

[>

Two kinases, one substrate, simplified model

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[> with(LinearAlgebra) :  
[> interface(rtablesize = 40) :  
[>
```

Consider the system with two kinases (K, G), both allosteric, and a simple substrate.
The reactions are as follows (the label of the reaction is indicated in the arrows).

$KR + S \xrightarrow{-1} KRS \xrightarrow{-2} KR + Sp$
 $KT + S \xrightarrow{-3} KTS \xrightarrow{-4} KT + Sp$
 $KR \xrightarrow{-5} KT$
 $KRS \xleftarrow{-6} KTS$

$GR + S \xrightarrow{-7} GRS \xrightarrow{-8} GR + Sp$
 $GT + S \xrightarrow{-9} GTS \xrightarrow{-10} GT + Sp$
 $GR \xrightarrow{-11} GT$
 $GRS \xleftarrow{-12} GTS$

$Sp \xrightarrow{-13} S$

The system has been further simplified such that the binding reaction

$KR + S \rightarrow KRS$

is not reversible and the allosteric part is only one way.

It might not be realistic, but due to some mathematical theorems, if we can show that this system has 5 steady states (3 stable), then the full system will as well.

To start with it makes sense to make the simplification since the equations become simpler.

Species

{S (1), Sp (2), KR (3), KT (4), KRS (5), KTS (6), GR (7), GT (8), GRS (9), GTS (10)}

There are a total of 13 reactions and 10 species.

I construct the mass-action ODE system by defining the stoichiometric matrix A, and the vector of rates "krates".

Then, the ODE system is

$dx/dt = A.krates$

and hence steady states are given as $A \cdot \text{krates} = 0$.

Stoichiometric matrix:

I enter first the reactions as rows and then transpose the matrix

```
[> A := Matrix(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 :  
[> A := Transpose(A) :
```

Vector of rates:

here x_i is the concentration of the i-th species

```
[> krates := Vector([k1·x3·x1, k2·x5, k3·x4·x1, k4·x6, k5·x3, k6·x6, k7·x7·x1, k8·x9, k9·x8·x1, k10  
·x10, k11·x7, k12·x10, k13·x2])
```

(1.1)

$$krates := \begin{bmatrix} k_1 x_3 x_1 \\ k_2 x_5 \\ k_3 x_4 x_1 \\ k_4 x_6 \\ k_5 x_3 \\ k_6 x_6 \\ k_7 x_7 x_1 \\ k_8 x_9 \\ k_9 x_8 x_1 \\ k_{10} x_{10} \\ k_{11} x_7 \\ k_{12} x_{10} \\ k_{13} x_2 \end{bmatrix} \quad (1.1)$$

Steady state equations:

$$\begin{aligned} &> eqs := A.krates \\ eqs := &\begin{bmatrix} -k_1 x_1 x_3 - k_3 x_1 x_4 - k_7 x_1 x_7 - k_9 x_1 x_8 + k_{13} x_2 \\ k_2 x_5 + k_4 x_6 + k_8 x_9 + k_{10} x_{10} - k_{13} x_2 \\ -k_1 x_1 x_3 + k_2 x_5 - k_5 x_3 \\ -k_3 x_1 x_4 + k_4 x_6 + k_5 x_3 \\ k_1 x_1 x_3 - k_2 x_5 + k_6 x_6 \\ k_3 x_1 x_4 - k_4 x_6 - k_6 x_6 \\ -k_7 x_1 x_7 + k_8 x_9 - k_{11} x_7 \\ -k_9 x_1 x_8 + k_{10} x_{10} + k_{11} x_7 \\ k_7 x_1 x_7 - k_8 x_9 + k_{12} x_{10} \\ k_9 x_1 x_8 - k_{10} x_{10} - k_{12} x_{10} \end{bmatrix} \quad (1.2) \end{aligned}$$

Conservation laws:

This system has total amount of kinase and total amount of substrate conserved:

$$\begin{aligned} & \text{[> } F := \text{ReducedRowEchelonForm}(\text{Transpose}(\text{Matrix}([\text{op}(\text{NullSpace}(\text{Transpose}(A))])))) \\ & F := \begin{bmatrix} 1 & 1 & 0 & 0 & 1 & 1 & 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 \end{bmatrix} \end{aligned} \quad (1.3)$$

the conservation laws are:

$$\text{[> } cons := [x_1 + x_2 + x_5 + x_6 - T_1, x_3 + x_4 + x_5 + x_6 - T_2, x_7 + x_8 + x_9 + x_{10} - T_3]:$$

Therefore, the steady states constrained by the conservation laws are solutions to $myeqs=0$ (because there are two conservation laws, two of the equations in eqs can be disregarded).

$$\begin{aligned} & \text{[> } myeqs2 := [eqs[2], eqs[4], eqs[5], eqs[6], eqs[8], eqs[9], eqs[10], x_1 + x_2 + x_5 + x_6 \\ & \quad - T_1, x_3 + x_4 + x_5 + x_6 - T_2, x_7 + x_8 + x_9 + x_{10} - T_3] \\ & myeqs2 := [k_2 x_5 + k_4 x_6 + k_8 x_9 + k_{10} x_{10} - k_{13} x_2, -k_3 x_1 x_4 + k_4 x_6 + k_5 x_3, k_1 x_1 x_3 \\ & \quad - k_2 x_5 + k_6 x_6, k_3 x_1 x_4 - k_4 x_6 - k_6 x_6, -k_9 x_1 x_8 + k_{10} x_{10} + k_{11} x_7, k_7 x_1 x_7 - k_8 x_9 \\ & \quad + k_{12} x_{10}, k_9 x_1 x_8 - k_{10} x_{10} - k_{12} x_{10}, x_1 + x_2 + x_5 + x_6 - T_1, x_3 + x_4 + x_5 + x_6 \\ & \quad - T_2, x_7 + x_8 + x_9 + x_{10} - T_3] \end{aligned} \quad (1.4)$$

We parameterise the steady states as functions of x_1 and x_3 , using the four steady state equations:
When x_1 and x_3 are positive, then so are the rest.

$$\begin{aligned} & \text{[> } soll := \text{solve}([eqs[4], eqs[5], eqs[6], cons[2]], [x_3, x_4, x_5, x_6]) \\ & soll := \left[\left[x_3 = \frac{T_2 x_1 k_6 k_3 k_2}{k_1 k_3 k_6 x_1^2 + k_2 k_3 k_5 x_1 + k_2 k_3 k_6 x_1 + k_3 k_5 k_6 x_1 + k_2 k_4 k_5 + k_2 k_5 k_6}, x_4 \right. \right. \\ & \quad = \frac{(k_6 + k_4) k_5 k_2 T_2}{k_1 k_3 k_6 x_1^2 + k_2 k_3 k_5 x_1 + k_2 k_3 k_6 x_1 + k_3 k_5 k_6 x_1 + k_2 k_4 k_5 + k_2 k_5 k_6}, x_5 \\ & \quad = \frac{x_1 k_3 T_2 k_6 (k_1 x_1 + k_5)}{k_1 k_3 k_6 x_1^2 + k_2 k_3 k_5 x_1 + k_2 k_3 k_6 x_1 + k_3 k_5 k_6 x_1 + k_2 k_4 k_5 + k_2 k_5 k_6}, x_6 \\ & \quad \left. \left. = \frac{x_1 k_5 k_3 k_2 T_2}{k_1 k_3 k_6 x_1^2 + k_2 k_3 k_5 x_1 + k_2 k_3 k_6 x_1 + k_3 k_5 k_6 x_1 + k_2 k_4 k_5 + k_2 k_5 k_6} \right] \right] \end{aligned} \quad (1.5)$$

> $sol2 := solve([eqs[8], eqs[9], eqs[10], cons[3]], [x_7, x_8, x_9, x_{10}])$

$$sol2 := \left[\begin{array}{l} x_7 \end{array} \right] \quad (1.6)$$

$$= \frac{T_3 k_{12} x_1 k_9 k_8}{k_7 k_9 k_{12} x_1^2 + k_8 k_9 k_{11} x_1 + k_8 k_9 k_{12} x_1 + k_9 k_{11} k_{12} x_1 + k_8 k_{10} k_{11} + k_8 k_{11} k_{12}},$$

x_8

$$= \frac{(k_{12} + k_{10}) k_{11} k_8 T_3}{k_7 k_9 k_{12} x_1^2 + k_8 k_9 k_{11} x_1 + k_8 k_9 k_{12} x_1 + k_9 k_{11} k_{12} x_1 + k_8 k_{10} k_{11} + k_8 k_{11} k_{12}},$$

x_9

$$= \frac{x_1 k_9 T_3 k_{12} (k_7 x_1 + k_{11})}{k_7 k_9 k_{12} x_1^2 + k_8 k_9 k_{11} x_1 + k_8 k_9 k_{12} x_1 + k_9 k_{11} k_{12} x_1 + k_8 k_{10} k_{11} + k_8 k_{11} k_{12}},$$

x_{10}

$$= \frac{k_{11} x_1 k_9 k_8 T_3}{k_7 k_9 k_{12} x_1^2 + k_8 k_9 k_{11} x_1 + k_8 k_9 k_{12} x_1 + k_9 k_{11} k_{12} x_1 + k_8 k_{10} k_{11} + k_8 k_{11} k_{12}} \right]$$

>

> $sol3 := solve(eqs[2], \{x_2\})$

$$sol3 := \left\{ x_2 = \frac{k_2 x_5 + k_4 x_6 + k_8 x_9 + k_{10} x_{10}}{k_{13}} \right\} \quad (1.7)$$

> $sol4 := simplify(subs(sol2[1], sol1[1], \{sol3[1]\}))$

$$sol4 := \left\{ x_2 = \left(x_1 \left(T_2 k_1 k_2 k_3 k_6 k_7 k_9 k_{12} x_1^3 + T_3 k_1 k_3 k_6 k_7 k_8 k_9 k_{12} x_1^3 \right. \right. \right. \quad (1.8)$$

$$+ T_2 k_1 k_2 k_3 k_6 k_8 k_9 k_{11} x_1^2 + T_2 k_1 k_2 k_3 k_6 k_8 k_9 k_{12} x_1^2 + T_2 k_1 k_2 k_3 k_6 k_9 k_{11} k_{12} x_1^2$$

$$+ T_2 k_2 k_3 k_4 k_5 k_7 k_9 k_{12} x_1^2 + T_2 k_2 k_3 k_5 k_6 k_7 k_9 k_{12} x_1^2 + T_3 k_1 k_3 k_6 k_8 k_9 k_{10} k_{11} x_1^2$$

$$+ T_3 k_1 k_3 k_6 k_8 k_9 k_{11} k_{12} x_1^2 + T_3 k_2 k_3 k_5 k_7 k_8 k_9 k_{12} x_1^2 + T_3 k_2 k_3 k_6 k_7 k_8 k_9 k_{12} x_1^2$$

$$+ T_3 k_3 k_5 k_6 k_7 k_8 k_9 k_{12} x_1^2 + T_2 k_1 k_2 k_3 k_6 k_8 k_{10} k_{11} x_1 + T_2 k_1 k_2 k_3 k_6 k_8 k_{11} k_{12} x_1$$

$$+ T_2 k_2 k_3 k_4 k_5 k_8 k_9 k_{11} x_1 + T_2 k_2 k_3 k_4 k_5 k_8 k_9 k_{12} x_1 + T_2 k_2 k_3 k_4 k_5 k_9 k_{11} k_{12} x_1$$

$$+ T_2 k_2 k_3 k_5 k_6 k_8 k_9 k_{11} x_1 + T_2 k_2 k_3 k_5 k_6 k_8 k_9 k_{12} x_1 + T_2 k_2 k_3 k_5 k_6 k_9 k_{11} k_{12} x_1$$

$$\begin{aligned}
& + T_3 k_2 k_3 k_5 k_8 k_9 k_{10} k_{11} x_1 + T_3 k_2 k_3 k_5 k_8 k_9 k_{11} k_{12} x_1 + T_3 k_2 k_3 k_6 k_8 k_9 k_{10} k_{11} x_1 \\
& + T_3 k_2 k_3 k_6 k_8 k_9 k_{11} k_{12} x_1 + T_3 k_2 k_4 k_5 k_7 k_8 k_9 k_{12} x_1 + T_3 k_2 k_5 k_6 k_7 k_8 k_9 k_{12} x_1 \\
& + T_3 k_3 k_5 k_6 k_8 k_9 k_{10} k_{11} x_1 + T_3 k_3 k_5 k_6 k_8 k_9 k_{11} k_{12} x_1 + T_2 k_2 k_3 k_4 k_5 k_8 k_{10} k_{11} \\
& + T_2 k_2 k_3 k_4 k_5 k_8 k_{11} k_{12} + T_2 k_2 k_3 k_5 k_6 k_8 k_{10} k_{11} + T_2 k_2 k_3 k_5 k_6 k_8 k_{11} k_{12} \\
& + T_3 k_2 k_4 k_5 k_8 k_9 k_{10} k_{11} + T_3 k_2 k_4 k_5 k_8 k_9 k_{11} k_{12} + T_3 k_2 k_5 k_6 k_8 k_9 k_{10} k_{11} \\
& + T_3 k_2 k_5 k_6 k_8 k_9 k_{11} k_{12} \Big) \Big/ \Big(\Big(k_1 k_3 k_6 x_1^2 + k_2 k_3 k_5 x_1 + k_2 k_3 k_6 x_1 + k_3 k_5 k_6 x_1 \\
& + k_2 k_4 k_5 + k_2 k_5 k_6 \Big) \Big(k_7 k_9 k_{12} x_1^2 + k_8 k_9 k_{11} x_1 + k_8 k_9 k_{12} x_1 + k_9 k_{11} k_{12} x_1 \\
& + k_8 k_{10} k_{11} + k_8 k_{11} k_{12} \Big) k_{13} \Big) \Big\}
\end{aligned}$$

$\triangleright \text{collect}(\text{numer}(\text{simplify}(\text{subs}(\text{sol2}[1], \text{sol1}[1], \text{sol4}, \text{cons}[1]))), x_1)$

$$\begin{aligned}
& k_1 k_3 k_6 k_7 k_9 k_{12} k_{13} x_1^5 + \Big(-T_1 k_1 k_3 k_6 k_7 k_9 k_{12} k_{13} + T_2 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_3 k_1 k_3 k_6 k_7 k_8 k_9 k_{12} + k_1 k_3 k_6 k_8 k_9 k_{11} 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} + 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} + k_3 k_5 k_6 k_7 k_9 k_{12} k_{13} \Big) x_1^4 + \Big(-T_1 k_1 k_3 k_6 k_8 k_9 k_{11} k_{13} \\
& - T_1 k_1 k_3 k_6 k_8 k_9 k_{12} k_{13} - T_1 k_1 k_3 k_6 k_9 k_{11} k_{12} k_{13} - T_1 k_2 k_3 k_5 k_7 k_9 k_{12} k_{13} \\
& - T_1 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_2 k_1 k_2 k_3 k_6 k_8 k_9 k_{11} \\
& + 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 k_1 k_3 k_6 k_8 k_9 k_{11} k_{13} \\
& + T_2 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_2 k_3 k_4 k_5 k_7 k_9 k_{12} \\
& + T_2 k_2 k_3 k_5 k_6 k_7 k_9 k_{12} + 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_3 k_1 k_3 k_6 k_8 k_9 k_{10} k_{11} + T_3 k_1 k_3 k_6 k_8 k_9 k_{11} k_{12} + T_3 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} + k_1 k_3 k_6 k_8 k_{10} k_{11} k_{13} \\
& + k_1 k_3 k_6 k_8 k_{11} k_{12} k_{13} + k_2 k_3 k_5 k_8 k_9 k_{11} k_{13} + k_2 k_3 k_5 k_8 k_9 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_8 k_9 k_{11} k_{13} + k_2 k_3 k_6 k_8 k_9 k_{12} k_{13} \\
& + k_2 k_3 k_6 k_9 k_{11} k_{12} k_{13} + 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_3 k_5 k_6 k_8 k_9 k_{11} k_{13} + k_3 k_5 k_6 k_8 k_9 k_{12} k_{13} + k_3 k_5 k_6 k_9 k_{11} k_{12} k_{13} \Big) x_1^3 + \Big(\\
& - T_1 k_1 k_3 k_6 k_8 k_{10} k_{11} k_{13} - T_1 k_1 k_3 k_6 k_8 k_{11} k_{12} k_{13} - T_1 k_2 k_3 k_5 k_8 k_9 k_{11} k_{13} \\
& - T_1 k_2 k_3 k_5 k_8 k_9 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_8 k_9 k_{11} k_{13} \\
& - T_1 k_2 k_3 k_6 k_8 k_9 k_{12} k_{13} - T_1 k_2 k_3 k_6 k_9 k_{11} k_{12} 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 k_3 k_5 k_6 k_8 k_9 k_{11} k_{13} - T_1 k_3 k_5 k_6 k_8 k_9 k_{12} k_{13} \\
& - T_1 k_3 k_5 k_6 k_9 k_{11} k_{12} k_{13} + T_2 k_1 k_2 k_3 k_6 k_8 k_{10} k_{11} + T_2 k_1 k_2 k_3 k_6 k_8 k_{11} k_{12}
\end{aligned}
\tag{1.9}$$

$$\begin{aligned}
& + T_2 k_1 k_3 k_6 k_8 k_{10} k_{11} k_{13} + T_2 k_1 k_3 k_6 k_8 k_{11} k_{12} k_{13} + T_2 k_2 k_3 k_4 k_5 k_8 k_9 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_4 k_5 k_9 k_{11} k_{12} + T_2 k_2 k_3 k_5 k_6 k_8 k_9 k_{11} \\
& + T_2 k_2 k_3 k_5 k_6 k_8 k_9 k_{12} + T_2 k_2 k_3 k_5 k_6 k_9 k_{11} k_{12} + T_2 k_2 k_3 k_5 k_8 k_9 k_{11} k_{13} \\
& + T_2 k_2 k_3 k_5 k_8 k_9 k_{12} k_{13} + T_2 k_2 k_3 k_5 k_9 k_{11} k_{12} k_{13} + T_2 k_3 k_5 k_6 k_8 k_9 k_{11} k_{13} \\
& + T_2 k_3 k_5 k_6 k_8 k_9 k_{12} k_{13} + T_2 k_3 k_5 k_6 k_9 k_{11} k_{12} k_{13} + T_3 k_2 k_3 k_5 k_8 k_9 k_{10} k_{11} \\
& + 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_{10} k_{11} + T_3 k_2 k_3 k_6 k_8 k_9 k_{11} k_{12} \\
& + T_3 k_2 k_4 k_5 k_7 k_8 k_9 k_{12} + T_3 k_2 k_5 k_6 k_7 k_8 k_9 k_{12} + T_3 k_3 k_5 k_6 k_8 k_9 k_{10} k_{11} \\
& + T_3 k_3 k_5 k_6 k_8 k_9 k_{11} k_{12} + k_2 k_3 k_5 k_8 k_{10} k_{11} 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_{10} k_{11} k_{13} + k_2 k_3 k_6 k_8 k_{11} k_{12} k_{13} + k_2 k_4 k_5 k_8 k_9 k_{11} k_{13} \\
& + k_2 k_4 k_5 k_8 k_9 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_8 k_9 k_{11} k_{13} \\
& + k_2 k_5 k_6 k_8 k_9 k_{12} k_{13} + k_2 k_5 k_6 k_9 k_{11} k_{12} k_{13} + k_3 k_5 k_6 k_8 k_{10} k_{11} k_{13} \\
& + k_3 k_5 k_6 k_8 k_{11} k_{12} k_{13}) x_1^2 + (-T_1 k_2 k_3 k_5 k_8 k_{10} k_{11} k_{13} - T_1 k_2 k_3 k_5 k_8 k_{11} k_{12} k_{13} \\
& - T_1 k_2 k_3 k_6 k_8 k_{10} k_{11} k_{13} - T_1 k_2 k_3 k_6 k_8 k_{11} k_{12} k_{13} - T_1 k_2 k_4 k_5 k_8 k_9 k_{11} k_{13} \\
& - T_1 k_2 k_4 k_5 k_8 k_9 k_{12} k_{13} - T_1 k_2 k_4 k_5 k_9 k_{11} k_{12} k_{13} - T_1 k_2 k_5 k_6 k_8 k_9 k_{11} k_{13} \\
& - T_1 k_2 k_5 k_6 k_8 k_9 k_{12} k_{13} - T_1 k_2 k_5 k_6 k_9 k_{11} k_{12} k_{13} - T_1 k_3 k_5 k_6 k_8 k_{10} k_{11} k_{13} \\
& - T_1 k_3 k_5 k_6 k_8 k_{11} k_{12} k_{13} + T_2 k_2 k_3 k_4 k_5 k_8 k_{10} k_{11} + T_2 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_{10} k_{11} + 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 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_{10} k_{11} k_{13} + T_2 k_3 k_5 k_6 k_8 k_{11} k_{12} k_{13} \\
& + T_3 k_2 k_4 k_5 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 k_2 k_5 k_6 k_8 k_9 k_{10} k_{11} \\
& + T_3 k_2 k_5 k_6 k_8 k_9 k_{11} k_{12} + k_2 k_4 k_5 k_8 k_{10} k_{11} k_{13} + k_2 k_4 k_5 k_8 k_{11} k_{12} k_{13} \\
& + k_2 k_5 k_6 k_8 k_{10} k_{11} k_{13} + k_2 k_5 k_6 k_8 k_{11} k_{12} k_{13}) x_1 - T_1 k_2 k_4 k_5 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_{10} k_{11} k_{13} - T_1 k_2 k_5 k_6 k_8 k_{11} k_{12} k_{13}
\end{aligned}$$

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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 x_1 (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 x_1) alternate.

This is a pre-check when you do the sampling: you need to impose the coefficient of x_1^4 to be negative, the coefficient of x_1^3 to be positive, the coefficient of x_1^2 to be negative and the coefficient of x_1 to be positive. The coefficients of x_1^5 and the independent term always have the right sign.

