Stability analysis of the singular points and Hopf bifurcations of a tumor growth control model

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1. a) Qualitative analysis

The tumor growth model

The following model describes the time evolution of the living tumor volume (x_1), the dead tumor volume (x_2), the drug level in the central compartment (x_3) and the drug level in the peripheral compartment (x_4):

$$x_1' = a\, x_1 - n\, x_1 - b\, x_1 \frac{x_3}{\mathrm{ED}_{50} + x_3}$$

$$x_2' = n\, x_1 - w\, x_2 + b\, x_1 \frac{x_3}{\mathrm{ED}_{50} + x_3}$$

$$x_3' = -c\, x_3 - k_1\, x_3 + k_2\, x_4 + k(x_1 + x_2)$$

$$x_4' = k_1\, x_3 - k_2\, x_4$$

The measured values in Table 2 are the following:

In[∘]:=

```
{a, b, n, w, ED, c, k1, k2} =
  {3131/12500, 3771/2500, 86643/1000000, 2993/100000, 17461/20000, 21471/25000, 8323/50, 8369/500};
% // N
```

Out[∘]=

```
{0.25048, 1.5084, 0.086643, 0.02993, 0.87305, 0.85884, 166.46, 16.738}
```

Calculations

System (1)

In[∘]:=

```
Quit
```

In[•]:=
```
f1 = a x1 - n x1 - b x1 x3/(ED + x3);
f2 = n x1 - w x2 + b x1 x3/(ED + x3);
f3 = -c x3 - k1 x3 + k2 x4 + k (x1 + x2);
f4 = k1 x3 - k2 x4;
```

Singular point (3)

In[•]:=
```
sol = Solve[{f1, f2, f3, f4} == 0, {x1, x2, x3, x4}] // Factor
```

Out[•]=

$$\left\{\{x1 \to 0,\ x2 \to 0,\ x3 \to 0,\ x4 \to 0\},\ \left\{x1 \to -\frac{c\ ED\ (a-n)\ w}{k\ (a-b-n)\ (a+w)},\ x2 \to -\frac{a\ c\ ED\ (a-n)}{k\ (a-b-n)\ (a+w)},\ x3 \to -\frac{ED\ (a-n)}{a-b-n},\ x4 \to -\frac{ED\ k1\ (a-n)}{k2\ (a-b-n)}\right\}\right\}$$

The Jacobian at the nontrivial singular point (4), (5)

In[•]:=
```
jac = D[{f1, f2, f3, f4}, {{x1, x2, x3, x4}}] // FullSimplify;
{x1, x2, x3, x4} = {x1, x2, x3, x4} /. sol⟦2⟧;
jac = jac // FullSimplify
jac // MatrixForm
```

Out[•]=

$$\left\{\left\{0,\ 0,\ -\frac{c\ (a-n)\ (-a+b+n)\ w}{b\ k\ (a+w)},\ 0\right\},\ \left\{a,\ -w,\ \frac{c\ (a-n)\ (-a+b+n)\ w}{b\ k\ (a+w)},\ 0\right\},\ \{k,\ k,\ -c-k1,\ k2\},\ \{0,\ 0,\ k1,\ -k2\}\right\}$$

Out[•]//MatrixForm=

$$\begin{pmatrix} 0 & 0 & -\frac{c\ (a-n)\ (-a+b+n)\ w}{b\ k\ (a+w)} & 0 \\ a & -w & \frac{c\ (a-n)\ (-a+b+n)\ w}{b\ k\ (a+w)} & 0 \\ k & k & -c-k1 & k2 \\ 0 & 0 & k1 & -k2 \end{pmatrix}$$

The characteristic polynomial (6)

In[•]:=
```
pol = CharacteristicPolynomial[jac, y] // Factor
```

Out[•]=

$$\frac{1}{b}\left(-a^2\ c\ k2\ w + a\ b\ c\ k2\ w + 2\ a\ c\ k2\ n\ w - b\ c\ k2\ n\ w - c\ k2\ n^2\ w - a^2\ c\ w\ y + a\ b\ c\ w\ y + b\ c\ k2\ w\ y + 2\ a\ c\ n\ w\ y - b\ c\ n\ w\ y - c\ n^2\ w\ y + b\ c\ k2\ y^2 + b\ c\ w\ y^2 + b\ k1\ w\ y^2 + b\ k2\ w\ y^2 + b\ c\ y^3 + b\ k1\ y^3 + b\ k2\ y^3 + b\ w\ y^3 + b\ y^4\right)$$

In[•]:=
```
Variables[pol]
```

Out[•]=
{b, a, c, k2, w, n, y, k1}

Initial parameter settings and characteristic polynomial (7)

In[•]:=
$$\{w, ED, c, k1, k2\} = \left\{\frac{2993}{100000}, \frac{17461}{20000}, \frac{21471}{25000}, \frac{8323}{50}, \frac{8369}{500}\right\};$$

In[•]:=
```
pol = pol // Factor
```

Out[•]=
$$\frac{1}{1250000000000\,b}\left(-537814561407\,a^2 + 537814561407\,a\,b + 1075629122814\,a\,n - 537814561407\,b\,n - 537814561407\,n^2 - 32131351500\,a^2\,y + 537814561407\,b\,y + 32131351500\,a\,b\,y + 64262703000\,a\,n\,y - 32131351500\,b\,n\,y - 32131351500\,n^2\,y + 24855106426500\,b\,y^2 + 230108462500000\,b\,y^3 + 1250000000000\,b\,y^4\right)$$

The method to find pure imaginary eigenvalues

In[•]:=
```
pb = (b0 + b1 y + b2 y^2) (y^2 + W) // Expand
eq = pol - pb;
uu = Series[eq, {y, 0, 7}] // FullSimplify
sys = LogicalExpand[uu == 0] // FullSimplify
```

Out[•]=
$$b0\,W + b1\,W\,y + b0\,y^2 + b2\,W\,y^2 + b1\,y^3 + b2\,y^4$$

Out[•]=
$$\left(\frac{537814561407\,(a-n)\,(-a+b+n)}{1250000000000\,b} - b0\,W\right) + \left(\frac{64262703\,(8369\,b - 500\,(a-n)\,(a-b-n))}{1250000000000\,b} - b1\,W\right) y + \left(\frac{49710212853}{2500000000} - b0 - b2\,W\right) y^2 + \left(\frac{18408677}{100000} - b1\right) y^3 + (1-b2)\,y^4 + O[y]^8$$

Out[•]=
$$100000\,b1 == 18408677\;\&\&\; b2 == 1\;\&\&\; \frac{537814561407\,(a-n)\,(-a+b+n)}{b} == 1250000000000\,b0\,W\;\&\&\; \frac{64262703\,(8369\,b - 500\,(a-n)\,(a-b-n))}{b} == 1250000000000\,b1\,W\;\&\&\; b0 + W == \frac{49710212853}{2500000000}$$

Elimination of b_0, b_2 in (9), (10)

In[ ]:=
```
b2 = 1;
eqs = Eliminate[sys, {b0, b1}] // FullSimplify
```

Out[ ]=

$$500\left(a^2+n^2-a\,(b+2\,n)\right)\left(-140\,889\,196\,154\,970\,607\,369\,b+6\,426\,270\,300\,000\left(a^2+n\,(2\,b+n)-a\,(b+2\,n)\right)\right)==b^2\,(7\,657\,565\,446\,076\,595\,113\,889+500\,(140\,889\,196\,154\,970\,607\,369-6\,426\,270\,300\,000\,n)\,n)\ \&\&\ \frac{64\,262\,703\,(8369\,b-500\,(a-n)\,(a-b-n))}{b}==230\,108\,462\,500\,000\,W\ \&\&\ b\neq 0$$

Setting the values *a*, *b*, *n*

In[∘]:=
```
ClearAll[a]; a = 3131/12500;
CylindricalDecomposition[eqs && x1 > 0 && x2 > 0 && x3 > 0 && x4 > 0 &&
   n > 0 && b > 0 && W > 0 && a > n && n > a - b, {b, n, k, W}] // FullSimplify
```

Out[∘]=

$$W == -\frac{64\,262\,703\,\left((3131 - 12\,500\,n)^2 + 50\,000\,b\,(-53\,089 + 3125\,n)\right)}{71\,908\,894\,531\,250\,000\,000\,b} \;\&\&$$

k > 0 && ((n == Root[12 351 544 145 099 676 844 926 − 4 316 123 451 959 740 176 251 390 553 125 b + 9 753 318 048 793 714 228 850 703 125 000 b^2 + (−197 245 994 013 089 697 300 000 + 34 462 819 396 927 808 044 744 609 375 000 b − 68 793 554 381 970 203 543 457 031 250 000 b^2) #1 + (1 181 208 044 632 843 125 000 000 − 68 793 557 525 822 126 871 582 031 250 000 b + 3 137 827 294 921 875 000 000 000 b^2) #1^2 + (−3 143 851 923 328 125 000 000 000 + 6 275 654 589 843 750 000 000 000 b) #1^3 + 3 137 827 294 921 875 000 000 000 #1^4 &, 2] &&

$$\frac{-140\,889\,196\,154\,970\,607\,369 + 7\,\sqrt{405\,097\,265\,038\,172\,811\,166\,168\,519\,191\,770\,258\,689}}{3\,213\,135\,150\,000} \le$$

$$b < \left(9\,803\,161\,\left(140\,889\,199\,374\,274\,976\,857 + 7\,\sqrt{405\,097\,265\,038\,172\,811\,166\,168\,519\,191\,770\,258\,689}\right)\right) / 6\,242\,123\,551\,227\,977\,106\,464\,450\,000 \Big) \;||$$

(n == Root[12 351 544 145 099 676 844 926 − 4 316 123 451 959 740 176 251 390 553 125 b + 9 753 318 048 793 714 228 850 703 125 000 b^2 + (−197 245 994 013 089 697 300 000 + 34 462 819 396 927 808 044 744 609 375 000 b − 68 793 554 381 970 203 543 457 031 250 000 b^2) #1 + (1 181 208 044 632 843 125 000 000 − 68 793 557 525 822 126 871 582 031 250 000 b + 3 137 827 294 921 875 000 000 000 b^2) #1^2 + (−3 143 851 923 328 125 000 000 000 + 6 275 654 589 843 750 000 000 000 b) #1^3 + 3 137 827 294 921 875 000 000 000 #1^4 &, 3] &&

$$140\,889\,196\,154\,970\,607\,369 + 3\,213\,135\,150\,000\,b > 7\,\sqrt{405\,097\,265\,038\,172\,811\,166\,168\,519\,191\,770\,258\,689}\Big)\Big)$$

In[∘]:=
```
Reduce[(-140 889 196 154 970 607 369 + 7 Sqrt[405 097 265 038 172 811 166 168 519 191 770 258 689])/3 213 135 150 000 ≤
   b < (9 803 161
       (140 889 199 374 274 976 857 + 7 Sqrt[405 097 265 038 172 811 166 168 519 191 770 258 689])) /
    6 242 123 551 227 977 106 464 450 000, b];
% // N
```

Out[∘]=

$0.434813 \le b < 0.442529$

In[•]:=
```
Reduce[140 889 196 154 970 607 369 + 3 213 135 150 000 b >
    7 √405 097 265 038 172 811 166 168 519 191 770 258 689 , b];
% // N
```

Out[•]=

b > 0.434813

The measured value is $b = 1.5084$.

In[•]:=
```
ClearAll[b]; b = 3/2;
CylindricalDecomposition[eqs && x1 > 0 && x2 > 0 && x3 > 0 &&
    x4 > 0 && n > 0 && W > 0 && a > n && n > a - b, {n, k, W}] // FullSimplify
```

Out[•]=

```
12 488 + 25 000 n == 125 [√ 126.…] && k > 0 &&
 W == - 21 420 901 (-3 971 871 839 + 50 000 n (3122 + 3125 n)) / 35 954 447 265 625 000 000
```

In[•]:=
```
Reduce[12 488 + 25 000 n == 125 [√ 126.…], n]
% // N
```

Out[•]=

```
n == (-12 488 + 125 [√ 126.…]) / 25 000
```

Out[•]=

n == 0.132497

The measured value is $n = 0.086643$.

In[•]:=
```
ClearAll[n];
n = (-12 488 + 125 [√ 126.…]) / 25 000;
```

The eigenvalues (13)

In[•]:=
```
Solve[pol == 0, y] // N
```

Out[•]=

```
{{y → -183.979}, {y → -0.108065}, {y → 0. - 0.0485016 i}, {y → 0. + 0.0485016 i}}
```

1. b) Stability of the equilibrium state and the Hopf bifurcation

Step 1 - Shifting the singular point into the origin

The singular point of the system in the first quadrant is shifted into the origin and the parameters are chosen in such a way that the Jacobian at the origin has a pair of pure imaginary eigenvalues.

System (1)

In[∘]:=
```
Quit
```

In[∘]:=
```
ClearAll[x1, x2, x3, a, b, n, w, ED, c, k1, k2, k, f1, f2, f3, f4];
```
$$f1 = a\,x1 - n\,x1 - b\,x1\,\frac{x3}{ED + x3};$$
$$f2 = n\,x1 - w\,x2 + b\,x1\,\frac{x3}{ED + x3};$$
$$f3 = -c\,x3 - k1\,x3 + k2\,x4 + k\,(x1 + x2);$$
$$f4 = k1\,x3 - k2\,x4;$$

Singular points

In[∘]:=
```
sol = Solve[{f1 == 0, f2 == 0, f3 == 0, f4 == 0}, {x1, x2, x3, x4}] // Factor
{y1, y2, y3, y4} = {x1, x2, x3, x4} /. sol[[2]]
```

Out[∘]=
$$\left\{\{x1 \to 0, x2 \to 0, x3 \to 0, x4 \to 0\}, \left\{x1 \to -\frac{c\,ED\,(a-n)\,w}{k\,(a-b-n)\,(a+w)}, x2 \to -\frac{a\,c\,ED\,(a-n)}{k\,(a-b-n)\,(a+w)}, x3 \to -\frac{ED\,(a-n)}{a-b-n}, x4 \to -\frac{ED\,k1\,(a-n)}{k2\,(a-b-n)}\right\}\right\}$$

Out[∘]=
$$\left\{-\frac{c\,ED\,(a-n)\,w}{k\,(a-b-n)\,(a+w)}, -\frac{a\,c\,ED\,(a-n)}{k\,(a-b-n)\,(a+w)}, -\frac{ED\,(a-n)}{a-b-n}, -\frac{ED\,k1\,(a-n)}{k2\,(a-b-n)}\right\}$$

The singular point is shifted into the origin (17)

In[∘]:=
```
x1d = f1 /. {x1 → x1 + y1, x2 → x2 + y2, x3 → x3 + y3, x4 → x4 + y4} // Factor
x2d = f2 /. {x1 → x1 + y1, x2 → x2 + y2, x3 → x3 + y3, x4 → x4 + y4} // Factor
x3d = f3 /. {x1 → x1 + y1, x2 → x2 + y2, x3 → x3 + y3, x4 → x4 + y4} // Factor
x4d = f4 /. {x1 → x1 + y1, x2 → x2 + y2, x3 → x3 + y3, x4 → x4 + y4} // Factor
```

Out[∘]=

$$\frac{(a-b-n)\left(-a\,c\,ED\,w+c\,ED\,n\,w+a^2\,k\,x1-a\,b\,k\,x1-a\,k\,n\,x1+a\,k\,w\,x1-b\,k\,w\,x1-k\,n\,w\,x1\right)x3}{k\,(a+w)\,(-b\,ED+a\,x3-b\,x3-n\,x3)}$$

Out[∘]=

$$-\frac{1}{k\,(a+w)\,(b\,ED-a\,x3+b\,x3+n\,x3)}\left(-a^2\,b\,ED\,k\,x1-a\,b\,ED\,k\,w\,x1+a\,b\,ED\,k\,w\,x2+b\,ED\,k\,w^2\,x2+a^2\,c\,ED\,w\,x3-a\,b\,c\,ED\,w\,x3-2\,a\,c\,ED\,n\,w\,x3+b\,c\,ED\,n\,w\,x3+c\,ED\,n^2\,w\,x3+a^2\,b\,k\,x1\,x3-a\,b^2\,k\,x1\,x3+a^2\,k\,n\,x1\,x3-2\,a\,b\,k\,n\,x1\,x3-a\,k\,n^2\,x1\,x3+a\,b\,k\,w\,x1\,x3-b^2\,k\,w\,x1\,x3+a\,k\,n\,w\,x1\,x3-2\,b\,k\,n\,w\,x1\,x3-k\,n^2\,w\,x1\,x3-a^2\,k\,w\,x2\,x3+a\,b\,k\,w\,x2\,x3+a\,k\,n\,w\,x2\,x3-a\,k\,w^2\,x2\,x3+b\,k\,w^2\,x2\,x3+k\,n\,w^2\,x2\,x3\right)$$

Out[∘]=

$$k\,x1+k\,x2-c\,x3-k1\,x3+k2\,x4$$

Out[∘]=

$$k1\,x3-k2\,x4$$

The Jacobian at the origin

In[∘]:=
```
Jac = D[{x1d, x2d, x3d, x4d}, {{x1, x2, x3, x4}}] // Simplify;
JacOrigin = Jac /. {x1 → 0, x2 → 0, x3 → 0, x4 → 0} // Simplify
```

Out[∘]=

$$\left\{\left\{0,\,0,\,-\frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)},\,0\right\},\left\{a,\,-w,\,\frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)},\,0\right\},\{k,\,k,\,-c-k1,\,k2\},\{0,\,0,\,k1,\,-k2\}\right\}$$

Eigenvalues of the Jacobian at the origin with the given parameter settings

In[∘]:=

$$\{w,\,ED,\,c,\,k1,\,k2\}=\left\{\frac{2993}{100\,000},\,\frac{17\,461}{20\,000},\,\frac{21\,471}{25\,000},\,\frac{8323}{50},\,\frac{8369}{500}\right\};$$

$$a=\frac{3131}{12\,500};\ b=\frac{3}{2};\ n=\frac{-12\,488+125\ \boxed{\sqrt{\ }\ 126.\ldots}}{25\,000};$$

$$k=\frac{1}{100};$$

```
Eigenvalues[JacOrigin] // N
```

Out[∘]=

{-183.979, -0.108065, 0. + 0.0485016 i, 0. - 0.0485016 i}

Step 2 - Taylor series expansion

Series expansion symbolically and the Jacobian at the origin

In[ ]:=
```
Quit
```

In[∘]:=
```
x1d =
  ((a - b - n) (-a c ED w + c ED n w + a^2 k x1 - a b k x1 - a k n x1 + a k w x1 - b k w x1 - k n w x1) x3) /
   (k (a + w) (-b ED + a x3 - b x3 - n x3));
x2d = - 1/(k (a + w) (b ED - a x3 + b x3 + n x3))
   (-a^2 b ED k x1 - a b ED k w x1 + a b ED k w x2 + b ED k w^2 x2 + a^2 c ED w x3 -
     a b c ED w x3 - 2 a c ED n w x3 + b c ED n w x3 + c ED n^2 w x3 + a^2 b k x1 x3 -
     a b^2 k x1 x3 + a^2 k n x1 x3 - 2 a b k n x1 x3 - a k n^2 x1 x3 + a b k w x1 x3 -
     b^2 k w x1 x3 + a k n w x1 x3 - 2 b k n w x1 x3 - k n^2 w x1 x3 - a^2 k w x2 x3 +
     a b k w x2 x3 + a k n w x2 x3 - a k w^2 x2 x3 + b k w^2 x2 x3 + k n w^2 x2 x3);
x3d = k x1 + k x2 - c x3 - k1 x3 + k2 x4;
x4d = k1 x3 - k2 x4;
r1 = Series[x1d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal
r2 = Series[x2d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal
r3 = Series[x3d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal
r4 = Series[x4d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal
```

Out[∘]=

$$-\frac{(-a+b+n)\,(a c w-c n w)\,x3}{b k\,(a+w)}+\frac{(-a+b+n)^2\,(a c w-c n w)\,x3^2}{b^2\,ED\,k\,(a+w)}-\frac{(-a+b+n)^3\,(a c w-c n w)\,x3^3}{b^3\,ED^2\,k\,(a+w)}+\frac{(-a+b+n)^4\,(a c w-c n w)\,x3^4}{b^4\,ED^3\,k\,(a+w)}+x1\left(-\frac{(-a+b+n)^2\,x3}{b\,ED}+\frac{(-a+b+n)^3\,x3^2}{b^2\,ED^2}-\frac{(-a+b+n)^4\,x3^3}{b^3\,ED^3}+\frac{(-a+b+n)^5\,x3^4}{b^4\,ED^4}\right)$$

Out[∘]=

$$-w\,x2+\frac{\left(-a^2 c w+a b c w+2 a c n w-b c n w-c n^2 w\right)x3}{b k\,(a+w)}-\frac{(-a+b+n)^2\,(a c w-c n w)\,x3^2}{b^2\,ED\,k\,(a+w)}+\frac{(-a+b+n)^3\,(a c w-c n w)\,x3^3}{b^3\,ED^2\,k\,(a+w)}-\frac{(-a+b+n)^4\,(a c w-c n w)\,x3^4}{b^4\,ED^3\,k\,(a+w)}+x1\left(a+\frac{\left(a^2-2 a b+b^2-2 a n+2 b n+n^2\right)x3}{b\,ED}+\frac{\left(a^3-3 a^2 b+3 a b^2-b^3-3 a^2 n+6 a b n-3 b^2 n+3 a n^2-3 b n^2-n^3\right)x3^2}{b^2\,ED^2}+\frac{1}{b^3\,ED^3}\left(a^4-4 a^3 b+6 a^2 b^2-4 a b^3+b^4-4 a^3 n+12 a^2 b n-12 a b^2 n+4 b^3 n+6 a^2 n^2-12 a b n^2+6 b^2 n^2-4 a n^3+4 b n^3+n^4\right)x3^3+\frac{1}{b^4\,ED^4}\left(a^5-5 a^4 b+10 a^3 b^2-10 a^2 b^3+5 a b^4-b^5-5 a^4 n+20 a^3 b n-30 a^2 b^2 n+20 a b^3 n-5 b^4 n+10 a^3 n^2-30 a^2 b n^2+30 a b^2 n^2-10 b^3 n^2-10 a^2 n^3+20 a b n^3-10 b^2 n^3+5 a n^4-5 b n^4-n^5\right)x3^4\right)$$

Out[∘]=

$$k\,x1+k\,x2+(-c-k1)\,x3+k2\,x4$$

Out[∘]=

$$k1\,x3-k2\,x4$$

In[•]:=
```
Jac = D[{r1, r2, r3, r4}, {{x1, x2, x3, x4}}] // Simplify;
JacOrigin = Jac /. {x1 → 0, x2 → 0, x3 → 0, x4 → 0} // Simplify
```

Out[•]=

$$\left\{\left\{0, 0, -\frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)}, 0\right\}, \left\{a, -w, \frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)}, 0\right\}, \{k, k, -c-k1, k2\}, \{0, 0, k1, -k2\}\right\}$$

Series expansion with numerical values

A series expansion of the transformed system about the origin up to degree 4 will be used instead of the original system.

In[•]:=
```
Quit
```

In[•]:=
```
{w, ED, c, k1, k2} = {2993/100000, 17461/20000, 21471/25000, 8323/50, 8369/500};
a = 3131/12500; b = 3/2; n = (-12488 + 125 [√ 126.…])/25000;
k = 1/100;
x1d =
  ((a - b - n) (-a c ED w + c ED n w + a^2 k x1 - a b k x1 - a k n x1 + a k w x1 - b k w x1 - k n w x1) x3) /
   (k (a + w) (-b ED + a x3 - b x3 - n x3));
x2d = - 1/(k (a + w) (b ED - a x3 + b x3 + n x3))
    (-a^2 b ED k x1 - a b ED k w x1 + a b ED k w x2 + b ED k w^2 x2 + a^2 c ED w x3 -
      a b c ED w x3 - 2 a c ED n w x3 + b c ED n w x3 + c ED n^2 w x3 + a^2 b k x1 x3 -
      a b^2 k x1 x3 + a^2 k n x1 x3 - 2 a b k n x1 x3 - a k n^2 x1 x3 + a b k w x1 x3 -
      b^2 k w x1 x3 + a k n w x1 x3 - 2 b k n w x1 x3 - k n^2 w x1 x3 - a^2 k w x2 x3 +
      a b k w x2 x3 + a k n w x2 x3 - a k w^2 x2 x3 + b k w^2 x2 x3 + k n w^2 x2 x3);
x3d = k x1 + k x2 - c x3 - k1 x3 + k2 x4;
x4d = k1 x3 - k2 x4;
r1 = Series[x1d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal;
r2 = Series[x2d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal;
r3 = Series[x3d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal;
r4 = Series[x4d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal;
```

Separation of the linear and nonlinear parts

In[ ]:=
```
g1 = r1 /. {x1 → t x1, x2 → t x2, x3 → t x3, x4 → t x4};
rr1 = Normal[Series[g1, {t, 0, 4}]] // Simplify;
g2 = r2 /. {x1 → t x1, x2 → t x2, x3 → t x3, x4 → t x4};
rr2 = Normal[Series[g2, {t, 0, 4}]] // Simplify;
f1p = D[rr1, t] /. t → 0 // Simplify;
f2p = D[rr2, t] /. t → 0 // Simplify;
f1deg2 = rr1 - f1p t // Simplify // Factor;
f2deg2 = rr2 - f2p t // Simplify // Factor;
```

The full system

In[ ]:=

```
ff1 = (SetPrecision[f1p, 100] t + SetPrecision[f1deg2, 100]) /. t → 1 // Expand
ff2 = (SetPrecision[f2p, 100] t + SetPrecision[f2deg2, 100]) /. t → 1 // Expand
ff3 = r3
ff4 = r4
```

Out[ ]=

```
-0.996479806391328353503051218563542279852193446000847479042671287973746984356032480981418503063597857 x3 -
 1.45846537314413581758059765516814447681811012183434275755826241555527303177390730060638360076054221 7 x1 x3 +
 1.05160193265734561726398085950713001916805371437992396576478041401320228247941969945311727254709154 x3^2 +
 1.53914308676906557527848975127873767360705354742049333749159402772006807659650625916062412578973900 6 x1 x3^2 -
 1.1097732414402572763332174370166047342464277170908044734301576443728521541127871239395264293072481 8 x3^3 -
 1.6242836375621582016466928334193106529139704516805678458653458961333211955860028509754220509336347 04 x1 x3^3 +
 1.1711624039189736832222134597810617995291851688320015607302527174548950480849929611465480775855134 8 x3^4
```

Out[ ]=

```
0.250480000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000 x1 -
 0.029900000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000000 x2 +
 0.996479806391328353503051218563542279852193446000847479042671287973746984356032480981418503063597857 x3 +
 1.45846537314413581758059765516814447681811012183434275755826241555527303177390730060638360076054221 7 x1 x3 -
 1.05160193265734561726398085950713001916805371437992396576478041401320228247941969945311727254709154 x3^2 -
 1.53914308676906557527848975127873767360705354742049333749159402772006807659650625916062412578973900 6 x1 x3^2 +
 1.1097732414402572763332174370166047342464277170908044734301576443728521541127871239395264293072481 8 x3^3 +
 1.6242836375621582016466928334193106529139704516805678458653458961333211955860028509754220509336347 04 x1 x3^3 -
 1.1711624039189736832222134597810617995291851688320015607302527174548950480849929611465480775855134 8 x3^4
```

Out[ ]=

$$\frac{x1}{100} + \frac{x2}{100} - \frac{4182971\,x3}{25000} + \frac{8369\,x4}{500}$$

Out[ ]=

$$\frac{8323\,x3}{50} - \frac{8369\,x4}{500}$$

The full system with shorter numerical values in (18)

In[•]:=
```
ff1 // N
ff2 // N
ff3 // N
ff4 // N
```

Out[•]=
```
-0.99648 x3 - 1.45847 x1 x3 + 1.0516 x3^2 +
 1.53914 x1 x3^2 - 1.10977 x3^3 - 1.62428 x1 x3^3 + 1.17116 x3^4
```

Out[•]=
```
0.25048 x1 - 0.02993 x2 + 0.99648 x3 + 1.45847 x1 x3 -
 1.0516 x3^2 - 1.53914 x1 x3^2 + 1.10977 x3^3 + 1.62428 x1 x3^3 - 1.17116 x3^4
```

Out[•]=
```
0.01 x1 + 0.01 x2 - 167.319 x3 + 16.738 x4
```

Out[•]=
```
166.46 x3 - 16.738 x4
```

The nonlinear part

In[•]:=
```
f1 = SetPrecision[f1deg2, 100] /. t → 1 // Expand
f2 = SetPrecision[f2deg2, 100] /. t → 1 // Expand
f3 = 0;
f4 = 0;
```

Out[•]=
```
-1.458465373144135817580597655168144476818110121834342757558262415555273031773907300 6
    06383600760542217 x1 x3 +
 1.051601932657345617263980859507130019168053714379923965764780414013202282479419699 4
   5311727254709154 x3^2 +
 1.539143086769065575278489751278737673607053547420493337491594027720068076596506259 1
   60624125789739006 x1 x3^2 -
 1.109773241440257276333217437016604734246427717090804473430157644372852154112787123 9
   3952642930724818 x3^3 -
 1.624283637562158201646692833419310652913970451680567845865345896133321195586002850 9
   75422050933634704 x1 x3^3 +
 1.171162403918973683222213459781061799529185168832001560730252717454895048084992961 1
   4654807758551348 x3^4
```

Out[•]=
```
1.4584653731441358175805976551681444768181101218343427575582624155552730317739073006 0
   6383600760542217 x1 x3 -
 1.051601932657345617263980859507130019168053714379923965764780414013202282479419699 4
   5311727254709154 x3^2 -
 1.539143086769065575278489751278737673607053547420493337491594027720068076596506259 1
   60624125789739006 x1 x3^2 +
 1.109773241440257276333217437016604734246427717090804473430157644372852154112787123 9
   3952642930724818 x3^3 +
 1.624283637562158201646692833419310652913970451680567845865345896133321195586002850 9
   75422050933634704 x1 x3^3 -
 1.171162403918973683222213459781061799529185168832001560730252717454895048084992961 1
   4654807758551348 x3^4
```

The Jacobian at the origin

In[ ]:=
```
Jac = D[{ff1, ff2, ff3, ff4}, {{x1, x2, x3, x4}}] // Simplify;
JacOrigin = Jac /. {x1 → 0, x2 → 0, x3 → 0, x4 → 0} // Simplify;
```

In[ ]:=
```
SetPrecision[Eigenvalues[JacOrigin], 100]
```

Out[ ]=
```
{-183.9787045976274199132968167380356649524306950139818002882859640724395101832839239⋱
  251272658890791462,
 -0.1080654023725800867031832619643350475693049860181997117140359275604898167160760749⋱
  872734110920853817 1, 0. × 10^-112 +
 0.0485015553497298715587390201887311967155049599905460509351769219452405327389311616⋱
  1696209557571688838 08 i, 0. × 10^-112 -
 0.0485015553497298715587390201887311967155049599905460509351769219452405327389311616⋱
  1696209557571688838 08 i}
```

The Jacobian the singular point

In[ ]:=
$$J = \left\{\left\{0,\ 0,\ -\frac{c\ (a-n)\ (-a+b+n)\ w}{b\ k\ (a+w)},\ 0\right\},\ \left\{a,\ -w,\ \frac{c\ (a-n)\ (-a+b+n)\ w}{b\ k\ (a+w)},\ 0\right\},\ \{k,\ k,\ -c-k1,\ k2\},\ \{0,\ 0,\ k1,\ -k2\}\right\}\ //\ \text{FullSimplify};$$

In[ ]:=
```
SetPrecision[Eigenvalues[J], 100]
```

Out[ ]=
```
{-183.9787045976274199132968167380356649524306950139818002882859640724395101832839239⋱
  251272658890791462,
 -0.1080654023725800867031832619643350475693049860181997117140359275604898167160760749⋱
  87273411092085382,
 0.04850155534972987155873902018873119671550495999054605093517692194524053273893116 16⋱
  9620955757169 i,
 -0.0485015553497298715587390201887311967155049599905460509351769219452405327389311616⋱
  1696209557571 69 i}
```

Step 3 - Transformation to real Jordan normal form

The system is transformed in such a way that its linear part has real Jordan normal form (RJNF).
We remark that for the eigenvectors of *J*, both the exact values
`ev=Eigenvectors[J]//FullSimplify` and the numerical values
`ev=SetPrecision[Eigenvectors[J],100]` can be used.
With **`SetPrecision`** the calculations are faster and provide more digits.

Transformation of *J*

In[∘]:=
```
ev = SetPrecision[Eigenvectors[J], 100];
```

In[∘]:=
```
SetPrecision[Transpose[ev], 100] // N // MatrixForm
```

Out[∘]//MatrixForm=

-0.00544168	0.921218	-0.0059863 + 2.06589 ⅈ	-0.0059863 - 2.06589 ⅈ
0.00544998	-4.22726	8.64044 + 3.29699 ⅈ	8.64044 - 3.29699 ⅈ
-1.00469	0.0999035	0.100553 + 0.000291371 ⅈ	0.100553 - 0.000291371 ⅈ
1.	1.	1.	1.

The matrix *S* for which the product $S^{-1} J S$ has real Jordan normal form (19)

In[∘]:=
```
S = Transpose[{ev⟦1⟧, ev⟦2⟧, Re[ev⟦3⟧], Im[ev⟦3⟧]}];
```

In[∘]:=
```
SetPrecision[S, 100] // N // MatrixForm
```

Out[∘]//MatrixForm=

-0.00544168	0.921218	-0.0059863	2.06589
0.00544998	-4.22726	8.64044	3.29699
-1.00469	0.0999035	0.100553	0.000291371
1.	1.	1.	0.

The inverse of *S*

In[∘]:=
```
Sinv = Inverse[S];
```

Verification that *S* transforms *J* to the real Jordan normal form (20)

In[∘]:=
```
RJNF = Sinv.J.S
```

Out[∘]=
```
{{-183.978704597627419913296816738035664952430695013981800288285964072439510183283923⋱
   9251273, 0. × 10^-87, 0. × 10^-87, 0. × 10^-89}, {0. × 10^-86,
  -0.108065402372580086703183261964335047569304986018199711714035927560489816716076077⋱
   48727, 0. × 10^-86, 0. × 10^-89}, {0. × 10^-86, 0. × 10^-87, 0. × 10^-87,
  0.0485015553497298715587390201887311967155049599905460509351769219452405327389311161⋱
  6962096}, {0. × 10^-86, 0. × 10^-87,
  -0.048501555349729871558739020188731196715504959990546050935176921945240532738931116⋱
   169621, 0. × 10^-89}}
```

In[∘]:=
```
SetPrecision[RJNF, 100]
```

Out[∘]=
```
{{-183.978704597627419913296816738035664952430695013981800288285964072439510183283923⋱
   9251272658890791456, 0, 0, 0}, {0,
  -0.1080654023725800867031832619643350475693049860181997117140359275604898167160760 7⋱
   4872734110920853588 1, 0, 0}, {0, 0, 0,
  0.04850155534972987155873902018873119671550495999054605093517692194524053273893116 1⋱
  6962095575716888378 4}, {0, 0,
  -0.04850155534972987155873902018873119671550495999054605093517692194524053273893116⋱
   16962095575716888759 4, 0}}
```

The entries a_1, a_2, β in (20)

In[∘]:=
```
a1 = RJNF[[1, 1]];
a2 = RJNF[[2, 2]];
beta = RJNF[[3, 4]];
```

Transformation of the system

Consider the system $\dot{\boldsymbol{x}} = J\,\boldsymbol{x} + f(\boldsymbol{x})$ where f contains the nonlinear terms.
With the substitution $\boldsymbol{x} = S\,\boldsymbol{y}$, this system is transformed into the form
$\dot{\boldsymbol{y}} = S^{-1}\,J\,S\,\boldsymbol{y} + S^{-1}\,f(S\,\boldsymbol{y})$.
The product $S\,\boldsymbol{y}$:

In[∘]:=
```
sy = S.{y1, y2, y3, y4} // FullSimplify;
```

The substitution $f(S\,\boldsymbol{y})$:

In[∘]:=
```
FF1 = f1 /. {x1 → sy[[1]], x2 → sy[[2]], x3 → sy[[3]], x4 → sy[[4]] } // Simplify // Expand;
FF2 = f2 /. {x1 → sy[[1]], x2 → sy[[2]], x3 → sy[[3]], x4 → sy[[4]] } // Simplify // Expand;
FF3 = f3 /. {x1 → sy[[1]], x2 → sy[[2]], x3 → sy[[3]], x4 → sy[[4]] } // Simplify
FF4 = f4 /. {x1 → sy[[1]], x2 → sy[[2]], x3 → sy[[3]], x4 → sy[[4]] } // Simplify
```

Out[∘]=
```
0
```

Out[∘]=
```
0
```

The product $S^{-1}\,f(S\,\boldsymbol{y})$, that is, the nonlinear part in $\dot{\boldsymbol{y}}$ in the new coordinates:

In[∘]:=
```
{h1, h2, h3, h4} = SetPrecision[Sinv.{FF1, FF2, FF3, FF4}, 100] // Simplify;
```

The full system in (21)

In[∘]:=
```
f1y = a1 y1 + h1 // Simplify;
f2y = a2 y2 + h2 // Simplify;
f3y = beta y4 + h3 // Simplify;
f4y = -beta y3 + h4 // Simplify;
jac = D[{f1y, f2y, f3y, f4y}, {{y1, y2, y3, y4}}] /. {y1 → 0, y2 → 0, y3 → 0, y4 → 0};
```

```
In[]:= jac // N // MatrixForm
```

Out[]//MatrixForm=

$$\begin{pmatrix} -183.979 & 0. & 0. & 0. \\ 0. & -0.108065 & 0. & 0. \\ 0. & 0. & 0. & 0.0485016 \\ 0. & 0. & -0.0485016 & 0. \end{pmatrix}$$

Step 4 - Search for a Lyapunov function

We look for a polynomial $\phi(x_1, x_2, x_3, x_4) = \phi_2\,(x_1, x_2, x_3, x_4) + \sum_{i+j+k+l=3}^{4} p_{\mathrm{ijkl}}\, x_1^i\, x_2^j\, x_3^k\, x_4^l$

such that the quadratic part of ϕ,

$\phi_2\,(x_1, x_2, x_3, x_4) = A\,x_1^2 + B\,x_2^2 + C\,x_3^2 + D\,x_4^2$

is positively defined and for the Lie derivative of the previous system we have that

$$\frac{\partial\phi}{\partial x_1}\,\dot{x}_1 + \frac{\partial\phi}{\partial x_2}\,\dot{x}_2 + \frac{\partial\phi}{\partial x_3}\,\dot{x}_3 + \frac{\partial\phi}{\partial x_4}\,\dot{x}_4 = g_0\left[\left(x_1^2 + x_2^2\right) + \left(x_3^2 + x_4^2\right)^2\right] + h.o.t.$$

The following program compares the coefficients of the corresponding terms on both sides and thus the focus (or Lyapunov) quantity g_0 can be calculated.

The system in (21)

```
In[]:= ClearAll[f1, f2, f3, f4];
f1 = f1y /. {y1 → x1, y2 → x2, y3 → x3, y4 → x4};
f2 = f2y /. {y1 → x1, y2 → x2, y3 → x3, y4 → x4};
f3 = f3y /. {y1 → x1, y2 → x2, y3 → x3, y4 → x4};
f4 = f4y /. {y1 → x1, y2 → x2, y3 → x3, y4 → x4};
```

Program

In[•]:=
```
Ser[s_] := Plus @@ (Table[x1^i x2^j x3^k x4^(s-i-j-k) p[i, j, k, s - i - j - k], {i, 0, s},
        {j, 0, s}, {k, 0, s}, {l, 0, s - i - j - k}] // Flatten // Union);
Hom[s_] := Table[p[i, j, k, s - i - j - k], {i, 0, s},
      {j, 0, s}, {k, 0, s}, {l, 0, s - i - j - k}] // Flatten // Union;
hh = Sum[Ser[i], {i, 3, 4}];
V = hh + aa x1^2 + bb x2^2 + cc x3^2 + dd x4^2;
Lie = D[V, x1] f1 + D[V, x2] f2 + D[V, x3] f3 + D[V, x4] f4 // Expand;
RHS = g0 ((x1^2 + x2^2) + (x3^2 + x4^2)^2) // Expand;
vv = Lie - RHS // Expand;
CoefPol[f_, s_] := Module[{m, lis, t}, lis = {};
   m = Expand[f]; Do[Do[Do[Do[If[i + j + k + l == s, lis = AppendTo[lis,
           Coefficient[m, x1^i x2^j x3^k x4^l] /. {x1 → 0, x2 → 0, x3 → 0, x4 → 0}]],
        {i, 0, s}], {j, 0, s}], {k, 0, s}], {l, 0, s}];
   ls[s] = lis];
Do[CoefPol[vv, i], {i, 1, 4}]
```

Degree 2

In[•]:=
```
ls[2] // FullSimplify
```

Out[•]=
```
{-367.957409195254839826593633476071329904861390027963600576571928144879020366567847850255 aa - g0, 0,
 -0.21613080474516017340636652392867009513860997203639942342807185512097963343215214974557455 bb - g0, 0, 0, 0, 0, 0,
 0.097003110699459743117478040377462393431009919981092101870353843890481065477862332339924191 cc -
  0.0970031106994597431174780403774623934310099199810921018703538438904810654778623233924191 dd,
 0}
```

In[•]:=
```
Variables[ls[2]]
```

Out[•]=
```
{aa, bb, cc, dd, g0}
```

In[•]:=
```
sol2 = Solve[ls[2] == 0, {aa, bb, cc, dd}] // FullSimplify // Factor
```

Solve: Equations may not give solutions for all "solve" variables.

Out[•]=
```
{{aa →
  -0.0027177058404315342415913759893163253770824613660240024685646468010243063089825⋱
    64411032 g0, bb →
  -4.6268277267513993461688257777451941249857746311818695673472131546238633967663190⋱
    56322 g0, dd →
  1.00000000000000000000000000000000000000000000000000000000000000000000000000000000⋱
   0000 cc}}
```

In[•]:=
```
{aa, bb, cc, dd} = {aa, bb, cc, dd} /. sol2[[1]]
```

Out[•]=
```
{-0.002717705840431534241591375989316325377082461366024002468564646801024306308982564⋱
    411032 g0,
 -4.626827726751399346168825777745194124985774631181869567347213154623863396766319056⋱
    322 g0, cc,
 1.0000000000000000000000000000000000000000000000000000000000000000000000000000000000⋱
   00 cc}
```

In[•]:=
```
{aa, bb, cc, dd} // N
```

Out[•]=
```
{-0.00271771 g0, -4.62683 g0, cc, 1. cc}
```

Positive definiteness of the quadratic part of *V*

In[•]:=
```
S2 = aa x1^2 + bb x2^2 + cc x3^2 + cc x4^2
```

Out[•]=
```
-0.0027177058404315342415913759893163253770824613660240024685646468010243063089825644⋱
    11032 g0 x1^2 -
 4.6268277267513993461688257777451941249857746311818695673472131546238633967663190563⋱
   22 g0 x2^2 + cc x3^2 + cc x4^2
```

It can be seen that S2 will be positively defined if $g_0 < 0$ and $c > 0$.

Degree 3

In[ ]:=
```
ls[3] // Factor;
sol3 = Solve[ls[3] == 0, Hom[3]] // Simplify;
{p[0, 0, 0, 3], p[0, 0, 1, 2], p[0, 0, 2, 1], p[0, 0, 3, 0], p[0, 1, 0, 2],
   p[0, 1, 1, 1], p[0, 1, 2, 0], p[0, 2, 0, 1], p[0, 2, 1, 0], p[0, 3, 0, 0],
   p[1, 0, 0, 2], p[1, 0, 1, 1], p[1, 0, 2, 0], p[1, 1, 0, 1], p[1, 1, 1, 0],
   p[1, 2, 0, 0], p[2, 0, 0, 1], p[2, 0, 1, 0], p[2, 1, 0, 0], p[3, 0, 0, 0]} =
  {p[0, 0, 0, 3], p[0, 0, 1, 2], p[0, 0, 2, 1], p[0, 0, 3, 0], p[0, 1, 0, 2], p[0, 1, 1, 1],
     p[0, 1, 2, 0], p[0, 2, 0, 1], p[0, 2, 1, 0], p[0, 3, 0, 0], p[1, 0, 0, 2],
     p[1, 0, 1, 1], p[1, 0, 2, 0], p[1, 1, 0, 1], p[1, 1, 1, 0], p[1, 2, 0, 0],
     p[2, 0, 0, 1], p[2, 0, 1, 0], p[2, 1, 0, 0], p[3, 0, 0, 0]} /. sol3[[1]] // Simplify;
ls[3] // Simplify
```

Out[ ]=

$\{0. \times 10^{-94}\ g0,\ 0. \times 10^{-94}\ g0,\ 0. \times 10^{-94}\ g0,\ 0. \times 10^{-94}\ g0,\ 0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,$
$0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,\ 0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,\ 0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,$
$0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,\ 0. \times 10^{-85}\ cc,\ 0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,\ 0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,$
$0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,\ 0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,\ 0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,$
$0. \times 10^{-85}\ cc,\ 0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,\ 0. \times 10^{-85}\ cc + 0. \times 10^{-94}\ g0,\ 0. \times 10^{-85}\ cc,\ 0. \times 10^{-85}\ cc\}$

Degree 4

In[ ]:=
```
ls[4] = ls[4] // Simplify;
```

In[ ]:=
```
sol4 = Solve[ls[4] == 0, AppendTo[Hom[4], g0]]
```

Solve: Equations may not give solutions for all "solve" variables.

Out[ ]=
```
{{p[0, 0, 1, 3] →
   -0.22434914917688472862068916999124932024323031196428786628938978716771464210356
    cc, p[0, 0, 2, 2] →
   -7.4653824223809246744201967770130702439874138884416658784404932604662563846222 cc +
    2.0000000000000000000000000000000000000000000000000000000000000000000000000000
     p[0, 0, 0, 4], p[0, 0, 3, 1] →
   0.27580084691135915969217244748212663583302110132943933104628109761805095563813 cc,
  p[0, 0, 4, 0] →
   -3.1216972731271275759047332656482617142259133948731368419196626338479703306865 cc +
    1.0000000000000000000000000000000000000000000000000000000000000000000000000000
     p[0, 0, 0, 4], p[0, 1, 0, 3] →
   5.752204264852997501471079728134515767698714310225940597821426903771997315591 cc,
  p[0, 1, 1, 2] →
   -2.073652984871214402592682928645351157071759114024068800945191974746034989548 cc,
  p[0, 1, 2, 1] →
   -1.434647021809576939215320817955467041934784229737540744268729077406092330047 cc,
  p[0, 1, 3, 0] →
   0.309439227941176515753700425191014118317256934936143299165501375432173799870 cc,
  p[0, 2, 0, 2] →
```

```
 3.5053384666137022231403416821551710472809047525672274452969290768570357190149 cc,
p[0, 2, 1, 1] →
 -1.6510611896269796142155068448916794174019007957892881149033465986846010310161 cc,
p[0, 2, 2, 0] →
 -0.2792858378830226508183409627185939693419246828056776732658314328330057494927 cc,
p[0, 3, 0, 1] →
 0.8434765917338929595148708418262786263401409060348541252654664091821679880137 0 cc,
p[0, 3, 1, 0] →
 -0.3461424255929168731830370436538117362514740511052882215672346295895944939 20 cc,
p[0, 4, 0, 0] →
 0.06445498963475192695884575081478698369792401257535416217844891982345294442891 2
  cc, p[1, 0, 0, 3] →
 -0.03934165492216551255724658539565607782230570070140716829053793220616503612217 5
  cc, p[1, 0, 1, 2] →
 0.00486668247656414473891107439584681858729196190646108242575192261525899463111 63
  cc, p[1, 0, 2, 1] →
 0.00700796393765999576891118346309125568049815704984543498469993717707172065831 29
  cc, p[1, 0, 3, 0] →
 -0.000504359166360540466991457646208171256651388756180080909864782454801692727490 90
  cc, p[1, 1, 0, 2] →
 -0.04576795707997799365788136082615002387584164731398625182910763625051480432222 3
  cc, p[1, 1, 1, 1] →
 0.01638396927829276696659688224743521267220069891678069204701565031549075292971 3
  cc, p[1, 1, 2, 0] →
 0.00176895931791150556907245335785845439059641836490605874552787704745345893607031
  cc, p[1, 2, 0, 1] →
 -0.01543017350476828050648335932484578134141621709564461923389832738620672506932 1
  cc, p[1, 2, 1, 0] →
 0.00536128379933840651497801095743322820501314487150679691575207107780441260 cc,
p[1, 3, 0, 0] →
 -0.00140446133535152605653715828414019263676823206213468056445560486572633442416672
  cc, p[2, 0, 0, 2] →
 0.00028517590367715126064766671800662651660085129936637640464602840349401912536793
  cc, p[2, 0, 1, 1] →
 -0.00311314503484652432879286849285372015956706807860598699747919316159824016310 07
  cc, p[2, 0, 2, 0] →
 0.00137520403924335127854010045625130770613482577145175717483873182748356259403903
  cc, p[2, 1, 0, 1] →
 -0.00231144205760785879815929170101746745730086644497697646037002027531327521713 11
  cc, p[2, 1, 1, 0] →
 0.00102955824813837874032679698462521650843598486799025346625346328251296000 5 cc,
p[2, 2, 0, 0] →
 -0.00058857453822528554314670122603292821694997078280532397426630899560834064889340
  cc, p[3, 0, 0, 1] →
 0.00166124423658153307903349816203941465458725530663384054061769058143858515009 07
  cc, p[3, 0, 1, 0] →
 -0.00073934261575552703265213260556433656508355126891169450747644542440640329 0 cc,
p[3, 1, 0, 0] →
 0.00003693527034508081101068691020864411324135353504089948186727004810829944864538 4
  cc, p[4, 0, 0, 0] →
```

```
1.60962292979464945695389276271263364244554057343410810451071885542587750902878 ×
  10^-6 cc, g0 →
-0.008782119554335957600174014936060177374054594634644197543040827324044547716697
 cc}}
```

```
In[•]:= {g0, p[0, 0, 0, 4], p[0, 0, 1, 3], p[0, 0, 2, 2], p[0, 0, 3, 1], p[0, 0, 4, 0],
    p[0, 1, 0, 3], p[0, 1, 1, 2], p[0, 1, 2, 1], p[0, 1, 3, 0], p[0, 2, 0, 2],
    p[0, 2, 1, 1], p[0, 2, 2, 0], p[0, 3, 0, 1], p[0, 3, 1, 0], p[0, 4, 0, 0],
    p[1, 0, 0, 3], p[1, 0, 1, 2], p[1, 0, 2, 1], p[1, 0, 3, 0], p[1, 1, 0, 2],
    p[1, 1, 1, 1], p[1, 1, 2, 0], p[1, 2, 0, 1], p[1, 2, 1, 0], p[1, 3, 0, 0],
    p[2, 0, 0, 2], p[2, 0, 1, 1], p[2, 0, 2, 0], p[2, 1, 0, 1], p[2, 1, 1, 0],
    p[2, 2, 0, 0], p[3, 0, 0, 1], p[3, 0, 1, 0], p[3, 1, 0, 0], p[4, 0, 0, 0]} =
  {g0, p[0, 0, 0, 4], p[0, 0, 1, 3], p[0, 0, 2, 2], p[0, 0, 3, 1], p[0, 0, 4, 0],
    p[0, 1, 0, 3], p[0, 1, 1, 2], p[0, 1, 2, 1], p[0, 1, 3, 0], p[0, 2, 0, 2],
    p[0, 2, 1, 1], p[0, 2, 2, 0], p[0, 3, 0, 1], p[0, 3, 1, 0], p[0, 4, 0, 0],
    p[1, 0, 0, 3], p[1, 0, 1, 2], p[1, 0, 2, 1], p[1, 0, 3, 0], p[1, 1, 0, 2],
    p[1, 1, 1, 1], p[1, 1, 2, 0], p[1, 2, 0, 1], p[1, 2, 1, 0], p[1, 3, 0, 0],
    p[2, 0, 0, 2], p[2, 0, 1, 1], p[2, 0, 2, 0], p[2, 1, 0, 1], p[2, 1, 1, 0],
    p[2, 2, 0, 0], p[3, 0, 0, 1], p[3, 0, 1, 0], p[3, 1, 0, 0], p[4, 0, 0, 0]} /. sol4[[1]];
```

```
In[•]:= g0
```

```
Out[•]= -0.008782119554335957600174014936060177374054594634644197543040827324044547716697 cc
```

```
In[•]:= g0 // N
```

```
Out[•]= -0.00878212 cc
```

From the above it can be seen that we can take e.g. cc=1.

```
In[•]:= S2 /. { cc → 1}
```

```
Out[•]= 0.000023867217604186814593430465769716919087932982493324291106571739118817387174652
   x1^2 +
  0.040633354253647251034350052899967875845605798985794628522783769783962578398730 x2^2 +
  x3^2 + x4^2
```

```
In[•]:= S2 // N
```

```
Out[•]= 0.0000238672 cc x1^2 + 0.0406334 cc x2^2 + cc x3^2 + cc x4^2
```

```
In[•]:= V1 = V  /. { cc → 1}  // Simplify // Expand;
```

```
In[•]:= vd = D[V1, x1] f1 + D[V1, x2] f2 + D[V1, x3] f3 + D[V1, x4] f4 // Simplify;
```

```
In[•]:= gg = vd /. {x1 → t x1, x2 → t x2, x3 → t x3, x4 → t x4};
        ff = Normal[Series[gg, {t, 0, 4}]] // Simplify;
```

In[•]:=
```
MonomialList[ff, t]
```

Out[•]=
```
{t^4 (-0.0087821195543359576001740149360601773740545946346441975430408273240445477 x3^4 -
    0.0175642391086719152003480298721203547481091892692883950860816546480890950 x3^2 x4^2 -
    0.0087821195543359576001740149360601773740545946346441975430408273240445477
     x4^4), 0,
 t^2 (-0.0087821195543359576001740149360601773740545946346441975430408273240445477 x1^2 -
    0.0087821195543359576001740149360601773740545946346441975430408273240445477 x2^2)}
```

In[•]:=
```
S2 /. { cc → 1}
```

Out[•]=
```
0.000023867217604186814593430465769716919087932982493324291106571739118817387174652
   x1^2 +
 0.0406333542536472510343500528999678758456057989857946285227837697839625783987300 x2^2 +
 x3^2 + x4^2
```

From the above we can see that the lowest degree part of V is positively defined, that is, V is a positively defined Lyapunov function, whose Lie derivative is negatively defined.

1. c) Evolution of system states under perturbations

Plotting the original system

Preparations

In[•]:=
```
Quit
```

In[•]:=
```
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@
  {Plot, ParametricPlot, ListPlot, ListLinePlot};
SetDirectory[NotebookDirectory[]];
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@ {Plot, ListPlot,
   ListLinePlot, ListLogLogPlot, ParametricPlot, DateListPlot, DiscretePlot};
LaunchKernels[];
```

The function creating the plots with the measured values

In[ ]:=
```
ClearAll[x1, x2, x3, a, b, n, w, ED, c, k1, k2, k];
f1[x1_, x2_, x3_, x4_] := a x1 - n x1 - b x1 x3/(ED + x3);
f2[x1_, x2_, x3_, x4_] := n x1 - w x2 + b x1 x3/(ED + x3);
f3[x1_, x2_, x3_, x4_] := -c x3 - k1 x3 + k2 x4 + k (x1 + x2);
f4[x1_, x2_, x3_, x4_] := k1 x3 - k2 x4;
{a, b, n, w, ED, c, k1, k2} =
  {3131/12500, 3771/2500, 86643/1000000, 2993/100000, 17461/20000, 21471/25000, 8323/50, 8369/500};
k = 1/100;
```

In[]:=
```
ClearAll[nsol, ev, plotter3D];
nsol = NSolve[Join @@ Thread /@ {{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3,
         x4], f4[x1, x2, x3, x4]} == 0, {x1, x2, x3, x4} > 0}, {x1, x2, x3, x4}, 20][[1]]
ev = Eigenvalues[
  D[{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3, x4], f4[x1, x2, x3, x4]},
    {{x1, x2, x3, x4}}] /. nsol]
plotter3D[τ_, shift_, ag_ : Automatic, pg_ : Automatic, pp_ : 1000,
  ar_ : Automatic, opts___] := Module[{startingpoint, sys, solution,
   solution1, solution2, solution3, solution4, plot1, imagesize, imagesize2},
  imagesize = 350; imagesize2 = 250;
  startingpoint = ({x1, x2, x3, x4} /. nsol) + shift;
  sys := NDSolveValue[Join[{u1'[t] == f1[u1[t], u2[t], u3[t], u4[t]],
      u2'[t] == f2[u1[t], u2[t], u3[t], u4[t]], u3'[t] ==
       f3[u1[t], u2[t], u3[t], u4[t]], u4'[t] == f4[u1[t], u2[t], u3[t], u4[t]]},
     Thread[{u1[0], u2[0], u3[0], u4[0]} == startingpoint]],
    {u1, u2, u3, u4}, {t, τ}, AccuracyGoal → ag, PrecisionGoal → pg, opts];
  solution[t_] := Through[sys[t]];
  solution4[t_] := Delete[Through[sys[t]], 4];
  solution3[t_] := Delete[Through[sys[t]], 3];
  solution2[t_] := Delete[Through[sys[t]], 2];
  solution1[t_] := Delete[Through[sys[t]], 1];
  {ParametricPlot3D[Evaluate[solution4[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1 [mm3]", "x2 [mm3]", "x3 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution3[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1 [mm3]", "x2 [mm3]", "x4 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution2[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1 [mm3]", "x3 [mg/kg]", "x4 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution1[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x2 [mm3]", "x3 [mg/kg]", "x4 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   Plot[Evaluate[solution[t][[1]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x1 [mm3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[2]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x2 [mm3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[3]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x3 [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[4]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x4 [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2]}]
```

Out[ ]=

```
{x1 → 0.9752039020806009366, x2 → 8.161345586139289095,
 x3 → 0.10638244013110579422, x4 → 1.0579771169927034596}
```

Out[ ]=

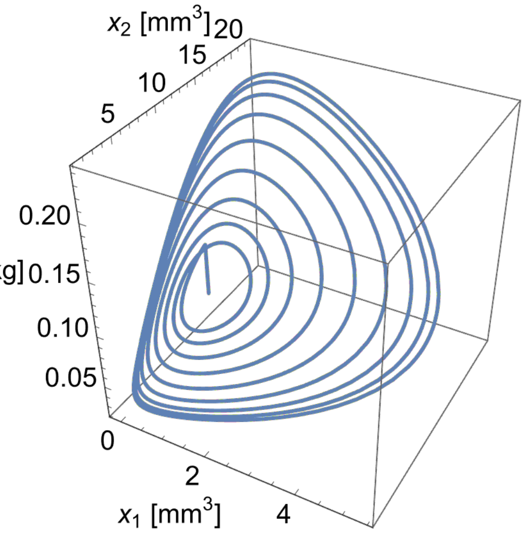
```
{-183.97870462341836626, -0.11374116433798663099,
 0.002837893878176444287 + 0.05472348796826117015 ⅈ,
 0.002837893878176444287 - 0.05472348796826117015 ⅈ}
```

Trajectories going outwards, approaching the limit cycle from inside

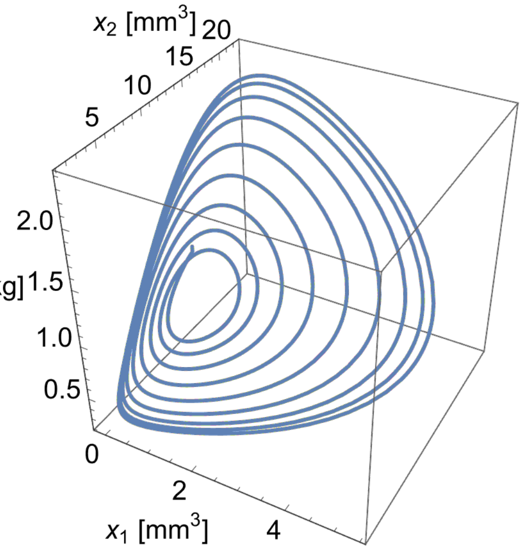
In[ ]:=

```
plotter3D[1200, {0, 0, 0, 0.5}, Automatic, 100, 1000, 1, Method → "BDF"]
```

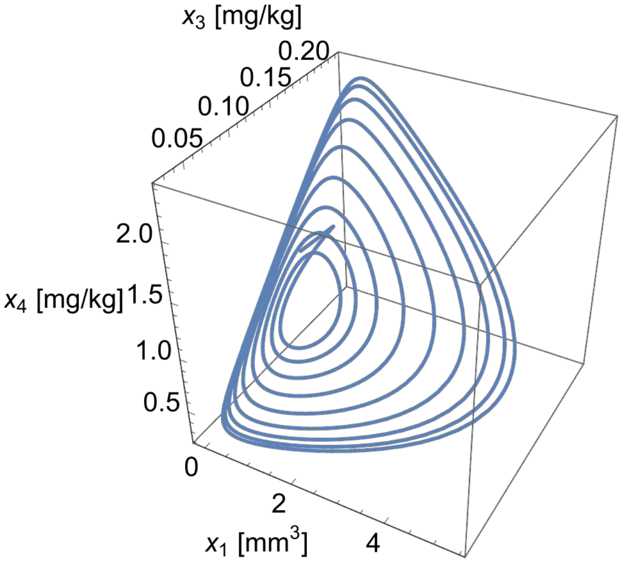
Out[ ]=

{

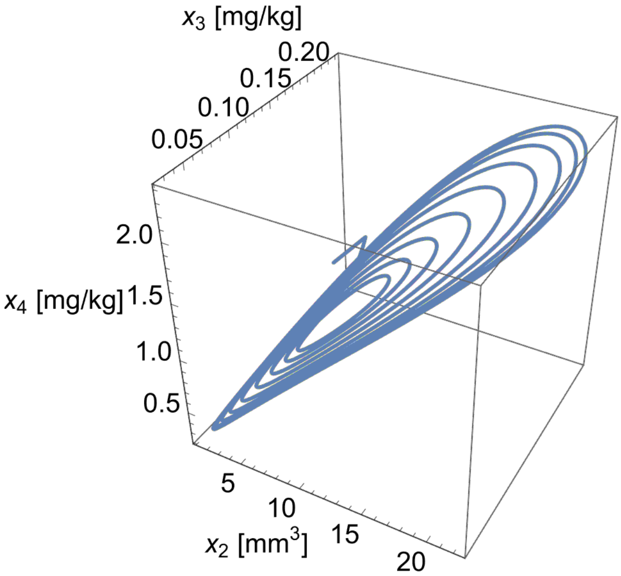
,



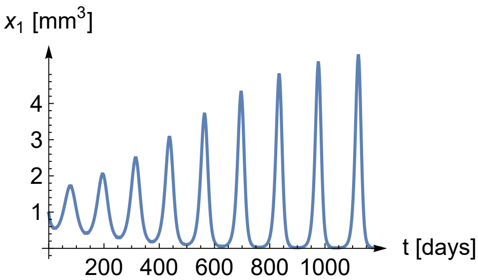
,


x3 [mg/kg]
0.20
0.15
0.10
0.05
2.0
x4 [mg/kg] 1.5
1.0
0.5
0
2
x1 [mm3]
4

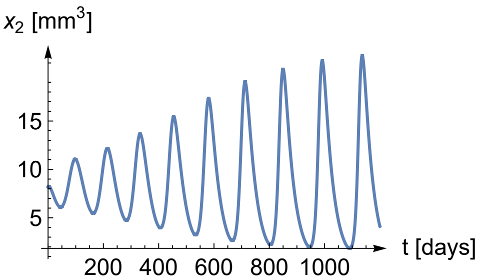
,


x3 [mg/kg]
0.20
0.15
0.10
0.05
2.0
x4 [mg/kg] 1.5
1.0
0.5
5
10
x2 [mm3]
15
20

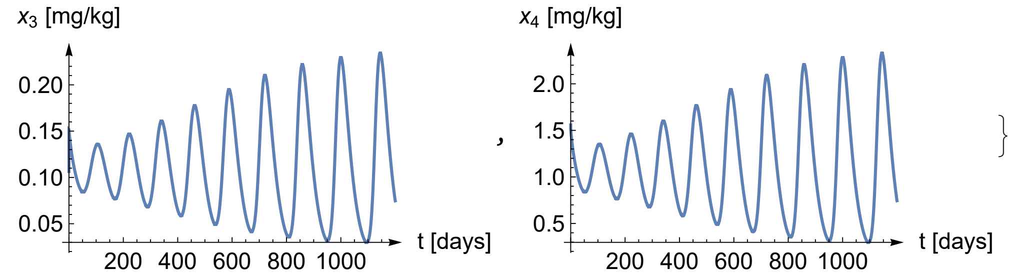
,


x1 [mm3]
4
3
2
1
200
400
600
800
1000
t [days]

,


x2 [mm3]
15
10
5
200
400
600
800
1000
t [days]

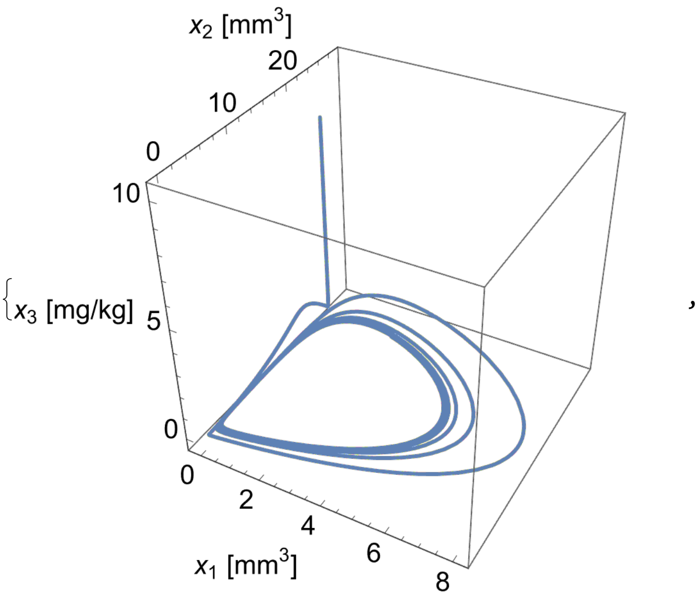
,

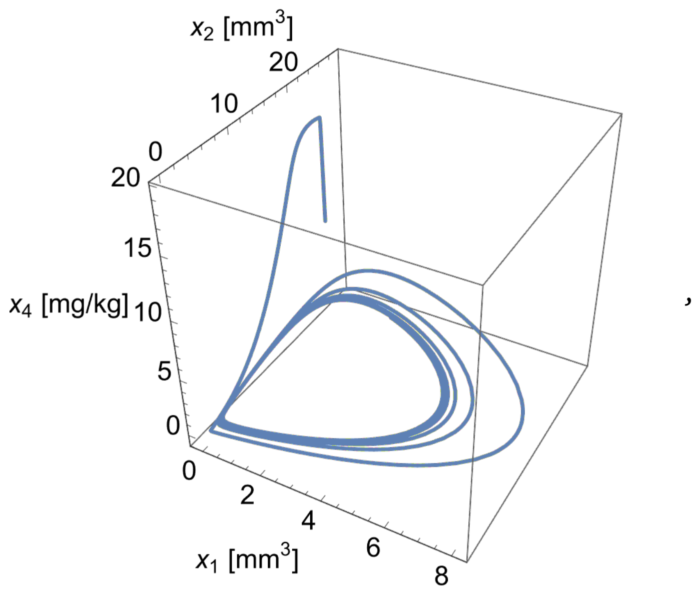


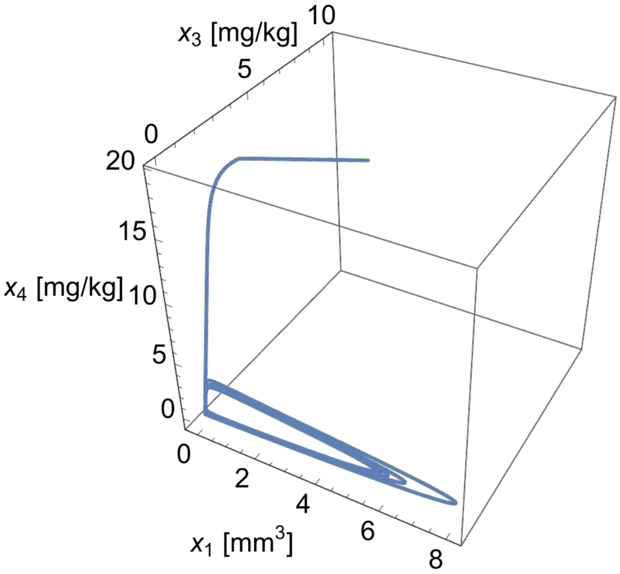
Trajectories going inwards, approaching the limit cycle from outside

In[◦]:=
```
plotter3D[1000, {0, 10, 10, 10}, Automatic, 100, 1000, 1, Method → "BDF"]
```

Out[◦]=

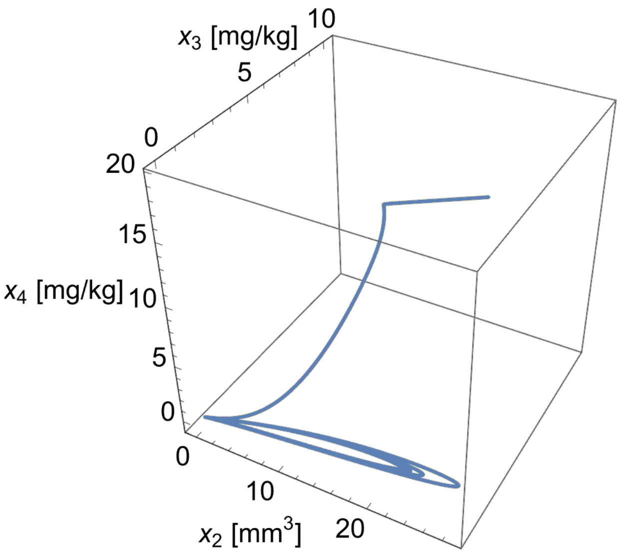






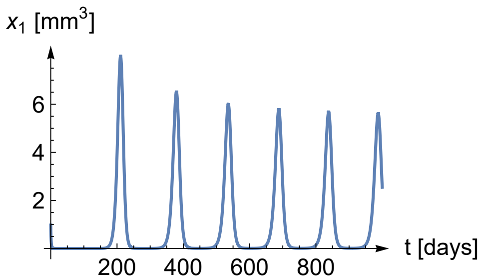
x3 [mg/kg]
10
5
0
20
15
x4 [mg/kg]
10
5
0
0
2
4
6
8
x1 [mm3]

,



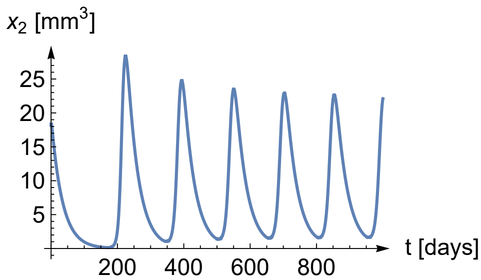
x3 [mg/kg]
10
5
0
20
15
x4 [mg/kg]
10
5
0
0
10
20
x2 [mm3]

,



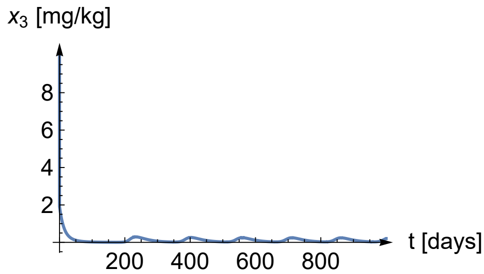
x1 [mm3]
6
4
2
200
400
600
800
t [days]

,

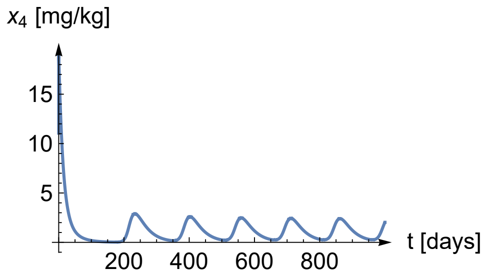


x2 [mm3]
25
20
15
10
5
200
400
600
800
t [days]

,



,



}

Positive perturbation

We perturb n by +1/50, so $n \approx 0.152497$. Each eigenvalue has a negative real part, the singular point is locally asymptotically stable.

Preparations

In[∘]:=

```
Quit
```

In[∘]:=

```
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@
  {Plot, ParametricPlot, ListPlot, ListLinePlot};
SetDirectory[NotebookDirectory[]];
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@ {Plot, ListPlot,
   ListLinePlot, ListLogLogPlot, ParametricPlot, DateListPlot, DiscretePlot};
LaunchKernels[];
```

The function creating the plots

In[∘]:=

```
ClearAll[x1, x2, x3, a, b, n, w, ED, c, k1, k2, k];
f1[x1_, x2_, x3_, x4_] := a x1 - n x1 - b x1 x3/(ED + x3);
f2[x1_, x2_, x3_, x4_] := n x1 - w x2 + b x1 x3/(ED + x3);
f3[x1_, x2_, x3_, x4_] := -c x3 - k1 x3 + k2 x4 + k (x1 + x2);
f4[x1_, x2_, x3_, x4_] := k1 x3 - k2 x4;
{w, ED, c, k1, k2} = {2993/100000, 17461/20000, 21471/25000, 8323/50, 8369/500};
a = 3131/12500; b = 3/2;
n = (-12488 + 125 [√ 126....])/25000 + 1/50;
k = 1/100;
```

In[ ]:=

```
ClearAll[nsol, ev, plotter3D];
nsol = NSolve[Join @@ Thread /@ {{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3,
          x4], f4[x1, x2, x3, x4]} == 0, {x1, x2, x3, x4} > 0}, {x1, x2, x3, x4}, 20][[1]]
ev = Eigenvalues[
  D[{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3, x4], f4[x1, x2, x3, x4]},
    {{x1, x2, x3, x4}}] /. nsol]
plotter3D[τ_, shift_, ag_ : Automatic, pg_ : Automatic, pp_ : 1000,
  ar_ : Automatic, opts___] := Module[{startingpoint, sys, solution,
   solution1, solution2, solution3, solution4, plot1, imagesize, imagesize2},
  imagesize = 350; imagesize2 = 250;
  startingpoint = ({x1, x2, x3, x4} /. nsol) + shift;
  sys := NDSolveValue[Join[{u1'[t] == f1[u1[t], u2[t], u3[t], u4[t]],
      u2'[t] == f2[u1[t], u2[t], u3[t], u4[t]], u3'[t] ==
       f3[u1[t], u2[t], u3[t], u4[t]], u4'[t] == f4[u1[t], u2[t], u3[t], u4[t]]},
     Thread[{u1[0], u2[0], u3[0], u4[0]} == startingpoint]],
    {u1, u2, u3, u4}, {t, τ}, AccuracyGoal → ag, PrecisionGoal → pg, opts];
  solution[t_] := Through[sys[t]];
  solution4[t_] := Delete[Through[sys[t]], 4];
  solution3[t_] := Delete[Through[sys[t]], 3];
  solution2[t_] := Delete[Through[sys[t]], 2];
  solution1[t_] := Delete[Through[sys[t]], 1];
  {ParametricPlot3D[Evaluate[solution4[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1 [mm3]", "x2 [mm3]", "x3 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution3[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1 [mm3]", "x2 [mm3]", "x4 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution2[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1 [mm3]", "x3 [mg/kg]", "x4 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution1[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x2 [mm3]", "x3 [mg/kg]", "x4 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   Plot[Evaluate[solution[t][[1]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x1 [mm3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[2]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x2 [mm3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[3]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x3 [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[4]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x4 [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2]}]
```

Out[ ]=

```
{x1 → 0.5593248387955557657, x2 → 4.680911647895449656,
 x3 → 0.06101528208619772509, x4 → 0.6067991310830728473}
```

Out[ ]=

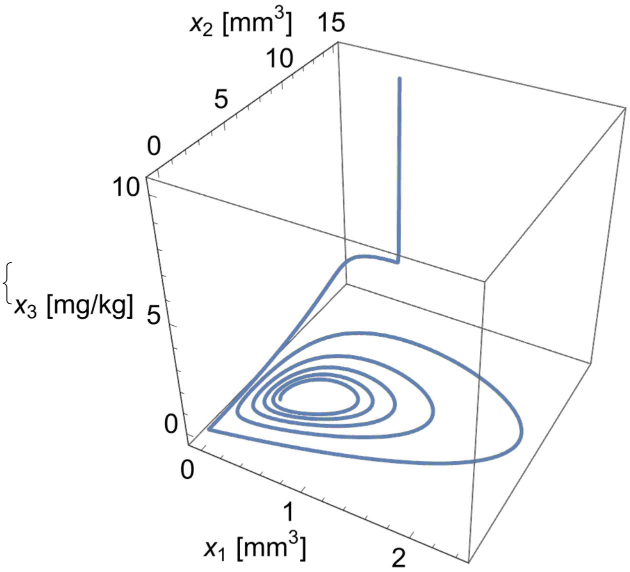
```
{-183.97870458580167773, -0.10509393683501969075,
 -0.0014857386816512905181 + 0.045119117797367824l2 ⅈ,
 -0.0014857386816512905181 - 0.045119117797367824l2 ⅈ}
```

Trajectories going inwards, towards the singular point

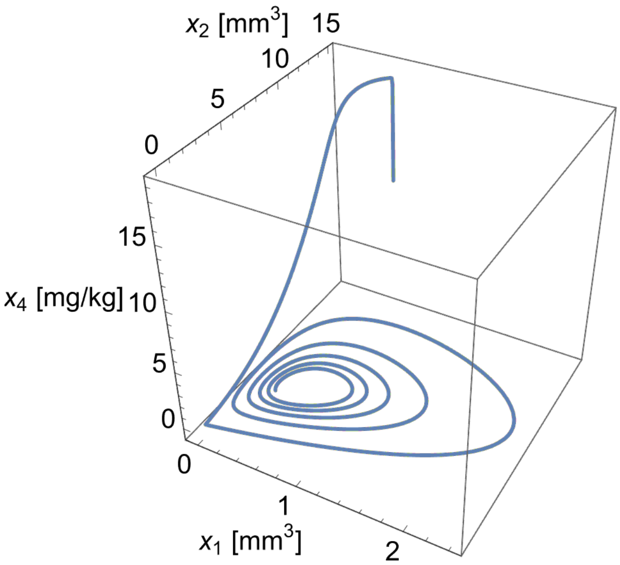
In[ ]:=

```
plotter3D[1000, {0, 10, 10, 10}, Automatic, 100, 1000, 1, Method → "BDF"]
```

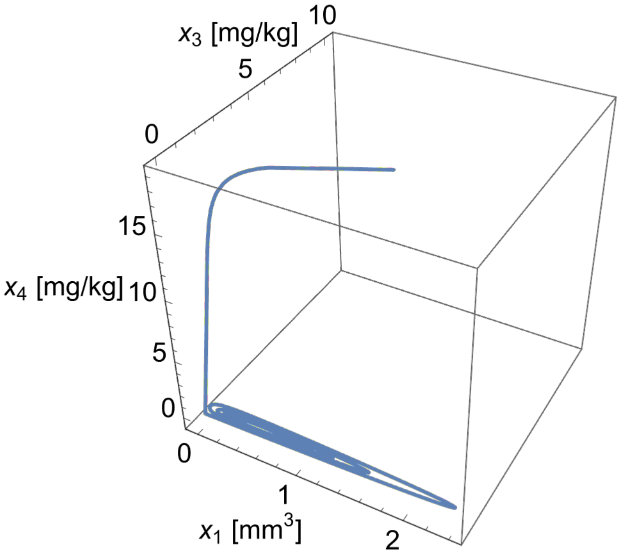
Out[ ]=

{

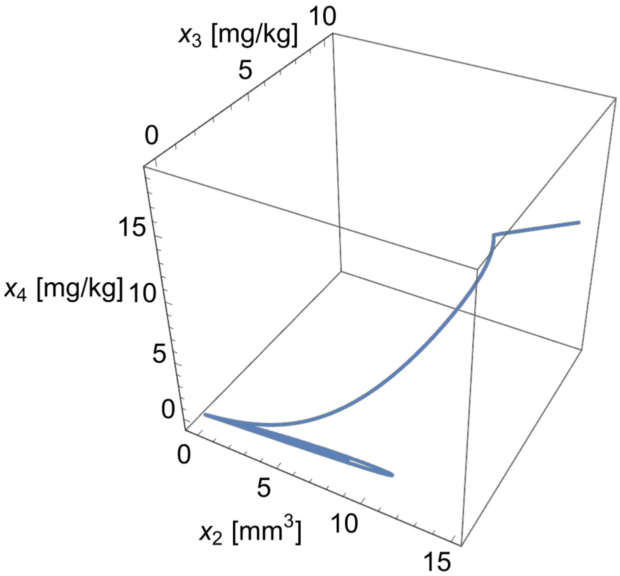
,



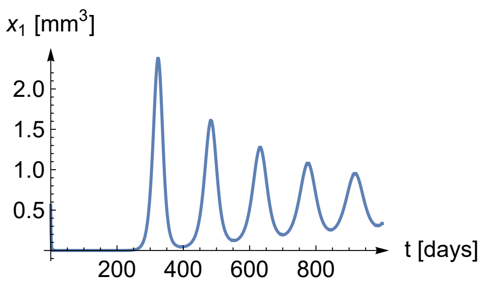
,


x3 [mg/kg]
10
5
0
15
x4 [mg/kg] 10
5
0
0
1
x1 [mm3]
2

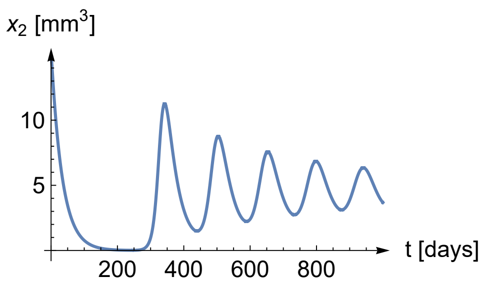
,


x3 [mg/kg]
10
5
0
15
x4 [mg/kg] 10
5
0
0
5
x2 [mm3]
10
15

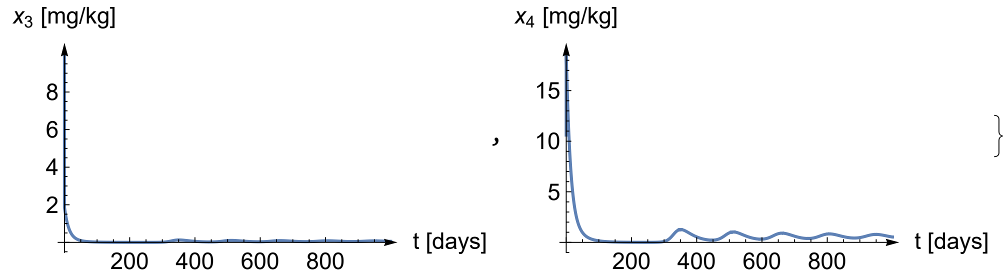
,


x1 [mm3]
2.0
1.5
1.0
0.5
200
400
600
800
t [days]

,

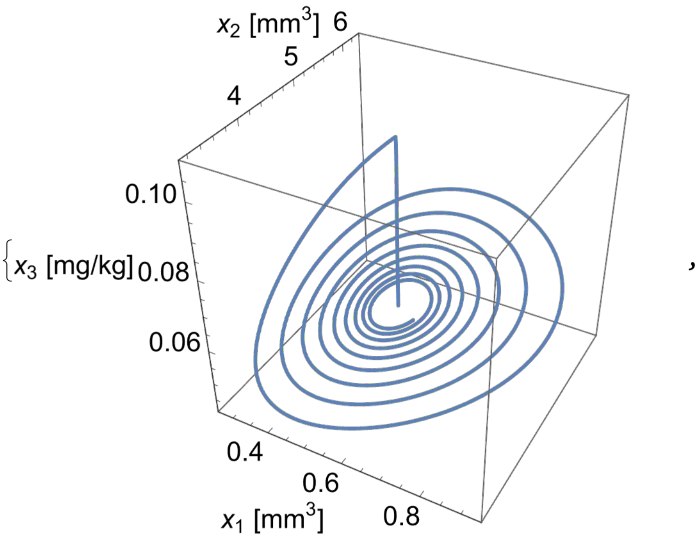

x2 [mm3]
10
5
200
400
600
800
t [days]

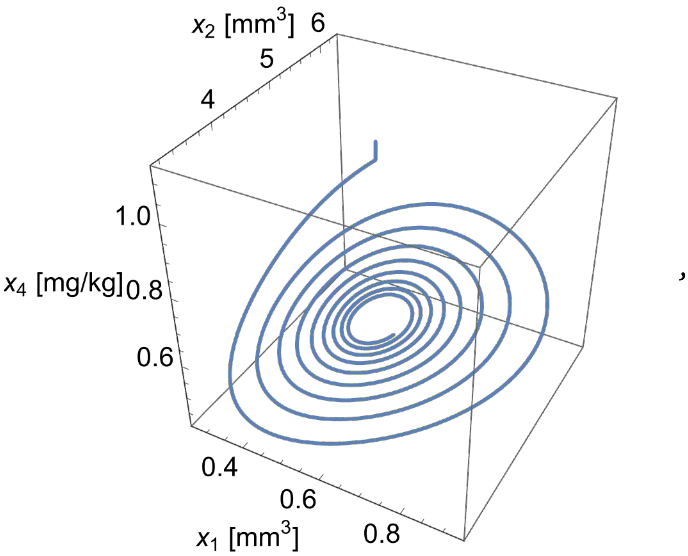
,

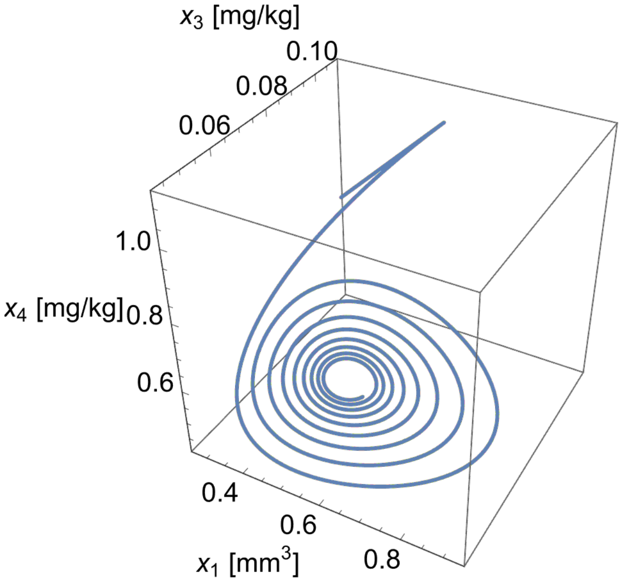


In[ ]:=
```
plotter3D[1200, {0, 0, 0, 0.5}, Automatic, 100, 1000, 1, Method → "BDF"]
```

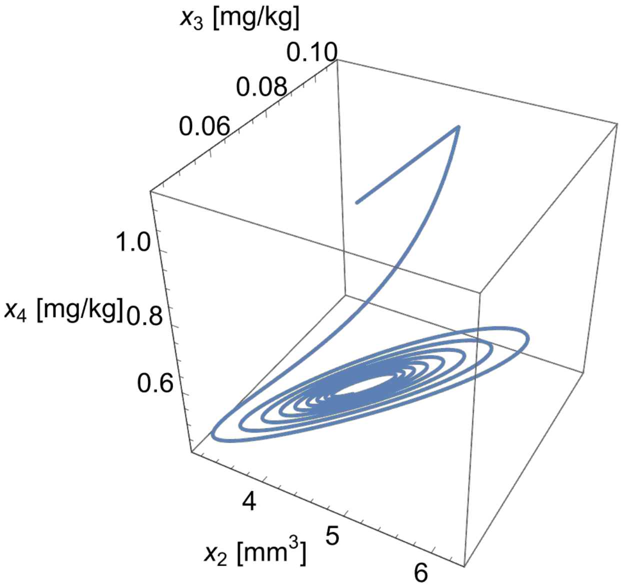
Out[ ]=



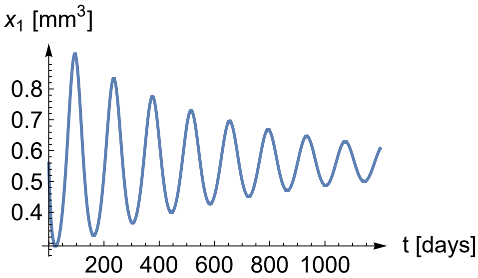



x3 [mg/kg]
0.10
0.08
0.06
1.0
x4 [mg/kg]
0.8
0.6
0.4
0.6
x1 [mm3]
0.8

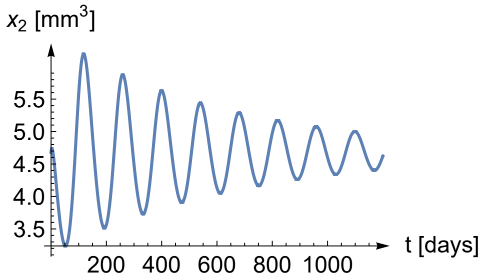
,


x3 [mg/kg]
0.10
0.08
0.06
1.0
x4 [mg/kg]
0.8
0.6
4
5
x2 [mm3]
6

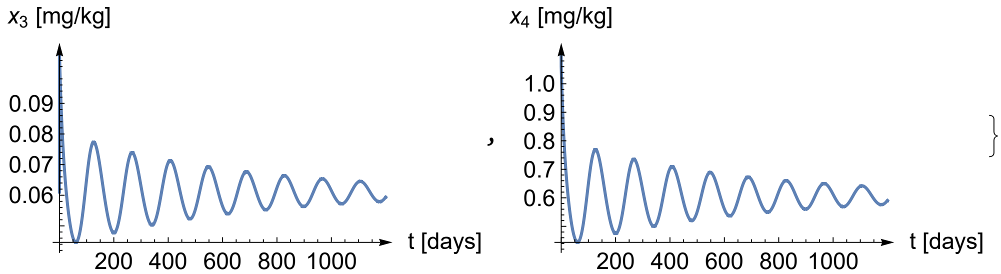
,


x1 [mm3]
0.8
0.7
0.6
0.5
0.4
200 400 600 800 1000
t [days]

,


x2 [mm3]
5.5
5.0
4.5
4.0
3.5
200 400 600 800 1000
t [days]

,



Negative perturbation

We perturb n by $-1/50$, so $n \approx 0.112497$. Two imaginary eigenvalues have positive real part, so the singular point becomes locally unstable and a stable limit cycle appears around it.

Preparations

In[◦]:=
```
Quit
```

In[◦]:=
```
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@
  {Plot, ParametricPlot, ListPlot, ListLinePlot};
SetDirectory[NotebookDirectory[]];
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@ {Plot, ListPlot,
   ListLinePlot, ListLogLogPlot, ParametricPlot, DateListPlot, DiscretePlot};
LaunchKernels[];
```

The function creating the plots

In[◦]:=
```
ClearAll[x1, x2, x3, a, b, n, w, ED, c, k1, k2, k];
f1[x1_, x2_, x3_, x4_] := a x1 - n x1 - b x1 x3/(ED + x3);
f2[x1_, x2_, x3_, x4_] := n x1 - w x2 + b x1 x3/(ED + x3);
f3[x1_, x2_, x3_, x4_] := -c x3 - k1 x3 + k2 x4 + k (x1 + x2);
f4[x1_, x2_, x3_, x4_] := k1 x3 - k2 x4;
{w, ED, c, k1, k2} = {2993/100000, 17461/20000, 21471/25000, 8323/50, 8369/500};
a = 3131/12500; b = 3/2;
n = (-12488 + 125 [√ 126.…])/25000 - 1/50;
k = 1/100;
```

In[∘]:=
```
ClearAll[nsol, ev, plotter3D];
nsol = NSolve[Join @@ Thread /@ {{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3,
        x4], f4[x1, x2, x3, x4]} == 0, {x1, x2, x3, x4} > 0}, {x1, x2, x3, x4}, 20][[1]]
ev = Eigenvalues[
  D[{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3, x4], f4[x1, x2, x3, x4]},
    {{x1, x2, x3, x4}}] /. nsol]
plotter3D[τ_, shift_, ag_ : Automatic, pg_ : Automatic, pp_ : 1000,
  ar_ : Automatic, opts___] := Module[{startingpoint, sys, solution,
   solution1, solution2, solution3, solution4, plot1, imagesize, imagesize2},
  imagesize = 350; imagesize2 = 250;
  startingpoint = ({x1, x2, x3, x4} /. nsol) + shift;
  sys := NDSolveValue[Join[{u1'[t] == f1[u1[t], u2[t], u3[t], u4[t]],
      u2'[t] == f2[u1[t], u2[t], u3[t], u4[t]], u3'[t] ==
       f3[u1[t], u2[t], u3[t], u4[t]], u4'[t] == f4[u1[t], u2[t], u3[t], u4[t]]},
     Thread[{u1[0], u2[0], u3[0], u4[0]} == startingpoint]],
    {u1, u2, u3, u4}, {t, τ}, AccuracyGoal → ag, PrecisionGoal → pg, opts];
  solution[t_] := Through[sys[t]];
  solution4[t_] := Delete[Through[sys[t]], 4];
  solution3[t_] := Delete[Through[sys[t]], 3];
  solution2[t_] := Delete[Through[sys[t]], 2];
  solution1[t_] := Delete[Through[sys[t]], 1];
  {ParametricPlot3D[Evaluate[solution4[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x_1 [mm^3]", "x_2 [mm^3]", "x_3 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution3[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x_1 [mm^3]", "x_2 [mm^3]", "x_4 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution2[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x_1 [mm^3]", "x_3 [mg/kg]", "x_4 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution1[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x_2 [mm^3]", "x_3 [mg/kg]", "x_4 [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   Plot[Evaluate[solution[t][[1]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x_1 [mm^3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[2]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x_2 [mm^3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[3]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x_3 [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[4]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x_4 [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2]}]
```

Out[∘]=

```
{x1 → 0.8107914412655531128, x2 → 6.785400608359363304,
 x3 → 0.0884471152906818082 2, x4 → 0.8796096792500235271}
```

Out[∘]=

```
{-183.97870460908476842, -0.11070486378595318174,
 0.0013197364353608002215 + 0.051429255504015888 12 ⅈ,
 0.0013197364353608002215 - 0.051429255504015888 12 ⅈ}
```

Case (i), Figures 1 and 3 (a)

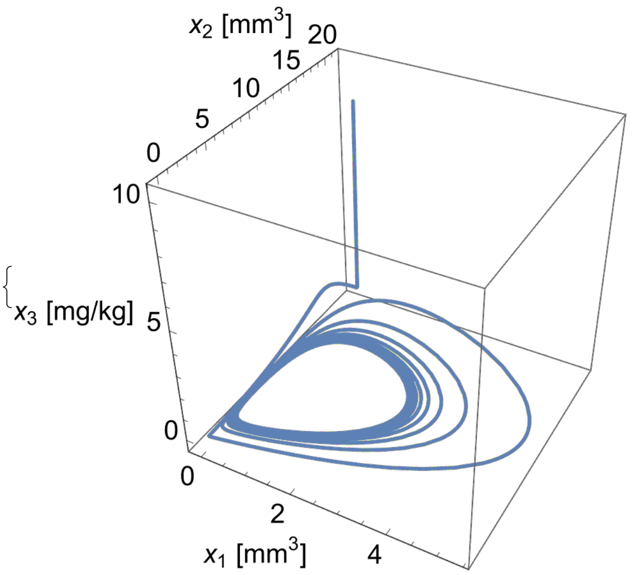
The trajectories are going inward, approaching the limit cycle from outside.

In[∘]:=

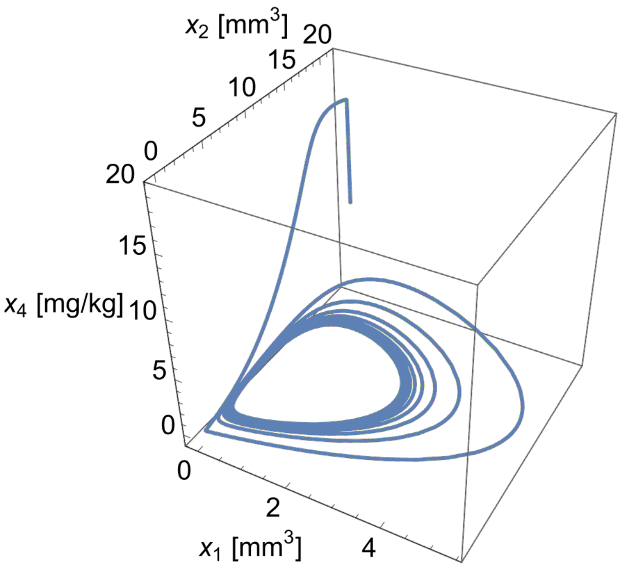
```
plotter3D[1800, {0, 10, 10, 10}, Automatic, 100, 1000, 1, Method → "BDF"]
```

Out[∘]=

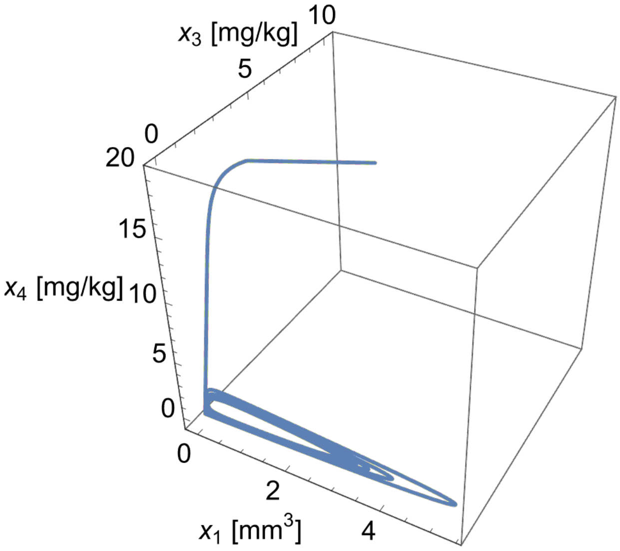
{



,

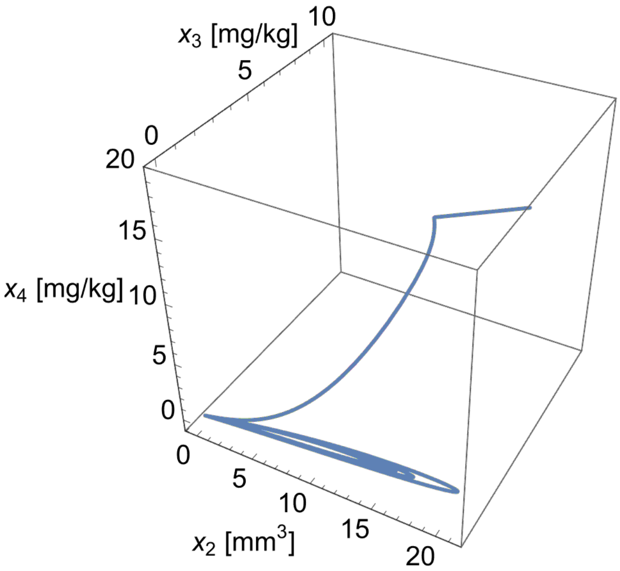


,



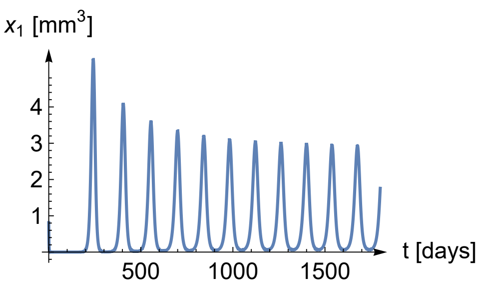
x₃ [mg/kg]
10
5
0
20
15
x₄ [mg/kg]
10
5
0
0
2
x₁ [mm³]
4

,



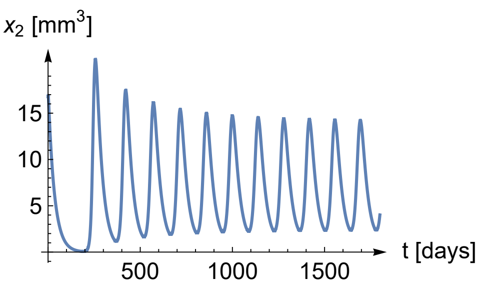
x₃ [mg/kg]
10
5
0
20
15
x₄ [mg/kg]
10
5
0
0
5
10
15
x₂ [mm³]
20

,



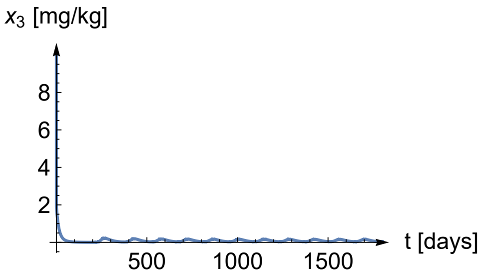
x₁ [mm³]
4
3
2
1
500
1000
1500
t [days]

,

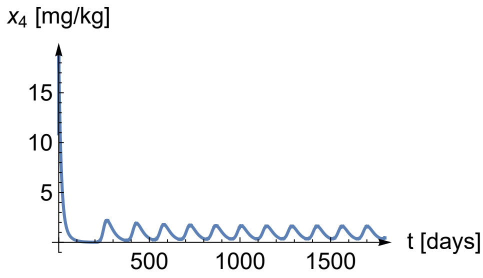


x₂ [mm³]
15
10
5
500
1000
1500
t [days]

,



,



}

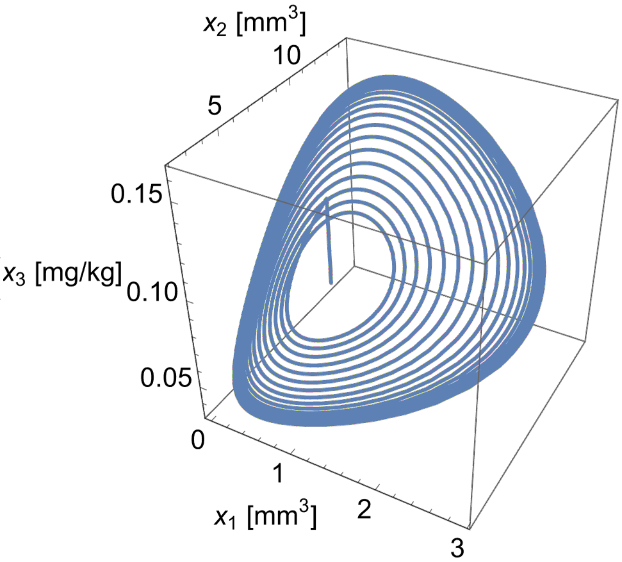
Case (ii) , Figures 2 and 3 (b)

The trajectories are going outward, approaching the limit cycle from inside.

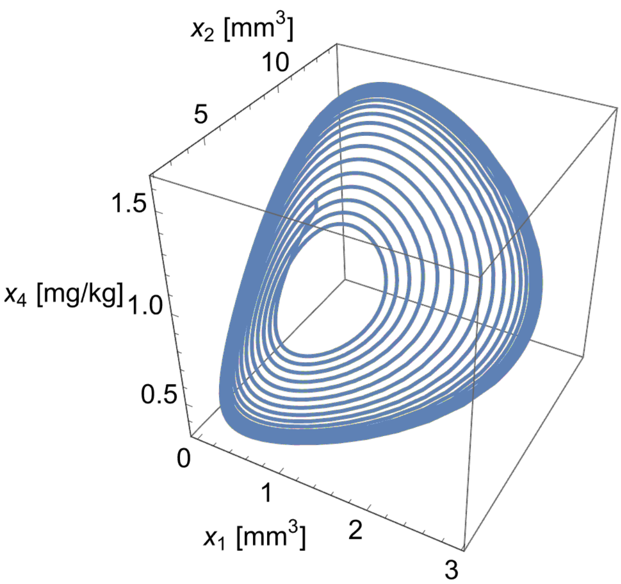
In[∘]:=
```
plotter3D[2500, {0, 0, 0, 0.5}, Automatic, 100, 1000, 1, Method → "BDF"]
```

Out[∘]=

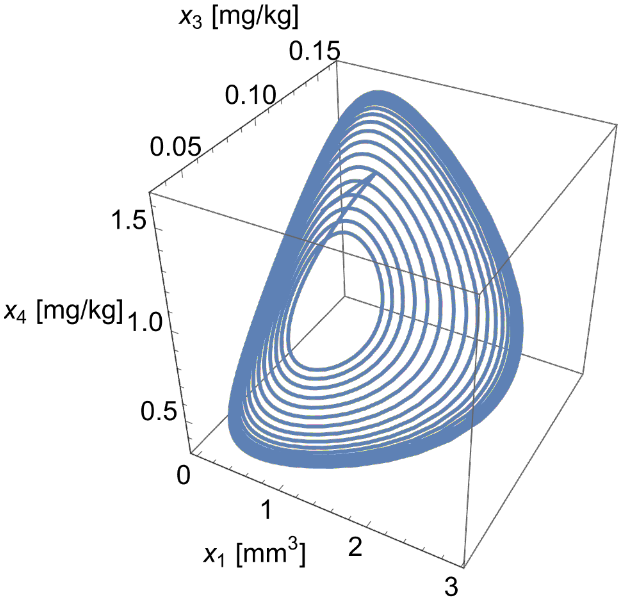
{



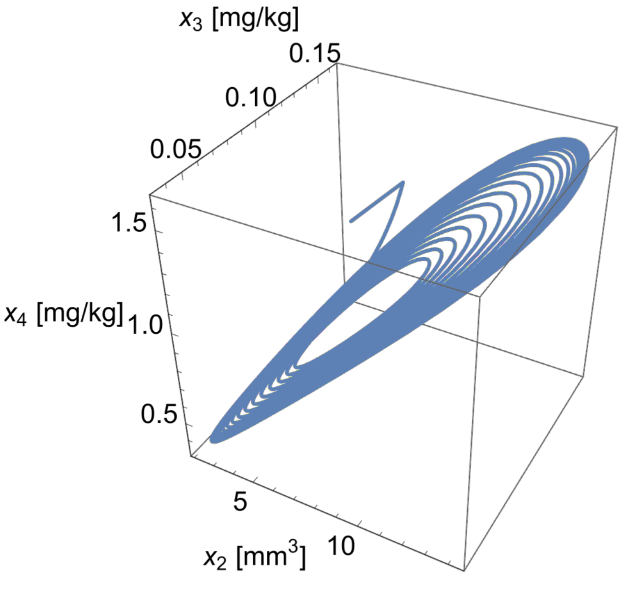
,



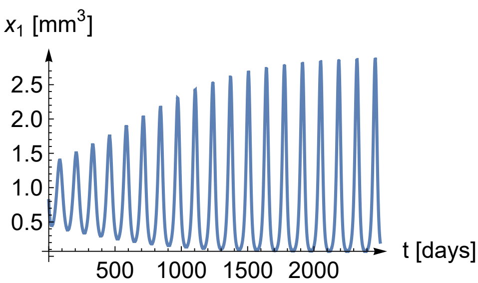
,


x3 [mg/kg]
0.15
0.10
0.05
1.5
x4 [mg/kg]
1.0
0.5
0
1
x1 [mm3]
2
3

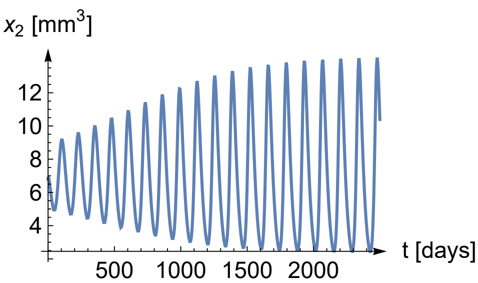
,


x3 [mg/kg]
0.15
0.10
0.05
1.5
x4 [mg/kg]
1.0
0.5
5
x2 [mm3]
10

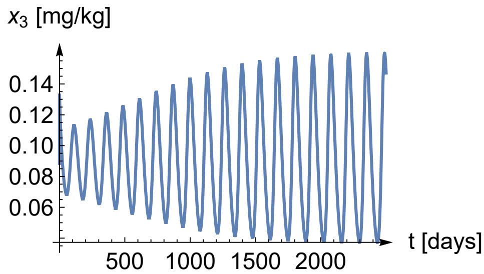
,


x1 [mm3]
2.5
2.0
1.5
1.0
0.5
500
1000
1500
2000
t [days]

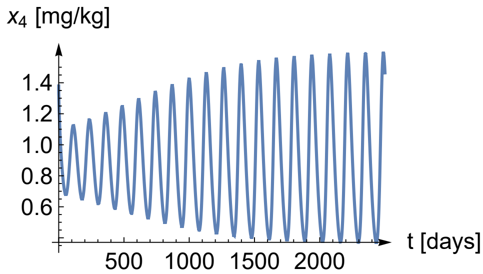
,


x2 [mm3]
12
10
8
6
4
500
1000
1500
2000
t [days]

,



,



}

2. a) Qualitative analysis

The tumor growth model

Here we repeat the procedure described in the previous section.
The measured values in Table 3 are the following:

In[◦]:=
```
Quit
```

In[◦]:=

$$\{a, b, n, w, ED, c, k1, k2\} = \left\{\frac{38437}{100000}, \frac{22229}{10000}, \frac{13881}{100000}, \frac{71159}{1000000}, \frac{117}{80}, \frac{22711}{100000}, \frac{21459}{100}, \frac{13953}{10}\right\};$$

```
% // N
```

Out[◦]=
```
{0.38437, 2.2229, 0.13881, 0.071159, 1.4625, 0.22711, 214.59, 1395.3}
```

Calculations

System (1)

In[◦]:=
```
Quit
```

In[◦]:=

$$f1 = a\,x1 - n\,x1 - b\,x1\,\frac{x3}{ED + x3};$$

$$f2 = n\,x1 - w\,x2 + b\,x1\,\frac{x3}{ED + x3};$$

```
f3 = - c x3 - k1 x3 + k2 x4 + k (x1 + x2);
f4 = k1 x3 - k2 x4;
```

Singular point (3)

In[∘]:=
```
sol = Solve[{f1, f2, f3, f4} == 0, {x1, x2, x3, x4}] // Factor
```

Out[∘]=

$$\left\{\{x1 \to 0, x2 \to 0, x3 \to 0, x4 \to 0\}, \left\{x1 \to -\frac{c\, ED\, (a-n)\, w}{k\, (a-b-n)\, (a+w)},\right.\right.$$
$$\left.\left. x2 \to -\frac{a\, c\, ED\, (a-n)}{k\, (a-b-n)\, (a+w)},\ x3 \to -\frac{ED\, (a-n)}{a-b-n},\ x4 \to -\frac{ED\, k1\, (a-n)}{k2\, (a-b-n)}\right\}\right\}$$

The Jacobian at the nontrivial singular point (4), (5)

In[∘]:=
```
jac = D[{f1, f2, f3, f4}, {{x1, x2, x3, x4}}] // FullSimplify;
{x1, x2, x3, x4} = {x1, x2, x3, x4} /. sol[[2]];
jac = jac // FullSimplify
jac // MatrixForm
```

Out[∘]=

$$\left\{\left\{0, 0, -\frac{c\, (a-n)\, (-a+b+n)\, w}{b\, k\, (a+w)}, 0\right\},\right.$$
$$\left.\left\{a, -w, \frac{c\, (a-n)\, (-a+b+n)\, w}{b\, k\, (a+w)}, 0\right\}, \{k, k, -c-k1, k2\}, \{0, 0, k1, -k2\}\right\}$$

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0 & 0 & -\frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)} & 0 \\ a & -w & \frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)} & 0 \\ k & k & -c-k1 & k2 \\ 0 & 0 & k1 & -k2 \end{pmatrix}$$

The characteristic polynomial (6)

In[∘]:=
```
pol = CharacteristicPolynomial[jac, y] // Factor
```

Out[∘]=

$$\frac{1}{b}\left(-a^2\, c\, k2\, w + a\, b\, c\, k2\, w + 2\, a\, c\, k2\, n\, w - b\, c\, k2\, n\, w - c\, k2\, n^2\, w - a^2\, c\, w\, y + a\, b\, c\, w\, y + b\, c\, k2\, w\, y + 2\, a\, c\, n\, w\, y - b\, c\, n\, w\, y - c\, n^2\, w\, y + b\, c\, k2\, y^2 + b\, c\, w\, y^2 + b\, k1\, w\, y^2 + b\, k2\, w\, y^2 + b\, c\, y^3 + b\, k1\, y^3 + b\, k2\, y^3 + b\, w\, y^3 + b\, y^4\right)$$

In[∘]:=
```
Variables[pol]
```

Out[∘]=

{b, a, c, k2, w, n, y, k1}

Initial parameter settings and characteristic polynomial

In[∘]:=

$$\{w, ED, c, k1, k2\} = \left\{\frac{71159}{1000000}, \frac{117}{80}, \frac{22711}{100000}, \frac{21459}{100}, \frac{13953}{10}\right\};$$

In[∘]:=
```
pol = pol // Factor
```

Out[∘]=

$$\frac{1}{1\,000\,000\,000\,000\,b}\left(-22\,549\,332\,359\,697\,a^2+22\,549\,332\,359\,697\,a\,b+45\,098\,664\,719\,394\,a\,n-22\,549\,332\,359\,697\,b\,n-22\,549\,332\,359\,697\,n^2-16\,160\,920\,490\,a^2\,y+22\,549\,332\,359\,697\,b\,y+16\,160\,920\,490\,a\,b\,y+32\,321\,840\,980\,a\,n\,y-16\,160\,920\,490\,b\,n\,y-16\,160\,920\,490\,n^2\,y+431\,460\,906\,430\,490\,b\,y^2+1\,610\,188\,269\,000\,000\,b\,y^3+1\,000\,000\,000\,000\,b\,y^4\right)$$

The method to find pure imaginary eigenvalues

In[∘]:=
```
pb = (b0 + b1 y + b2 y^2) (y^2 + W) // Expand
eq = pol - pb;
uu = Series[eq, {y, 0, 7}] // FullSimplify
sys = LogicalExpand[uu == 0] // FullSimplify
```

Out[∘]=

$$b0\,W+b1\,W\,y+b0\,y^2+b2\,W\,y^2+b1\,y^3+b2\,y^4$$

Out[∘]=

$$\left(\frac{22\,549\,332\,359\,697\,(a-n)\,(-a+b+n)}{1\,000\,000\,000\,000\,b}-b0\,W\right)+\left(\frac{1\,616\,092\,049\,(13\,953\,b-10\,(a-n)\,(a-b-n))}{1\,000\,000\,000\,000\,b}-b1\,W\right)y+\left(\frac{43\,146\,090\,643\,049}{100\,000\,000\,000}-b0-b2\,W\right)y^2+\left(\frac{1\,610\,188\,269}{1\,000\,000}-b1\right)y^3+(1-b2)\,y^4+O[y]^8$$

Out[∘]=

$$1\,000\,000\,b1==1\,610\,188\,269\;\&\&\;b2==1\;\&\&\;\frac{22\,549\,332\,359\,697\,(a-n)\,(-a+b+n)}{b}==1\,000\,000\,000\,000\,b0\,W\;\&\&\;\frac{1\,616\,092\,049\,(13\,953\,b-10\,(a-n)\,(a-b-n))}{b}==1\,000\,000\,000\,000\,b1\,W\;\&\&\;b0+W==\frac{43\,146\,090\,643\,049}{100\,000\,000\,000}$$

Elimination of b_0, b_2

In[∘]:=
```
b2 = 1;
eqs = Eliminate[sys, {b0, b1}] // FullSimplify
```

Out[∘]=

$$10\,a\,(a-b-2\,n)\left(-361\,690\,835\,865\,426\,262\,623\,537\,819\,b+1\,616\,092\,049\,000\,000\left(a^2+2\,n\,(b+n)-a\,(b+2\,n)\right)\right)==10\,b\,(361\,690\,835\,865\,426\,262\,623\,537\,819-3\,232\,184\,098\,000\,000\,n)\,n^2-16\,160\,920\,490\,000\,000\,n^4+b^2\,(969\,329\,896\,546\,320\,377\,655\,401\,493+10\,(361\,690\,835\,865\,426\,262\,623\,537\,819-1\,616\,092\,049\,000\,000\,n)\,n)\;\&\&\;\frac{1\,616\,092\,049\,(13\,953\,b-10\,(a-n)\,(a-b-n))}{b}==1\,610\,188\,269\,000\,000\,W\;\&\&\;b\neq 0$$

Setting the values *a*, *b*, *n*

In[•]:=
```
ClearAll[a]; a = 38437/100000;
CylindricalDecomposition[eqs && x1 > 0 && x2 > 0 && x3 > 0 && x4 > 0 &&
    n > 0 && b > 0 && W > 0 && a > n && n > a - b, {b, n, k, W}] // FullSimplify
```

Out[•]=

$$17\,179\,639\,562\,122\,700\,701\,308\,600\,627\,400\,000\, b > 30\,151\,081\left(361\,690\,835\,866\,668\,617\,225\,286\,079 + 1\,610\,188\,269\sqrt{50\,457\,031\,205\,553\,435\,413\,138\,389\,202\,156\,401}\right) \;\&\&\; n == \mathrm{Root}\Big[3\,527\,475\,682\,171\,259\,806\,043\,145\,089 - 5\,343\,631\,147\,695\,079\,032\,277\,621\,949\,889\,685\,510\,000\, b + 4\,209\,011\,692\,720\,061\,671\,820\,607\,153\,713\,000\,000\,000\, b^2 + \left(-36\,709\,167\,543\,473\,838\,291\,678\,800\,000 + 27\,804\,621\,316\,462\,035\,664\,404\,039\,906\,666\,000\,000\,000\, b - 36\,169\,083\,586\,666\,861\,722\,528\,607\,900\,000\,000\,000\,000\, b^2\right) \#1 + \left(143\,257\,151\,482\,193\,608\,860\,000\,000\,000 - 36\,169\,083\,586\,915\,332\,642\,878\,259\,900\,000\,000\,000\,000\, b + 161\,609\,204\,900\,000\,000\,000\,000\,000\,000\, b^2\right) \#1^2 + \left(-248\,470\,920\,349\,652\,000\,000\,000\,000\,000 + 323\,218\,409\,800\,000\,000\,000\,000\,000\,000\, b\right) \#1^3 + 161\,609\,204\,900\,000\,000\,000\,000\,000\,000\, \#1^4 \;\&,\; 3\Big] \;\&\&\; k > 0 \;\&\&\; W == -\frac{1\,616\,092\,049\left((38\,437 - 100\,000\, n)^2 + 100\,000\, b\,(-139\,568\,437 + 100\,000\, n)\right)}{1\,610\,188\,269\,000\,000\,000\,000\,000\, b}$$

In[•]:=
```
Reduce[17 179 639 562 122 700 701 308 600 627 400 000 b >
    30 151 081 (361 690 835 866 668 617 225 286 079 +
        1 610 188 269 √50 457 031 205 553 435 413 138 389 202 156 401), b];
% // N
```

Out[•]=

$b > 1.26957$

The measured value is $b = 2.2229$, this is set for *b*.

In[•]:=
```
ClearAll[b]; b = 22229/10000;
CylindricalDecomposition[eqs && x1 > 0 && x2 > 0 && x3 > 0 &&
    x4 > 0 && n > 0 && W > 0 && a > n && n > a - b, {n, k, W}] // FullSimplify
```

Out[•]=

$$18\,177 + 25\,000\, n == 2.00\ldots \times 10^4 \;\&\&\; k > 0 \;\&\&\; W == -\frac{1\,616\,092\,049\,(-31\,023\,190\,457\,761 + 800\,000\, n\,(18\,177 + 12\,500\, n))}{3\,579\,287\,503\,160\,100\,000\,000\,000}$$

In[∘]:=
```
Reduce[18 177 + 25 000 n == (√) 2.00… × 10^4, n]
% // N
```

Out[∘]=

$$n == \frac{-18177 + 2.00\ldots \times 10^4}{25000}$$

Out[∘]=

```
n == 0.0726605
```

The measured value is $n = 0.13881$.

In[∘]:=
```
ClearAll[n];
n = (-18 177 + (√) 2.00… × 10^4) / 25 000;
```

The eigenvalues

In[∘]:=
```
Solve[pol == 0, y] // N
```

Out[∘]=

```
{{y → -1609.92}, {y → -0.267993}, {y → 0. - 0.118351 i}, {y → 0. + 0.118351 i}}
```

2. b) Stability of the equilibrium state and the Hopf bifurcation

Step 1 - Shifting the singular point into the origin

The singular point of the system in the first quadrant is shifted into the origin and the parameters are chosen in such a way that the Jacobian at the origin has a pair of pure imaginary eigenvalues.

System (1)

In[∘]:=
```
Quit
```

In[∘]:=
```
ClearAll[x1, x2, x3, a, b, n, w, ED, c, k1, k2, k, f1, f2, f3, f4];
f1 = a x1 - n x1 - b x1 x3/(ED + x3);
f2 = n x1 - w x2 + b x1 x3/(ED + x3);
f3 = -c x3 - k1 x3 + k2 x4 + k (x1 + x2);
f4 = k1 x3 - k2 x4;
```

Singular points

In[•]:=
```
sol = Solve[{f1 == 0, f2 == 0, f3 == 0, f4 == 0}, {x1, x2, x3, x4}] // Factor
{y1, y2, y3, y4} = {x1, x2, x3, x4} /. sol[[2]]
```

Out[•]=

$$\left\{\{x1 \to 0, x2 \to 0, x3 \to 0, x4 \to 0\}, \left\{x1 \to -\frac{c\,ED\,(a-n)\,w}{k\,(a-b-n)\,(a+w)}, x2 \to -\frac{a\,c\,ED\,(a-n)}{k\,(a-b-n)\,(a+w)}, x3 \to -\frac{ED\,(a-n)}{a-b-n}, x4 \to -\frac{ED\,k1\,(a-n)}{k2\,(a-b-n)}\right\}\right\}$$

Out[•]=

$$\left\{-\frac{c\,ED\,(a-n)\,w}{k\,(a-b-n)\,(a+w)}, -\frac{a\,c\,ED\,(a-n)}{k\,(a-b-n)\,(a+w)}, -\frac{ED\,(a-n)}{a-b-n}, -\frac{ED\,k1\,(a-n)}{k2\,(a-b-n)}\right\}$$

The singular point is shifted into the origin (17)

In[•]:=
```
x1d = f1 /. {x1 → x1 + y1, x2 → x2 + y2, x3 → x3 + y3, x4 → x4 + y4} // Factor
x2d = f2 /. {x1 → x1 + y1, x2 → x2 + y2, x3 → x3 + y3, x4 → x4 + y4} // Factor
x3d = f3 /. {x1 → x1 + y1, x2 → x2 + y2, x3 → x3 + y3, x4 → x4 + y4} // Factor
x4d = f4 /. {x1 → x1 + y1, x2 → x2 + y2, x3 → x3 + y3, x4 → x4 + y4} // Factor
```

Out[•]=

$$\frac{(a-b-n)\left(-a\,c\,ED\,w + c\,ED\,n\,w + a^2\,k\,x1 - a\,b\,k\,x1 - a\,k\,n\,x1 + a\,k\,w\,x1 - b\,k\,w\,x1 - k\,n\,w\,x1\right)x3}{k\,(a+w)\,(-b\,ED + a\,x3 - b\,x3 - n\,x3)}$$

Out[•]=

$$-\frac{1}{k\,(a+w)\,(b\,ED - a\,x3 + b\,x3 + n\,x3)}\left(-a^2\,b\,ED\,k\,x1 - a\,b\,ED\,k\,w\,x1 + a\,b\,ED\,k\,w\,x2 + b\,ED\,k\,w^2\,x2 + a^2\,c\,ED\,w\,x3 - a\,b\,c\,ED\,w\,x3 - 2\,a\,c\,ED\,n\,w\,x3 + b\,c\,ED\,n\,w\,x3 + c\,ED\,n^2\,w\,x3 + a^2\,b\,k\,x1\,x3 - a\,b^2\,k\,x1\,x3 + a^2\,k\,n\,x1\,x3 - 2\,a\,b\,k\,n\,x1\,x3 - a\,k\,n^2\,x1\,x3 + a\,b\,k\,w\,x1\,x3 - b^2\,k\,w\,x1\,x3 + a\,k\,n\,w\,x1\,x3 - 2\,b\,k\,n\,w\,x1\,x3 - k\,n^2\,w\,x1\,x3 - a^2\,k\,w\,x2\,x3 + a\,b\,k\,w\,x2\,x3 + a\,k\,n\,w\,x2\,x3 - a\,k\,w^2\,x2\,x3 + b\,k\,w^2\,x2\,x3 + k\,n\,w^2\,x2\,x3\right)$$

Out[•]=

$$k\,x1 + k\,x2 - c\,x3 - k1\,x3 + k2\,x4$$

Out[•]=

$$k1\,x3 - k2\,x4$$

The Jacobian at the origin

In[•]:=
```
Jac = D[{x1d, x2d, x3d, x4d}, {{x1, x2, x3, x4}}] // Simplify;
JacOrigin = Jac /. {x1 → 0, x2 → 0, x3 → 0, x4 → 0} // Simplify
```

Out[•]=

$$\left\{\left\{0, 0, -\frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)}, 0\right\}, \left\{a, -w, \frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)}, 0\right\}, \{k, k, -c-k1, k2\}, \{0, 0, k1, -k2\}\right\}$$

Eigenvalues of the Jacobian at the origin with the given parameter settings

In[◦]:=

$$\{w, ED, c, k1, k2\} = \left\{\frac{71159}{1000000}, \frac{117}{80}, \frac{22711}{100000}, \frac{21459}{100}, \frac{13953}{10}\right\};$$

$$a = \frac{38437}{100000};\ b = \frac{22229}{10000};\ n = \frac{-18177 + \boxed{2.00\ldots \times 10^4}}{25000};$$

$$k = \frac{1}{100};$$

```
Eigenvalues[JacOrigin] // N
```

Out[◦]=

```
{-1609.92, -0.267993, 0. + 0.118351 ⅈ, 0. - 0.118351 ⅈ}
```

Step 2 - Taylor series expansion

Series expansion symbolically and the Jacobian at the origin

In[◦]:=

```
Quit
```

In[•]:=

```
x1d =
  ((a - b - n) (-a c ED w + c ED n w + a^2 k x1 - a b k x1 - a k n x1 + a k w x1 - b k w x1 - k n w x1) x3) /
   (k (a + w) (-b ED + a x3 - b x3 - n x3));
x2d = - 1/(k (a + w) (b ED - a x3 + b x3 + n x3))
   (-a^2 b ED k x1 - a b ED k w x1 + a b ED k w x2 + b ED k w^2 x2 + a^2 c ED w x3 -
     a b c ED w x3 - 2 a c ED n w x3 + b c ED n w x3 + c ED n^2 w x3 + a^2 b k x1 x3 -
     a b^2 k x1 x3 + a^2 k n x1 x3 - 2 a b k n x1 x3 - a k n^2 x1 x3 + a b k w x1 x3 -
     b^2 k w x1 x3 + a k n w x1 x3 - 2 b k n w x1 x3 - k n^2 w x1 x3 - a^2 k w x2 x3 +
     a b k w x2 x3 + a k n w x2 x3 - a k w^2 x2 x3 + b k w^2 x2 x3 + k n w^2 x2 x3);
x3d = k x1 + k x2 - c x3 - k1 x3 + k2 x4;
x4d = k1 x3 - k2 x4;
r1 = Series[x1d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal
r2 = Series[x2d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal
r3 = Series[x3d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal
r4 = Series[x4d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal
```

Out[•]=

$$-\frac{(-a+b+n)\,(a c w-c n w)\,x3}{b k\,(a+w)}+\frac{(-a+b+n)^2\,(a c w-c n w)\,x3^2}{b^2\,ED\,k\,(a+w)}-\frac{(-a+b+n)^3\,(a c w-c n w)\,x3^3}{b^3\,ED^2\,k\,(a+w)}+\frac{(-a+b+n)^4\,(a c w-c n w)\,x3^4}{b^4\,ED^3\,k\,(a+w)}+x1\left(-\frac{(-a+b+n)^2\,x3}{b\,ED}+\frac{(-a+b+n)^3\,x3^2}{b^2\,ED^2}-\frac{(-a+b+n)^4\,x3^3}{b^3\,ED^3}+\frac{(-a+b+n)^5\,x3^4}{b^4\,ED^4}\right)$$

Out[•]=

$$-w\,x2+\frac{\left(-a^2 c w+a b c w+2 a c n w-b c n w-c n^2 w\right)x3}{b k\,(a+w)}-\frac{(-a+b+n)^2\,(a c w-c n w)\,x3^2}{b^2\,ED\,k\,(a+w)}+\frac{(-a+b+n)^3\,(a c w-c n w)\,x3^3}{b^3\,ED^2\,k\,(a+w)}-\frac{(-a+b+n)^4\,(a c w-c n w)\,x3^4}{b^4\,ED^3\,k\,(a+w)}+x1\left(a+\frac{\left(a^2-2 a b+b^2-2 a n+2 b n+n^2\right)x3}{b\,ED}+\frac{\left(a^3-3 a^2 b+3 a b^2-b^3-3 a^2 n+6 a b n-3 b^2 n+3 a n^2-3 b n^2-n^3\right)x3^2}{b^2\,ED^2}+\frac{1}{b^3\,ED^3}\left(a^4-4 a^3 b+6 a^2 b^2-4 a b^3+b^4-4 a^3 n+12 a^2 b n-12 a b^2 n+4 b^3 n+6 a^2 n^2-12 a b n^2+6 b^2 n^2-4 a n^3+4 b n^3+n^4\right)x3^3+\frac{1}{b^4\,ED^4}\left(a^5-5 a^4 b+10 a^3 b^2-10 a^2 b^3+5 a b^4-b^5-5 a^4 n+20 a^3 b n-30 a^2 b^2 n+20 a b^3 n-5 b^4 n+10 a^3 n^2-30 a^2 b n^2+30 a b^2 n^2-10 b^3 n^2-10 a^2 n^3+20 a b n^3-10 b^2 n^3+5 a n^4-5 b n^4-n^5\right)x3^4\right)$$

Out[•]=

$$k\,x1+k\,x2+(-c-k1)\,x3+k2\,x4$$

Out[•]=

$$k1\,x3-k2\,x4$$

In[ ]:=
```
Jac = D[{r1, r2, r3, r4}, {{x1, x2, x3, x4}}] // Simplify;
JacOrigin = Jac /. {x1 → 0, x2 → 0, x3 → 0, x4 → 0} // Simplify
```

Out[ ]=

$$\left\{\left\{0, 0, -\frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)}, 0\right\}, \left\{a, -w, \frac{c\,(a-n)\,(-a+b+n)\,w}{b\,k\,(a+w)}, 0\right\}, \{k, k, -c-k1, k2\}, \{0, 0, k1, -k2\}\right\}$$

Series expansion with numerical values

A series expansion of the transformed system about the origin up to degree 4 will be used instead of the original system.

In[ ]:=
```
Quit
```

In[ ]:=

$$\{w, ED, c, k1, k2\} = \left\{\frac{71159}{1000000}, \frac{117}{80}, \frac{22711}{100000}, \frac{21459}{100}, \frac{13953}{10}\right\};$$

$$a = \frac{38437}{100000};\ b = \frac{22229}{10000};\ n = \frac{-18177 + \boxed{2.00\ldots\times 10^4}}{25000};$$

$$k = \frac{1}{100};$$

$$x1d = \left((a-b-n)\left(-a\,c\,ED\,w + c\,ED\,n\,w + a^2\,k\,x1 - a\,b\,k\,x1 - a\,k\,n\,x1 + a\,k\,w\,x1 - b\,k\,w\,x1 - k\,n\,w\,x1\right)x3\right) / (k\,(a+w)\,(-b\,ED + a\,x3 - b\,x3 - n\,x3));$$

$$x2d = -\frac{1}{k\,(a+w)\,(b\,ED - a\,x3 + b\,x3 + n\,x3)}\left(-a^2\,b\,ED\,k\,x1 - a\,b\,ED\,k\,w\,x1 + a\,b\,ED\,k\,w\,x2 + b\,ED\,k\,w^2\,x2 + a^2\,c\,ED\,w\,x3 - a\,b\,c\,ED\,w\,x3 - 2\,a\,c\,ED\,n\,w\,x3 + b\,c\,ED\,n\,w\,x3 + c\,ED\,n^2\,w\,x3 + a^2\,b\,k\,x1\,x3 - a\,b^2\,k\,x1\,x3 + a^2\,k\,n\,x1\,x3 - 2\,a\,b\,k\,n\,x1\,x3 - a\,k\,n^2\,x1\,x3 + a\,b\,k\,w\,x1\,x3 - b^2\,k\,w\,x1\,x3 + a\,k\,n\,w\,x1\,x3 - 2\,b\,k\,n\,w\,x1\,x3 - k\,n^2\,w\,x1\,x3 - a^2\,k\,w\,x2\,x3 + a\,b\,k\,w\,x2\,x3 + a\,k\,n\,w\,x2\,x3 - a\,k\,w^2\,x2\,x3 + b\,k\,w^2\,x2\,x3 + k\,n\,w^2\,x2\,x3\right);$$

```
x3d = k x1 + k x2 - c x3 - k1 x3 + k2 x4;
x4d = k1 x3 - k2 x4;
r1 = Series[x1d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal;
r2 = Series[x2d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal;
r3 = Series[x3d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal;
r4 = Series[x4d, {x1, 0, 4}, {x2, 0, 4}, {x3, 0, 4}, {x4, 0, 4}] // Normal;
```

Separation of the linear and nonlinear parts

```
In[*]:= g1 = r1 /. {x1 → t x1, x2 → t x2, x3 → t x3, x4 → t x4};
rr1 = Normal[Series[g1, {t, 0, 4}]] // Simplify;
g2 = r2 /. {x1 → t x1, x2 → t x2, x3 → t x3, x4 → t x4};
rr2 = Normal[Series[g2, {t, 0, 4}]] // Simplify;
f1p = D[rr1, t] /. t → 0 // Simplify;
f2p = D[rr2, t] /. t → 0 // Simplify;
f1deg2 = rr1 - f1p t // Simplify // Factor;
f2deg2 = rr2 - f2p t // Simplify // Factor;
```

The full system

In[∘]:=
```
ff1 = (SetPrecision[f1p, 100] t + SetPrecision[f1deg2, 100]) /. t → 1 // Expand
ff2 = (SetPrecision[f2p, 100] t + SetPrecision[f2deg2, 100]) /. t → 1 // Expand
ff3 = r3
ff4 = r4
```

Out[∘]=

$-0.9507890374456097868269365664492773909901497236202468413681612924838358362632250850\backslash 10328979893718833\,x3 -$
$1.1235493447174995634570940932786588208104339966486407889341848793596228006240963899\backslash 74466701599436690\,x1\,x3 +$
$0.5589492024167124596942973164484929999640065765039747602018990683307990419287235910\backslash 81969084293701890\,x3^2 +$
$0.6605114124925863630222485702382269509104130916205154389887911055064574641400765057\backslash 51577890430427140\,x1\,x3^2 -$
$0.3285946709289349920509321986182023588444768459191006123607932196880276191219633987\backslash 47037059213954962\,x3^3 -$
$0.3883009928172284881418288975278369168807594369886906836971704139933827918198517890\backslash 66870175169450716\,x1\,x3^3 +$
$0.1931740081138841291728596018311260830019630534519817969602278421700742060581751440\backslash 99672861897208510\,x3^4$

Out[∘]=

$0.3843000000000000000000000000000000000000000000000000000000000000000000000000000000\backslash 0000000000000000\,x1 -$
$0.0711590000000000000000000000000000000000000000000000000000000000000000000000000000\backslash 000000000000000000\,x2 +$
$0.9507890374456097868269365664492773909901497236202468413681612924838358362632250850\backslash 10328979893718833\,x3 +$
$1.1235493447174995634570940932786588208104339966486407889341848793596228006240963899\backslash 74466701599436690\,x1\,x3 -$
$0.5589492024167124596942973164484929999640065765039747602018990683307990419287235910\backslash 81969084293701890\,x3^2 -$
$0.6605114124925863630222485702382269509104130916205154389887911055064574641400765057\backslash 51577890430427140\,x1\,x3^2 +$
$0.3285946709289349920509321986182023588444768459191006123607932196880276191219633987\backslash 47037059213954962\,x3^3 +$
$0.3883009928172284881418288975278369168807594369886906836971704139933827918198517890\backslash 66870175169450716\,x1\,x3^3 -$
$0.1931740081138841291728596018311260830019630534519817969602278421700742060581751440\backslash 99672861897208510\,x3^4$

Out[∘]=

$$\frac{x1}{100} + \frac{x2}{100} - \frac{21\,481\,711\,x3}{100\,000} + \frac{13\,953\,x4}{10}$$

Out[∘]=

$$\frac{21\,459\,x3}{100} - \frac{13\,953\,x4}{10}$$

The full system with shorter numerical values

In[◦]:=
```
ff1 // N
ff2 // N
ff3 // N
ff4 // N
```

Out[◦]=
```
-0.950789 x3 - 1.12355 x1 x3 + 0.558949 x3^2 +
 0.660511 x1 x3^2 - 0.328595 x3^3 - 0.388301 x1 x3^3 + 0.193174 x3^4
```

Out[◦]=
```
0.38437 x1 - 0.071159 x2 + 0.950789 x3 + 1.12355 x1 x3 -
 0.558949 x3^2 - 0.660511 x1 x3^2 + 0.328595 x3^3 + 0.388301 x1 x3^3 - 0.193174 x3^4
```

Out[◦]=
```
0.01 x1 + 0.01 x2 - 214.817 x3 + 1395.3 x4
```

Out[◦]=
```
214.59 x3 - 1395.3 x4
```

The nonlinear part

In[◦]:=
```
f1 = SetPrecision[f1deg2, 100] /. t → 1 // Expand
f2 = SetPrecision[f2deg2, 100] /. t → 1 // Expand
f3 = 0;
f4 = 0;
```

Out[◦]=
```
-1.1235493447174995634570940932786588208104339966486407889341848793596228006240963899\
   74466701599436690 x1 x3 +
 0.5589492024167124596942973164484929999640065765039747602018990683307990419287235910\
   81969084293701890 x3^2 +
 0.6605114124925863630222485702382269509104130916205154389887911055064574641400765057\
   51577890430427140 x1 x3^2 -
 0.3285946709289349920509321986182023588444768459191006123607932196880276191219633987\
   47037059213954962 x3^3 -
 0.3883009928172284881418288975278369168807594369886906836971704139933827918198517890\
   66870175169450716 x1 x3^3 +
 0.1931740081138841291728596018311260830019630534519817969602278421700742060581751440\
   99672861897208510 x3^4
```

Out[◦]=
```
1.123549344717499563457094093278658820810433996648640788934184879359622800624096389974\
   4466701599436690 x1 x3 -
 0.5589492024167124596942973164484929999640065765039747602018990683307990419287235910\
   81969084293701890 x3^2 -
 0.6605114124925863630222485702382269509104130916205154389887911055064574641400765057\
   51577890430427140 x1 x3^2 +
 0.3285946709289349920509321986182023588444768459191006123607932196880276191219633987\
   47037059213954962 x3^3 +
 0.3883009928172284881418288975278369168807594369886906836971704139933827918198517890\
   66870175169450716 x1 x3^3 -
 0.1931740081138841291728596018311260830019630534519817969602278421700742060581751440\
   99672861897208510 x3^4
```

The Jacobian at the origin

In[•]:=
```
Jac = D[{ff1, ff2, ff3, ff4}, {{x1, x2, x3, x4}}] // Simplify;
JacOrigin = Jac /. {x1 → 0, x2 → 0, x3 → 0, x4 → 0} // Simplify;
```

In[•]:=
```
SetPrecision[Eigenvalues[JacOrigin], 100]
```

Out[•]=
```
{-1609.920276288847655759450296027891023536738867821765609599276655914324074518625353⋱
  638643883628453122,
 -0.267992711152344240549703972108976463261132178234390400723344085675925481374646361⋱
  3561163715468778511, 0. × 10^-108 +
 0.118350533207991210283791907224299374530370226502253306124848798184753069547924592⋱
   68619885412857468650 i, 0. × 10^-108 -
 0.118350533207991210283791907224299374530370226502253306124848798184753069547924592⋱
   68619885412857468650 i}
```

The Jacobian the singular point

In[•]:=
$$J = \left\{\left\{0, 0, -\frac{c\ (a - n)\ (-a + b + n)\ w}{b\,k\ (a + w)}, 0\right\}, \left\{a, -w, \frac{c\ (a - n)\ (-a + b + n)\ w}{b\,k\ (a + w)}, 0\right\}, \{k, k, -c - k1, k2\}, \{0, 0, k1, -k2\}\right\}\ //\ \text{FullSimplify};$$

In[•]:=
```
SetPrecision[Eigenvalues[J], 100]
```

Out[•]=
```
{-1609.920276288847655759450296027891023536738867821765609599276655914324074518625353⋱
  638643883628453122,
 -0.267992711152344240549703972108976463261132178234390400723344085675925481374646361⋱
  356116371546878,
 0.1183505332079912102837919072242993745303702265022533061248487981847530695479245926⋱
  86198854129 i,
 -0.118350533207991210283791907224299374530370226502253306124848798184753069547924592⋱
   686198854129 i}
```

Step 3 - Transformation to real Jordan normal form

The system is transformed in such a way that its linear part has real Jordan normal form (RJNF).

Transformation of *J*

In[•]:=
```
ev = SetPrecision[Eigenvectors[J], 100];
```

In[•]:=
```
SetPrecision[Transpose[ev], 100] // N // MatrixForm
```

Out[•]//MatrixForm=

$$\begin{pmatrix} -0.000590665 & 23.0641 & -0.00443072 + 52.2363\,i & -0.00443072 - 52.2363\,i \\ 0.000590832 & -76.4409 & 147.669 + 36.5648\,i & 147.669 - 36.5648\,i \\ -1.00014 & 6.50092 & 6.50217 + 0.000551519\,i & 6.50217 - 0.000551519\,i \\ 1. & 1. & 1. & 1. \end{pmatrix}$$

The matrix S for which the product $S^{-1}\,J\,S$ has real Jordan normal form

In[•]:=
```
S = Transpose[{ev[[1]], ev[[2]], Re[ev[[3]]], Im[ev[[3]]]}];
```

In[•]:=
```
SetPrecision[S, 100] // N // MatrixForm
```

Out[•]//MatrixForm=

$$\begin{pmatrix} -0.000590665 & 23.0641 & -0.00443072 & 52.2363 \\ 0.000590832 & -76.4409 & 147.669 & 36.5648 \\ -1.00014 & 6.50092 & 6.50217 & 0.000551519 \\ 1. & 1. & 1. & 0. \end{pmatrix}$$

The inverse of S

In[•]:=
```
Sinv = Inverse[S];
```

Verification that S transforms J to the real Jordan normal form

In[•]:=
```
RJNF = Sinv.J.S
```

Out[•]=

$\{\{-1609.920276288847655759450296027891023536738867821765609599276655914324074518625354, 0.\times 10^{-79}, 0.\times 10^{-79}, 0.\times 10^{-83}\}, \{0.\times 10^{-80},$
$-0.267992711152344240549703972108976463261132178234390400723344085675925481374646, 0.\times 10^{-79}, 0.\times 10^{-83}\}, \{0.\times 10^{-80}, 0.\times 10^{-80}, 0.\times 10^{-80},$
$0.1183505332079912102837919072242993745303702265022533061248487981847530695479245927\}, \{0.\times 10^{-80}, 0.\times 10^{-80},$
$-0.1183505332079912102837919072242993745303702265022533061248487981847530695479246, 0.\times 10^{-83}\}\}$

In[•]:=
```
SetPrecision[RJNF, 100]
```

Out[•]=

```
{{-1609.92027628884765575945029602789102353673886782176560959927665591432407451862535⋱
    3638643883628452938, 0, 0, 0}, {0,
  -0.26799271115234424054970397210897646326113217823439040072334408567592548137464636⋱
    13561163715468816461, 0, 0}, {0, 0, 0,
  0.118350533207991210283791907224299374530370226502253306124848798184753069547924592⋱
   6861988541285616129}, {0, 0,
  -0.11835053320799121028379190722429937453037022650225330612484879818475306954792459⋱
    26861988541286042161, 0}}
```

The entries a_1, a_2, β

In[•]:=
```
a1 = RJNF[[1, 1]];
a2 = RJNF[[2, 2]];
beta = RJNF[[3, 4]];
```

Transformation of the system

Consider the system $\dot{\boldsymbol{x}} = J\,\boldsymbol{x} + f(\boldsymbol{x})$ where f contains the nonlinear terms.
With the substitution $\boldsymbol{x} = S\,\boldsymbol{y}$, this system is transformed into the form
$\dot{\boldsymbol{y}} = S^{-1}\,J\,S\,\boldsymbol{y} + S^{-1}\,f(S\,\boldsymbol{y})$.
The product $S\,\boldsymbol{y}$:

In[•]:=
```
sy = S.{y1, y2, y3, y4} // FullSimplify;
```

The substitution $f(S\,\boldsymbol{y})$:

In[•]:=
```
FF1 = f1 /. {x1 → sy[[1]], x2 → sy[[2]], x3 → sy[[3]], x4 → sy[[4]] } // Simplify // Expand;
FF2 = f2 /. {x1 → sy[[1]], x2 → sy[[2]], x3 → sy[[3]], x4 → sy[[4]] } // Simplify // Expand;
FF3 = f3 /. {x1 → sy[[1]], x2 → sy[[2]], x3 → sy[[3]], x4 → sy[[4]] } // Simplify
FF4 = f4 /. {x1 → sy[[1]], x2 → sy[[2]], x3 → sy[[3]], x4 → sy[[4]] } // Simplify
```

Out[•]=
```
0
```

Out[•]=
```
0
```

The product $S^{-1}\,f(S\,\boldsymbol{y})$, that is, the nonlinear part in $\dot{\boldsymbol{y}}$ in the new coordinates:

In[•]:=
```
{h1, h2, h3, h4} = SetPrecision[Sinv.{FF1, FF2, FF3, FF4}, 100] // Simplify;
```

The full system

In[•]:=
```
f1y = a1 y1 + h1 // Simplify;
f2y = a2 y2 + h2 // Simplify;
f3y = beta y4 + h3 // Simplify;
f4y = -beta y3 + h4 // Simplify;
jac = D[{f1y, f2y, f3y, f4y}, {{y1, y2, y3, y4}}] /. {y1 → 0, y2 → 0, y3 → 0, y4 → 0};
```

In[•]:=
```
jac // N // MatrixForm
```

Out[•]//MatrixForm=

$$\begin{pmatrix} -1609.92 & 0. & 0. & 0. \\ 0. & -0.267993 & 0. & 0. \\ 0. & 0. & 0. & 0.118351 \\ 0. & 0. & -0.118351 & 0. \end{pmatrix}$$

Step 4 - Search for a Lyapunov function

We look for a polynomial $\phi(x_1, x_2, x_3, x_4) = \phi_2\,(x_1, x_2, x_3, x_4) + \sum_{i+j+k+l=3}^{4} p_{\text{ijkl}}\, x_1^i\, x_2^j\, x_3^k\, x_4^l$

such that the quadratic part of ϕ,

$\phi_2\,(x_1, x_2, x_3, x_4) = A\,x_1^2 + B\,x_2^2 + C\,x_3^2 + D\,x_4^2$

is positively defined and for the Lie derivative of the previous system we have that

$$\frac{\partial\phi}{\partial x_1}\dot{x}_1 + \frac{\partial\phi}{\partial x_2}\dot{x}_2 + \frac{\partial\phi}{\partial x_3}\dot{x}_3 + \frac{\partial\phi}{\partial x_4}\dot{x}_4 = g_0\left[\left(x_1^2 + x_2^2\right) + \left(x_3^2 + x_4^2\right)^2\right] + h.o.t.$$

The following program compares the coefficients of the corresponding terms on both sides and thus the focus (or Lyapunov) quantity g_0 can be calculated.

The system

In[∘]:=
```
ClearAll[f1, f2, f3, f4];
f1 = f1y /. {y1 → x1, y2 → x2, y3 → x3, y4 → x4};
f2 = f2y /. {y1 → x1, y2 → x2, y3 → x3, y4 → x4};
f3 = f3y /. {y1 → x1, y2 → x2, y3 → x3, y4 → x4};
f4 = f4y /. {y1 → x1, y2 → x2, y3 → x3, y4 → x4};
```

Program

In[∘]:=
```
Ser[s_] := Plus @@ (Table[x1^i x2^j x3^k x4^(s-i-j-k) p[i, j, k, s - i - j - k], {i, 0, s},
        {j, 0, s}, {k, 0, s}, {l, 0, s - i - j - k}] // Flatten // Union);
Hom[s_] := Table[p[i, j, k, s - i - j - k], {i, 0, s},
      {j, 0, s}, {k, 0, s}, {l, 0, s - i - j - k}] // Flatten // Union;
hh = Sum[Ser[i], {i, 3, 4}];
V = hh + aa x1^2 + bb x2^2 + cc x3^2 + dd x4^2;
Lie = D[V, x1] f1 + D[V, x2] f2 + D[V, x3] f3 + D[V, x4] f4 // Expand;
RHS = g0 ((x1^2 + x2^2) + (x3^2 + x4^2)^2) // Expand;
vv = Lie - RHS // Expand;
CoefPol[f_, s_] := Module[{m, lis, t}, lis = {};
   m = Expand[f]; Do[Do[Do[Do[If[i + j + k + l == s, lis = AppendTo[lis,
            Coefficient[m, x1^i x2^j x3^k x4^l] /. {x1 → 0, x2 → 0, x3 → 0, x4 → 0}]],
        {i, 0, s}], {j, 0, s}], {k, 0, s}], {l, 0, s}];
   ls[s] = lis];
Do[CoefPol[vv, i], {i, 1, 4}]
```

Degree 2

In[•]:=
```
ls[2] // FullSimplify
```

Out[•]=
```
{-3219.84055257769531151890059205578204707347773564353121919855331182864814903725071
   aa - g0, 0,
 -0.535985422304688481099407944217952926522264356468780801446688171351850962749293 bb -
  g0, 0, 0, 0, 0, 0,
 0.2367010664159824205675838144485987490607404530045066122496975963695061390958491854
   cc -
  0.2367010664159824205675838144485987490607404530045066122496975963695061390958491854
   dd,
 0}
```

In[•]:=
```
Variables[ls[2]]
```

Out[•]=
```
{aa, bb, cc, dd, g0}
```

In[•]:=
```
sol2 = Solve[ls[2] == 0, {aa, bb, cc, dd}] // FullSimplify // Factor
```

Solve: Equations may not give solutions for all "solve" variables.

Out[•]=
```
{{aa →
   -0.00031057438518172394078309408290383188664420152348122954109805527740495784321577
     50 g0, bb →
   -1.86572238420233728036771834197407834386431725946530280464680778547093410474108
    g0,
  dd → 1.00000000000000000000000000000000000000000000000000000000000000000000000000000
    cc}}
```

In[•]:=
```
{aa, bb, cc, dd} = {aa, bb, cc, dd} /. sol2[[1]]
```

Out[•]=
```
{-0.000310574385181723940783094082903831886644201523481229541098055277404957843215750
  g0, -1.86572238420233728036771834197407834386431725946530280464680778547093410474108
  g0, cc,
 1.00000000000000000000000000000000000000000000000000000000000000000000000000000 cc}
```

In[•]:=
```
{aa, bb, cc, dd} // N
```

Out[•]=
```
{-0.000310574 g0, -1.86572 g0, cc, 1. cc}
```

Positive definiteness of the quadratic part of *V*

In[•]:=
```
S2 = aa x1^2 + bb x2^2 + cc x3^2 + cc x4^2
```

Out[•]=
```
-0.00031057438518172394078309408290383188664420152348122954109805527740495784321575O
  g0 x1^2 -
 1.8657223842023372803677183419740783438643172594653028046468077854709341047410 8
  g0 x2^2 + cc x3^2 + cc x4^2
```

It can be seen that S2 will be positively defined if $g_0 < 0$ and $c > 0$.

Degree 3

In[•]:=
```
ls[3] // Factor;
sol3 = Solve[ls[3] == 0, Hom[3]] // Simplify;
{p[0, 0, 0, 3], p[0, 0, 1, 2], p[0, 0, 2, 1], p[0, 0, 3, 0], p[0, 1, 0, 2],
   p[0, 1, 1, 1], p[0, 1, 2, 0], p[0, 2, 0, 1], p[0, 2, 1, 0], p[0, 3, 0, 0],
   p[1, 0, 0, 2], p[1, 0, 1, 1], p[1, 0, 2, 0], p[1, 1, 0, 1], p[1, 1, 1, 0],
   p[1, 2, 0, 0], p[2, 0, 0, 1], p[2, 0, 1, 0], p[2, 1, 0, 0], p[3, 0, 0, 0]} =
  {p[0, 0, 0, 3], p[0, 0, 1, 2], p[0, 0, 2, 1], p[0, 0, 3, 0], p[0, 1, 0, 2], p[0, 1, 1, 1],
     p[0, 1, 2, 0], p[0, 2, 0, 1], p[0, 2, 1, 0], p[0, 3, 0, 0], p[1, 0, 0, 2],
     p[1, 0, 1, 1], p[1, 0, 2, 0], p[1, 1, 0, 1], p[1, 1, 1, 0], p[1, 2, 0, 0],
     p[2, 0, 0, 1], p[2, 0, 1, 0], p[2, 1, 0, 0], p[3, 0, 0, 0]} /. sol3[[1]] // Simplify;
ls[3] // Simplify
```

Out[•]=
```
{0. × 10^-91 g0, 0. × 10^-91 g0, 0. × 10^-91 g0, 0. × 10^-77 g0, 0. × 10^-74 cc + 0. × 10^-84 g0,
 0. × 10^-74 cc + 0. × 10^-73 g0, 0. × 10^-74 cc + 0. × 10^-73 g0, 0. × 10^-74 cc + 0. × 10^-84 g0,
 0. × 10^-74 cc + 0. × 10^-73 g0, 0. × 10^-78 cc, 0. × 10^-79 cc + 0. × 10^-84 g0, 0. × 10^-74 cc + 0. × 10^-73 g0,
 0. × 10^-74 cc + 0. × 10^-73 g0, 0. × 10^-74 cc + 0. × 10^-84 g0, 0. × 10^-74 cc + 0. × 10^-73 g0,
 0. × 10^-74 cc, 0. × 10^-74 cc + 0. × 10^-84 g0, 0. × 10^-74 cc + 0. × 10^-73 g0, 0. × 10^-74 cc, 0. × 10^-78 cc}
```

Degree 4

In[•]:=
```
ls[4] = ls[4] // Simplify;
```

In[•]:=
```
sol4 = Solve[ls[4] == 0, AppendTo[Hom[4], g0]]
```

Solve: Equations may not give solutions for all "solve" variables.

Out[•]=
```
{{p[0, 0, 1, 3] →
   -9.5173531376348982189019398083396751592128292824106539175120986109721 73 cc,
  p[0, 0, 2, 2] →
   -3295.022722606268167276817340051106522091954071374888606184542336764668 cc +
    2.0000000000000000000000000000000000000000000000000000000000000000000000
     p[0, 0, 0, 4], p[0, 0, 3, 1] →
   91.969392526669543519103713542028146118482968034648736460140347621700 6 cc, p[0, 0, 4,
    0] → -1311.5069889413909363639768270549118395560952216272355536421395176684 08 cc +
```

```
  1.0000000000000000000000000000000000000000000000000000000000000000
   p[0, 0, 0, 4], p[0, 1, 0, 3] →
 2751.3728598012838373442091299847476754412290947916983870748191436186000 cc,
p[0, 1, 1, 2] →
 -359.34162579285360616424964749866600029978418842710422785209688475191 cc, p[0, 1,
  2, 1] → -467.83602970434197014503634724200076502177650001240963959122485959658 0 cc,
p[0, 1, 3, 0] → 22.987379549264944007680588925886175769605406090613688200155420333912
  cc, p[0, 2, 0, 2] →
 1916.7315570938029985286148612652006546188911186915993978463362996101 66 cc, p[0,
  2, 1, 1] → -16.571869727856480201431589505622265044867094519398809321111789920620
  cc, p[0, 2, 2, 0] →
 -149.40713929236783820842889790007055973720480754025170387506052532133 31 cc, p[0, 3,
  0, 1] → 670.61032328808129103984751641475119507660044130264834062775252218146 69 cc,
p[0, 3, 1, 0] → -3.9594609680482496656808374227016035829776510173623736172237684722 79
  cc, p[0, 4, 0, 0] →
 92.523286848659776138196277542751336891707556681199055675078927152502 1 cc, p[1, 0,
  0, 3] → -0.074517370939414166984543827240085256752349124039076548735335746822 1138
  cc, p[1, 0, 1, 2] →
 0.0037948548289247305049428852388382508380746638893331960925340153466067 3 cc,
p[1, 0, 2, 1] →
 0.017510092097531364684775047353903844821686760418068077914745428787010 70 cc,
p[1, 0, 3, 0] →
 -0.0019986945141468154337719108201246608244267439460484723408347331566064 88 cc,
p[1, 1, 0, 2] →
 -0.098208695301692848317146560886653104724122061465032480840918029441619 3 cc,
p[1, 1, 1, 1] →
 0.0067432559176296512285251072481916338703801994932067712710562120346404 5 cc,
p[1, 1, 2, 0] →
 0.0054661629922031174664959119515111552730830113604735134096475130224760855 cc,
p[1, 2, 0, 1] →
 -0.052822420885000964794002120483539060249684501253957037843461959093251 04 cc,
p[1, 2, 1, 0] → 0.0031490183991747186866617927984121863654432992214984101023876209 49
  cc, p[1, 3, 0, 0] →
 -0.0094126856035535239083197014905093639464762713872226443748485471406463 2 cc,
p[2, 0, 0, 2] →
 -0.000010133424997031488071508137680468957499179872848430691393788346431619 27 cc,
p[2, 0, 1, 1] →
 -0.00019923748663990835923259396643473258561428281793478936032525054247117 90 cc,
p[2, 0, 2, 0] →
 0.000090832569321227782749719459053958792924293499207892597725207402476033 70 cc,
p[2, 1, 0, 1] →
 0.000076662262203538835431642941062510903414642490996420375649607923373097 7 cc,
p[2, 1, 1, 0] →
 -0.000077349549137150155729558409489800685576852759822117173993758682 56 cc,
p[2, 2, 0, 0] →
 -0.000023251586896488541375656622983888325852208476697452550952139232259927 29 cc,
p[3, 0, 0, 1] →
 2.1857485088044288267306810773790717972342627543213634593154737324156 84 × 10^-6 cc,
p[3, 0, 1, 0] →
 -9.6389262467219953102657003983090061310985666409780880939300056368058 68 × 10^-7 cc,
```

```
p[3, 1, 0, 0] →
 1.906829067130223877461865406376300977466591361639065979282479173678063 × 10^-6 cc,
p[4, 0, 0, 0] →
 1.220380201925954489961413615523729489572572050772810485806108564979383 × 10^-11 cc,
g0 → -1.060228760573803395928677515259228169180820577214517868413576063535516 cc}}
```

In[ ]:=
```
{g0, p[0, 0, 0, 4], p[0, 0, 1, 3], p[0, 0, 2, 2], p[0, 0, 3, 1], p[0, 0, 4, 0],
   p[0, 1, 0, 3], p[0, 1, 1, 2], p[0, 1, 2, 1], p[0, 1, 3, 0], p[0, 2, 0, 2],
   p[0, 2, 1, 1], p[0, 2, 2, 0], p[0, 3, 0, 1], p[0, 3, 1, 0], p[0, 4, 0, 0],
   p[1, 0, 0, 3], p[1, 0, 1, 2], p[1, 0, 2, 1], p[1, 0, 3, 0], p[1, 1, 0, 2],
   p[1, 1, 1, 1], p[1, 1, 2, 0], p[1, 2, 0, 1], p[1, 2, 1, 0], p[1, 3, 0, 0],
   p[2, 0, 0, 2], p[2, 0, 1, 1], p[2, 0, 2, 0], p[2, 1, 0, 1], p[2, 1, 1, 0],
   p[2, 2, 0, 0], p[3, 0, 0, 1], p[3, 0, 1, 0], p[3, 1, 0, 0], p[4, 0, 0, 0]} =
  {g0, p[0, 0, 0, 4], p[0, 0, 1, 3], p[0, 0, 2, 2], p[0, 0, 3, 1], p[0, 0, 4, 0],
    p[0, 1, 0, 3], p[0, 1, 1, 2], p[0, 1, 2, 1], p[0, 1, 3, 0], p[0, 2, 0, 2],
    p[0, 2, 1, 1], p[0, 2, 2, 0], p[0, 3, 0, 1], p[0, 3, 1, 0], p[0, 4, 0, 0],
    p[1, 0, 0, 3], p[1, 0, 1, 2], p[1, 0, 2, 1], p[1, 0, 3, 0], p[1, 1, 0, 2],
    p[1, 1, 1, 1], p[1, 1, 2, 0], p[1, 2, 0, 1], p[1, 2, 1, 0], p[1, 3, 0, 0],
    p[2, 0, 0, 2], p[2, 0, 1, 1], p[2, 0, 2, 0], p[2, 1, 0, 1], p[2, 1, 1, 0],
    p[2, 2, 0, 0], p[3, 0, 0, 1], p[3, 0, 1, 0], p[3, 1, 0, 0], p[4, 0, 0, 0]} /. sol4[[1]];
```

In[ ]:=
```
g0
```

Out[ ]=
```
-1.060228760573803395928677515259228169180820577214517868413576063535516 cc
```

In[ ]:=
```
g0 // N
```

Out[ ]=
```
-1.06023 cc
```

From the above it can be seen that we can take e.g. cc=1.

In[ ]:=
```
S2 /. { cc → 1}
```

Out[ ]=
```
0.0003292798954671901853045076059883110658074407734479166845240084655909496 x1^2 +
 1.978092530977645483781488288075046308266814225142902562421661710671039 x2^2 + x3^2 + x4^2
```

In[ ]:=
```
S2 // N
```

Out[ ]=
```
0.00032928 cc x1^2 + 1.97809 cc x2^2 + cc x3^2 + cc x4^2
```

In[ ]:=
```
V1 = V  /. { cc → 1} // Simplify // Expand;
```

In[ ]:=
```
vd = D[V1, x1] f1 + D[V1, x2] f2 + D[V1, x3] f3 + D[V1, x4] f4 // Simplify;
```

In[ ]:=
```
gg = vd /. {x1 → t x1, x2 → t x2, x3 → t x3, x4 → t x4};
ff = Normal[Series[gg, {t, 0, 4}]] // Simplify;
```

In[∘]:=
```
MonomialList[ff, t]
```

Out[∘]=
```
{t^4 (-1.06022876057380339592867751525922816918082057721451786841357 61 x3^4 -
    2.1204575211476067918573550305184563383616411544290357368271521 x3^2 x4^2 -
    1.0602287605738033959286775152592281691808205772145178684135761 x4^4), 0,
 t^2 (-1.0602287605738033959286775152592281691808205772145178684135761 x1^2 -
    1.0602287605738033959286775152592281691808205772145178684135761 x2^2)}
```

In[∘]:=
```
S2 /. { cc → 1}
```

Out[∘]=
```
0.00032927989546719018530450760598831106580744077344791668452400846559094 96 x1^2 +
 1.9780925309776454837814882880750463082668142251429025624216617106710 39 x2^2 + x3^2 + x4^2
```

From the above we can see that the lowest degree part of V is positively defined, that is, V is a positively defined Lyapunov function, whose Lie derivative is negatively defined.

2. c) Evolution of system states under perturbations

Plotting the original system

Preparations

In[∘]:=
```
Quit
```

In[∘]:=
```
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@
  {Plot, ParametricPlot, ListPlot, ListLinePlot};
SetDirectory[NotebookDirectory[]];
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@ {Plot, ListPlot,
   ListLinePlot, ListLogLogPlot, ParametricPlot, DateListPlot, DiscretePlot};
LaunchKernels[];
```

The function creating the plots with the measured values

In[∘]:=

```
ClearAll[x1, x2, x3, a, b, n, w, ED, c, k1, k2, k];
f1[x1_, x2_, x3_, x4_] := a x1 - n x1 - b x1 x3/(ED + x3);
f2[x1_, x2_, x3_, x4_] := n x1 - w x2 + b x1 x3/(ED + x3);
f3[x1_, x2_, x3_, x4_] := -c x3 - k1 x3 + k2 x4 + k (x1 + x2);
f4[x1_, x2_, x3_, x4_] := k1 x3 - k2 x4;
{a, b, n, w, ED, c, k1, k2} =
  {38437/100000, 22229/10000, 13881/100000, 71159/1000000, 117/80, 22711/100000, 21459/100, 13953/10};
k = 1/100;
n // N
```

Out[∘]=

```
0.13881
```

In[•]:=
```
ClearAll[nsol, ev, plotter3D];
nsol = NSolve[Join @@ Thread /@ {{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3,
          x4], f4[x1, x2, x3, x4]} == 0, {x1, x2, x3, x4} > 0}, {x1, x2, x3, x4}, 20]⟦1⟧
ev = Eigenvalues[
  D[{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3, x4], f4[x1, x2, x3, x4]},
    {{x1, x2, x3, x4}}] /. nsol]
plotter3D[τ_, shift_, ag_ : Automatic, pg_ : Automatic, pp_ : 100000,
  ar_ : Automatic, opts___] := Module[{startingpoint, sys, solution,
   solution1, solution2, solution3, solution4, plot1, imagesize, imagesize2},
  imagesize = 350; imagesize2 = 250;
  startingpoint = ({x1, x2, x3, x4} /. nsol) + shift;
  sys := NDSolveValue[Join[{u1'[t] == f1[u1[t], u2[t], u3[t], u4[t]],
      u2'[t] == f2[u1[t], u2[t], u3[t], u4[t]], u3'[t] ==
       f3[u1[t], u2[t], u3[t], u4[t]], u4'[t] == f4[u1[t], u2[t], u3[t], u4[t]]},
     Thread[{u1[0], u2[0], u3[0], u4[0]} == startingpoint]],
    {u1, u2, u3, u4}, {t, τ}, AccuracyGoal → ag, PrecisionGoal → pg, opts];
  solution[t_] := Through[sys[t]];
  solution4[t_] := Delete[Through[sys[t]], 4];
  solution3[t_] := Delete[Through[sys[t]], 3];
  solution2[t_] := Delete[Through[sys[t]], 2];
  solution1[t_] := Delete[Through[sys[t]], 1];
  {ParametricPlot3D[Evaluate[solution4[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x₁ [mm³]", "x₂ [mm³]", "x₃ [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution3[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x₁ [mm³]", "x₂ [mm³]", "x₄ [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution2[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x₁ [mm³]", "x₃ [mg/kg]", "x₄ [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution1[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x₂ [mm³]", "x₃ [mg/kg]", "x₄ [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   Plot[Evaluate[solution[t]⟦1⟧], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x₁ [mm³]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t]⟦2⟧], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x₂ [mm³]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t]⟦3⟧], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x₃ [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t]⟦4⟧], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t [days]", "x₄ [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2]}]
```

Out[∘]=

```
{x1 → 0.6443505607794775852, x2 → 3.480501764313829585,
 x3 → 0.1816235447621552186 3, x4 → 0.0279327717842119174 12}
```

Out[∘]=

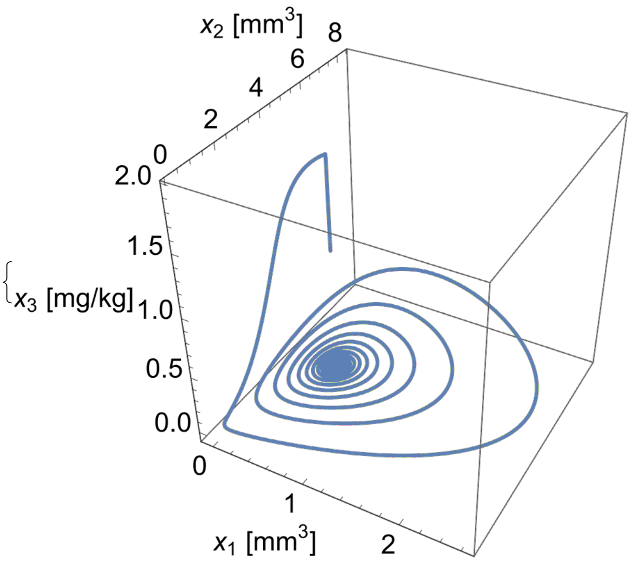
```
{-1609.9202762888064478, -0.2594561416409449572,
 -0.0042682847763036351 45 + 0.1085066759521500905 4 ⅈ,
 -0.0042682847763036351 45 - 0.1085066759521500905 4 ⅈ}
```

Figure 4: Trajectories going inwards, converging to the singular point

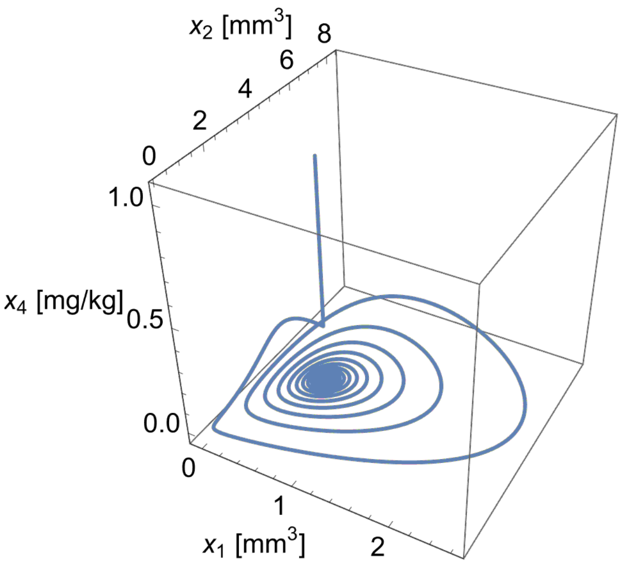
In[∘]:=

```
plotter3D[1200, {0, 0, 1, 1}, Automatic, 100, 10000, 1, Method → "BDF"]
```

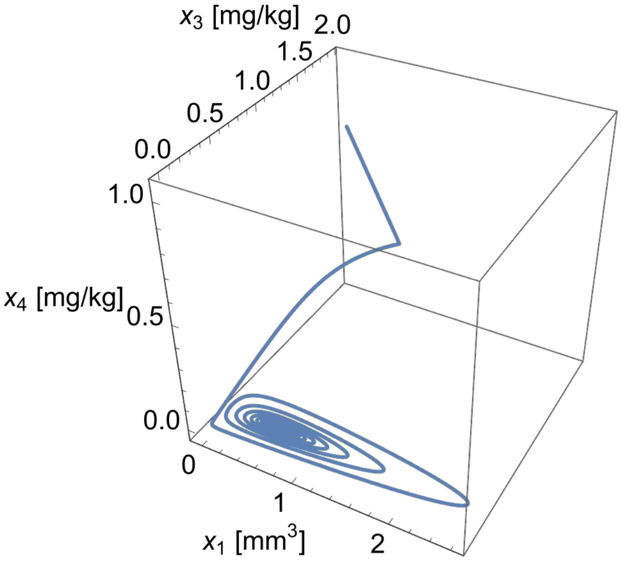
Out[∘]=

{

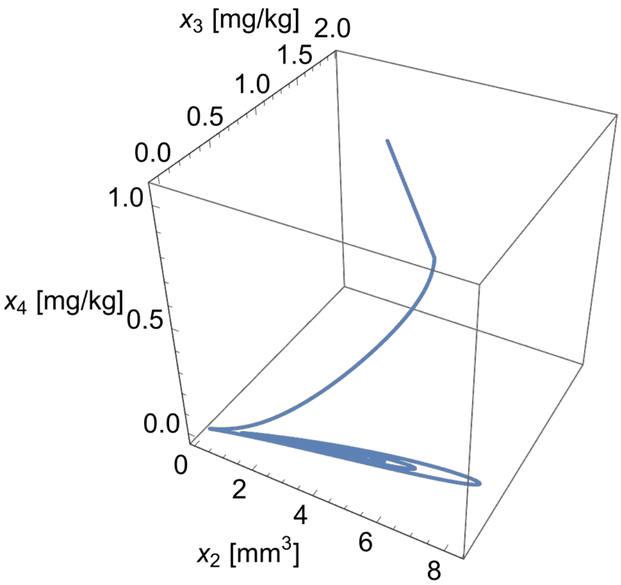
,



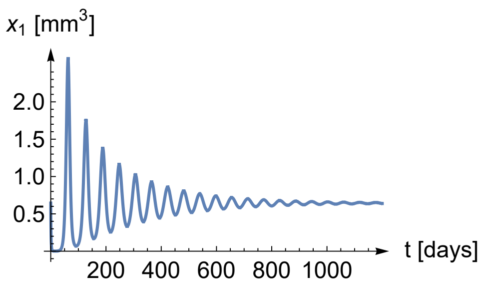
,


x_3 [mg/kg]
2.0
1.5
1.0
0.5
0.0
1.0
x_4 [mg/kg]
0.5
0.0
0
1
x_1 [mm^3]
2

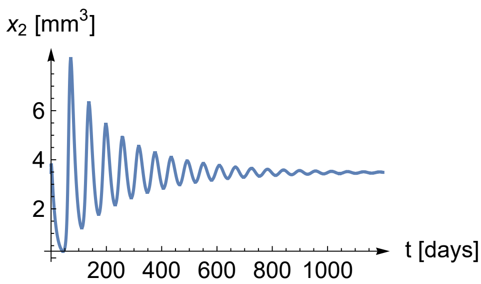
,


x_3 [mg/kg]
2.0
1.5
1.0
0.5
0.0
1.0
x_4 [mg/kg]
0.5
0.0
0
2
4
x_2 [mm^3]
6
8

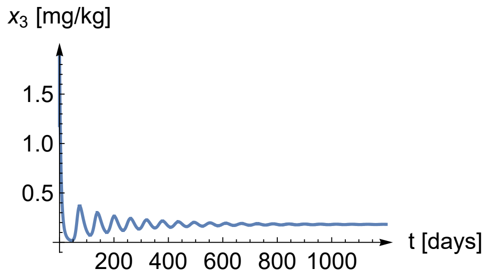
,


x_1 [mm^3]
2.0
1.5
1.0
0.5
200 400 600 800 1000
t [days]

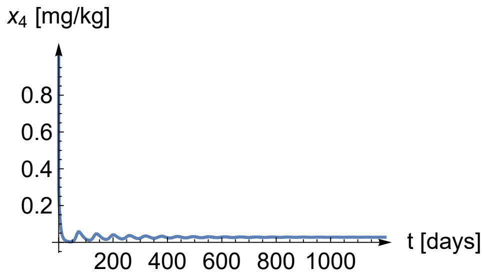
,


x_2 [mm^3]
6
4
2
200 400 600 800 1000
t [days]

,



,



}

Positive perturbation

If *n* is perturbed with a positive value then each eigenvalue has a negative real part and the singular point is locally asymptotically stable.

Preparations

In[∘]:=
```
Quit
```

In[∘]:=
```
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@
  {Plot, ParametricPlot, ListPlot, ListLinePlot};
SetDirectory[NotebookDirectory[]];
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@ {Plot, ListPlot,
   ListLinePlot, ListLogLogPlot, ParametricPlot, DateListPlot, DiscretePlot};
LaunchKernels[];
```

The function creating the plots

In[∘]:=
```
ClearAll[x1, x2, x3, a, b, n, w, ED, c, k1, k2, k];
```

$$f1[x1\_, x2\_, x3\_, x4\_] := a\,x1 - n\,x1 - b\,x1\,\frac{x3}{ED + x3};$$

$$f2[x1\_, x2\_, x3\_, x4\_] := n\,x1 - w\,x2 + b\,x1\,\frac{x3}{ED + x3};$$

```
f3[x1_, x2_, x3_, x4_] := -c x3 - k1 x3 + k2 x4 + k (x1 + x2);
f4[x1_, x2_, x3_, x4_] := k1 x3 - k2 x4;
```

$$\{w, ED, c, k1, k2\} = \left\{\frac{71159}{1000000}, \frac{117}{80}, \frac{22711}{100000}, \frac{21459}{100}, \frac{13953}{10}\right\};$$

$$a = \frac{38437}{100000};\ b = \frac{22229}{10000};$$

$$n = \frac{-18177 + \boxed{2.00\ldots \times 10^4}}{25000} + \frac{1}{100};$$

$$k = \frac{1}{100};$$

```
n // N
```

Out[∘]=

0.0826605

In[*]:=
```
ClearAll[nsol, ev, plotter3D];
nsol = NSolve[Join @@ Thread /@ {{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3,
          x4], f4[x1, x2, x3, x4]} == 0, {x1, x2, x3, x4} > 0}, {x1, x2, x3, x4}, 20][[1]]
ev = Eigenvalues[
  D[{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3, x4], f4[x1, x2, x3, x4]},
    {{x1, x2, x3, x4}}] /. nsol]
plotter3D[τ_, shift_, ag_ : Automatic, pg_ : Automatic, pp_ : 1000,
  ar_ : Automatic, opts___] := Module[{startingpoint, sys, solution,
   solution1, solution2, solution3, solution4, plot1, imagesize, imagesize2},
  imagesize = 350; imagesize2 = 250;
  startingpoint = ({x1, x2, x3, x4} /. nsol) + shift;
  sys := NDSolveValue[Join[{u1'[t] == f1[u1[t], u2[t], u3[t], u4[t]],
      u2'[t] == f2[u1[t], u2[t], u3[t], u4[t]], u3'[t] ==
       f3[u1[t], u2[t], u3[t], u4[t]], u4'[t] == f4[u1[t], u2[t], u3[t], u4[t]]},
     Thread[{u1[0], u2[0], u3[0], u4[0]} == startingpoint]],
    {u1, u2, u3, u4}, {t, τ}, AccuracyGoal → ag, PrecisionGoal → pg, opts];
  solution[t_] := Through[sys[t]];
  solution4[t_] := Delete[Through[sys[t]], 4];
  solution3[t_] := Delete[Through[sys[t]], 3];
  solution2[t_] := Delete[Through[sys[t]], 2];
  solution1[t_] := Delete[Through[sys[t]], 1];
  {ParametricPlot3D[Evaluate[solution4[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1  [mm^3]", "x2  [mm^3]", "x3  [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution3[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1  [mm^3]", "x2  [mm^3]", "x4  [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution2[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1  [mm^3]", "x3  [mg/kg]", "x4  [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution1[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x2  [mm^3]", "x3  [mg/kg]", "x4  [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   Plot[Evaluate[solution[t][[1]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t  [days]", "x1  [mm^3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[2]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t  [days]", "x2  [mm^3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[3]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t  [days]", "x3  [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[4]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t  [days]", "x4  [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2]}]
```

Out[•]=

{x1 → 0.8148253080817211190, x2 → 4.401332279365521529,
 x3 → 0.22967538142077595210, x4 → 0.03532289837245345916}

Out[•]=

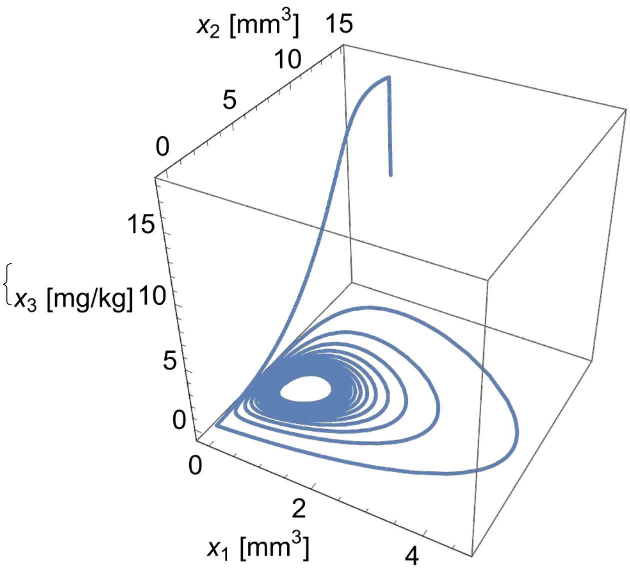
{-1609.9202762888416362, -0.2668023084178325956,
 -0.0005952013702655830927 + 0.11699949810784607569 ⅈ,
 -0.0005952013702655830927 - 0.11699949810784607569 ⅈ}

Trajectories going inwards, towards the singular point

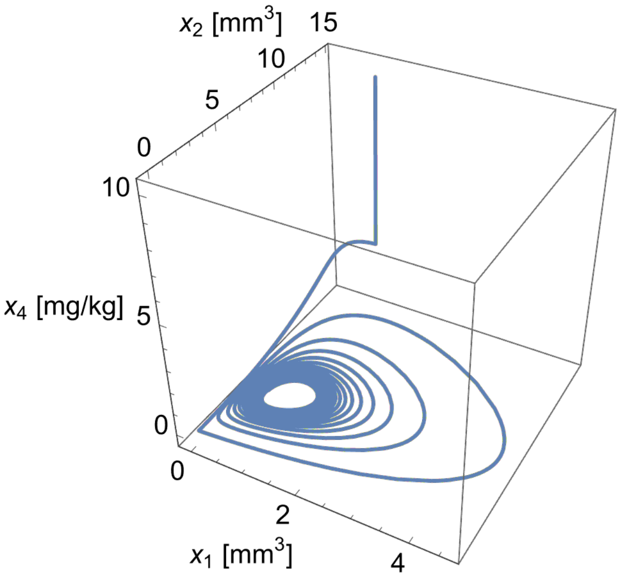
In[•]:=

```
plotter3D[1000, {0, 10, 10, 10}, Automatic, 100, 1000, 1, Method → "BDF"]
```

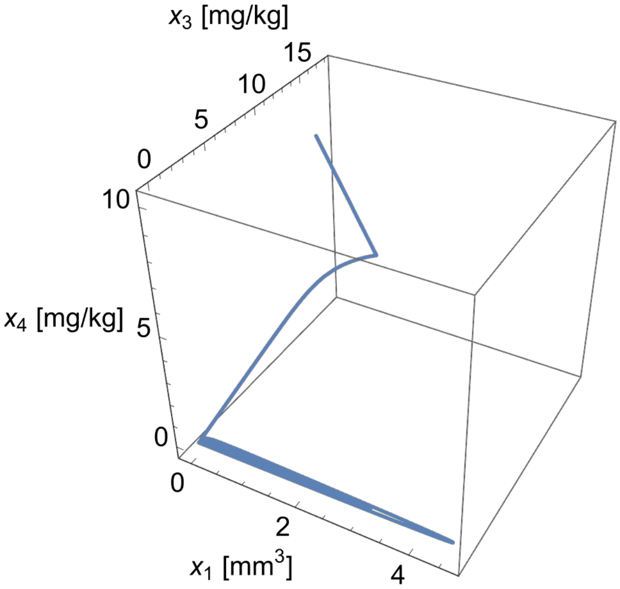
Out[•]=

{

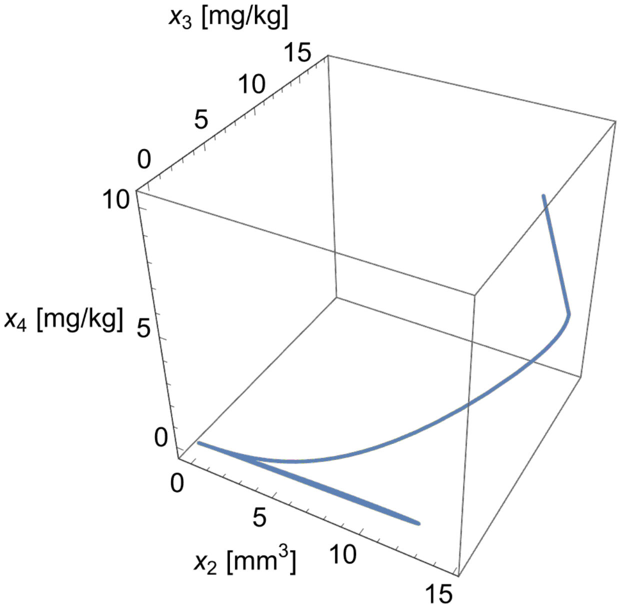
,



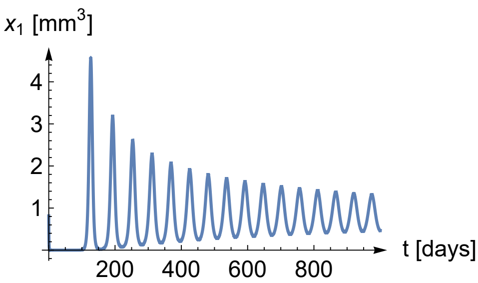
,


x3 [mg/kg]
15
10
5
0
10
x4 [mg/kg]
5
0
0
2
4
x1 [mm3]

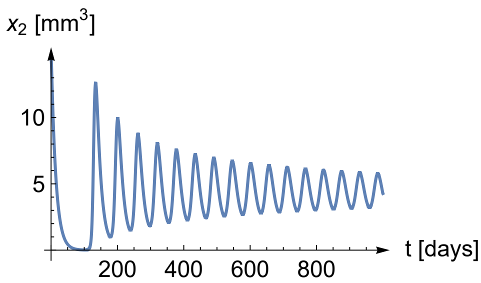
,


x3 [mg/kg]
15
10
5
0
10
x4 [mg/kg]
5
0
0
5
10
15
x2 [mm3]

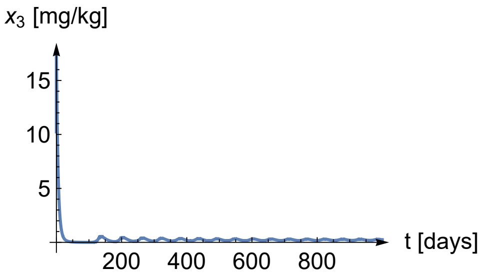
,


x1 [mm3]
4
3
2
1
200
400
600
800
t [days]

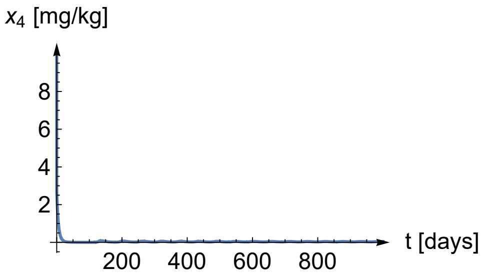
,


x2 [mm3]
10
5
200
400
600
800
t [days]

,



,



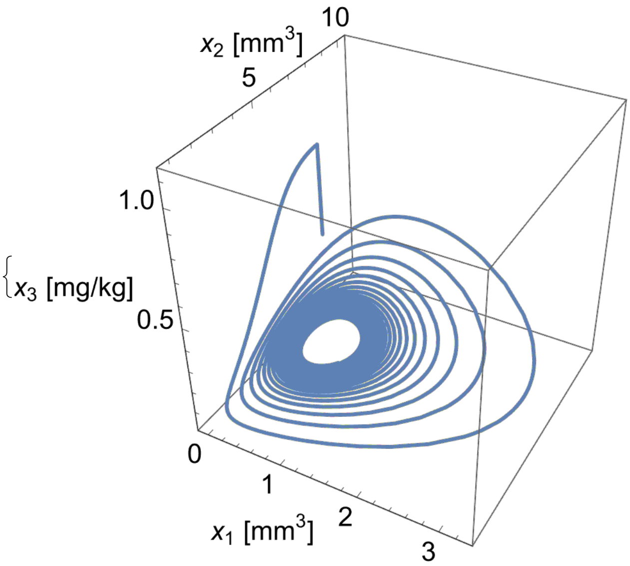
}

In[∘]:=

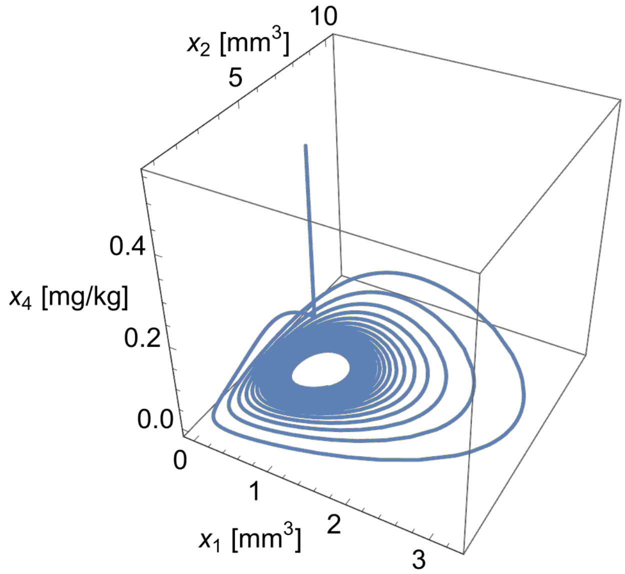
```
plotter3D[1200, {0, 0, 0.5, 0.5}, Automatic, 100, 1000, 1, Method → "BDF"]
```

Out[∘]=

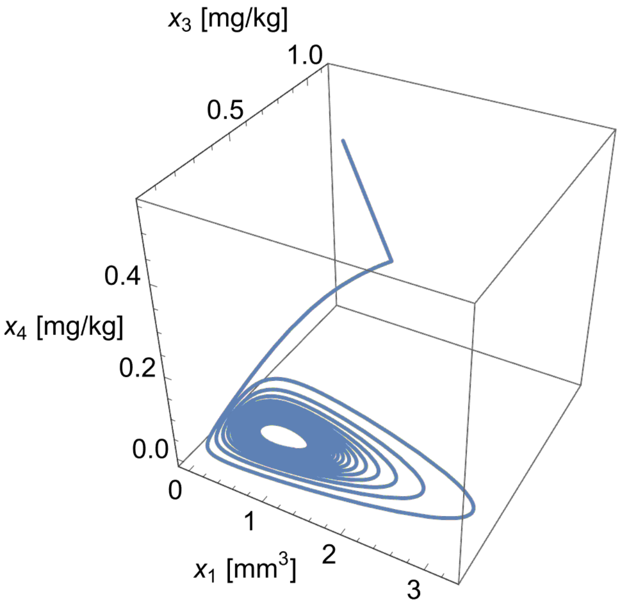
{



,

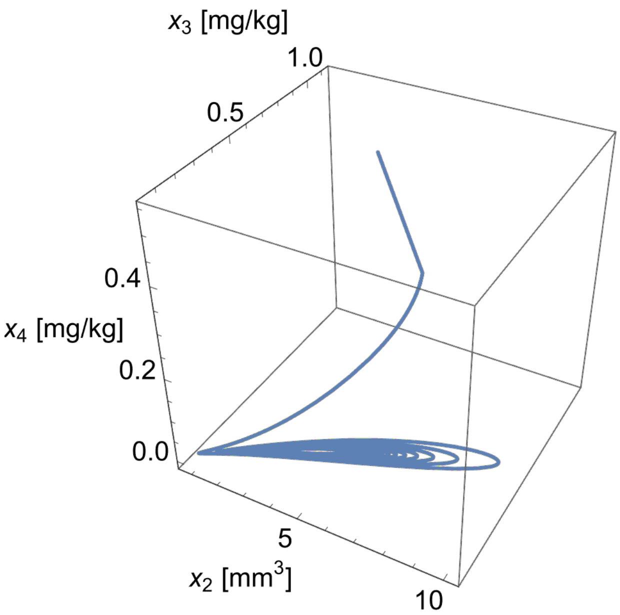


,



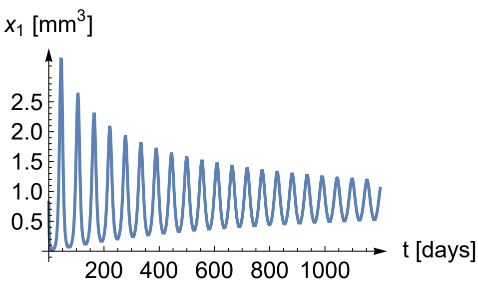
x3 [mg/kg]
1.0
0.5
0.4
x4 [mg/kg]
0.2
0.0
0
1
x1 [mm3]
2
3

,



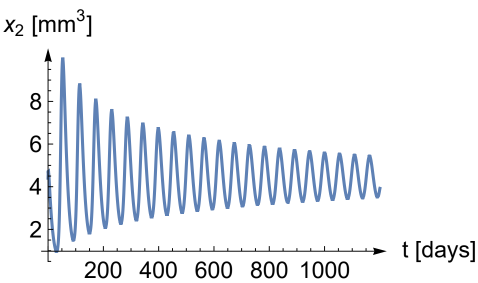
x3 [mg/kg]
1.0
0.5
0.4
x4 [mg/kg]
0.2
0.0
5
x2 [mm3]
10

,



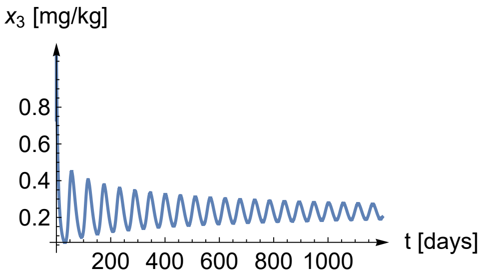
x1 [mm3]
2.5
2.0
1.5
1.0
0.5
200 400 600 800 1000
t [days]

,

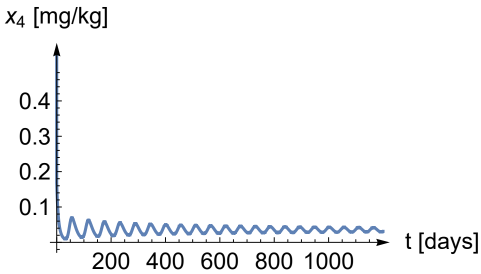


x2 [mm3]
8
6
4
2
200 400 600 800 1000
t [days]

,



,



}

Negative perturbation

If *n* is perturbed with a negative value then two imaginary eigenvalues have positive real part, so the singular point becomes locally unstable and a stable limit cycle appears around it.

Preparations

In[∘]:=
```
Quit
```

In[∘]:=
```
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@
  {Plot, ParametricPlot, ListPlot, ListLinePlot};
SetDirectory[NotebookDirectory[]];
SetOptions[#, AxesStyle → Arrowheads[Automatic]] & /@ {Plot, ListPlot,
   ListLinePlot, ListLogLogPlot, ParametricPlot, DateListPlot, DiscretePlot};
LaunchKernels[];
```

The function creating the plots

In[∘]:=
```
ClearAll[x1, x2, x3, a, b, n, w, ED, c, k1, k2, k];
```

$$f1[x1\_, x2\_, x3\_, x4\_] := a\,x1 - n\,x1 - b\,x1 \frac{x3}{ED + x3};$$

$$f2[x1\_, x2\_, x3\_, x4\_] := n\,x1 - w\,x2 + b\,x1 \frac{x3}{ED + x3};$$

```
f3[x1_, x2_, x3_, x4_] := -c x3 - k1 x3 + k2 x4 + k (x1 + x2);
f4[x1_, x2_, x3_, x4_] := k1 x3 - k2 x4;
```

$$\{w, ED, c, k1, k2\} = \left\{\frac{71159}{1000000}, \frac{117}{80}, \frac{22711}{100000}, \frac{21459}{100}, \frac{13953}{10}\right\};$$

$$a = \frac{38437}{100000};\ b = \frac{22229}{10000};$$

$$n = \frac{-18177 + \boxed{2.00\ldots \times 10^4}}{25000} - \frac{5}{100};$$

$$k = \frac{1}{100};$$

```
n // N
```

Out[∘]=

0.0226605

```
In[•]:= ClearAll[nsol, ev, plotter3D];
nsol = NSolve[Join @@ Thread /@ {{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3,
          x4], f4[x1, x2, x3, x4]} == 0, {x1, x2, x3, x4} > 0}, {x1, x2, x3, x4}, 20][[1]]
ev = Eigenvalues[
  D[{f1[x1, x2, x3, x4], f2[x1, x2, x3, x4], f3[x1, x2, x3, x4], f4[x1, x2, x3, x4]},
    {{x1, x2, x3, x4}}] /. nsol]
plotter3D[τ_, shift_, ag_ : Automatic, pg_ : Automatic, pp_ : 1000,
  ar_ : Automatic, opts___] := Module[{startingpoint, sys, solution,
   solution1, solution2, solution3, solution4, plot1, imagesize, imagesize2},
  imagesize = 350; imagesize2 = 250;
  startingpoint = ({x1, x2, x3, x4} /. nsol) + shift;
  sys := NDSolveValue[Join[{u1'[t] == f1[u1[t], u2[t], u3[t], u4[t]],
      u2'[t] == f2[u1[t], u2[t], u3[t], u4[t]], u3'[t] ==
       f3[u1[t], u2[t], u3[t], u4[t]], u4'[t] == f4[u1[t], u2[t], u3[t], u4[t]]},
     Thread[{u1[0], u2[0], u3[0], u4[0]} == startingpoint]],
    {u1, u2, u3, u4}, {t, τ}, AccuracyGoal → ag, PrecisionGoal → pg, opts];
  solution[t_] := Through[sys[t]];
  solution4[t_] := Delete[Through[sys[t]], 4];
  solution3[t_] := Delete[Through[sys[t]], 3];
  solution2[t_] := Delete[Through[sys[t]], 2];
  solution1[t_] := Delete[Through[sys[t]], 1];
  {ParametricPlot3D[Evaluate[solution4[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1  [mm^3]", "x2  [mm^3]", "x3  [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution3[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1  [mm^3]", "x2  [mm^3]", "x4  [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution2[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x1  [mm^3]", "x3  [mg/kg]", "x4  [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   ParametricPlot3D[Evaluate[solution1[t]], {t, 0, τ}, PlotRange → All,
    PlotPoints → pp, AxesLabel → {"x2  [mm^3]", "x3  [mg/kg]", "x4  [mg/kg]"},
    LabelStyle → Directive[14], ImageSize → imagesize, BoxRatios → {1, 1, 1}],
   Plot[Evaluate[solution[t][[1]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t  [days]", "x1  [mm^3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[2]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t  [days]", "x2  [mm^3]"}, LabelStyle → Directive[12],
    ImagePadding → {{22, 48}, {10, 22}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[3]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t  [days]", "x3  [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2],
   Plot[Evaluate[solution[t][[4]]], {t, 0, τ}, PlotRange → All, PlotPoints → pp,
    AxesLabel → {"t  [days]", "x4  [mg/kg]"}, LabelStyle → Directive[12],
    ImagePadding → {{25, 48}, {10, 20}}, ImageSize → imagesize2]}]
```

Out[∘]=

```
{x1 → 1.0083586790820129192, x2 → 5.4467154608518009777,
 x3 → 0.28422676852335053043, x4 → 0.043712622559611402804}
```

Out[∘]=

```
{-1609.9202762888766314, -0.27348969423683937723,
 0.002748491556735363216 + 0.12450987662165104041 ⅈ,
 0.002748491556735363216 - 0.12450987662165104041 ⅈ}
```

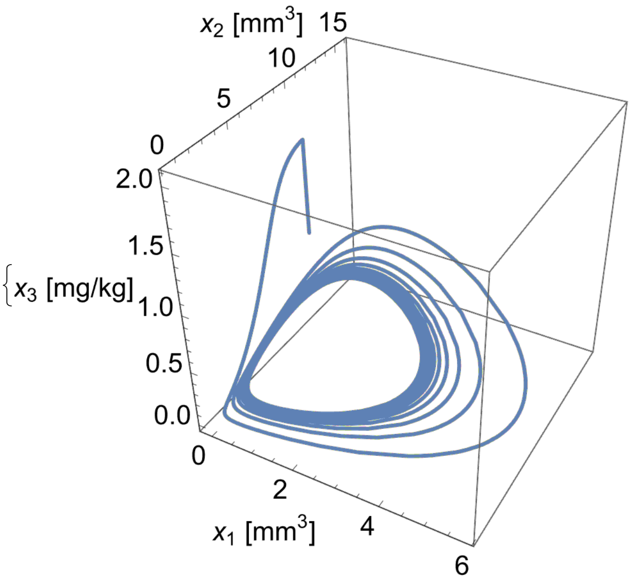
Figure 5. (a)

The trajectories are going inward, approaching the limit cycle from outside.

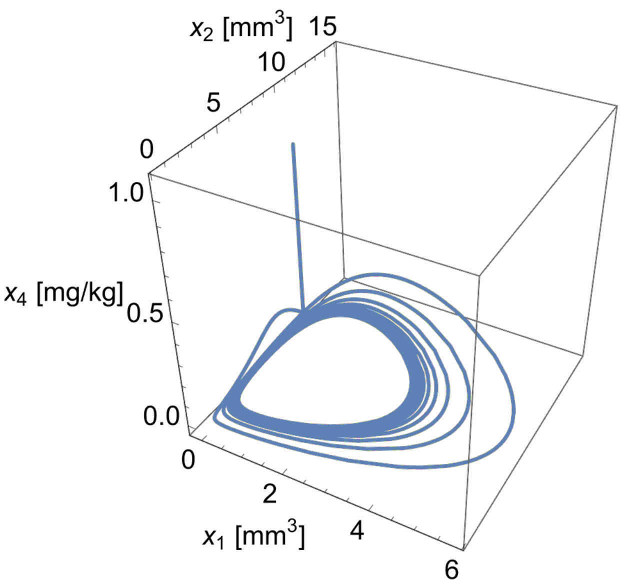
In[∘]:=

```
plotter3D[1300, {0, 1, 1, 1}, Automatic, 100, 1000, 1, Method → "BDF"]
```

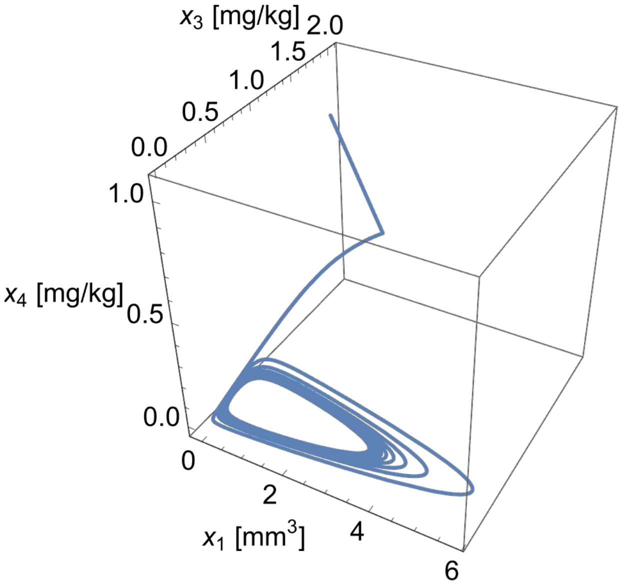
Out[∘]=

{

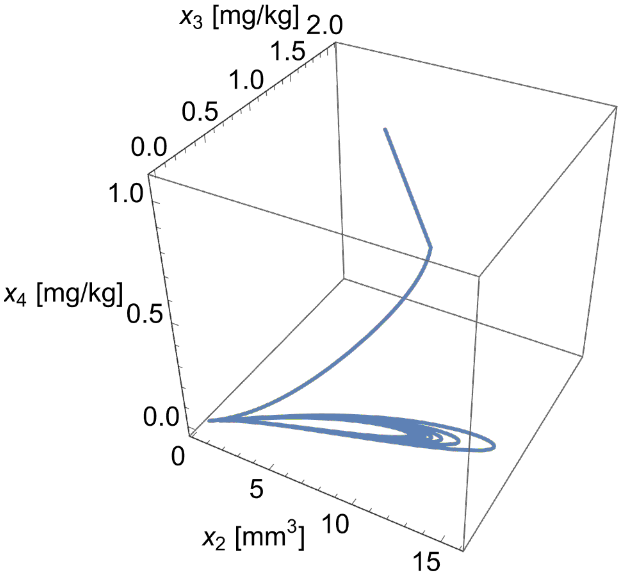
,



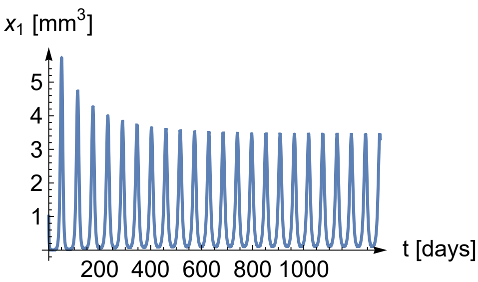
,


x3 [mg/kg]
2.0
1.5
1.0
0.5
0.0
1.0
x4 [mg/kg]
0.5
0.0
0
2
4
6
x1 [mm3]

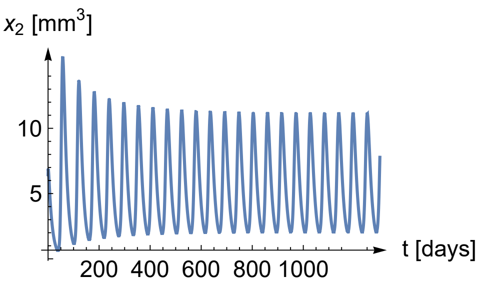
,


x3 [mg/kg]
2.0
1.5
1.0
0.5
0.0
1.0
x4 [mg/kg]
0.5
0.0
0
5
10
15
x2 [mm3]

,


x1 [mm3]
5
4
3
2
1
200 400 600 800 1000
t [days]

,


x2 [mm3]
10
5
200 400 600 800 1000
t [days]

,

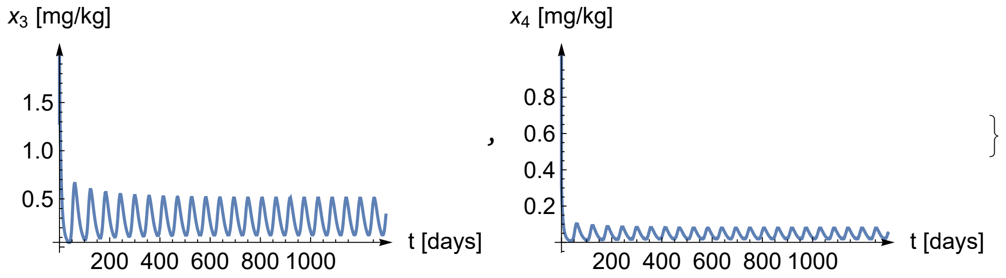
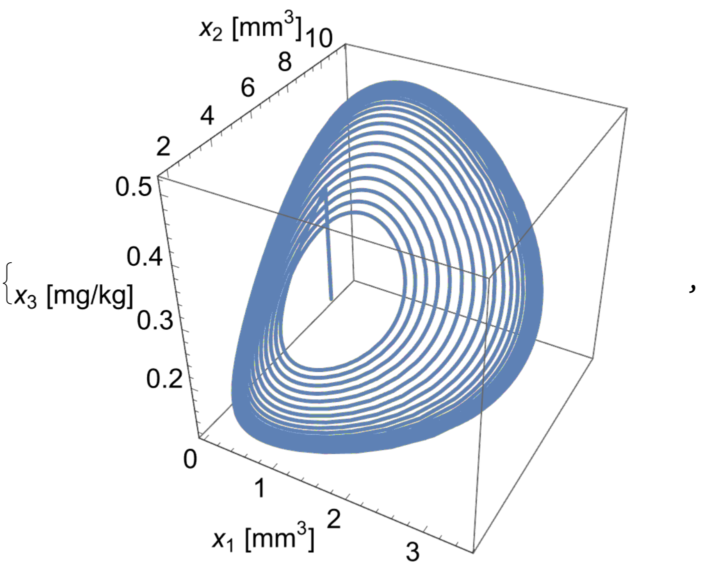


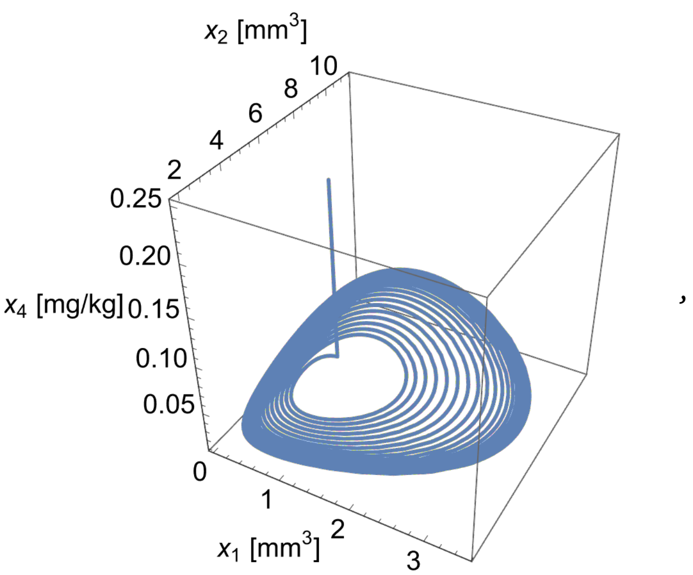
Figure 5. (b)

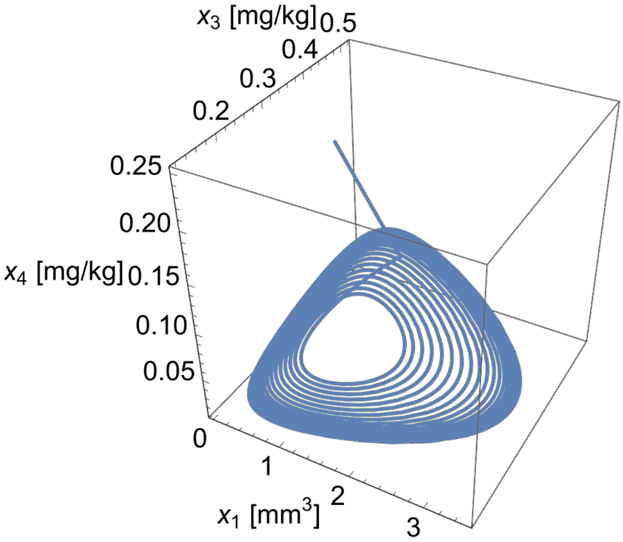
The trajectories are going outward, approaching the limit cycle from inside.

In[ ]:=
```
plotter3D[1300, {0, 0, 0, 0.2}, Automatic, 100, 1000, 1, Method → "BDF"]
```

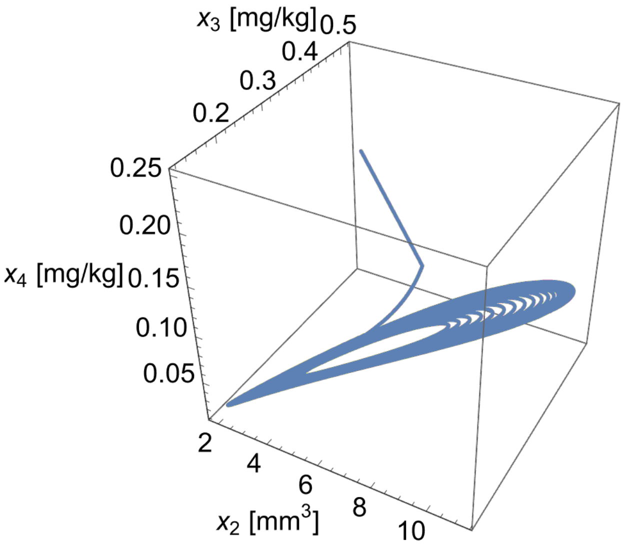
Out[ ]=



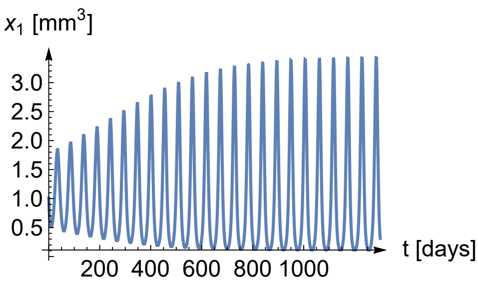



x3 [mg/kg]
0.5
0.4
0.3
0.2
0.25
0.20
x4 [mg/kg]
0.15
0.10
0.05
0
1
2
3
x1 [mm3]

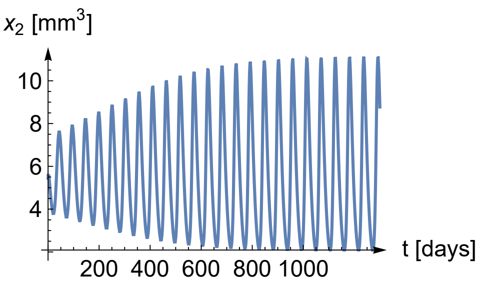
,


x3 [mg/kg]
0.5
0.4
0.3
0.2
0.25
0.20
x4 [mg/kg]
0.15
0.10
0.05
2
4
6
8
10
x2 [mm3]

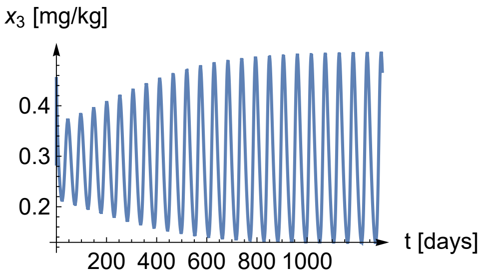
,


x1 [mm3]
3.0
2.5
2.0
1.5
1.0
0.5
200 400 600 800 1000
t [days]

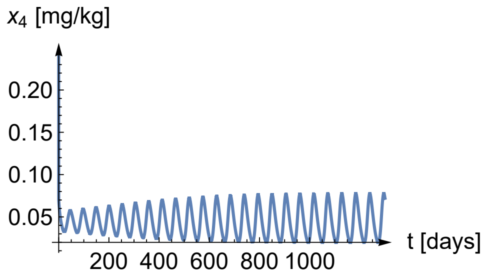
,


x2 [mm3]
10
8
6
4
200 400 600 800 1000
t [days]

,


x_3 [mg/kg]
0.4
0.3
0.2
200 400 600 800 1000
t [days]

,


x_4 [mg/kg]
0.20
0.15
0.10
0.05
200 400 600 800 1000
t [days]

}