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

Simplification of minimal system extend 4

We consider the following reactions:

K + S <-> K_S -> K + Sp
Sp->S
A + K <-> A_K
A_K + S <-> A_K_S
A + K_S <-> A_K_S
A_K_S -> A_K + Sp

$$K + S \rightleftharpoons KS \rightarrow K + S_p$$
$$S_p \rightarrow S$$
$$A + K \rightleftharpoons AK$$
$$AK + S \rightleftharpoons AKS$$
$$A + KS \rightleftharpoons AKS$$
$$AKS \rightarrow AK + S_p$$

The species of the networ are (in parentesis the order in which I consider them)

{S (1) , Sp (2) , K (3) , A (4), K_S (5), A_K (6), A_K_S (7) }

There are a total of 11 reactions and 7 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, 7) :
> A[1, 1] := -1 : A[1, 3] := -1 : A[1, 5] := 1 : A[2] := -A[1] :
```

> $A[3,3] := 1 : A[3,2] := 1 : A[3,5] := -1 :$
> $A[4,2] := -1 : A[4,1] := 1 :$
> $A[5,4] := -1 : A[5,3] := -1 : A[5,6] := 1 : A[6] := -A[5] :$
> $A[7,6] := -1 : A[7,1] := -1 : A[7,7] := 1 : A[8] := -A[7] :$
> $A[9,4] := -1 : A[9,5] := -1 : A[9,7] := 1 : A[10] := -A[9] :$
> $A[11,7] := -1 : A[11,6] := 1 : A[11,2] := 1 :$
> $A := Transpose(A) :$

Vector of rates:

here x_i is the concentration of the i-th species

> $ks := Vector([k_1 \cdot x_3 \cdot x_1, k_2 \cdot x_5, k_3 \cdot x_5, k_4 \cdot x_2, k_5 \cdot x_3 \cdot x_4, k_6 \cdot x_6, k_1 \cdot x_1 \cdot x_6, k_2 \cdot x_7, k_5 \cdot x_4 \cdot x_5, k_6 \cdot x_7, k_3 \cdot x_7])$

$$ks := \begin{bmatrix} k_1 x_3 x_1 \\ k_2 x_5 \\ k_3 x_5 \\ k_4 x_2 \\ k_5 x_3 x_4 \\ k_6 x_6 \\ k_1 x_1 x_6 \\ k_2 x_7 \\ k_5 x_4 x_5 \\ k_6 x_7 \\ k_3 x_7 \end{bmatrix} \qquad \textbf{(1)}$$

Steady state equations:

> $ssEqs := A.ks$

(2)

$$ssEqs := \begin{bmatrix} -k_1 x_1 x_3 - k_1 x_1 x_6 + k_2 x_5 + k_2 x_7 + k_4 x_2 \\ k_3 x_5 + k_3 x_7 - k_4 x_2 \\ -k_1 x_1 x_3 - k_5 x_3 x_4 + k_2 x_5 + k_3 x_5 + k_6 x_6 \\ -k_5 x_3 x_4 - k_5 x_4 x_5 + k_6 x_6 + k_6 x_7 \\ k_1 x_1 x_3 - k_5 x_4 x_5 - k_2 x_5 - k_3 x_5 + k_6 x_7 \\ -k_1 x_1 x_6 + k_5 x_3 x_4 + k_2 x_7 + k_3 x_7 - k_6 x_6 \\ k_1 x_1 x_6 + k_5 x_4 x_5 - k_2 x_7 - k_3 x_7 - k_6 x_7 \end{bmatrix} \quad \textbf{(2)}$$

Conservation laws:

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

> $F := ReducedRowEchelonForm(Transpose(Matrix([op(NullSpace(Transpose(A)))])))$

$$F := \begin{bmatrix} 1 & 1 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 0 & 1 & 1 & 1 \\ 0 & 0 & 0 & 1 & 0 & 1 & 1 \end{bmatrix} \quad \textbf{(3)}$$

>

the conservation laws are:

$x_1 + x_2 + x_5 + x_7 - T_1, x_3 + x_7 + x_5 + x_6 - T_2, x_4 + x_6 + x_7 - T_3$

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).

> $subsEqs := [ssEqs[2], ssEqs[6], ssEqs[5], ssEqs[7], x_1 + x_2 + x_5 + x_7 - T_1, x_3 + x_7 + x_5 + x_6 - T_2, x_4 + x_6 + x_7 - T_3]$

$$subsEqs := [k_3 x_5 + k_3 x_7 - k_4 x_2, -k_1 x_1 x_6 + k_5 x_3 x_4 + k_2 x_7 + k_3 x_7 - k_6 x_6, k_1 x_1 x_3 - k_5 x_4 x_5 - k_2 x_5 - k_3 x_5 + k_6 x_7, k_1 x_1 x_6 + k_5 x_4 x_5 - k_2 x_7 - k_3 x_7 - k_6 x_7, x_1 + x_2 + x_5 + x_7 - T_1, x_3 + x_7 + x_5 + x_6 - T_2, x_4 + x_6 + x_7 - T_3] \quad \textbf{(4)}$$

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)

> $J := VectorCalculus[Jacobian]\left(subsEqs, \left[seq\left(x_i, i = 1..7\right)\right]\right)$

$$J := \begin{bmatrix} 0 & -k_4 & 0 & 0 & k_3 & 0 & k_3 \\ -k_1 x_6 & 0 & k_5 x_4 & k_5 x_3 & 0 & -k_1 x_1 - k_6 & k_2 + k_3 \\ k_1 x_3 & 0 & k_1 x_1 & -k_5 x_5 & -k_5 x_4 - k_2 - k_3 & 0 & k_6 \\ k_1 x_6 & 0 & 0 & k_5 x_5 & k_5 x_4 & k_1 x_1 & -k_2 - k_3 - k_6 \\ 1 & 1 & 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 0 & 1 & 1 & 1 \\ 0 & 0 & 0 & 1 & 0 & 1 & 1 \end{bmatrix} \tag{1.1}$$

> $Determinant(J)$:

> $detJ := collect\left(\%, \left\{seq\left(x_i, i = 1..7\right)\right\}, 'distributed'\right)$

$$detJ := -k_1^2 k_4 k_6 x_1^2 + \left(-k_1^2 k_3 k_5 - k_1^2 k_4 k_5\right) x_1 x_3^2 + \left(-k_1^2 k_3 k_6 - k_1^2 k_4 k_6 - 2 k_1 k_2 k_4 k_5 - 2 k_1 k_3 k_4 k_5 - k_1 k_4 k_5 k_6\right) x_1 x_3 + \left(-2 k_1 k_2 k_4 k_5 - 2 k_1 k_3 k_4 k_5 - 2 k_1 k_4 k_5 k_6\right) x_1 x_4 + \left(-2 k_1 k_2 k_4 k_5 - 2 k_1 k_3 k_4 k_5 - k_1 k_4 k_5 k_6\right) x_1 x_5 + \left(-k_1^2 k_3 k_6 - k_1^2 k_4 k_6\right) x_1 x_6 + \left(-k_1 k_3 k_5^2 - k_1 k_4 k_5^2\right) x_3^2 x_4 + \left(-k_1 k_3 k_5^2 - k_1 k_4 k_5^2\right) x_3 x_4^2 + \left(-k_1 k_2 k_3 k_5 - k_1 k_2 k_4 k_5 - k_1 k_3^2 k_5 - k_1 k_3 k_4 k_5 - 2 k_1 k_3 k_5 k_6 - 2 k_1 k_4 k_5 k_6 - k_2 k_4 k_5^2 - k_3 k_4 k_5^2\right) x_3 x_4 + \left(-k_1 k_2 k_3 k_5 - k_1 k_2 k_4 k_5 - k_1 k_3^2 k_5 - k_1 k_3 k_4 k_5 - k_1 k_3 k_5 k_6 - k_1 k_4 k_5 k_6\right) x_3 x_5 + \left(-k_1 k_2 k_3 k_5 - k_1 k_2 k_4 k_5 - k_1 k_3^2 k_5 - k_1 k_3 k_4 k_5 - k_1 k_3 k_5 k_6 - k_1 k_4 k_5 k_6\right) x_3 x_6 + \left(-k_1 k_3 k_5^2 - k_1 k_4 k_5^2\right) x_4^2 x_6 + \left(-k_2 k_4 k_5^2 - k_3 k_4 k_5^2\right) x_4 x_5 + \left(-k_1 k_2 k_3 k_5 - k_1 k_2 k_4 k_5 - k_1 k_3^2 k_5 - k_1 k_3 k_4 k_5 - 2 k_1 k_3 k_5 k_6 - 2 k_1 k_4 k_5 k_6\right) x_4 x_6 + \left(-k_1 k_2 k_3 k_5 - k_1 k_2 k_4 k_5 - k_1 k_3^2 k_5 - k_1 k_3 k_4 k_5 - k_1 k_3 k_5 k_6 - k_1 k_4 k_5 k_6\right) x_5 x_6 - 2 k_2 k_3 k_4 k_6 - k_1 k_4 k_5^2 x_1 x_4 x_5 - k_1^2 k_4 k_5 x_1^2 x_3 - k_1^2 k_4 k_5 x_1^2 x_4 - k_1^2 k_4 k_5 x_1^2 x_5 + \left(-k_1^2 k_3 k_5 - k_1^2 k_4 k_5 - k_1 k_4 k_5^2\right) x_1 x_3 x_4 + \left(-k_1^2 k_3 k_5 - k_1^2 k_4 k_5\right) x_1 x_3 x_5 + \left(-k_1^2 k_3 k_5 - k_1^2 k_4 k_5\right) x_1 x_3 x_6 - k_1 k_4 k_5^2 x_1 x_4^2 + \left(-k_1^2 k_3 k_5 - k_1^2 k_4 k_5\right) x_1 x_4 x_6 + \left(-k_1^2 k_3 k_5 - k_1^2 k_4 k_5\right) x_1 x_5 x_6 + \left(-k_1 k_3 k_5^2 - k_1 k_4 k_5^2\right) x_3 x_4 x_5 + \left(-k_1 k_3 k_5^2 - k_1 k_4 k_5^2\right) x_3 x_4 x_6 + \left(-k_1 k_3 k_5^2 - k_1 k_4 k_5^2\right) x_4 x_5 x_6 + \left(-2 k_1 k_2 k_4 k_6 \right.$$

(1.2)

$$- 2 k_1 k_3 k_4 k_6 - k_1 k_4 k_6^2 \big) x_1 + \big(-k_1 k_2 k_3 k_6 - k_1 k_2 k_4 k_6 - k_1 k_3^2 k_6 - k_1 k_3 k_4 k_6 - k_1 k_3 k_6^2 - k_1 k_4 k_6^2 - k_2^2 k_4 k_5 - 2 k_2 k_3 k_4 k_5 - k_2 k_4 k_5 k_6 - k_3^2 k_4 k_5 - k_3 k_4 k_5 k_6 \big) x_3 + \big(-k_2 k_4 k_5^2 - k_3 k_4 k_5^2 \big) x_4^2 + \big(-k_2^2 k_4 k_5 - 2 k_2 k_3 k_4 k_5 - 2 k_2 k_4 k_5 k_6 - k_3^2 k_4 k_5 - 2 k_3 k_4 k_5 k_6 \big) x_4 + \big(-k_2^2 k_4 k_5 - 2 k_2 k_3 k_4 k_5 - k_2 k_4 k_5 k_6 - k_3^2 k_4 k_5 - k_3 k_4 k_5 k_6 \big) x_5 + \big(-k_1 k_2 k_3 k_6 - k_1 k_2 k_4 k_6 - k_1 k_3^2 k_6 - k_1 k_3 k_4 k_6 - k_1 k_3 k_6^2 - k_1 k_4 k_6^2 \big) x_6 - k_2^2 k_4 k_6 - k_2 k_4 k_6^2 - k_3^2 k_4 k_6 - k_3 k_4 k_6^2 + \big(-k_1 k_2 k_3 k_5 - k_1 k_2 k_4 k_5 - k_1 k_3^2 k_5 - k_1 k_3 k_4 k_5 - k_1 k_3 k_5 k_6 - k_1 k_4 k_5 k_6 \big) x_3^2$$

We parameterise the steady states as functions of x1 and x3, using the four steady state equations: When x1 and x3 are positive, then so are the rest.

```
> solution := solve([ssEqs[1], ssEqs[2], ssEqs[3], ssEqs[4]], [x2, x5, x7, x6])
```

$$solution := \left[\left[x_2 = \frac{x_3 x_1 k_3 k_1 (k_5 x_4 + k_6)}{k_6 k_4 (k_2 + k_3)}, x_5 = \frac{x_3 x_1 k_1}{k_2 + k_3}, x_7 = \frac{k_5 x_4 k_1 x_1 x_3}{k_6 (k_2 + k_3)}, x_6 = \frac{k_5 x_4 x_3}{k_6}\right]\right] \quad \textbf{(1.3)}$$

We evaluate the determinant of the Jacobian at the parameterisation. We then write it as a polynomial in x1 and x3

```
> detSubs := subs(solution[1], detJ) :
> polSubs := numer(detSubs) :
> finalPol := collect(polSubs, {x1, x3, x4},'distributed')
```

$$finalPol := \big(-k_1^3 k_3 k_5^2 - k_1^3 k_4 k_5^2 \big) x_1^2 x_3^2 x_4 + \big(-k_1^2 k_3 k_5^3 - k_1^2 k_4 k_5^3 \big) x_1 x_3^2 x_4^2 + \big(-2 k_1^2 k_2 k_3 k_5^2 - 2 k_1^2 k_2 k_4 k_5^2 - 2 k_1^2 k_3^2 k_5^2 - 2 k_1^2 k_3 k_4 k_5^2 - 2 k_1^2 k_3 k_5^2 k_6 - 2 k_1^2 k_4 k_5^2 k_6 \big) x_1 x_3^2 x_4 + \big(-k_1^2 k_2 k_3 k_5^2 - k_1^2 k_2 k_4 k_5^2 - k_1^2 k_3^2 k_5^2 - k_1^2 k_3 k_4 k_5^2 \big) x_1 x_3 x_4^2 + \big(-2 k_1^2 k_2 k_3 k_5 k_6 - 2 k_1^2 k_2 k_4 k_5 k_6 - 2 k_1^2 k_3^2 k_5 k_6 - 2 k_1^2 k_3 k_4 k_5 k_6 - 2 k_1 k_2 k_4 k_5^2 k_6 - 2 k_1 k_3 k_4 k_5^2 k_6 \big) x_1 x_3 x_4 + \big(-k_1 k_2^2 k_3 k_5 k_6 - k_1 k_2^2 k_4 k_5 k_6 - 2 k_1 k_2 k_3^2 k_5 k_6 - 2 k_1 k_2 k_3 k_4 k_5 k_6 - k_1 k_2 k_3 k_5 k_6^2 - k_1 k_2 k_4 k_5 k_6^2 - k_1 k_3^3 k_5 k_6 - k_1 k_3^2 k_4 k_5 k_6 - k_1 k_3^2 k_5 k_6^2 - k_1 k_3 k_4 k_5 k_6^2 \big) x_3^2 + \big(-2 k_1 k_2^2 k_4 k_6^2 - 4 k_1 k_2 k_3 k_4 k_6^2 - k_1 k_2 k_4 k_6^3 - 2 k_1 k_3^2 k_4 k_6^2 - k_1 k_3 k_4 k_6^3 \big) x_1 + \big(-k_2^2 k_4 k_5^2 k_6 - 2 k_2 k_3 k_4 k_5^2 k_6 - k_3^2 k_4 k_5^2 k_6 \big) x_4^2 + \big(-k_1 k_2^2 k_3 k_6^2 \quad \textbf{(1.4)}$$

$$
\begin{aligned}
& - k_1 k_2^2 k_4 k_6^2 - 2 k_1 k_2 k_3^2 k_6^2 - 2 k_1 k_2 k_3 k_4 k_6^2 - k_1 k_2 k_3 k_6^3 - k_1 k_2 k_4 k_6^3 - k_1 k_3^3 k_6^2 \\
& - k_1 k_3^2 k_4 k_6^2 - k_1 k_3^2 k_6^3 - k_1 k_3 k_4 k_6^3 - k_2^3 k_4 k_5 k_6 - 3 k_2^2 k_3 k_4 k_5 k_6 - k_2^2 k_4 k_5 k_6^2 \\
& - 3 k_2 k_3^2 k_4 k_5 k_6 - 2 k_2 k_3 k_4 k_5 k_6^2 - k_3^3 k_4 k_5 k_6 - k_3^2 k_4 k_5 k_6^2) x_3 + (-k_2^3 k_4 k_5 k_6 - 3 \\
& k_2^2 k_3 k_4 k_5 k_6 - 2 k_2^2 k_4 k_5 k_6^2 - 3 k_2 k_3^2 k_4 k_5 k_6 - 4 k_2 k_3 k_4 k_5 k_6^2 - k_3^3 k_4 k_5 k_6 - 2 \\
& k_3^2 k_4 k_5 k_6^2) x_4 + (-k_1^2 k_2 k_4 k_6^2 - k_1^2 k_3 k_4 k_6^2) x_1^2 - k_2^3 k_4 k_6^2 - k_2^2 k_4 k_6^3 - k_3^3 k_4 k_6^2 - \\
& k_3^2 k_4 k_6^3 + (-k_1^3 k_3 k_5 k_6 - k_1^3 k_4 k_5 k_6) x_1^2 x_3^2 + (-3 k_1^2 k_2 k_4 k_5 k_6 - 3 k_1^2 k_3 k_4 k_5 k_6 - \\
& k_1^2 k_4 k_5 k_6^2) x_1^2 x_3 + (-k_1^2 k_2 k_4 k_5 k_6 - k_1^2 k_3 k_4 k_5 k_6) x_1^2 x_4 + (-2 k_1^2 k_2 k_3 k_5 k_6 - 2 \\
& k_1^2 k_2 k_4 k_5 k_6 - 2 k_1^2 k_3^2 k_5 k_6 - 2 k_1^2 k_3 k_4 k_5 k_6 - k_1^2 k_3 k_5 k_6^2 - k_1^2 k_4 k_5 k_6^2) x_1 x_3^2 + (- \\
& k_1^2 k_2 k_3 k_6^2 - k_1^2 k_2 k_4 k_6^2 - k_1^2 k_3^2 k_6^2 - k_1^2 k_3 k_4 k_6^2 - 3 k_1 k_2^2 k_4 k_5 k_6 - 6 k_1 k_2 k_3 k_4 k_5 k_6 \\
& - 2 k_1 k_2 k_4 k_5 k_6^2 - 3 k_1 k_3^2 k_4 k_5 k_6 - 2 k_1 k_3 k_4 k_5 k_6^2) x_1 x_3 + (-k_1 k_2 k_4 k_5^2 k_6 \\
& - k_1 k_3 k_4 k_5^2 k_6) x_1 x_4^2 + (-2 k_1 k_2^2 k_4 k_5 k_6 - 4 k_1 k_2 k_3 k_4 k_5 k_6 - 2 k_1 k_2 k_4 k_5 k_6^2 \\
& - 2 k_1 k_3^2 k_4 k_5 k_6 - 2 k_1 k_3 k_4 k_5 k_6^2) x_1 x_4 + (-k_1 k_2 k_3 k_5^3 - k_1 k_2 k_4 k_5^3 - k_1 k_3^2 k_5^3 \\
& - k_1 k_3 k_4 k_5^3) x_3^2 x_4^2 + (-k_1 k_2^2 k_3 k_5^2 - k_1 k_2^2 k_4 k_5^2 - 2 k_1 k_2 k_3^2 k_5^2 - 2 k_1 k_2 k_3 k_4 k_5^2 \\
& - 2 k_1 k_2 k_3 k_5^2 k_6 - 2 k_1 k_2 k_4 k_5^2 k_6 - k_1 k_3^3 k_5^2 - k_1 k_3^2 k_4 k_5^2 - 2 k_1 k_3^2 k_5^2 k_6 - 2 k_1 k_3 k_4 \\
& k_5^2 k_6) x_3^2 x_4 + (-k_1 k_2 k_3 k_5^3 - k_1 k_2 k_4 k_5^3 - k_1 k_3^2 k_5^3 - k_1 k_3 k_4 k_5^3) x_3 x_4^3 + (-k_1 k_2^2 k_3 \\
& k_5^2 - k_1 k_2^2 k_4 k_5^2 - 2 k_1 k_2 k_3^2 k_5^2 - 2 k_1 k_2 k_3 k_4 k_5^2 - 3 k_1 k_2 k_3 k_5^2 k_6 - 3 k_1 k_2 k_4 k_5^2 k_6 \\
& - k_1 k_3^3 k_5^2 - k_1 k_3^2 k_4 k_5^2 - 3 k_1 k_3^2 k_5^2 k_6 - 3 k_1 k_3 k_4 k_5^2 k_6) x_3 x_4^2 + (-2 k_1 k_2^2 k_3 k_5 k_6 \\
& - 2 k_1 k_2^2 k_4 k_5 k_6 - 4 k_1 k_2 k_3^2 k_5 k_6 - 4 k_1 k_2 k_3 k_4 k_5 k_6 - 3 k_1 k_2 k_3 k_5 k_6^2 \\
& - 3 k_1 k_2 k_4 k_5 k_6^2 - 2 k_1 k_3^3 k_5 k_6 - 2 k_1 k_3^2 k_4 k_5 k_6 - 3 k_1 k_3^2 k_5 k_6^2 - 3 k_1 k_3 k_4 k_5 k_6^2 - \\
& k_2^2 k_4 k_5^2 k_6 - 2 k_2 k_3 k_4 k_5^2 k_6 - k_3^2 k_4 k_5^2 k_6) x_3 x_4 - 3 k_2^2 k_3 k_4 k_6^2 - 3 k_2 k_3^2 k_4 k_6^2 \\
& - 2 k_2 k_4 k_6^3 k_3 - k_1^3 k_4 k_5 x_1^3 x_3 k_6 - k_1^2 k_4 k_5^2 x_1^2 x_4 x_3 k_6
\end{aligned}
$$

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Here, we get a polynomial without any positive coefficient of x1, x3 and x4. Then there is no bistability allowed when consider non-allosteric regulated situition.