k_3^2 k_6^2 k_8 k_9 - k_2^2 k_4 k_6^2 k_8 k_9 - 2 k_2 k_3 k_4 k_6^2 k_8 k_9 - k_3^2 k_4 k_6^2 k_8 k_9 - k_2^2 k_4 k_5 k_7 k_8 k_9 -$

$2 k_2 k_3 k_4 k_5 k_7 k_8 k_9 - k_3^2 k_4 k_5 k_7 k_8 k_9 - k_1 k_2 k_5^2 k_7 k_8 k_9 - k_1 k_3 k_5^2 k_7 k_8 k_9 -$

$k_2^2 k_4 k_6 k_7 k_8 k_9 - 2 k_2 k_3 k_4 k_6 k_7 k_8 k_9 - k_3^2 k_4 k_6 k_7 k_8 k_9 - 2 k_1 k_2 k_5 k_6 k_7 k_8 k_9 -$

$2 k_1 k_3 k_5 k_6 k_7 k_8 k_9 - k_1 k_2 k_6^2 k_7 k_8 k_9 - k_1 k_3 k_6^2 k_7 k_8 k_9 - k_1 k_2 k_3 k_5^2 k_9^2 - k_1 k_3^2 k_5^2 k_9^2 -$

$2 k_1 k_2 k_3 k_5 k_6 k_9^2 - 2 k_1 k_3^2 k_5 k_6 k_9^2 - k_1 k_2 k_3 k_6^2 k_9^2 - k_1 k_3^2 k_6^2 k_9^2 - k_1 k_2 k_5^2 k_7 k_9^2 -$

$k_1 k_3 k_5^2 k_7 k_9^2 - 2 k_1 k_2 k_5 k_6 k_7 k_9^2 - 2 k_1 k_3 k_5 k_6 k_7 k_9^2 - k_1 k_2 k_6^2 k_7 k_9^2 - k_1 k_3 k_6^2 k_7 k_9^2 -$

$2 k_2 k_4 k_5 k_6 k_8^2 k_{10} - 2 k_3 k_4 k_5 k_6 k_8^2 k_{10} - 2 k_2 k_4 k_6^2 k_8^2 k_{10} - 2 k_3 k_4 k_6^2 k_8^2 k_{10} -$

$2 k_2 k_4 k_5 k_7 k_8^2 k_{10} - 2 k_3 k_4 k_5 k_7 k_8^2 k_{10} - 2 k_2 k_4 k_6 k_7 k_8^2 k_{10} - 2 k_3 k_4 k_6 k_7 k_8^2 k_{10} -$

$k_1 k_3 k_5^2 k_8 k_9 k_{10} - k_1 k_2 k_5 k_6 k_8 k_9 k_{10} - 3 k_1 k_3 k_5 k_6 k_8 k_9 k_{10} - 2 k_2 k_4 k_5 k_6 k_8 k_9 k_{10} -$

$2 k_3 k_4 k_5 k_6 k_8 k_9 k_{10} - k_1 k_2 k_6^2 k_8 k_9 k_{10} - 2 k_1 k_3 k_6^2 k_8 k_9 k_{10} - 2 k_2 k_4 k_6^2 k_8 k_9 k_{10} -$

$2 k_3 k_4 k_6^2 k_8 k_9 k_{10} - k_1 k_2 k_5 k_7 k_8 k_9 k_{10} - k_1 k_3 k_5 k_7 k_8 k_9 k_{10} - 2 k_2 k_4 k_5 k_7 k_8 k_9 k_{10} -$

$2 k_3 k_4 k_5 k_7 k_8 k_9 k_{10} - k_1 k_5^2 k_7 k_8 k_9 k_{10} - k_1 k_2 k_6 k_7 k_8 k_9 k_{10} - k_1 k_3 k_6 k_7 k_8 k_9 k_{10} -$

$2 k_2 k_4 k_6 k_7 k_8 k_9 k_{10} - 2 k_3 k_4 k_6 k_7 k_8 k_9 k_{10} - 2 k_1 k_5 k_6 k_7 k_8 k_9 k_{10} - k_1 k_6^2 k_7 k_8 k_9 k_{10} -$

$k_1 k_3 k_5^2 k_9^2 k_{10} - k_1 k_2 k_5 k_6 k_9^2 k_{10} - 3 k_1 k_3 k_5 k_6 k_9^2 k_{10} - k_1 k_2 k_6^2 k_9^2 k_{10} - 2 k_1 k_3 k_6^2 k_9^2 k_{10} -$

$k_1 k_2 k_5 k_7 k_9^2 k_{10} - k_1 k_3 k_5 k_7 k_9^2 k_{10} - k_1 k_5^2 k_7 k_9^2 k_{10} - k_1 k_2 k_6 k_7 k_9^2 k_{10} - k_1 k_3 k_6 k_7 k_9^2 k_{10} -$

$2 k_1 k_5 k_6 k_7 k_9^2 k_{10} - k_1 k_6^2 k_7 k_9^2 k_{10} - k_4 k_5 k_6 k_8^2 k_{10}^2 - k_4 k_6^2 k_8^2 k_{10}^2 - k_4 k_5 k_7 k_8^2 k_{10}^2 -$

$k_4 k_6 k_7 k_8^2 k_{10}^2 - k_1 k_5 k_6 k_8 k_9 k_{10}^2 - k_4 k_5 k_6 k_8 k_9 k_{10}^2 - k_1 k_6^2 k_8 k_9 k_{10}^2 - k_4 k_6^2 k_8 k_9 k_{10}^2 -$

$k_1 k_5 k_7 k_8 k_9 k_{10}^2 - k_4 k_5 k_7 k_8 k_9 k_{10}^2 - k_1 k_6 k_7 k_8 k_9 k_{10}^2 - k_4 k_6 k_7 k_8 k_9 k_{10}^2 -$

$k_1 k_5 k_6 k_9^2 k_{10}^2 - k_1 k_6^2 k_9^2 k_{10}^2 - k_1 k_5 k_7 k_9^2 k_{10}^2 - k_1 k_6 k_7 k_9^2 k_{10}^2 - k_2 k_3 k_4 k_5 k_8^2 k_{11} -$

$k_3^2 k_4 k_5 k_8^2 k_{11} - k_2^2 k_4 k_6 k_8^2 k_{11} - 3 k_2 k_3 k_4 k_6 k_8^2 k_{11} - 2 k_3^2 k_4 k_6 k_8^2 k_{11} - k_2^2 k_4 k_7 k_8^2 k_{11} -$

$2 k_2 k_3 k_4 k_7 k_8^2 k_{11} - k_3^2 k_4 k_7 k_8^2 k_{11} - k_2 k_4 k_5 k_7 k_8^2 k_{11} - k_3 k_4 k_5 k_7 k_8^2 k_{11} -$

$k_2 k_4 k_6 k_7 k_8^2 k_{11} - k_3 k_4 k_6 k_7 k_8^2 k_{11} - 2 k_1 k_2 k_3 k_5 k_8 k_9 k_{11} - 2 k_1 k_3^2 k_5 k_8 k_9 k_{11} -$

$k_2 k_3 k_4 k_5 k_8 k_9 k_{11} - k_3^2 k_4 k_5 k_8 k_9 k_{11} - 2 k_1 k_2 k_3 k_6 k_8 k_9 k_{11} - 2 k_1 k_3^2 k_6 k_8 k_9 k_{11} -$

$k_2^2 k_4 k_6 k_8 k_9 k_{11} - 3 k_2 k_3 k_4 k_6 k_8 k_9 k_{11} - 2 k_3^2 k_4 k_6 k_8 k_9 k_{11} - k_2^2 k_4 k_7 k_8 k_9 k_{11} -$

$2 k_2 k_3 k_4 k_7 k_8 k_9 k_{11} - k_3^2 k_4 k_7 k_8 k_9 k_{11} - 2 k_1 k_2 k_5 k_7 k_8 k_9 k_{11} - 2 k_1 k_3 k_5 k_7 k_8 k_9 k_{11} -$

$k_2 k_4 k_5 k_7 k_8 k_9 k_{11} - k_3 k_4 k_5 k_7 k_8 k_9 k_{11} - 2 k_1 k_2 k_6 k_7 k_8 k_9 k_{11} - 2 k_1 k_3 k_6 k_7 k_8 k_9 k_{11} -$

$k_2 k_4 k_6 k_7 k_8 k_9 k_{11} - k_3 k_4 k_6 k_7 k_8 k_9 k_{11} - 2 k_1 k_2 k_3 k_5 k_9^2 k_{11} - 2 k_1 k_3^2 k_5 k_9^2 k_{11} -$

$2 k_1 k_2 k_3 k_6 k_9^2 k_{11} - 2 k_1 k_3^2 k_6 k_9^2 k_{11} - 2 k_1 k_2 k_5 k_7 k_9^2 k_{11} - 2 k_1 k_3 k_5 k_7 k_9^2 k_{11} -$

$2 k_1 k_2 k_6 k_7 k_9^2 k_{11} - 2 k_1 k_3 k_6 k_7 k_9^2 k_{11} - k_3 k_4 k_5 k_8^2 k_{10} k_{11} - k_2 k_4 k_6 k_8^2 k_{10} k_{11} -$

$2 k_3 k_4 k_6 k_8^2 k_{10} k_{11} - k_2 k_4 k_7 k_8^2 k_{10} k_{11} - k_3 k_4 k_7 k_8^2 k_{10} k_{11} - k_4 k_5 k_7 k_8^2 k_{10} k_{11} -$

$k_4 k_6 k_7 k_8^2 k_{10} k_{11} - k_1 k_3 k_5 k_8 k_9 k_{10} k_{11} - k_3 k_4 k_5 k_8 k_9 k_{10} k_{11} - k_1 k_2 k_6 k_8 k_9 k_{10} k_{11} -$

$2 k_1 k_3 k_6 k_8 k_9 k_{10} k_{11} - k_2 k_4 k_6 k_8 k_9 k_{10} k_{11} - 2 k_3 k_4 k_6 k_8 k_9 k_{10} k_{11} -$

$k_1 k_2 k_7 k_8 k_9 k_{10} k_{11} - k_1 k_3 k_7 k_8 k_9 k_{10} k_{11} - k_2 k_4 k_7 k_8 k_9 k_{10} k_{11} - k_3 k_4 k_7 k_8 k_9 k_{10} k_{11} -$

$k_1 k_5 k_7 k_8 k_9 k_{10} k_{11} - k_4 k_5 k_7 k_8 k_9 k_{10} k_{11} - k_1 k_6 k_7 k_8 k_9 k_{10} k_{11} - k_4 k_6 k_7 k_8 k_9 k_{10} k_{11} -$

$k_1 k_3 k_5 k_9^2 k_{10} k_{11} - k_1 k_2 k_6 k_9^2 k_{10} k_{11} - 2 k_1 k_3 k_6 k_9^2 k_{10} k_{11} - k_1 k_2 k_7 k_9^2 k_{10} k_{11} -$

$k_1 k_3 k_7 k_9^2 k_{10} k_{11} - k_1 k_5 k_7 k_9^2 k_{10} k_{11} - k_1 k_6 k_7 k_9^2 k_{10} k_{11} - k_2 k_3 k_4 k_8^2 k_{11}^2 -$

$k_3^2 k_4 k_8^2 k_{11}^2 - k_2 k_4 k_7 k_8^2 k_{11}^2 - k_3 k_4 k_7 k_8^2 k_{11}^2 - k_1 k_2 k_3 k_8 k_9 k_{11}^2 - k_1 k_3^2 k_8 k_9 k_{11}^2 -$

$k_2 k_3 k_4 k_8 k_9 k_{11}^2 - k_3^2 k_4 k_8 k_9 k_{11}^2 - k_1 k_2 k_7 k_8 k_9 k_{11}^2 - k_1 k_3 k_7 k_8 k_9 k_{11}^2 - k_2 k_4 k_7 k_8 k_9 k_{11}^2 -$

$k_3 k_4 k_7 k_8 k_9 k_{11}^2 - k_1 k_2 k_3 k_9^2 k_{11}^2 - k_1 k_3^2 k_9^2 k_{11}^2 - k_1 k_2 k_7 k_9^2 k_{11}^2 - k_1 k_3 k_7 k_9^2 k_{11}^2\Big) x_3 +$

$x_1^2 \Big(-k_1 k_2 k_4 k_5 k_7 k_9 k_{10} - k_1 k_3 k_4 k_5 k_7 k_9 k_{10} - k_1 k_2 k_4 k_6 k_7 k_9 k_{10} - k_1 k_3 k_4 k_6 k_7 k_9 k_{10} -$

$$
\begin{aligned}
&k_1 k_4 k_5 k_7 k_9 k_{10}^2 - k_1 k_4 k_6 k_7 k_9 k_{10}^2 - k_2^2 k_4^2 k_7 k_8 k_{11} - 2 k_2 k_3 k_4^2 k_7 k_8 k_{11} - \\
&k_3^2 k_4^2 k_7 k_8 k_{11} - 2 k_1 k_2 k_4 k_5 k_7 k_9 k_{11} - 2 k_1 k_3 k_4 k_5 k_7 k_9 k_{11} - 2 k_1 k_2 k_4 k_6 k_7 k_9 k_{11} - \\
&2 k_1 k_3 k_4 k_6 k_7 k_9 k_{11} - k_1 k_2 k_4 k_5 k_7 k_{10} k_{11} - k_1 k_3 k_4 k_5 k_7 k_{10} k_{11} - \\
&k_1 k_2 k_4 k_6 k_7 k_{10} k_{11} - k_1 k_3 k_4 k_6 k_7 k_{10} k_{11} - k_2 k_4^2 k_7 k_8 k_{10} k_{11} - k_3 k_4^2 k_7 k_8 k_{10} k_{11} - \\
&2 k_1 k_2 k_4 k_7 k_9 k_{10} k_{11} - 2 k_1 k_3 k_4 k_7 k_9 k_{10} k_{11} - k_1 k_4 k_5 k_7 k_9 k_{10} k_{11} - \\
&k_1 k_4 k_6 k_7 k_9 k_{10} k_{11} - k_2^2 k_4^2 k_7 k_{11}^2 - 2 k_2 k_3 k_4^2 k_7 k_{11}^2 - k_3^2 k_4^2 k_7 k_{11}^2 - \\
&k_2 k_4^2 k_7 k_8 k_{11}^2 - k_3 k_4^2 k_7 k_8 k_{11}^2 - 2 k_1 k_2 k_4 k_7 k_9 k_{11}^2 - 2 k_1 k_3 k_4 k_7 k_9 k_{11}^2 + \\
&(k_1^2 k_3 k_4 k_5 k_9 k_{10} + k_1^2 k_3 k_4 k_6 k_9 k_{10} - k_1^2 k_4 k_5 k_6 k_9 k_{10} - k_1^2 k_4 k_6^2 k_9 k_{10} - k_1^2 k_4 k_5 k_6 k_{10}^2 - \\
&\quad k_1^2 k_4 k_6^2 k_{10}^2 - k_1^2 k_4 k_5 k_7 k_{10}^2 - k_1^2 k_4 k_6 k_7 k_{10}^2 - k_1 k_2 k_3 k_4^2 k_8 k_{11} - k_1 k_3^2 k_4^2 k_8 k_{11} + k_1 k_2 \\
&\quad\; k_4^2 k_6 k_8 k_{11} + k_1 k_3 k_4^2 k_6 k_8 k_{11} - k_1^2 k_3 k_4 k_5 k_{10} k_{11} - k_1^2 k_3 k_4 k_6 k_{10} k_{11} - k_1 k_2 k_4^2 k_6 k_{10} \\
&\quad\; k_{11} - k_1 k_3 k_4^2 k_6 k_{10} k_{11} - k_1 k_2 k_4^2 k_7 k_{10} k_{11} - k_1 k_3 k_4^2 k_7 k_{10} k_{11} - k_1^2 k_4 k_5 k_7 k_{10} k_{11} - \\
&\quad k_1^2 k_4 k_6 k_7 k_{10} k_{11} - k_1 k_2 k_3 k_4^2 k_{11}^2 - k_1 k_3^2 k_4^2 k_{11}^2 - k_1 k_2 k_4^2 k_7 k_{11}^2 - k_1 k_3 k_4^2 k_7 k_{11}^2)\ x_3) + \\
x_1\ &(-k_2^2 k_4 k_5 k_7 k_8 k_9 - 2 k_2 k_3 k_4 k_5 k_7 k_8 k_9 - k_3^2 k_4 k_5 k_7 k_8 k_9 - k_2^2 k_4 k_6 k_7 k_8 k_9 - \\
&2 k_2 k_3 k_4 k_6 k_7 k_8 k_9 - k_3^2 k_4 k_6 k_7 k_8 k_9 - k_1 k_2 k_5^2 k_7 k_9^2 - k_1 k_3 k_5^2 k_7 k_9^2 - \\
&2 k_1 k_2 k_5 k_6 k_7 k_9^2 - 2 k_1 k_3 k_5 k_6 k_7 k_9^2 - k_1 k_2 k_6^2 k_7 k_9^2 - k_1 k_3 k_6^2 k_7 k_9^2 - k_1 k_2 k_5^2 k_7 k_9 k_{10} - \\
&k_1 k_3 k_5^2 k_7 k_9 k_{10} - 2 k_1 k_2 k_5 k_6 k_7 k_9 k_{10} - 2 k_1 k_3 k_5 k_6 k_7 k_9 k_{10} - k_1 k_2 k_6^2 k_7 k_9 k_{10} - \\
&k_1 k_3 k_6^2 k_7 k_9 k_{10} - 2 k_2 k_4 k_5 k_7 k_8 k_9 k_{10} - 2 k_3 k_4 k_5 k_7 k_8 k_9 k_{10} - 2 k_2 k_4 k_6 k_7 k_8 k_9 k_{10} - \\
&2 k_3 k_4 k_6 k_7 k_8 k_9 k_{10} - k_1 k_2 k_5 k_7 k_9^2 k_{10} - k_1 k_3 k_5 k_7 k_9^2 k_{10} - k_1 k_5^2 k_7 k_9^2 k_{10} - \\
&k_1 k_2 k_6 k_7 k_9^2 k_{10} - k_1 k_3 k_6 k_7 k_9^2 k_{10} - 2 k_1 k_5 k_6 k_7 k_9^2 k_{10} - k_1 k_6^2 k_7 k_9^2 k_{10} - k_1 k_5^2 k_7 k_9 k_{10}^2 - \\
&2 k_1 k_5 k_6 k_7 k_9 k_{10}^2 - k_1 k_6^2 k_7 k_9 k_{10}^2 - k_4 k_5 k_7 k_8 k_9 k_{10}^2 - k_4 k_6 k_7 k_8 k_9 k_{10}^2 - \\
&k_1 k_5 k_7 k_9^2 k_{10}^2 - k_1 k_6 k_7 k_9^2 k_{10}^2 - k_2^2 k_4 k_5 k_7 k_8 k_{11} - 2 k_2 k_3 k_4 k_5 k_7 k_8 k_{11} - \\
&k_3^2 k_4 k_5 k_7 k_8 k_{11} - k_2^2 k_4 k_6 k_7 k_8 k_{11} - 2 k_2 k_3 k_4 k_6 k_7 k_8 k_{11} - k_3^2 k_4 k_6 k_7 k_8 k_{11} - \\
&2 k_2^2 k_4 k_5 k_7 k_9 k_{11} - 4 k_2 k_3 k_4 k_5 k_7 k_9 k_{11} - 2 k_3^2 k_4 k_5 k_7 k_9 k_{11} - 2 k_2^2 k_4 k_6 k_7 k_9 k_{11} - \\
&4 k_2 k_3 k_4 k_6 k_7 k_9 k_{11} - 2 k_3^2 k_4 k_6 k_7 k_9 k_{11} - k_2^2 k_4 k_7 k_8 k_9 k_{11} - 2 k_2 k_3 k_4 k_7 k_8 k_9 k_{11} - \\
&k_3^2 k_4 k_7 k_8 k_9 k_{11} - k_2 k_4 k_5 k_7 k_8 k_9 k_{11} - k_3 k_4 k_5 k_7 k_8 k_9 k_{11} - k_2 k_4 k_6 k_7 k_8 k_9 k_{11} - \\
&k_3 k_4 k_6 k_7 k_8 k_9 k_{11} - 2 k_1 k_2 k_5 k_7 k_9^2 k_{11} - 2 k_1 k_3 k_5 k_7 k_9^2 k_{11} - 2 k_1 k_2 k_6 k_7 k_9^2 k_{11} - \\
&2 k_1 k_3 k_6 k_7 k_9^2 k_{11} - k_2 k_4 k_5 k_7 k_8 k_{10} k_{11} - k_3 k_4 k_5 k_7 k_8 k_{10} k_{11} - k_2 k_4 k_6 k_7 k_8 k_{10} k_{11} - \\
&k_3 k_4 k_6 k_7 k_8 k_{10} k_{11} - k_1 k_2 k_5 k_7 k_9 k_{10} k_{11} - k_1 k_3 k_5 k_7 k_9 k_{10} k_{11} - 2 k_2 k_4 k_5 k_7 k_9 k_{10} k_{11} - \\
&2 k_3 k_4 k_5 k_7 k_9 k_{10} k_{11} - k_1 k_2 k_6 k_7 k_9 k_{10} k_{11} - k_1 k_3 k_6 k_7 k_9 k_{10} k_{11} - \\
&2 k_2 k_4 k_6 k_7 k_9 k_{10} k_{11} - 2 k_3 k_4 k_6 k_7 k_9 k_{10} k_{11} - k_2 k_4 k_7 k_8 k_9 k_{10} k_{11} - \\
&k_3 k_4 k_7 k_8 k_9 k_{10} k_{11} - k_4 k_5 k_7 k_8 k_9 k_{10} k_{11} - k_4 k_6 k_7 k_8 k_9 k_{10} k_{11} - k_1 k_2 k_7 k_9^2 k_{10} k_{11} - \\
&k_1 k_3 k_7 k_9^2 k_{10} k_{11} - k_1 k_5 k_7 k_9^2 k_{10} k_{11} - k_1 k_6 k_7 k_9^2 k_{10} k_{11} - k_2^2 k_4 k_7 k_8 k_{11}^2 - \\
&2 k_2 k_3 k_4 k_7 k_8 k_{11}^2 - k_3^2 k_4 k_7 k_8 k_{11}^2 - 2 k_2^2 k_4 k_7 k_9 k_{11}^2 - 4 k_2 k_3 k_4 k_7 k_9 k_{11}^2 - \\
&2 k_3^2 k_4 k_7 k_9 k_{11}^2 - k_2 k_4 k_7 k_8 k_9 k_{11}^2 - k_3 k_4 k_7 k_8 k_9 k_{11}^2 - k_1 k_2 k_7 k_9^2 k_{11}^2 - k_1 k_3 k_7 k_9^2 k_{11}^2 - \\
&2\ (k_1 k_2 k_4 k_5 k_6 k_8 k_{10} + k_1 k_3 k_4 k_5 k_6 k_8 k_{10} + k_1 k_2 k_4 k_6^2 k_8 k_{10} + k_1 k_3 k_4 k_6^2 k_8 k_{10} + \\
&\quad k_1 k_2 k_4 k_5 k_7 k_8 k_{10} + k_1 k_3 k_4 k_5 k_7 k_8 k_{10} + k_1 k_2 k_4 k_6 k_7 k_8 k_{10} + k_1 k_3 k_4 k_6 k_7 k_8 k_{10} + \\
&\quad k_1 k_2 k_4 k_5 k_6 k_9 k_{10} + k_1 k_3 k_4 k_5 k_6 k_9 k_{10} + k_1 k_2 k_4 k_6^2 k_9 k_{10} + k_1 k_3 k_4 k_6^2 k_9 k_{10} + \\
&\quad k_1 k_2 k_4 k_5 k_7 k_9 k_{10} + k_1 k_3 k_4 k_5 k_7 k_9 k_{10} + k_1 k_2 k_4 k_6 k_7 k_9 k_{10} + k_1 k_3 k_4 k_6 k_7 k_9 k_{10} + \\
&\quad k_1 k_4 k_5 k_6 k_8 k_{10}^2 + k_1 k_4 k_6^2 k_8 k_{10}^2 + k_1 k_4 k_5 k_7 k_8 k_{10}^2 + k_1 k_4 k_6 k_7 k_8 k_{10}^2 + \\
&\quad k_1 k_4 k_5 k_6 k_9 k_{10}^2 + k_1 k_4 k_6^2 k_9 k_{10}^2 + k_1 k_4 k_5 k_7 k_9 k_{10}^2 + k_1 k_4 k_6 k_7 k_9 k_{10}^2 + \\
&\quad k_1 k_2 k_3 k_4 k_5 k_8 k_{11} + k_1 k_3^2 k_4 k_5 k_8 k_{11} + k_1 k_2 k_3 k_4 k_6 k_8 k_{11} + k_1 k_3^2 k_4 k_6 k_8 k_{11} + \\
&\quad k_1 k_2 k_4 k_5 k_7 k_8 k_{11} + k_1 k_3 k_4 k_5 k_7 k_8 k_{11} + k_1 k_2 k_4 k_6 k_7 k_8 k_{11} + k_1 k_3 k_4 k_6 k_7 k_8 k_{11} + \\
&\quad k_1 k_2 k_3 k_4 k_5 k_9 k_{11} + k_1 k_3^2 k_4 k_5 k_9 k_{11} + k_1 k_2 k_3 k_4 k_6 k_9 k_{11} + k_1 k_3^2 k_4 k_6 k_9 k_{11} + \\
&\quad k_1 k_2 k_4 k_5 k_7 k_9 k_{11} + k_1 k_3 k_4 k_5 k_7 k_9 k_{11} + k_1 k_2 k_4 k_6 k_7 k_9 k_{11} + k_1 k_3 k_4 k_6 k_7 k_9 k_{11} + \\
&\quad k_1 k_3 k_4 k_5 k_8 k_{10} k_{11} + k_1 k_2 k_4 k_6 k_8 k_{10} k_{11} + 2 k_1 k_3 k_4 k_6 k_8 k_{10} k_{11} + k_1 k_2 k_4 k_7 \\
&\quad\; k_8 k_{10} k_{11} + k_1 k_3 k_4 k_7 k_8 k_{10} k_{11} + k_1 k_4 k_5 k_7 k_8 k_{10} k_{11} + k_1 k_4 k_6 k_7 k_8 k_{10} k_{11} + \\
&\quad k_1 k_3 k_4 k_5 k_9 k_{10} k_{11} + k_1 k_2 k_4 k_6 k_9 k_{10} k_{11} + 2 k_1 k_3 k_4 k_6 k_9 k_{10} k_{11} + k_1 k_2 k_4 \\
&\quad\; k_7 k_9 k_{10} k_{11} + k_1 k_3 k_4 k_7 k_9 k_{10} k_{11} + k_1 k_4 k_5 k_7 k_9 k_{10} k_{11} + k_1 k_4 k_6 k_7 k_9 k_{10} k_{11} + \\
&\quad k_1 k_2 k_3 k_4 k_8 k_{11}^2 + k_1 k_3^2 k_4 k_8 k_{11}^2 + k_1 k_2 k_4 k_7 k_8 k_{11}^2 + k_1 k_3 k_4 k_7 k_8 k_{11}^2 + \\
&\quad k_1 k_2 k_3 k_4 k_9 k_{11}^2 + k_1 k_3^2 k_4 k_9 k_{11}^2 + k_1 k_2 k_4 k_7 k_9 k_{11}^2 + k_1 k_3 k_4 k_7 k_9 k_{11}^2)\ x_3)
\end{aligned}
$$

In[24]:=

$$
\begin{aligned}
&\mathbf{factor} = k_1^2 k_3 k_4 k_5 k_9 k_{10} + k_1^2 k_3 k_4 k_6 k_9 k_{10} - k_1^2 k_4 k_5 k_6 k_9 k_{10} - \\
&\quad k_1^2 k_4 k_6^2 k_9 k_{10} - k_1^2 k_4 k_5 k_6 k_{10}^2 - k_1^2 k_4 k_6^2 k_{10}^2 - k_1^2 k_4 k_5 k_7 k_{10}^2 - k_1^2 k_4 k_6 k_7 k_{10}^2 - \\
&\quad k_1 k_2 k_3 k_4^2 k_8 k_{11} - k_1 k_3^2 k_4^2 k_8 k_{11} + k_1 k_2 k_4^2 k_6 k_8 k_{11} + k_1 k_3 k_4^2 k_6 k_8 k_{11} - \\
&\quad k_1^2 k_3 k_4 k_5 k_{10} k_{11} - k_1^2 k_3 k_4 k_6 k_{10} k_{11} - k_1 k_2 k_4^2 k_6 k_{10} k_{11} - k_1 k_3 k_4^2 k_6 k_{10} k_{11} - \\
&\quad k_1 k_2 k_4^2 k_7 k_{10} k_{11} - k_1 k_3 k_4^2 k_7 k_{10} k_{11} - k_1^2 k_4 k_5 k_7 k_{10} k_{11} - k_1^2 k_4 k_6 k_7 k_{10} k_{11} - \\
&\quad k_1 k_2 k_3 k_4^2 k_{11}^2 - k_1 k_3^2 k_4^2 k_{11}^2 - k_1 k_2 k_4^2 k_7 k_{11}^2 - k_1 k_3 k_4^2 k_7 k_{11}^2;
\end{aligned}
$$

In[25]:= `Factor[factor]`

Out[25]= $k_1 k_4 \left(k_1 k_3 k_5 k_9 k_{10} + k_1 k_3 k_6 k_9 k_{10} - k_1 k_5 k_6 k_9 k_{10} - k_1 k_6^2 k_9 k_{10} - k_1 k_5 k_6 k_{10}^2 - k_1 k_6^2 k_{10}^2 - k_1 k_5 k_7 k_{10}^2 - k_1 k_6 k_7 k_{10}^2 - k_2 k_3 k_4 k_8 k_{11} - k_3^2 k_4 k_8 k_{11} + k_2 k_4 k_6 k_8 k_{11} + k_3 k_4 k_6 k_8 k_{11} - k_1 k_3 k_5 k_{10} k_{11} - k_1 k_3 k_6 k_{10} k_{11} - k_2 k_4 k_6 k_{10} k_{11} - k_3 k_4 k_6 k_{10} k_{11} - k_2 k_4 k_7 k_{10} k_{11} - k_3 k_4 k_7 k_{10} k_{11} - k_1 k_5 k_7 k_{10} k_{11} - k_1 k_6 k_7 k_{10} k_{11} - k_2 k_3 k_4 k_{11}^2 - k_3^2 k_4 k_{11}^2 - k_2 k_4 k_7 k_{11}^2 - k_3 k_4 k_7 k_{11}^2\right)$

In[26]:= $\mathbf{term} = k_1 k_3 k_5 k_9 k_{10} + k_1 k_3 k_6 k_9 k_{10} - k_1 k_5 k_6 k_9 k_{10} - k_1 k_6^2 k_9 k_{10} - k_1 k_5 k_6 k_{10}^2 - k_1 k_6^2 k_{10}^2 - k_1 k_5 k_7 k_{10}^2 - k_1 k_6 k_7 k_{10}^2 - k_2 k_3 k_4 k_8 k_{11} - k_3^2 k_4 k_8 k_{11} + k_2 k_4 k_6 k_8 k_{11} + k_3 k_4 k_6 k_8 k_{11} - k_1 k_3 k_5 k_{10} k_{11} - k_1 k_3 k_6 k_{10} k_{11} - k_2 k_4 k_6 k_{10} k_{11} - k_3 k_4 k_6 k_{10} k_{11} - k_2 k_4 k_7 k_{10} k_{11} - k_3 k_4 k_7 k_{10} k_{11} - k_1 k_5 k_7 k_{10} k_{11} - k_1 k_6 k_7 k_{10} k_{11} - k_2 k_3 k_4 k_{11}^2 - k_3^2 k_4 k_{11}^2 - k_2 k_4 k_7 k_{11}^2 - k_3 k_4 k_7 k_{11}^2;$

In[27]:= `simpTerm = FullSimplify[term]`

Out[27]= $-(k_2 + k_3)\, k_4\, k_{11}\, (k_6\, (-k_8 + k_{10}) + k_3\, (k_8 + k_{11}) + k_7\, (k_{10} + k_{11})) - k_1\, (k_5 + k_6)\, k_{10}\, (k_6\, (k_9 + k_{10}) + k_3\, (-k_9 + k_{11}) + k_7\, (k_{10} + k_{11}))$

In[28]:= `simplerTerm = Distribute[simpTerm / (k1 * k4)] /. {(k2 + k3) / k1 → M1, (k5 + k6) / k4 → M2}`

Out[28]= $-k_{11}\, (k_6\, (-k_8 + k_{10}) + k_3\, (k_8 + k_{11}) + k_7\, (k_{10} + k_{11}))\, M_1 - k_{10}\, (k_6\, (k_9 + k_{10}) + k_3\, (-k_9 + k_{11}) + k_7\, (k_{10} + k_{11}))\, M_2$

This above term larger than 0 should be the necessary condition.

In[36]:= `condition = simplerTerm > 0`

Out[36]= $-k_{11}\, (k_6\, (-k_8 + k_{10}) + k_3\, (k_8 + k_{11}) + k_7\, (k_{10} + k_{11}))\, M_1 - k_{10}\, (k_6\, (k_9 + k_{10}) + k_3\, (-k_9 + k_{11}) + k_7\, (k_{10} + k_{11}))\, M_2 > 0$

In[37]:= `Simplify[condition]`

Out[37]= $k_{11}\, (k_6\, (-k_8 + k_{10}) + k_3\, (k_8 + k_{11}) + k_7\, (k_{10} + k_{11}))\, M_1 + k_{10}\, (k_6\, (k_9 + k_{10}) + k_3\, (-k_9 + k_{11}) + k_7\, (k_{10} + k_{11}))\, M_2 < 0$

By mannual simplying the term, we can have:

In[38]:= `simpleCond = (k3 - k6) * (M2 * k9 * k10 - M1 * k8 * k11) > (k11 * M1 + k10 * M2) * ((k6 * k10 + k3 * k11) + k7 * (k10 + k11))`

Out[38]= $(k_3 - k_6)\, (-k_8 k_{11} M_1 + k_9 k_{10} M_2) > (k_6 k_{10} + k_3 k_{11} + k_7\, (k_{10} + k_{11}))\, (k_{11} M_1 + k_{10} M_2)$

In[39]:= `left = (k3 - k6) * (M2 * k9 * k10 - M1 * k8 * k11) /. {M1 → (k2 + k3) / k1, M2 → (k5 + k6) / k4}`

Out[39]= $(k_3 - k_6)\left(\frac{(k_5 + k_6)\, k_9\, k_{10}}{k_4} - \frac{(k_2 + k_3)\, k_8\, k_{11}}{k_1}\right)$

In[40]:= `right = (k11 * M1 + k10 * M2) * ((k6 * k10 + k3 * k11) + k7 * (k10 + k11)) /. {M1 → (k2 + k3) / k1, M2 → (k5 + k6) / k4}`

Out[40]= $\left(\frac{(k_5 + k_6)\, k_{10}}{k_4} + \frac{(k_2 + k_3)\, k_{11}}{k_1}\right)(k_6 k_{10} + k_3 k_{11} + k_7\, (k_{10} + k_{11}))$

To fullfile the assumption of thermodynamic conditions for the reversible reactions, we have the the constraint:

$\frac{k_1 k_{10}}{k_2 k_{11}} = \frac{k_4 k_8}{k_5 k_9}.$

This will give us a even simple condition. Then we will example how will this condition result in the parameter space for multistationarity.

In[41]:=
```
oriCond = simpleCond /. {M1 → (k2 + k3) / k1, M2 → (k5 + k6) / k4}
```

Out[41]=
$$(k_3 - k_6)\left(\frac{(k_5 + k_6)\, k_9\, k_{10}}{k_4} - \frac{(k_2 + k_3)\, k_8\, k_{11}}{k_1}\right) > \left(\frac{(k_5 + k_6)\, k_{10}}{k_4} + \frac{(k_2 + k_3)\, k_{11}}{k_1}\right)(k_6\, k_{10} + k_3\, k_{11} + k_7\, (k_{10} + k_{11}))$$

In[42]:=
$$\text{Simplify}\left[\text{oriCond, Assumptions} \to \frac{k_1\, k_{10}}{k_2\, k_{11}} == \frac{k_4\, k_8}{k_5\, k_9}\right]$$

Out[42]=
$$\frac{(k_3 - k_6)\,(k_1\, k_6\, k_9\, k_{10} - k_3\, k_4\, k_8\, k_{11})}{k_1\, k_4} > \left(\frac{(k_5 + k_6)\, k_{10}}{k_4} + \frac{(k_2 + k_3)\, k_{11}}{k_1}\right)((k_6 + k_7)\, k_{10} + (k_3 + k_7)\, k_{11})$$

Better to do it manually, then we have the condition with thermodynamic constraint:

In[43]:=
$$\text{thermoCond} = (k_3 - k_6)\,(k_6\, k_2 - k_3\, k_5) > \left(\frac{k_2}{k_9} \times \frac{k_5\text{^}2 + k_6}{k_5} + \frac{k_5}{k_8} \times \frac{k_2\text{^}2 + k_3}{k_2}\right)((k_6 + k_7)\, k_{10} + (k_3 + k_7)\, k_{11})$$

Out[43]=
$$(k_3 - k_6)\,(-k_3\, k_5 + k_2\, k_6) > \left(\frac{(k_2^2 + k_3)\, k_5}{k_2\, k_8} + \frac{k_2\, (k_5^2 + k_6)}{k_5\, k_9}\right)((k_6 + k_7)\, k_{10} + (k_3 + k_7)\, k_{11})$$

Fromt the above condition, we can get some general idea that in order to satisfy the thermodynamic condition we should have:
Necessarily:
$k_3 > k_6$ and $k_2 > k_5$
or
$k_3 < k_6$ and $k_5 > k_2$
With additional (sufficiently):
$k_8,\ k_9 \gg k_{10},\ k_{11}$ and $k_7,\ k_{10},\ k_{11} \approx 0$

Sampling the parameters

Here we try to sampling the parameters by enforcing the thermodynamc constraint. The parameters are sampled in biologically meaningful ranges.

```
reactionRates = Array[10^(-3) * (10^6)^((# - 1)/1023) &, 1024];
(* association rates are set as 10^-3~10^3 μM^-1 s^-1,
disassociation and catalytic rates are set as 10^-3~10^3 s^-1 *)
switchingRates = Array[10^(-3) * (10^9)^((# - 1)/1535) &, 1536];
(* The switching rate between
  different conformations are set as 10^-3~10^6 s^-1 *)
concentrations = Array[10^(-3) * (10^4)^((# - 1)/1023) &, 1024];
(* The concentration values are set as 10^-3~
 10μM (1 molecule in a cell is approximately 2nM) *)

bistableKs = {};
bistableParSets = {};
SeedRandom[];
Do[{
   k1 = reactionRates[[RandomInteger[1023]]];
   k2 = reactionRates[[RandomInteger[1023]]];
   k3 = reactionRates[[RandomInteger[1023]]];
```

```
k4 = reactionRates[[RandomInteger[1023]]];
k5 = reactionRates[[RandomInteger[1023]]];
k6 = reactionRates[[RandomInteger[1023]]];
k7 = reactionRates[[RandomInteger[1023]]];
(*k8=switchingRates[[RandomInteger[1023]]];*)
k9 = switchingRates[[RandomInteger[1535]]];
k10 = switchingRates[[RandomInteger[1535]]];
k11 = switchingRates[[RandomInteger[1535]]];
k8 = (k1 × k10 × k5 × k9)/(k11 × k4 × k2);
If[ 10^(-3) ≤ k8 ≤ 10^6, {
  left = (k3 - k6) ((k5 + k6) k9 k10/k4 - (k2 + k3) k8 k11/k1);
  right = ((k5 + k6) k10/k4 + (k2 + k3) k11/k1) (k6 k10 + k3 k11 + k7 (k10 + k11));
  If[left > right, {
    AppendTo[bistableKs,
     {k1, k2, k3, k4, k5, k6, k7, k8, k9, k10, k11, left, right}];
    counter = 0; hitQ = 0;
    randCons = RandomSample[Range[1024]] - 1;
    While[hitQ == 0 && counter < 1024, {
      x1 = concentrations[[randCons[counter]]];
      subSol = finalSubs /. {k1 → k1, k2 → k2, k3 → k3, k4 → k4, k5 → k5,
          k6 → k6, k7 → k7, k8 → k8, k9 → k9, k10 → k10, k11 → k11, x1 → x1};
      finalSol = Solve[subSol == 0];
      x3 = x3 /. finalSol[[1]];
      If[x3 > 0, {
        otherSpecies = solution /. {k1 → k1, k2 → k2, k3 → k3, k4 → k4, k5 → k5, k6 →
             k6, k7 → k7, k8 → k8, k9 → k9, k10 → k10, k11 → k11, x1 → x1, x3 → x3};
        T1 = x1 + x2 + x5 + x6 /. {x1 → x1, x3 → x3, otherSpecies[[1]]};
        T2 = x3 + x4 + x5 + x6 /. {x1 → x1, x3 → x3, otherSpecies[[1]]};
        If[10^(-3) ≤ T1 ≤ 10 && 10^(-3) ≤ T2 ≤ 10, {
          AppendTo[bistableParSets,
           {k1, k2, k3, k4, k5, k6, k7, k8, k9, k10, k11, T1, T2, left, right}];
          hitQ = 1;
         }];
       }];
      counter++;
     }];
   }];
 }];
}, {i, 100000}];
```

In[74]:=
```
bistableParSets (*This table is to record all parameter
 set that could give rise to proper concentration values*)
```

Out[74]= { }

In[78]:=
```
Length[bistableParSets]
```

Out[78]= 0

In[75]:=
```
bistableKs
```

$$\Big\{\Big\{10\times 10^{14/341},\ 100\times 10^{17/31},\ 10^{97/341},\ \frac{1}{10\times 10^{208/341}},\ \frac{1}{10^{301/341}},\ \frac{1}{10\times 10^{58/341}},\ \frac{1}{10\times 10^{2/31}},$$
$$10\,000\times 10^{328\,591/523\,435},\ 100\,000\times 10^{145/307},\ 100\times 10^{488/1535},\ 100\times 10^{587/1535},$$
$$\left(-\frac{1}{10\times 10^{58/341}}+10^{97/341}\right)\left(1\,000\,000\,000\times 10^{209\,478/523\,435}\left(\frac{1}{10^{301/341}}+\frac{1}{10\times 10^{58/341}}\right)-\right.$$
$$\left.100\,000\times 10^{507\,268/523\,435}\left(10^{97/341}+100\times 10^{17/31}\right)\right),$$
$$\left(10\times 10^{77\,378/523\,435}+100\times 10^{349\,062/523\,435}+\frac{100\times 10^{488/1535}+100\times 10^{587/1535}}{10\times 10^{2/31}}\right)$$
$$\left(1000\times 10^{485\,688/523\,435}\left(\frac{1}{10^{301/341}}+\frac{1}{10\times 10^{58/341}}\right)+\right.$$
$$\left.10\times 10^{178\,677/523\,435}\left(10^{97/341}+100\times 10^{17/31}\right)\right)\Big\},\ \cdots 247 \cdots,$$
$$\Big\{100\times 10^{23/31},\ \frac{1}{10\times 10^{182/341}},\ 100\times 10^{151/341},\ 100\times 10^{65/341},\ 10\times 10^{252/341},$$
$$100\times 10^{293/341},\ \frac{1}{10\ \cdots 1 \cdots},\ 10\,000\times 10^{66\,489/\cdots 6 \cdots},$$
$$100\times 10^{713/1535},\ 10^{804/1535},\ 100\times 10^{272/1535},$$
$$\left(100\times 10^{151/341}-100\times 10^{293/341}\right)\left(-10\,000\ 10^{36\,842/523\,435}\left(\frac{1}{10\times 10^{182/341}}+100\times 10^{151/341}\right)+\right.$$
$$\left.10^{417\,522/523\,435}\left(10\times 10^{252/341}+100\times 10^{293/341}\right)\right),$$
$$\left(1000\times 10^{200\,484/523\,435}+10\,000\times 10^{324\,537/523\,435}+\frac{100\times 10^{272/1535}+10^{804/1535}}{10\times 10^{206/341}}\right)$$
$$\left(\frac{\frac{1}{10\times 10^{182/341}}+100\times 10^{151/341}}{10^{26\,873/47\,585}}+\frac{10\times 10^{252/341}+100\times 10^{293/341}}{10\times 10^{349\,046/523\,435}}\right)\Big\}\Big\}$$

largeoutput | **showless** | **showmore** | **showall** | **setsizelimit..**

In[79]:=
```
Length[bistableKs]
```

Out[79]= 249

In[76]:=
```
transposedKs = Transpose[bistableKs];
parK1 = (transposedKs[[1]] * transposedKs[[10]]) / (transposedKs[[2]] * transposedKs[[11]]);
parK2 = (transposedKs[[4]] * transposedKs[[8]]) / (transposedKs[[5]] * transposedKs[[9]]);
```

In[84]:=
```
ListLogLogPlot[Transpose[{parK1, parK2}], AxesLabel → {"K1", "K2"}]
```

Out[84]=