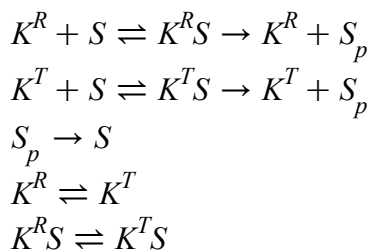
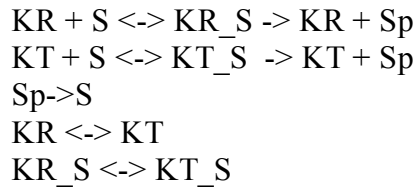


```
[> with(LinearAlgebra) :
[> interface(rtablesize = 40) :
[>
```

Simplification of minimal system extend 8

We consider the following reactions:



The species of the network are (in parenthesis the order in which I consider them)

{S (1), Sp (2), KR (3), KT (4), KR_S (5), KT_S (6) }

There are a total of 11 reactions and 6 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

$$\frac{dx}{dt} = A \cdot k_{rs}$$

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

Stoichiometric matrix:

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

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

```

Vector of rates:

here x_i is the concentration of the i-th species

$$\begin{aligned}
 & \text{> } ks := \text{Vector}([k_1 \cdot x_3 \cdot x_1, k_2 \cdot x_5, k_3 \cdot x_5, k_4 \cdot x_4 \cdot x_1, k_5 \cdot x_6, k_6 \cdot x_6, k_7 \cdot x_2, k_8 \cdot x_3, k_9 \cdot x_4, k_{10} \cdot x_5, k_{11} \cdot x_6]) \\
 & \hspace{15em} ks := \begin{bmatrix} k_1 x_3 x_1 \\ k_2 x_5 \\ k_3 x_5 \\ k_4 x_4 x_1 \\ k_5 x_6 \\ k_6 x_6 \\ k_7 x_2 \\ k_8 x_3 \\ k_9 x_4 \\ k_{10} x_5 \\ k_{11} x_6 \end{bmatrix} \hspace{10em} \textbf{(1)}
 \end{aligned}$$

Steady state equations:

$$\begin{aligned}
 & \text{> } ssEqs := A.ks \\
 & \hspace{10em} ssEqs := \begin{bmatrix} -k_1 x_1 x_3 - k_4 x_1 x_4 + k_2 x_5 + k_5 x_6 + k_7 x_2 \\ k_3 x_5 + k_6 x_6 - k_7 x_2 \\ -k_1 x_1 x_3 + k_2 x_5 + k_3 x_5 - k_8 x_3 + k_9 x_4 \\ -k_4 x_1 x_4 + k_5 x_6 + k_6 x_6 + k_8 x_3 - k_9 x_4 \\ k_1 x_1 x_3 - k_2 x_5 - k_3 x_5 - k_{10} x_5 + k_{11} x_6 \\ k_4 x_1 x_4 - k_5 x_6 - k_6 x_6 + k_{10} x_5 - k_{11} x_6 \end{bmatrix} \hspace{10em} \textbf{(2)}
 \end{aligned}$$

Conservation laws:

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

$$\begin{aligned} & \text{> } F := \text{ReducedRowEchelonForm}(\text{Transpose}(\text{Matrix}([\text{op}(\text{NullSpace}(\text{Transpose}(A)))]))) \\ & \qquad \qquad \qquad F := \begin{bmatrix} 1 & 1 & 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 1 & 1 & 1 \end{bmatrix} \end{aligned} \quad (3)$$

the conservation laws are:

$$x_1 + x_2 + x_5 + x_6 - T_1, x_3 + x_4 + x_5 + x_6 - T_2$$

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

$$\begin{aligned} & \text{> } \text{subsEqs} := [\text{ssEqs}[2], \text{ssEqs}[4], \text{ssEqs}[5], \text{ssEqs}[6], x_1 + x_2 + x_5 + x_6 - T_1, x_3 + x_4 + x_5 \\ & \qquad \qquad \qquad + x_6 - T_2] \\ & \text{subsEqs} := [k_3 x_5 + k_6 x_6 - k_7 x_2, -k_4 x_1 x_4 + k_5 x_6 + k_6 x_6 + k_8 x_3 - k_9 x_4, k_1 x_1 x_3 - k_2 x_5 \\ & \qquad \qquad \qquad - k_3 x_5 - k_{10} x_5 + k_{11} x_6, k_4 x_1 x_4 - k_5 x_6 - k_6 x_6 + k_{10} x_5 - k_{11} x_6, x_1 + x_2 + x_5 + x_6 \\ & \qquad \qquad \qquad - T_1, x_3 + x_4 + x_5 + x_6 - T_2] \end{aligned} \quad (4)$$

New parameter set:

$$\begin{aligned} \text{params} &:= \{k_1 = 10, k_2 = 0.01, k_3 = 1, k_4 = 0.01, k_5 = 10, k_6 = 100, k_7 = 0.1, k_8 = 100, k_9 = 0.01, k_{10} \\ &= 0.01, k_{11} = 1, T_1 = 84614.84435, T_2 = 3504.020816\} \end{aligned}$$

This considered the thermodynamic constraint of allosteric regulation: $\frac{k_1}{k_2} \cdot \frac{k_{10}}{k_{11}} = \frac{k_4}{k_5} \cdot \frac{k_8}{k_9}$

Original computed paramters

The following set of parameters give three steady states, two stable and one unstable:

$$\begin{aligned} \text{params} &:= \{k_1 = 0.1, k_2 = 0.1, k_3 = 0.1, k_4 = 0.1, k_5 = 0.1, k_7 = 0.1, k_9 = 0.1, k_{10} = 0.1, k_{11} = 0.1, k_6 \\ &= 10, k_8 = 10000, T_1 := 3.081835511 \cdot 10^6, T_2 := 41216.17056\} : \end{aligned}$$

These parameters are for sure not reasonable, but one can play to change them. To do that, look at the Computations section.

There are three positive steady states for some total amounts if and only if the following expression on the

rate constants is positive

$$\begin{aligned} \text{term} := & \left(k_1^2 k_3 k_4 k_5 k_9 k_{10} - k_1^2 k_3 k_4 k_5 k_{10} k_{11} + k_1^2 k_3 k_4 k_6 k_9 k_{10} - k_1^2 k_3 k_4 k_6 k_{10} k_{11} - \right. \\ & k_1^2 k_4 k_5 k_6 k_9 k_{10} - k_1^2 k_4 k_5 k_6 k_{10}^2 - k_1^2 k_4 k_5 k_7 k_{10}^2 - k_1^2 k_4 k_5 k_7 k_{10} k_{11} - k_1^2 k_4 k_6^2 k_9 k_{10} - k_1^2 k_4 k_6^2 k_{10}^2 \\ & k_6^2 k_{10}^2 - k_1^2 k_4 k_6 k_7 k_{10}^2 - k_1^2 k_4 k_6 k_7 k_{10} k_{11} - k_1 k_2 k_3 k_4^2 k_8 k_{11} - k_1 k_2 k_3 k_4^2 k_{11}^2 + k_1 k_2 \\ & k_4^2 k_6 k_8 k_{11} - k_1 k_2 k_4^2 k_6 k_{10} k_{11} - k_1 k_2 k_4^2 k_7 k_{10} k_{11} - k_1 k_2 k_4^2 k_7 k_{11}^2 - k_1 k_3^2 k_4^2 k_8 k_{11} - k_1 k_3^2 k_4^2 \\ & k_{11}^2 + k_1 k_3 k_4^2 k_6 k_8 k_{11} - k_1 k_3 k_4^2 k_6 k_{10} k_{11} - k_1 k_3 k_4^2 k_7 k_{10} k_{11} - k_1 k_3 k_4^2 k_7 k_{11}^2 \left. \right) \end{aligned}$$

As I said, the theory supporting this claim is not yet published, but the procedure above gives a way to generate parameters with three steady states.

Original computed parameters #####
#####

Computations

The way to find different sets of parameters is highlighted in bold. These are two steps where there is a choice.

We compute the Jacobian of myeqs (steady state equations together with the conservation laws)

$$\begin{aligned} & \text{> } J := \text{VectorCalculus}[\text{Jacobian}](\text{subsEqs}, [\text{seq}(x_i, i = 1..6)]) \\ & J := \begin{bmatrix} 0 & -k_7 & 0 & 0 & k_3 & k_6 \\ -k_4 x_4 & 0 & k_8 & -k_4 x_1 - k_9 & 0 & k_5 + k_6 \\ k_1 x_3 & 0 & k_1 x_1 & 0 & -k_2 - k_3 - k_{10} & k_{11} \\ k_4 x_4 & 0 & 0 & k_4 x_1 & k_{10} & -k_5 - k_6 - k_{11} \\ 1 & 1 & 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 1 & 1 & 1 \end{bmatrix} \end{aligned} \quad (1.1)$$

$$\begin{aligned} & \text{> } \text{Determinant}(J) : \\ & \text{> } \text{detJ} := \text{collect}(\%, \{\text{seq}(x_i, i = 1..6)\}, \text{'distributed'}) \\ & \text{detJ} := (-k_1 k_4 k_7 k_{10} - k_1 k_4 k_7 k_{11}) x_1^2 + (-k_1 k_3 k_4 k_8 - k_1 k_3 k_4 k_{11} + k_1 k_4 k_6 k_8 \\ & \quad - k_1 k_4 k_6 k_{10} - k_1 k_4 k_7 k_{10} - k_1 k_4 k_7 k_{11}) x_1 x_3 + (k_1 k_3 k_4 k_9 - k_1 k_3 k_4 k_{11} \\ & \quad - k_1 k_4 k_6 k_9 - k_1 k_4 k_6 k_{10} - k_1 k_4 k_7 k_{10} - k_1 k_4 k_7 k_{11}) x_1 x_4 + (-k_1 k_5 k_7 k_9 \end{aligned} \quad (1.2)$$

$$\begin{aligned}
& -k_1 k_5 k_7 k_{10} - k_1 k_6 k_7 k_9 - k_1 k_6 k_7 k_{10} - k_1 k_7 k_9 k_{10} - k_1 k_7 k_9 k_{11} - k_2 k_4 k_7 k_8 \\
& - k_2 k_4 k_7 k_{11} - k_3 k_4 k_7 k_8 - k_3 k_4 k_7 k_{11} - k_4 k_7 k_8 k_{10} - k_4 k_7 k_8 k_{11}) x_1 + (\\
& -k_1 k_3 k_5 k_8 - k_1 k_3 k_5 k_9 - k_1 k_3 k_6 k_8 - k_1 k_3 k_6 k_9 - k_1 k_3 k_8 k_{11} - k_1 k_3 k_9 k_{11} \\
& - k_1 k_5 k_7 k_8 - k_1 k_5 k_7 k_9 - k_1 k_6 k_7 k_8 - k_1 k_6 k_7 k_9 - k_1 k_6 k_8 k_{10} - k_1 k_6 k_9 k_{10} \\
& - k_1 k_7 k_8 k_{10} - k_1 k_7 k_8 k_{11} - k_1 k_7 k_9 k_{10} - k_1 k_7 k_9 k_{11}) x_3 + (-k_2 k_4 k_6 k_8 \\
& - k_2 k_4 k_6 k_9 - k_2 k_4 k_7 k_8 - k_2 k_4 k_7 k_9 - k_3 k_4 k_6 k_8 - k_3 k_4 k_6 k_9 - k_3 k_4 k_7 k_8 \\
& - k_3 k_4 k_7 k_9 - k_3 k_4 k_8 k_{11} - k_3 k_4 k_9 k_{11} - k_4 k_6 k_8 k_{10} - k_4 k_6 k_9 k_{10} - k_4 k_7 k_8 k_{10} \\
& - k_4 k_7 k_8 k_{11} - k_4 k_7 k_9 k_{10} - k_4 k_7 k_9 k_{11}) x_4 - k_2 k_5 k_7 k_8 - k_2 k_5 k_7 k_9 - k_2 k_6 k_7 k_8 \\
& - k_2 k_6 k_7 k_9 - k_2 k_7 k_8 k_{11} - k_2 k_7 k_9 k_{11} - k_3 k_5 k_7 k_8 - k_3 k_5 k_7 k_9 - k_3 k_6 k_7 k_8 \\
& - k_3 k_6 k_7 k_9 - k_3 k_7 k_8 k_{11} - k_3 k_7 k_9 k_{11} - k_5 k_7 k_8 k_{10} - k_5 k_7 k_9 k_{10} - k_6 k_7 k_8 k_{10} \\
& - k_6 k_7 k_9 k_{10}
\end{aligned}$$

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.

$$\begin{aligned}
& \text{solution} := \text{solve}([subsEqs[2], subsEqs[3], subsEqs[4], subsEqs[1]], [x_2, x_4, x_5, x_6]) \\
& \text{solution} := \left[\left[x_2 = \left((k_1 k_3 k_4 k_{11} x_1 + k_1 k_4 k_6 k_{10} x_1 + k_1 k_3 k_5 k_9 + k_1 k_3 k_6 k_9 \right. \right. \right. \quad (1.3) \\
& \quad \left. \left. \left. + k_1 k_3 k_9 k_{11} + k_1 k_6 k_9 k_{10} + k_2 k_4 k_6 k_8 + k_3 k_4 k_6 k_8 + k_3 k_4 k_8 k_{11} + k_4 k_6 k_8 k_{10} \right) \right. \right. \\
& \quad \left. \left. x_1 x_3 \right) / \left(k_7 \left(k_2 k_4 k_{11} x_1 + k_3 k_4 k_{11} x_1 + k_2 k_5 k_9 + k_2 k_6 k_9 + k_2 k_9 k_{11} + k_3 k_5 k_9 \right. \right. \right. \\
& \quad \left. \left. \left. + k_3 k_6 k_9 + k_3 k_9 k_{11} + k_5 k_9 k_{10} + k_6 k_9 k_{10} \right) \right), x_4 = \left(x_3 \left(k_1 k_5 k_{10} x_1 \right. \right. \right. \\
& \quad \left. \left. \left. + k_1 k_6 k_{10} x_1 + k_2 k_5 k_8 + k_2 k_6 k_8 + k_2 k_8 k_{11} + k_3 k_5 k_8 + k_3 k_6 k_8 + k_3 k_8 k_{11} \right. \right. \right. \\
& \quad \left. \left. \left. + k_5 k_8 k_{10} + k_6 k_8 k_{10} \right) \right) / \left(k_2 k_4 k_{11} x_1 + k_3 k_4 k_{11} x_1 + k_2 k_5 k_9 + k_2 k_6 k_9 + k_2 k_9 k_{11} \right. \right. \\
& \quad \left. \left. + k_3 k_5 k_9 + k_3 k_6 k_9 + k_3 k_9 k_{11} + k_5 k_9 k_{10} + k_6 k_9 k_{10} \right), x_5 = \left(x_1 x_3 \left(k_1 k_4 k_{11} x_1 \right. \right. \right. \\
& \quad \left. \left. \left. + k_1 k_5 k_9 + k_1 k_6 k_9 + k_1 k_9 k_{11} + k_4 k_8 k_{11} \right) \right) / \left(k_2 k_4 k_{11} x_1 + k_3 k_4 k_{11} x_1 + k_2 k_5 k_9 \right. \right.
\end{aligned}$$

$$\begin{aligned}
& + k_2 k_6 k_9 + k_2 k_9 k_{11} + k_3 k_5 k_9 + k_3 k_6 k_9 + k_3 k_9 k_{11} + k_5 k_9 k_{10} + k_6 k_9 k_{10}), x_6 \\
& = \left((k_1 k_4 k_{10} x_1 + k_1 k_9 k_{10} + k_2 k_4 k_8 + k_3 k_4 k_8 + k_4 k_8 k_{10}) x_1 x_3 \right) / \left((k_2 k_4 k_{11} x_1 \right. \\
& + k_3 k_4 k_{11} x_1 + k_2 k_5 k_9 + k_2 k_6 k_9 + k_2 k_9 k_{11} + k_3 k_5 k_9 + k_3 k_6 k_9 + k_3 k_9 k_{11} \\
& \left. + k_5 k_9 k_{10} + k_6 k_9 k_{10}) \right)]]
\end{aligned}$$

We evaluate the determinant of the Jacobian at the parameterisation. We then write it as a polynomial in x_1 and x_3

$$\begin{aligned}
& \text{> } \text{detSubs} := \text{subs}(\text{solution}[1], \text{detJ}) \\
& \text{detSubs} := \left(-k_1 k_4 k_7 k_{10} - k_1 k_4 k_7 k_{11} \right) x_1^2 + \left(-k_1 k_3 k_4 k_8 - k_1 k_3 k_4 k_{11} + k_1 k_4 k_6 k_8 \right. \\
& \quad - k_1 k_4 k_6 k_{10} - k_1 k_4 k_7 k_{10} - k_1 k_4 k_7 k_{11} \left. \right) x_1 x_3 + \left((k_1 k_3 k_4 k_9 - k_1 k_3 k_4 k_{11} \right. \\
& \quad - k_1 k_4 k_6 k_9 - k_1 k_4 k_6 k_{10} - k_1 k_4 k_7 k_{10} - k_1 k_4 k_7 k_{11} \left. \right) x_1 x_3 \left(k_1 k_5 k_{10} x_1 \right. \\
& \quad + k_1 k_6 k_{10} x_1 + k_2 k_5 k_8 + k_2 k_6 k_8 + k_2 k_8 k_{11} + k_3 k_5 k_8 + k_3 k_6 k_8 + k_3 k_8 k_{11} \\
& \quad + k_5 k_8 k_{10} + k_6 k_8 k_{10} \left. \right) \left. \right) / \left((k_2 k_4 k_{11} x_1 + k_3 k_4 k_{11} x_1 + k_2 k_5 k_9 + k_2 k_6 k_9 + k_2 k_9 k_{11} \right. \\
& \quad + k_3 k_5 k_9 + k_3 k_6 k_9 + k_3 k_9 k_{11} + k_5 k_9 k_{10} + k_6 k_9 k_{10}) + \left(-k_1 k_5 k_7 k_9 \right. \\
& \quad - k_1 k_5 k_7 k_{10} - k_1 k_6 k_7 k_9 - k_1 k_6 k_7 k_{10} - k_1 k_7 k_9 k_{10} - k_1 k_7 k_9 k_{11} - k_2 k_4 k_7 k_8 \\
& \quad - k_2 k_4 k_7 k_{11} - k_3 k_4 k_7 k_8 - k_3 k_4 k_7 k_{11} - k_4 k_7 k_8 k_{10} - k_4 k_7 k_8 k_{11} \left. \right) x_1 + \left(\right. \\
& \quad - k_1 k_3 k_5 k_8 - k_1 k_3 k_5 k_9 - k_1 k_3 k_6 k_8 - k_1 k_3 k_6 k_9 - k_1 k_3 k_8 k_{11} - k_1 k_3 k_9 k_{11} \\
& \quad - k_1 k_5 k_7 k_8 - k_1 k_5 k_7 k_9 - k_1 k_6 k_7 k_8 - k_1 k_6 k_7 k_9 - k_1 k_6 k_8 k_{10} - k_1 k_6 k_9 k_{10} \\
& \quad - k_1 k_7 k_8 k_{10} - k_1 k_7 k_8 k_{11} - k_1 k_7 k_9 k_{10} - k_1 k_7 k_9 k_{11} \left. \right) x_3 + \left(\left(-k_2 k_4 k_6 k_8 \right. \right. \\
& \quad - k_2 k_4 k_6 k_9 - k_2 k_4 k_7 k_8 - k_2 k_4 k_7 k_9 - k_3 k_4 k_6 k_8 - k_3 k_4 k_6 k_9 - k_3 k_4 k_7 k_8 \\
& \quad - k_3 k_4 k_7 k_9 - k_3 k_4 k_8 k_{11} - k_3 k_4 k_9 k_{11} - k_4 k_6 k_8 k_{10} - k_4 k_6 k_9 k_{10} - k_4 k_7 k_8 k_{10} \\
& \quad - k_4 k_7 k_8 k_{11} - k_4 k_7 k_9 k_{10} - k_4 k_7 k_9 k_{11} \left. \right) x_3 \left(k_1 k_5 k_{10} x_1 + k_1 k_6 k_{10} x_1 + k_2 k_5 k_8 \right. \\
& \quad + k_2 k_6 k_8 + k_2 k_8 k_{11} + k_3 k_5 k_8 + k_3 k_6 k_8 + k_3 k_8 k_{11} + k_5 k_8 k_{10} + k_6 k_8 k_{10} \left. \right) \left. \right) / \\
& \left((k_2 k_4 k_{11} x_1 + k_3 k_4 k_{11} x_1 + k_2 k_5 k_9 + k_2 k_6 k_9 + k_2 k_9 k_{11} + k_3 k_5 k_9 + k_3 k_6 k_9 \right. \\
& \quad + k_3 k_9 k_{11} + k_5 k_9 k_{10} + k_6 k_9 k_{10}) - k_2 k_5 k_7 k_8 - k_2 k_5 k_7 k_9 - k_2 k_6 k_7 k_8 \\
& \quad - k_2 k_6 k_7 k_9 - k_2 k_7 k_8 k_{11} - k_2 k_7 k_9 k_{11} - k_3 k_5 k_7 k_8 - k_3 k_5 k_7 k_9 - k_3 k_6 k_7 k_8 \\
& \quad - k_3 k_6 k_7 k_9 - k_3 k_7 k_8 k_{11} - k_3 k_7 k_9 k_{11} - k_5 k_7 k_8 k_{10} - k_5 k_7 k_9 k_{10} - k_6 k_7 k_8 k_{10} \\
& \quad \left. - k_6 k_7 k_9 k_{10} \right)
\end{aligned}
\tag{1.4}$$

$$\begin{aligned}
& \text{> } \text{polSubs} := \text{numer}(\text{detSubs}) : \\
& \text{> } \text{finalPol} := \text{collect}(\text{polSubs}, \{x_1, x_3\}, 'distributed')
\end{aligned}$$

(1.5)

(1.5)

$$\begin{aligned}
finalPol := & -4 k_2 k_3 k_5 k_6 k_7 k_8 k_9 - 4 k_2 k_3 k_5 k_7 k_8 k_9 k_{11} - 4 k_2 k_3 k_6 k_7 k_8 k_9 k_{11} \\
& - 4 k_2 k_5 k_6 k_7 k_8 k_9 k_{10} - 2 k_2 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} \\
& - 4 k_3 k_5 k_6 k_7 k_8 k_9 k_{10} - 2 k_3 k_5 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} + (\\
& - k_1 k_2 k_4 k_5 k_7 k_9 k_{10} - 2 k_1 k_2 k_4 k_5 k_7 k_9 k_{11} - k_1 k_2 k_4 k_5 k_7 k_{10} k_{11} \\
& - k_1 k_2 k_4 k_6 k_7 k_9 k_{10} - 2 k_1 k_2 k_4 k_6 k_7 k_9 k_{11} - k_1 k_2 k_4 k_6 k_7 k_{10} k_{11} \\
& - 2 k_1 k_2 k_4 k_7 k_9 k_{10} k_{11} - 2 k_1 k_2 k_4 k_7 k_9 k_{11}^2 - k_1 k_3 k_4 k_5 k_7 k_9 k_{10} \\
& - 2 k_1 k_3 k_4 k_5 k_7 k_9 k_{11} - k_1 k_3 k_4 k_5 k_7 k_{10} k_{11} - k_1 k_3 k_4 k_6 k_7 k_9 k_{10} \\
& - 2 k_1 k_3 k_4 k_6 k_7 k_9 k_{11} - k_1 k_3 k_4 k_6 k_7 k_{10} k_{11} - 2 k_1 k_3 k_4 k_7 k_9 k_{10} k_{11} \\
& - 2 k_1 k_3 k_4 k_7 k_9 k_{11}^2 - k_1 k_4 k_5 k_7 k_9 k_{10}^2 - 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}^2 \\
& - k_1 k_4 k_6 k_7 k_9 k_{10} k_{11} - k_2^2 k_4^2 k_7 k_8 k_{11} - k_2^2 k_4^2 k_7 k_{11}^2 - 2 k_2 k_3 k_4^2 k_7 k_8 k_{11} - 2 k_2 k_3 \\
& k_4^2 k_7 k_{11}^2 - k_2 k_4^2 k_7 k_8 k_{10} k_{11} - k_2 k_4^2 k_7 k_8 k_{11}^2 - k_3^2 k_4^2 k_7 k_8 k_{11} - k_3^2 k_4^2 k_7 k_{11}^2 - k_3 \\
& k_4^2 k_7 k_8 k_{10} k_{11} - k_3 k_4^2 k_7 k_8 k_{11}^2) x_1^2 + (-k_1 k_2 k_5^2 k_7 k_9^2 - k_1 k_2 k_5^2 k_7 k_9 k_{10} \\
& - 2 k_1 k_2 k_5 k_6 k_7 k_9^2 - 2 k_1 k_2 k_5 k_6 k_7 k_9 k_{10} - k_1 k_2 k_5 k_7 k_9^2 k_{10} - 2 k_1 k_2 k_5 k_7 k_9^2 k_{11} \\
& - k_1 k_2 k_5 k_7 k_9 k_{10} k_{11} - k_1 k_2 k_6^2 k_7 k_9^2 - k_1 k_2 k_6^2 k_7 k_9 k_{10} - k_1 k_2 k_6 k_7 k_9^2 k_{10} \\
& - 2 k_1 k_2 k_6 k_7 k_9^2 k_{11} - k_1 k_2 k_6 k_7 k_9 k_{10} k_{11} - k_1 k_2 k_7 k_9^2 k_{10} k_{11} - k_1 k_2 k_7 k_9^2 k_{11}^2 \\
& - k_1 k_3 k_5^2 k_7 k_9^2 - k_1 k_3 k_5^2 k_7 k_9 k_{10} - 2 k_1 k_3 k_5 k_6 k_7 k_9^2 - 2 k_1 k_3 k_5 k_6 k_7 k_9 k_{10} \\
& - k_1 k_3 k_5 k_7 k_9^2 k_{10} - 2 k_1 k_3 k_5 k_7 k_9^2 k_{11} - k_1 k_3 k_5 k_7 k_9 k_{10} k_{11} - k_1 k_3 k_6^2 k_7 k_9^2 \\
& - k_1 k_3 k_6^2 k_7 k_9 k_{10} - k_1 k_3 k_6 k_7 k_9^2 k_{10} - 2 k_1 k_3 k_6 k_7 k_9^2 k_{11} - k_1 k_3 k_6 k_7 k_9 k_{10} k_{11} \\
& - k_1 k_3 k_7 k_9^2 k_{10} k_{11} - k_1 k_3 k_7 k_9^2 k_{11}^2 - k_1 k_5^2 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_5 k_6 k_7 k_9 k_{10}^2 - k_1 k_5 k_7 k_9^2 k_{10}^2 - k_1 k_5 k_7 k_9^2 k_{10} k_{11} - k_1 k_6^2 k_7 k_9^2 k_{10} - k_1 \\
& k_6^2 k_7 k_9 k_{10}^2 - k_1 k_6 k_7 k_9^2 k_{10}^2 - k_1 k_6 k_7 k_9^2 k_{10} k_{11} - k_2^2 k_4 k_5 k_7 k_8 k_9 - k_2^2 k_4 k_5 k_7 k_8 k_{11} \\
& - 2 k_2^2 k_4 k_5 k_7 k_9 k_{11} - k_2^2 k_4 k_6 k_7 k_8 k_9 - k_2^2 k_4 k_6 k_7 k_8 k_{11} - 2 k_2^2 k_4 k_6 k_7 k_9 k_{11} - \\
& k_2^2 k_4 k_7 k_8 k_9 k_{11} - k_2^2 k_4 k_7 k_8 k_{11}^2 - 2 k_2^2 k_4 k_7 k_9 k_{11}^2 - 2 k_2 k_3 k_4 k_5 k_7 k_8 k_9 \\
& - 2 k_2 k_3 k_4 k_5 k_7 k_8 k_{11} - 4 k_2 k_3 k_4 k_5 k_7 k_9 k_{11} - 2 k_2 k_3 k_4 k_6 k_7 k_8 k_9 \\
& - 2 k_2 k_3 k_4 k_6 k_7 k_8 k_{11} - 4 k_2 k_3 k_4 k_6 k_7 k_9 k_{11} - 2 k_2 k_3 k_4 k_7 k_8 k_9 k_{11} \\
& - 2 k_2 k_3 k_4 k_7 k_8 k_{11}^2 - 4 k_2 k_3 k_4 k_7 k_9 k_{11}^2 - 2 k_2 k_4 k_5 k_7 k_8 k_9 k_{10} \\
& - k_2 k_4 k_5 k_7 k_8 k_9 k_{11} - k_2 k_4 k_5 k_7 k_8 k_{10} k_{11} - 2 k_2 k_4 k_5 k_7 k_9 k_{10} k_{11}
\end{aligned}$$

$$\begin{aligned}
& -2k_2k_4k_6k_7k_8k_9k_{10} - k_2k_4k_6k_7k_8k_9k_{11} - k_2k_4k_6k_7k_8k_{10}k_{11} \\
& -2k_2k_4k_6k_7k_9k_{10}k_{11} - k_2k_4k_7k_8k_9k_{10}k_{11} - k_2k_4k_7k_8k_9k_{11}^2 - k_3^2k_4k_5k_7k_8k_9 \\
& - k_3^2k_4k_5k_7k_8k_{11} - 2k_3^2k_4k_5k_7k_9k_{11} - k_3^2k_4k_6k_7k_8k_9 - k_3^2k_4k_6k_7k_8k_{11} - 2 \\
& k_3^2k_4k_6k_7k_9k_{11} - k_3^2k_4k_7k_8k_9k_{11} - k_3^2k_4k_7k_8k_{11}^2 - 2k_3^2k_4k_7k_9k_{11}^2 \\
& -2k_3k_4k_5k_7k_8k_9k_{10} - k_3k_4k_5k_7k_8k_9k_{11} - k_3k_4k_5k_7k_8k_{10}k_{11} \\
& -2k_3k_4k_5k_7k_9k_{10}k_{11} - 2k_3k_4k_6k_7k_8k_9k_{10} - k_3k_4k_6k_7k_8k_9k_{11} \\
& -k_3k_4k_6k_7k_8k_{10}k_{11} - 2k_3k_4k_6k_7k_9k_{10}k_{11} - k_3k_4k_7k_8k_9k_{10}k_{11} \\
& -k_3k_4k_7k_8k_9k_{11}^2 - k_4k_5k_7k_8k_9k_{10}^2 - k_4k_5k_7k_8k_9k_{10}k_{11} - k_4k_6k_7k_8k_9k_{10}^2 \\
& -k_4k_6k_7k_8k_9k_{10}k_{11} \big) x_1 - 2k_2k_6^2k_7k_9^2k_{10} - k_3^2k_5^2k_7k_8k_9 - 2k_3^2k_5k_6k_7k_9^2 - 2 \\
& k_3^2k_5k_7k_9^2k_{11} - k_3^2k_6^2k_7k_8k_9 - 2k_3^2k_6k_7k_9^2k_{11} - k_3^2k_7k_8k_9k_{11}^2 - 2k_3k_5^2k_7k_9^2k_{10} \\
& -2k_3k_6^2k_7k_9^2k_{10} - k_5^2k_7k_8k_9k_{10}^2 - 2k_5k_6k_7k_9^2k_{10}^2 - k_6^2k_7k_8k_9k_{10}^2 - k_2^2k_5^2k_7k_8k_9 \\
& -2k_2^2k_5k_6k_7k_9^2 - 2k_2^2k_5k_7k_9^2k_{11} - k_2^2k_6^2k_7k_8k_9 - 2k_2^2k_6k_7k_9^2k_{11} - k_2^2k_7k_8k_9 \\
& k_{11}^2 - 2k_2k_3k_5^2k_7k_9^2 - 2k_2k_3k_6^2k_7k_9^2 - 2k_2k_3k_7k_9^2k_{11}^2 - 2k_2k_5^2k_7k_9^2k_{10} + \big(\\
& -k_1k_2k_4^2k_7k_{10}k_{11} - k_1k_2k_4^2k_7k_{11}^2 - k_1k_3k_4^2k_7k_{10}k_{11} - k_1k_3k_4^2k_7k_{11}^2 \big) x_1^3 + \big(\\
& -k_1k_2k_3k_5^2k_8k_9 - k_1k_2k_3k_5^2k_9^2 - 2k_1k_2k_3k_5k_6k_8k_9 - 2k_1k_2k_3k_5k_6k_9^2 \\
& -2k_1k_2k_3k_5k_8k_9k_{11} - 2k_1k_2k_3k_5k_9^2k_{11} - k_1k_2k_3k_6^2k_8k_9 - k_1k_2k_3k_6^2k_9^2 \\
& -2k_1k_2k_3k_6k_8k_9k_{11} - 2k_1k_2k_3k_6k_9^2k_{11} - k_1k_2k_3k_8k_9k_{11}^2 - k_1k_2k_3k_9^2k_{11}^2 \\
& -k_1k_2k_5^2k_7k_8k_9 - k_1k_2k_5^2k_7k_9^2 - 2k_1k_2k_5k_6k_7k_8k_9 - 2k_1k_2k_5k_6k_7k_9^2 \\
& -k_1k_2k_5k_6k_8k_9k_{10} - k_1k_2k_5k_6k_9^2k_{10} - k_1k_2k_5k_7k_8k_9k_{10} \\
& -2k_1k_2k_5k_7k_8k_9k_{11} - k_1k_2k_5k_7k_9^2k_{10} - 2k_1k_2k_5k_7k_9^2k_{11} - k_1k_2k_6^2k_7k_8k_9 \\
& -k_1k_2k_6^2k_7k_9^2 - k_1k_2k_6^2k_8k_9k_{10} - k_1k_2k_6^2k_9^2k_{10} - k_1k_2k_6k_7k_8k_9k_{10} \\
& -2k_1k_2k_6k_7k_8k_9k_{11} - k_1k_2k_6k_7k_9^2k_{10} - 2k_1k_2k_6k_7k_9^2k_{11} \\
& -k_1k_2k_6k_8k_9k_{10}k_{11} - k_1k_2k_6k_9^2k_{10}k_{11} - k_1k_2k_7k_8k_9k_{10}k_{11} - k_1k_2k_7k_8k_9k_{11}^2 \\
& -k_1k_2k_7k_9^2k_{10}k_{11} - k_1k_2k_7k_9^2k_{11}^2 - k_1k_3^2k_5^2k_8k_9 - k_1k_3^2k_5^2k_9^2 - 2k_1k_3^2k_5k_6k_8k_9 \\
& -2k_1k_3^2k_5k_6k_9^2 - 2k_1k_3^2k_5k_8k_9k_{11} - 2k_1k_3^2k_5k_9^2k_{11} - k_1k_3^2k_6^2k_8k_9 - k_1k_3^2k_6^2k_9^2 \\
& -2k_1k_3^2k_6k_8k_9k_{11} - 2k_1k_3^2k_6k_9^2k_{11} - k_1k_3^2k_8k_9k_{11}^2 - k_1k_3^2k_9^2k_{11}^2 - k_1k_3 \\
& k_5^2k_7k_8k_9 - k_1k_3k_5^2k_7k_9^2 - k_1k_3k_5^2k_8k_9k_{10} - k_1k_3k_5^2k_9^2k_{10} - 2k_1k_3k_5k_6k_7k_8k_9
\end{aligned}$$

$$\begin{aligned}
& -2 k_1 k_3 k_5 k_6 k_7 k_9^2 - 3 k_1 k_3 k_5 k_6 k_8 k_9 k_{10} - 3 k_1 k_3 k_5 k_6 k_9^2 k_{10} \\
& - k_1 k_3 k_5 k_7 k_8 k_9 k_{10} - 2 k_1 k_3 k_5 k_7 k_8 k_9 k_{11} - k_1 k_3 k_5 k_7 k_9^2 k_{10} - 2 k_1 k_3 k_5 k_7 k_9^2 k_{11} \\
& - k_1 k_3 k_5 k_8 k_9 k_{10} k_{11} - k_1 k_3 k_5 k_9^2 k_{10} k_{11} - k_1 k_3 k_6^2 k_7 k_8 k_9 - k_1 k_3 k_6^2 k_7 k_9^2 \\
& - 2 k_1 k_3 k_6^2 k_8 k_9 k_{10} - 2 k_1 k_3 k_6^2 k_9^2 k_{10} - k_1 k_3 k_6 k_7 k_8 k_9 k_{10} - 2 k_1 k_3 k_6 k_7 k_8 k_9 k_{11} \\
& - k_1 k_3 k_6 k_7 k_9^2 k_{10} - 2 k_1 k_3 k_6 k_7 k_9^2 k_{11} - 2 k_1 k_3 k_6 k_8 k_9 k_{10} k_{11} - 2 k_1 k_3 k_6 \\
& k_9^2 k_{10} k_{11} - k_1 k_3 k_7 k_8 k_9 k_{10} k_{11} - k_1 k_3 k_7 k_8 k_9 k_{11}^2 - k_1 k_3 k_7 k_9^2 k_{10} k_{11} - k_1 k_3 k_7 k_9^2 \\
& k_{11}^2 - k_1 k_5^2 k_7 k_8 k_9 k_{10} - k_1 k_5^2 k_7 k_9^2 k_{10} - 2 k_1 k_5 k_6 k_7 k_8 k_9 k_{10} - 2 k_1 k_5 k_6 k_7 k_9^2 k_{10} \\
& - k_1 k_5 k_6 k_8 k_9 k_{10}^2 - k_1 k_5 k_6 k_9^2 k_{10}^2 - k_1 k_5 k_7 k_8 k_9 k_{10}^2 - k_1 k_5 k_7 k_8 k_9 k_{10} k_{11} \\
& - k_1 k_5 k_7 k_9^2 k_{10}^2 - k_1 k_5 k_7 k_9^2 k_{10} k_{11} - k_1 k_6^2 k_7 k_8 k_9 k_{10} - k_1 k_6^2 k_7 k_9^2 k_{10} - k_1 \\
& k_6^2 k_8 k_9 k_{10}^2 - k_1 k_6^2 k_9^2 k_{10}^2 - k_1 k_6 k_7 k_8 k_9 k_{10}^2 - k_1 k_6 k_7 k_8 k_9 k_{10} k_{11} - k_1 k_6 k_7 k_9^2 k_{10}^2 \\
& - k_1 k_6 k_7 k_9^2 k_{10} k_{11} - k_2^2 k_4 k_5 k_6 k_8^2 - k_2^2 k_4 k_5 k_6 k_8 k_9 - k_2^2 k_4 k_5 k_7 k_8^2 - \\
& k_2^2 k_4 k_5 k_7 k_8 k_9 - k_2^2 k_4 k_6^2 k_8^2 - k_2^2 k_4 k_6^2 k_8 k_9 - k_2^2 k_4 k_6 k_7 k_8^2 - k_2^2 k_4 k_6 k_7 k_8 k_9 - \\
& k_2^2 k_4 k_6 k_8^2 k_{11} - k_2^2 k_4 k_6 k_8 k_9 k_{11} - k_2^2 k_4 k_7 k_8^2 k_{11} - k_2^2 k_4 k_7 k_8 k_9 k_{11} \\
& - 2 k_2 k_3 k_4 k_5 k_6 k_8^2 - 2 k_2 k_3 k_4 k_5 k_6 k_8 k_9 - 2 k_2 k_3 k_4 k_5 k_7 k_8^2 - 2 k_2 k_3 k_4 k_5 k_7 k_8 k_9 \\
& - k_2 k_3 k_4 k_5 k_8^2 k_{11} - k_2 k_3 k_4 k_5 k_8 k_9 k_{11} - 2 k_2 k_3 k_4 k_6^2 k_8^2 - 2 k_2 k_3 k_4 k_6^2 k_8 k_9 \\
& - 2 k_2 k_3 k_4 k_6 k_7 k_8^2 - 2 k_2 k_3 k_4 k_6 k_7 k_8 k_9 - 3 k_2 k_3 k_4 k_6 k_8^2 k_{11} \\
& - 3 k_2 k_3 k_4 k_6 k_8 k_9 k_{11} - 2 k_2 k_3 k_4 k_7 k_8^2 k_{11} - 2 k_2 k_3 k_4 k_7 k_8 k_9 k_{11} - k_2 k_3 k_4 k_8^2 k_{11}^2 \\
& - k_2 k_3 k_4 k_8 k_9 k_{11}^2 - 2 k_2 k_4 k_5 k_6 k_8^2 k_{10} - 2 k_2 k_4 k_5 k_6 k_8 k_9 k_{10} - 2 k_2 k_4 k_5 k_7 k_8^2 k_{10} \\
& - k_2 k_4 k_5 k_7 k_8^2 k_{11} - 2 k_2 k_4 k_5 k_7 k_8 k_9 k_{10} - k_2 k_4 k_5 k_7 k_8 k_9 k_{11} - 2 k_2 k_4 k_6^2 k_8^2 k_{10} \\
& - 2 k_2 k_4 k_6^2 k_8 k_9 k_{10} - 2 k_2 k_4 k_6 k_7 k_8^2 k_{10} - k_2 k_4 k_6 k_7 k_8^2 k_{11} - 2 k_2 k_4 k_6 k_7 k_8 k_9 k_{10} \\
& - k_2 k_4 k_6 k_7 k_8 k_9 k_{11} - k_2 k_4 k_6 k_8^2 k_{10} k_{11} - k_2 k_4 k_6 k_8 k_9 k_{10} k_{11} - k_2 k_4 k_7 k_8^2 k_{10} k_{11} \\
& - k_2 k_4 k_7 k_8^2 k_{11}^2 - k_2 k_4 k_7 k_8 k_9 k_{10} k_{11} - k_2 k_4 k_7 k_8 k_9 k_{11}^2 - k_3^2 k_4 k_5 k_6 k_8^2 - \\
& k_3^2 k_4 k_5 k_6 k_8 k_9 - k_3^2 k_4 k_5 k_7 k_8^2 - k_3^2 k_4 k_5 k_7 k_8 k_9 - k_3^2 k_4 k_5 k_8^2 k_{11} - k_3^2 k_4 k_5 k_8 k_9 k_{11} \\
& - k_3^2 k_4 k_6^2 k_8^2 - k_3^2 k_4 k_6^2 k_8 k_9 - k_3^2 k_4 k_6 k_7 k_8^2 - k_3^2 k_4 k_6 k_7 k_8 k_9 - 2 k_3^2 k_4 k_6 k_8^2 k_{11} - 2 \\
& k_3^2 k_4 k_6 k_8 k_9 k_{11} - k_3^2 k_4 k_7 k_8^2 k_{11} - k_3^2 k_4 k_7 k_8 k_9 k_{11} - k_3^2 k_4 k_8^2 k_{11}^2 - k_3^2 k_4 k_8 k_9 k_{11}^2 \\
& - 2 k_3 k_4 k_5 k_6 k_8^2 k_{10} - 2 k_3 k_4 k_5 k_6 k_8 k_9 k_{10} - 2 k_3 k_4 k_5 k_7 k_8^2 k_{10} - k_3 k_4 k_5 k_7 k_8^2 k_{11} \\
& - 2 k_3 k_4 k_5 k_7 k_8 k_9 k_{10} - k_3 k_4 k_5 k_7 k_8 k_9 k_{11} - k_3 k_4 k_5 k_8^2 k_{10} k_{11}
\end{aligned}$$

$$\begin{aligned}
& -k_3 k_4 k_5 k_8 k_9 k_{10} k_{11} - 2 k_3 k_4 k_6^2 k_8^2 k_{10} - 2 k_3 k_4 k_6^2 k_8 k_9 k_{10} - 2 k_3 k_4 k_6 k_7 k_8^2 k_{10} \\
& - k_3 k_4 k_6 k_7 k_8^2 k_{11} - 2 k_3 k_4 k_6 k_7 k_8 k_9 k_{10} - k_3 k_4 k_6 k_7 k_8 k_9 k_{11} - 2 k_3 k_4 k_6 \\
& k_8^2 k_{10} k_{11} - 2 k_3 k_4 k_6 k_8 k_9 k_{10} k_{11} - k_3 k_4 k_7 k_8^2 k_{10} k_{11} - k_3 k_4 k_7 k_8^2 k_{11}^2 \\
& - k_3 k_4 k_7 k_8 k_9 k_{10} k_{11} - k_3 k_4 k_7 k_8 k_9 k_{11}^2 - k_4 k_5 k_6 k_8^2 k_{10}^2 - k_4 k_5 k_6 k_8 k_9 k_{10}^2 \\
& - k_4 k_5 k_7 k_8^2 k_{10}^2 - k_4 k_5 k_7 k_8^2 k_{10} k_{11} - k_4 k_5 k_7 k_8 k_9 k_{10}^2 - k_4 k_5 k_7 k_8 k_9 k_{10} k_{11} - k_4 \\
& k_6^2 k_8^2 k_{10}^2 - k_4 k_6^2 k_8 k_9 k_{10}^2 - k_4 k_6 k_7 k_8^2 k_{10}^2 - k_4 k_6 k_7 k_8^2 k_{10} k_{11} - k_4 k_6 k_7 k_8 k_9 k_{10}^2 \\
& - k_4 k_6 k_7 k_8 k_9 k_{10} k_{11} \Big) x_3 - 2 k_2^2 k_6 k_7 k_8 k_9 k_{11} - 2 k_2 k_3 k_5^2 k_7 k_8 k_9 - 4 k_2 k_3 k_5 k_6 k_7 \\
& k_9^2 - 4 k_2 k_3 k_5 k_7 k_9^2 k_{11} - 2 k_2 k_3 k_6^2 k_7 k_8 k_9 - 4 k_2 k_3 k_6 k_7 k_9^2 k_{11} - 2 k_2 k_3 k_7 k_8 k_9 k_{11}^2 \\
& - 2 k_2 k_5^2 k_7 k_8 k_9 k_{10} - 4 k_2 k_5 k_6 k_7 k_9^2 k_{10} - 2 k_2 k_5 k_7 k_9^2 k_{10} k_{11} - 2 k_2 k_6^2 k_7 k_8 k_9 k_{10} \\
& - 2 k_2 k_6 k_7 k_9^2 k_{10} k_{11} - 2 k_3^2 k_5 k_6 k_7 k_8 k_9 - 2 k_3^2 k_5 k_7 k_8 k_9 k_{11} - 2 k_3^2 k_6 k_7 k_8 k_9 k_{11} \\
& - 2 k_3 k_5^2 k_7 k_8 k_9 k_{10} - 4 k_3 k_5 k_6 k_7 k_9^2 k_{10} - 2 k_3 k_5 k_7 k_9^2 k_{10} k_{11} - 2 k_3 k_6^2 k_7 k_8 k_9 k_{10} \\
& - 2 k_3 k_6 k_7 k_9^2 k_{10} k_{11} - 2 k_5 k_6 k_7 k_8 k_9 k_{10}^2 - 2 k_2^2 k_5 k_6 k_7 k_8 k_9 - 2 k_2^2 k_5 k_7 k_8 k_9 k_{11} \\
& + \left(k_1^2 k_3 k_4 k_5 k_9 k_{10} - k_1^2 k_3 k_4 k_5 k_{10} k_{11} + k_1^2 k_3 k_4 k_6 k_9 k_{10} - k_1^2 k_3 k_4 k_6 k_{10} k_{11} - \right. \\
& k_1^2 k_4 k_5 k_6 k_9 k_{10} - k_1^2 k_4 k_5 k_6 k_{10}^2 - k_1^2 k_4 k_5 k_7 k_{10}^2 - k_1^2 k_4 k_5 k_7 k_{10} k_{11} - k_1^2 k_4 \\
& k_6^2 k_9 k_{10} - k_1^2 k_4 k_6^2 k_{10}^2 - k_1^2 k_4 k_6 k_7 k_{10}^2 - k_1^2 k_4 k_6 k_7 k_{10} k_{11} - k_1 k_2 k_3 k_4^2 k_8 k_{11} \\
& - k_1 k_2 k_3 k_4^2 k_{11}^2 + k_1 k_2 k_4^2 k_6 k_8 k_{11} - k_1 k_2 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_2 \\
& k_4^2 k_7 k_{11}^2 - k_1 k_3^2 k_4^2 k_8 k_{11} - k_1 k_3^2 k_4^2 k_{11}^2 + k_1 k_3 k_4^2 k_6 k_8 k_{11} - k_1 k_3 k_4^2 k_6 k_{10} k_{11} \\
& - k_1 k_3 k_4^2 k_7 k_{10} k_{11} - k_1 k_3 k_4^2 k_7 k_{11}^2 \Big) x_1^2 x_3 + \left(-2 k_1 k_2 k_3 k_4 k_5 k_8 k_{11} \right. \\
& - 2 k_1 k_2 k_3 k_4 k_5 k_9 k_{11} - 2 k_1 k_2 k_3 k_4 k_6 k_8 k_{11} - 2 k_1 k_2 k_3 k_4 k_6 k_9 k_{11} \\
& - 2 k_1 k_2 k_3 k_4 k_8 k_{11}^2 - 2 k_1 k_2 k_3 k_4 k_9 k_{11}^2 - 2 k_1 k_2 k_4 k_5 k_6 k_8 k_{10} \\
& - 2 k_1 k_2 k_4 k_5 k_6 k_9 k_{10} - 2 k_1 k_2 k_4 k_5 k_7 k_8 k_{10} - 2 k_1 k_2 k_4 k_5 k_7 k_8 k_{11} \\
& - 2 k_1 k_2 k_4 k_5 k_7 k_9 k_{10} - 2 k_1 k_2 k_4 k_5 k_7 k_9 k_{11} - 2 k_1 k_2 k_4 k_6^2 k_8 k_{10} - 2 k_1 k_2 k_4 \\
& k_6^2 k_9 k_{10} - 2 k_1 k_2 k_4 k_6 k_7 k_8 k_{10} - 2 k_1 k_2 k_4 k_6 k_7 k_8 k_{11} - 2 k_1 k_2 k_4 k_6 k_7 k_9 k_{10} \\
& - 2 k_1 k_2 k_4 k_6 k_7 k_9 k_{11} - 2 k_1 k_2 k_4 k_6 k_8 k_{10} k_{11} - 2 k_1 k_2 k_4 k_6 k_9 k_{10} k_{11} \\
& - 2 k_1 k_2 k_4 k_7 k_8 k_{10} k_{11} - 2 k_1 k_2 k_4 k_7 k_8 k_{11}^2 - 2 k_1 k_2 k_4 k_7 k_9 k_{10} k_{11} \\
& - 2 k_1 k_2 k_4 k_7 k_9 k_{11}^2 - 2 k_1 k_3^2 k_4 k_5 k_8 k_{11} - 2 k_1 k_3^2 k_4 k_5 k_9 k_{11} - 2 k_1 k_3^2 k_4 k_6 k_8 k_{11} \\
& - 2 k_1 k_3^2 k_4 k_6 k_9 k_{11} - 2 k_1 k_3^2 k_4 k_8 k_{11}^2 - 2 k_1 k_3^2 k_4 k_9 k_{11}^2 - 2 k_1 k_3 k_4 k_5 k_6 k_8 k_{10}
\end{aligned}$$

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

We look at the coefficients of mpol in x1 and x3 that do not have necessarily negative sign. (????)

I did it manually, but I only see one such term:

$$\begin{aligned}
> \text{term} := & \left(k_1^2 k_3 k_4 k_5 k_9 k_{10} - k_1^2 k_3 k_4 k_5 k_{10} k_{11} + k_1^2 k_3 k_4 k_6 k_9 k_{10} - k_1^2 k_3 k_4 k_6 k_{10} k_{11} - \right. \\
& k_1^2 k_4 k_5 k_6 k_9 k_{10} - k_1^2 k_4 k_5 k_6 k_{10}^2 - k_1^2 k_4 k_5 k_7 k_{10}^2 - k_1^2 k_4 k_5 k_7 k_{10} k_{11} - k_1^2 k_4 k_6^2 k_9 k_{10} \\
& - k_1^2 k_4 k_6^2 k_{10}^2 - k_1^2 k_4 k_6 k_7 k_{10}^2 - k_1^2 k_4 k_6 k_7 k_{10} k_{11} - k_1 k_2 k_3 k_4^2 k_8 k_{11} - k_1 k_2 k_3 k_4^2 k_{11}^2 \\
& + k_1 k_2 k_4^2 k_6 k_8 k_{11} - k_1 k_2 k_4^2 k_6 k_{10} k_{11} - k_1 k_2 k_4^2 k_7 k_{10} k_{11} - k_1 k_2 k_4^2 k_7 k_{11}^2 - k_1 k_3^2 \\
& k_4^2 k_8 k_{11} - k_1 k_3^2 k_4^2 k_{11}^2 + k_1 k_3 k_4^2 k_6 k_8 k_{11} - k_1 k_3 k_4^2 k_6 k_{10} k_{11} - k_1 k_3 k_4^2 k_7 k_{10} k_{11} \\
& \left. - k_1 k_3 k_4^2 k_7 k_{11}^2 \right) :
\end{aligned}$$

$$\begin{aligned}
> \text{factor}(\text{term}) \\
k_1 k_4 \left(k_1 k_3 k_5 k_9 k_{10} - k_1 k_3 k_5 k_{10} k_{11} + k_1 k_3 k_6 k_9 k_{10} - k_1 k_3 k_6 k_{10} k_{11} - k_1 k_5 k_6 k_9 k_{10} \right. \\
- k_1 k_5 k_6 k_{10}^2 - k_1 k_5 k_7 k_{10}^2 - k_1 k_5 k_7 k_{10} k_{11} - k_1 k_6^2 k_9 k_{10} - k_1 k_6^2 k_{10}^2 - k_1 k_6 k_7 k_{10}^2 \\
- k_1 k_6 k_7 k_{10} k_{11} - k_2 k_3 k_4 k_8 k_{11} - k_2 k_3 k_4 k_{11}^2 + k_2 k_4 k_6 k_8 k_{11} - k_2 k_4 k_6 k_{10} k_{11} \\
- k_2 k_4 k_7 k_{10} k_{11} - k_2 k_4 k_7 k_{11}^2 - k_3^2 k_4 k_8 k_{11} - k_3^2 k_4 k_{11}^2 + k_3 k_4 k_6 k_8 k_{11} \\
\left. - k_3 k_4 k_6 k_{10} k_{11} - k_3 k_4 k_7 k_{10} k_{11} - k_3 k_4 k_7 k_{11}^2 \right) \quad (1.6)
\end{aligned}$$

"Now the trick resides on finding parameters of the rate constants k such that the term is

positive." Thus we try to search parameter set that make *term* positive.

Orignal computation of parameters #####
Now **the trick resides on finding parameters of the rate constants k such that the term is positive.**

For example

```
[> params := {k1 = 10, k2 = 0.01, k3 = 1, k4 = 0.01, k5 = 10, k6 = 100, k7 = 0.1, k8 = 100, k9
= 0.01, k10 = 0.01, k11 = 1} :
> subs(params, term)
6.596777990 (1.7)
```

Once you have such a set, then substitute into the polynomial, and **find values of x1 and x3 such that the polynomial is positive:**

```
[> finalPol2 := subs(params, finalPol)
finalPol2 := -1281.778574 - 0.035806621 x12 - 14.16723525 x1 - 0.000102010 x13
- 1.307843255 106 x3 + 6.596777990 x12 x3 - 4757.559908 x1 x3 (1.8)
```

```
[> finalPol2 := collect(%, x3)
finalPol2 := (-1.307843255 106 + 6.596777990 x12 - 4757.559908 x1) x3 - 1281.778574
- 0.035806621 x12 - 14.16723525 x1 - 0.000102010 x13 (1.9)
```

```
[> x1 := 1000 :
> subs(x1 = x1, finalPol2)
5.31374827 105 x3 - 1.532656348 105 (1.10)
```

```
[> x3 := solve(%, x3)
x3 := 0.2884322460 (1.11)
```

```
[> subs(params, x1 = x1, x3 = x3, finalPol)
0. (1.12)
```

This choice of rate constants and x1 with x3 will give total amounts such that the system has three steady states.

To find the total amounts, we find the values of x2, x4, x5, x6 corresponding to x1 and x3, as given by the expressions above in sol2[1].

Then we substitute these values into the conservation laws:

```
[> solution2 := subs(params, x1 = x1, x3 = x3, solution)
solution2 := [[x2 = 80684.29918, x4 = 573.1872191, x5 = 2878.647339, x6 = 51.89782579]] (1.13)
```

$$\begin{aligned} > B_1 := \text{subs}(\text{solution2}[1], x_1 = x1, x_3 = x3, x_1 + x_2 + x_5 + x_6) \\ & \quad B_1 := 84614.84435 \end{aligned} \quad (1.14)$$

$$\begin{aligned} > B_2 := \text{subs}(\text{solution2}[1], x_1 = x1, x_3 = x3, x_3 + x_4 + x_5 + x_6) \\ & \quad B_2 := 3504.020816 \end{aligned} \quad (1.15)$$

We now check that we have three steady states. We substitute into myeqs the values of the parameters and solve the equations:

$$\begin{aligned} > \text{subs}(\text{params}, T_1 = B_1, T_2 = B_2, \text{subsEqs}) \\ & \quad [-0.1 x_2 + x_5 + 100 x_6, -0.01 x_1 x_4 + 100 x_3 - 0.01 x_4 + 110 x_6, 10 x_1 x_3 - 1.02 x_5 + x_6, \\ & \quad 0.01 x_1 x_4 + 0.01 x_5 - 111 x_6, x_1 + x_2 + x_5 + x_6 - 84614.84435, x_3 + x_4 + x_5 + x_6 \\ & \quad - 3504.020816] \end{aligned} \quad (1.16)$$

$$\begin{aligned} > \text{solutionSS} := \text{solve}(\%) \\ \text{solutionSS} := \{x_1 = 9485.350939, x_2 = 71668.95903, x_3 = 0.03641531393, x_4 \\ & \quad = 43.45001595, x_5 = 3423.096390, x_6 = 37.43799513\}, \{x_1 = 1000.019288, x_2 \\ & \quad = 80684.26702, x_3 = 0.2884280291, x_4 = 573.1743463, x_5 = 2878.660378, x_6 \\ & \quad = 51.89766324\}, \{x_1 = 999.9807131, x_2 = 80684.33135, x_3 = 0.2884364628, x_4 \\ & \quad = 573.2000917, x_5 = 2878.634300, x_6 = 51.89798835\} \end{aligned} \quad (1.17)$$

We find indeed three positive steady states.

The last step is to find their asymptotic stability properties.

To do that, we compute the eigenvalues of the Jacobian of eqs evaluated at the three steady states. Two of them (because there are two conservation laws) should be zero.

Due to numerical issues, we get small numbers instead of zero. We disregard the bottom two eigenvalues.

$$\begin{aligned} > \text{ssEqs} \\ & \quad \begin{bmatrix} -k_1 x_1 x_3 - k_4 x_1 x_4 + k_2 x_5 + k_5 x_6 + k_7 x_2 \\ k_3 x_5 + k_6 x_6 - k_7 x_2 \\ -k_1 x_1 x_3 + k_2 x_5 + k_3 x_5 - k_8 x_3 + k_9 x_4 \\ -k_4 x_1 x_4 + k_5 x_6 + k_6 x_6 + k_8 x_3 - k_9 x_4 \\ k_1 x_1 x_3 - k_2 x_5 - k_3 x_5 - k_{10} x_5 + k_{11} x_6 \\ k_4 x_1 x_4 - k_5 x_6 - k_6 x_6 + k_{10} x_5 - k_{11} x_6 \end{bmatrix} \end{aligned} \quad (1.18)$$

$$> J := \text{VectorCalculus}[\text{Jacobian}](\text{ssEqs}, [\text{seq}(x_i, i = 1..6)])$$

$$J := \begin{bmatrix} -k_1 x_3 - k_4 x_4 & k_7 & -k_1 x_1 & -k_4 x_1 & k_2 & k_5 \\ 0 & -k_7 & 0 & 0 & k_3 & k_6 \\ -k_1 x_3 & 0 & -k_1 x_1 - k_8 & k_9 & k_2 + k_3 & 0 \\ -k_4 x_4 & 0 & k_8 & -k_4 x_1 - k_9 & 0 & k_5 + k_6 \\ k_1 x_3 & 0 & k_1 x_1 & 0 & -k_2 - k_3 - k_{10} & k_{11} \\ k_4 x_4 & 0 & 0 & k_4 x_1 & k_{10} & -k_5 - k_6 - k_{11} \end{bmatrix} \quad (1.19)$$

> subs(params, solutionSS[1], J); Eigenvalues(%)

$$\begin{bmatrix} -0.7986532988 & 0.1 & -94853.50939 & -94.85350939 & 0.01 & 10 \\ 0 & -0.1 & 0 & 0 & 1 & 100 \\ -0.3641531393 & 0 & -94953.50939 & 0.01 & 1.01 & 0 \\ -0.4345001595 & 0 & 100 & -94.86350939 & 0 & 110 \\ 0.3641531393 & 0 & 94853.50939 & 0 & -1.02 & 1 \\ 0.4345001595 & 0 & 0 & 94.85350939 & 0.01 & -111 \end{bmatrix}$$

$$\begin{bmatrix} -94954.8821040290 + 0. \text{I} \\ -205.617900135784 + 0. \text{I} \\ -0.741304286052932 + 0. \text{I} \\ -0.0502442377746779 + 0. \text{I} \\ -2.29666343149062 \cdot 10^{-14} + 0. \text{I} \\ -1.54079147505976 \cdot 10^{-10} + 0. \text{I} \end{bmatrix}$$

(1.20)

> subs(params, solutionSS[2], J); Eigenvalues(%)

$$\begin{bmatrix} -8.616023754 & 0.1 & -10000.19288 & -10.00019288 & 0.01 & 10 \\ 0 & -0.1 & 0 & 0 & 1 & 100 \\ -2.884280291 & 0 & -10100.19288 & 0.01 & 1.01 & 0 \\ -5.731743463 & 0 & 100 & -10.01019288 & 0 & 110 \\ 2.884280291 & 0 & 10000.19288 & 0 & -1.02 & 1 \\ 5.731743463 & 0 & 0 & 10.00019288 & 0.01 & -111 \end{bmatrix}$$

(1.21)

$$\begin{bmatrix} -10104.0500258180 + 0. I \\ -121.899052736275 + 0. I \\ -4.99001861764499 + 0. I \\ 4.78856057554162 \cdot 10^{-7} + 0. I \\ 5.90299837429996 \cdot 10^{-8} + 0. I \\ -6.62696688098225 \cdot 10^{-14} + 0. I \end{bmatrix} \quad (1.21)$$

> *subs(params, solutionSS[3], J); Eigenvalues(%)*

$$\begin{bmatrix} -8.616365545 & 0.1 & -9999.807131 & -9.999807131 & 0.01 & 10 \\ 0 & -0.1 & 0 & 0 & 1 & 100 \\ -2.884364628 & 0 & -10099.80713 & 0.01 & 1.01 & 0 \\ -5.732000917 & 0 & 100 & -10.00980713 & 0 & 110 \\ 2.884364628 & 0 & 9999.807131 & 0 & -1.02 & 1 \\ 5.732000917 & 0 & 0 & 9.999807131 & 0.01 & -111 \end{bmatrix}$$

$$\begin{bmatrix} -10103.6643580139 + 0. I \\ -121.898700136404 + 0. I \\ -4.99024398796287 + 0. I \\ -0.00000713107524108617 + 0. I \\ 0.00000659432624812686 + 0. I \\ -9.65253945655092 \cdot 10^{-13} + 0. I \end{bmatrix} \quad (1.22)$$

>