practical_4_oscillations_solutions

October 27, 2019

Name: Write your name here

1 SYSTEMS AND NETWORK BIOLOGY - PRACTICAL 4

2 Oscillations

To submit your report, answer the questions below and save the *notebook* clicking on `File > Download as > iPython Notebook` in the menu at the top of the page. **Rename the notebook file** to ''`practicalN_name1_name2.ipynb`'', where `N` is the number of the practical, and `name1` and `name2` are the first surnames of the two team members (only one name if the report is sent individually). Finally, **submit the resulting file through the *Aula ESCI***.

Remember to label the axes in all the plots.

IMPORTANT REMINDER: Before the final submission, remember to ***reset the kernel*** *and re-run the whole notebook again to check that it works.*

The aim of this practical is to explore the dynamics of oscillatory systems and the requirements for oscillations.

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In [1]:
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A. **Oscillations from a negative feedback: the Goodwin oscillator**

We will begin by studying the following two-dimensional system:

$$\frac{dx_1}{dt} = \frac{1}{1+x_2^n} - k_1\, x_1$$

$$\frac{dx_2}{dt} = x_1 - k_2\, x_2$$

a) Consider that $k_1 = k_2 = 0.1$. Is there any vaue of n lower than 12 for which the system shows sustained oscillations?

b) For each of the previous cases, how does the system behave on the phase plane? (Draw the nullclines and plot the trajectory of the system on the phase plane.)

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In [3]:
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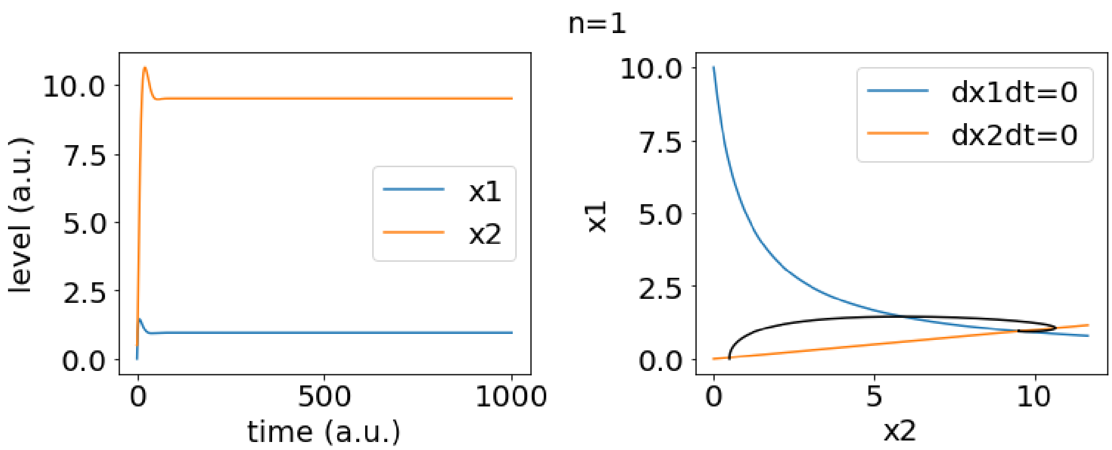
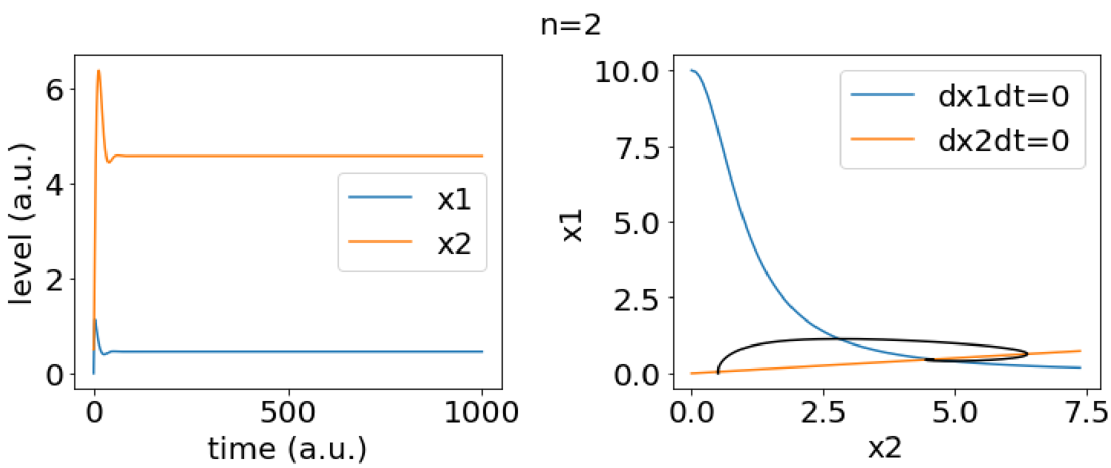
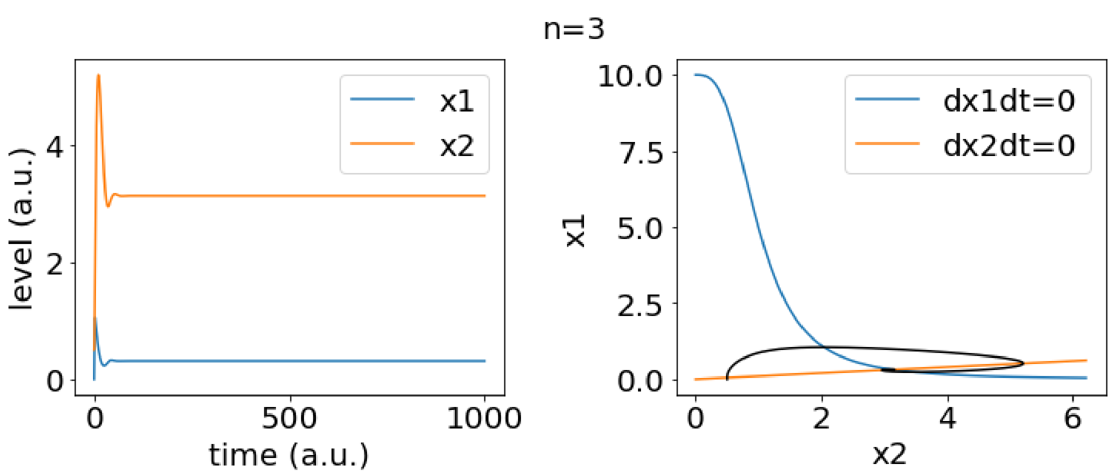

n=1
level (a.u.)
time (a.u.)
x1
x2
dx1dt=0
dx2dt=0
0.0
2.5
5.0
7.5
10.0
0
500
1000
5
10


n=2
level (a.u.)
time (a.u.)
x1
x2
dx1dt=0
dx2dt=0
0
2
4
6
500
1000
0.0
2.5
5.0
7.5
10.0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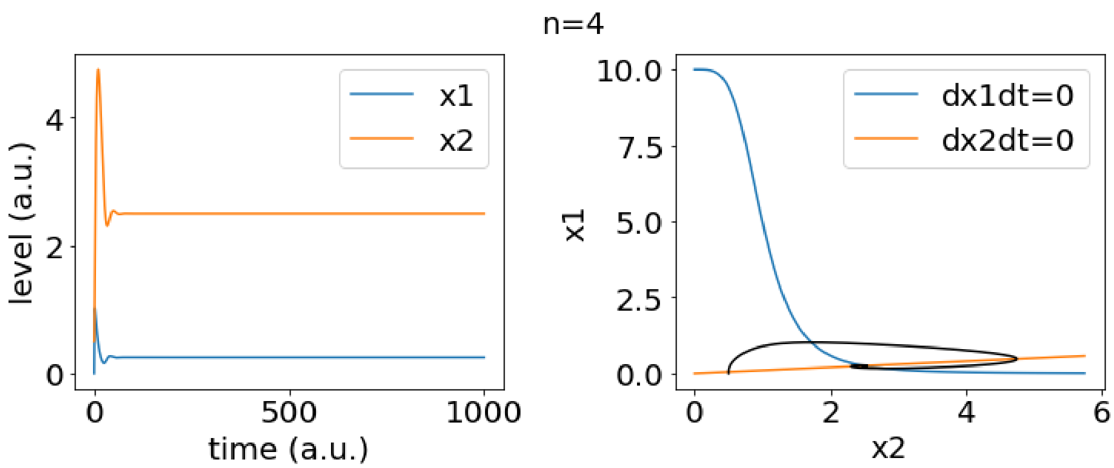
level (a.u.)
time (a.u.)
x1
x2
dx1dt=0
dx2dt=0
0
2
4
6
500
1000
0.0
2.5
5.0
7.5
10.0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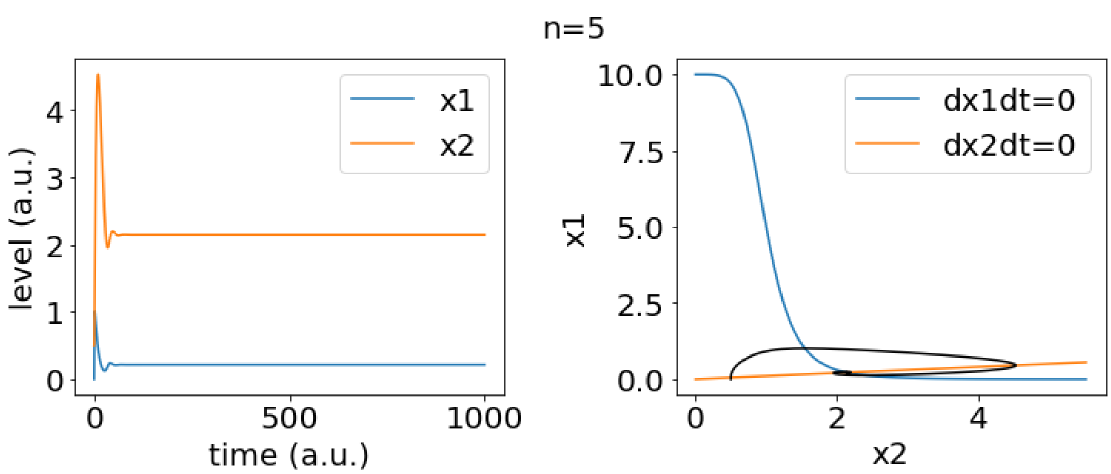
x2
dx1dt=0
dx2dt=0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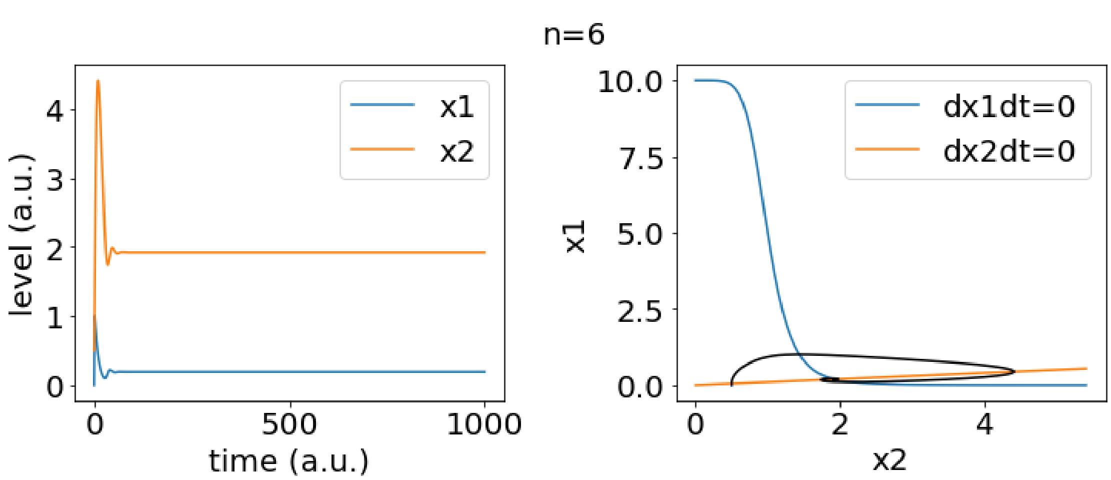
time (a.u.)
x1
x2
dx1dt=0
dx2dt=0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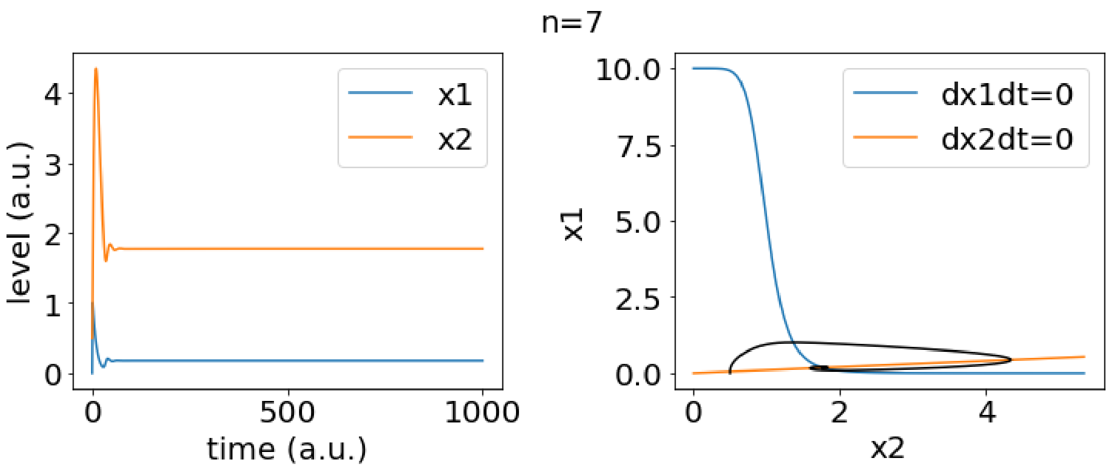
time (a.u.)
x1
x2
dx1dt=0
dx2dt=0


n=7
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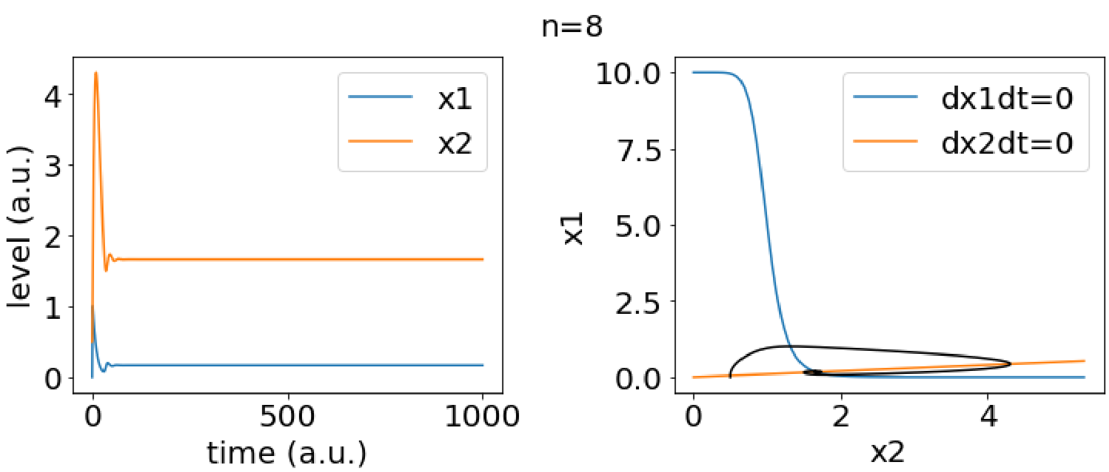
time (a.u.)
x1
x2
dx1dt=0
dx2dt=0
x1
x2


n=8
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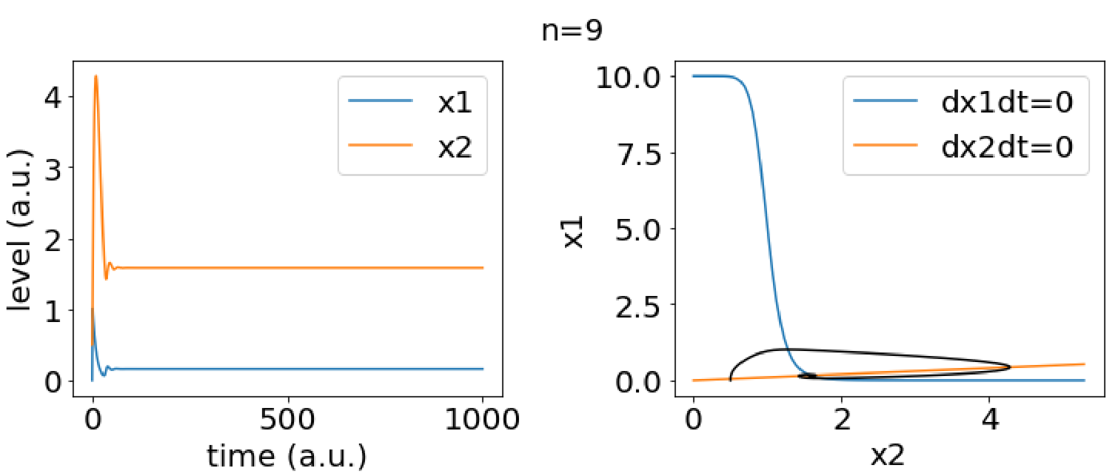
time (a.u.)
x1
x2
dx1dt=0
dx2dt=0
x1
x2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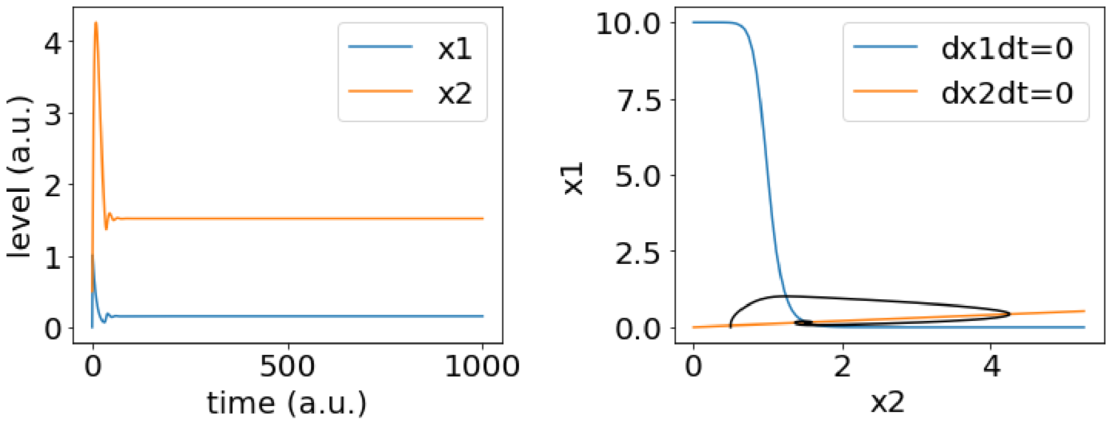
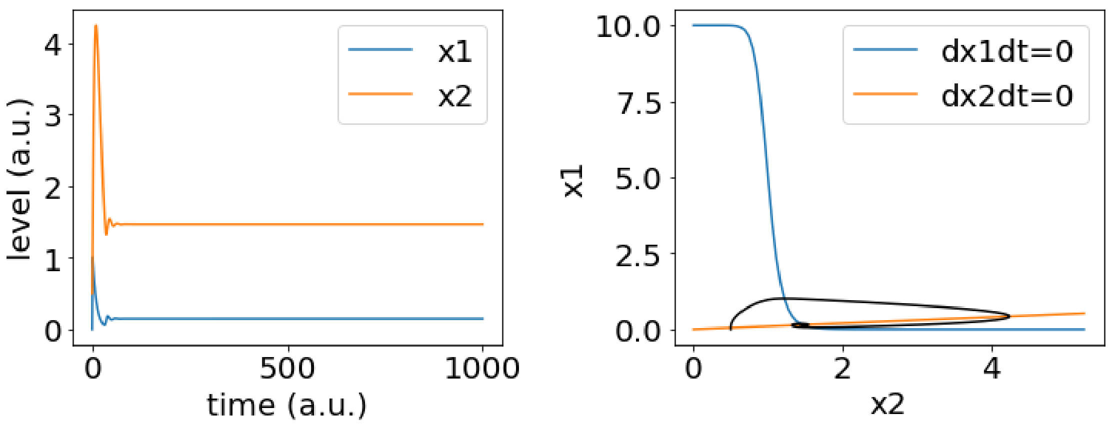
level (a.u.)
time (a.u.)
x1
x2
dx1dt=0
dx2dt=0
x1
x2

n=10



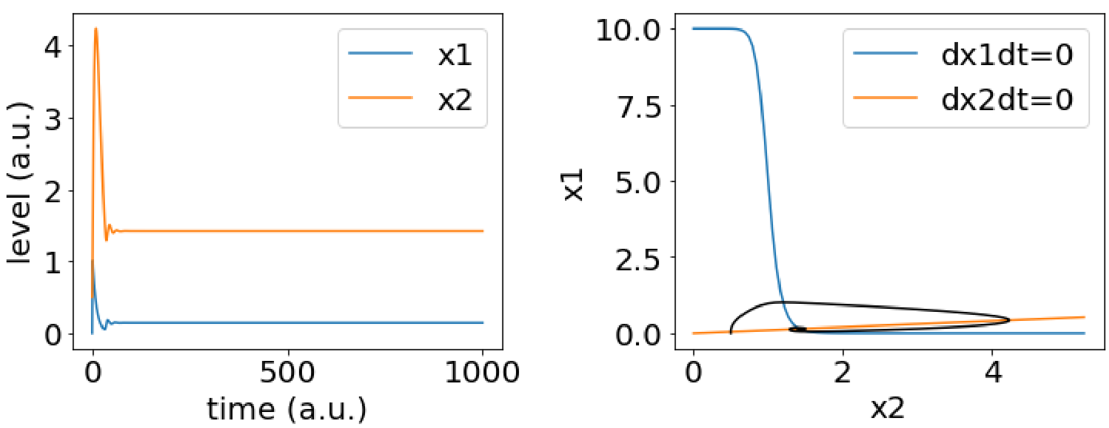
x1
x2
level (a.u.)
0
1
2
3
4
0
500
1000
time (a.u.)
dx1dt=0
dx2dt=0
x1
0.0
2.5
5.0
7.5
10.0
0
2
4
x2

n=11



x1
x2
level (a.u.)
0
1
2
3
4
0
500
1000
time (a.u.)
dx1dt=0
dx2dt=0
x1
0.0
2.5
5.0
7.5
10.0
0
2
4
x2

n=12



x1
x2
level (a.u.)
0
1
2
3
4
0
500
1000
time (a.u.)
dx1dt=0
dx2dt=0
x1
0.0
2.5
5.0
7.5
10.0
0
2
4
x2

Comment your result here

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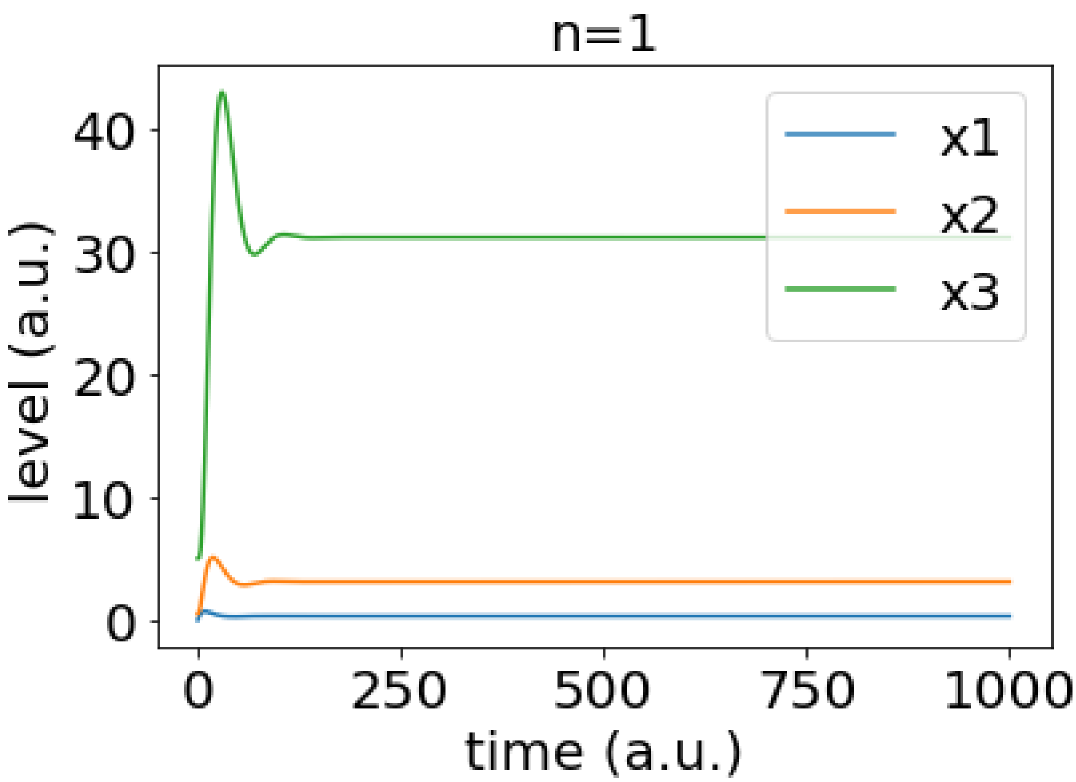
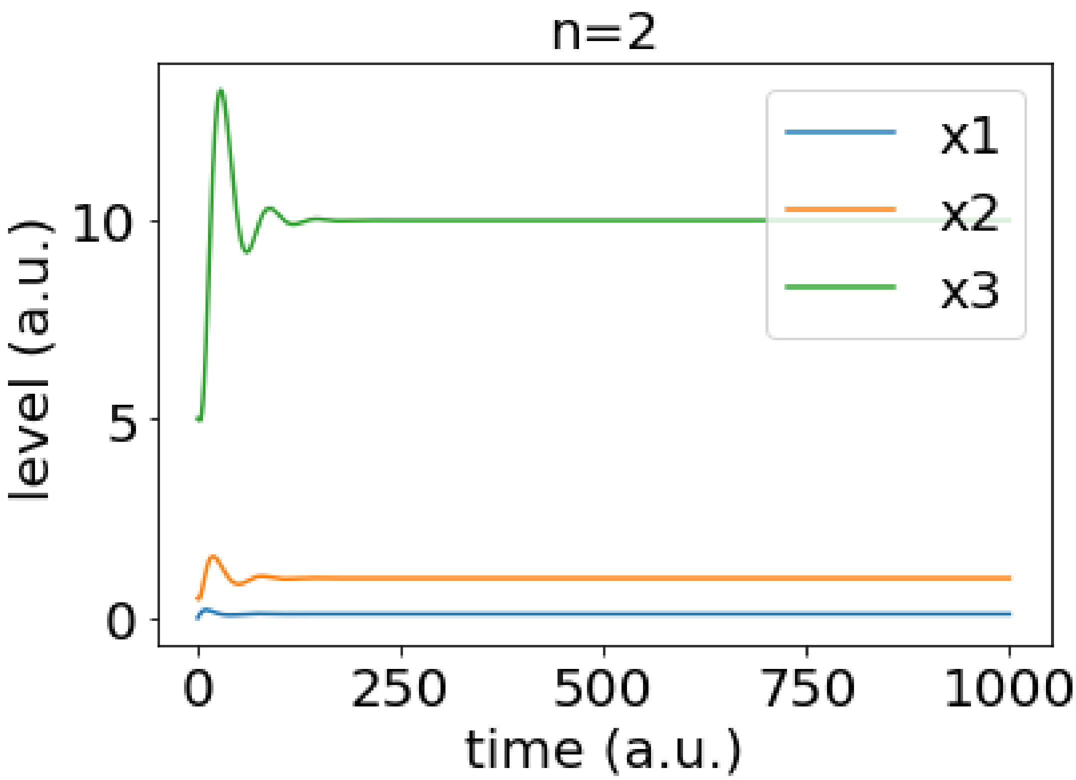
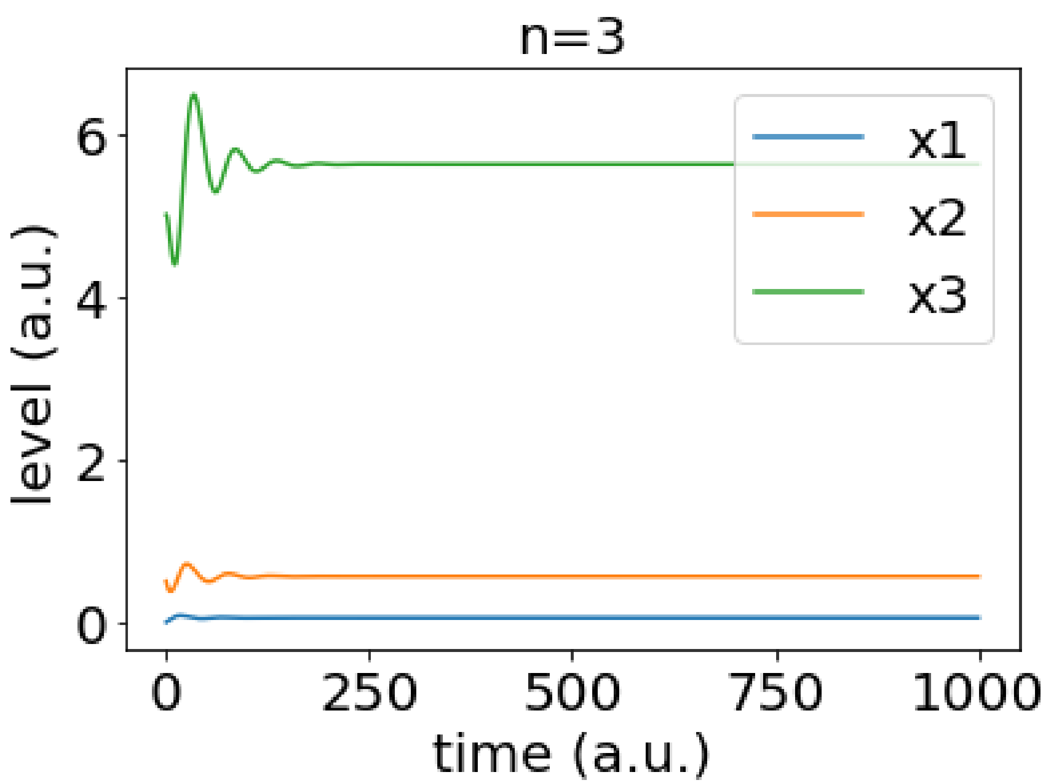
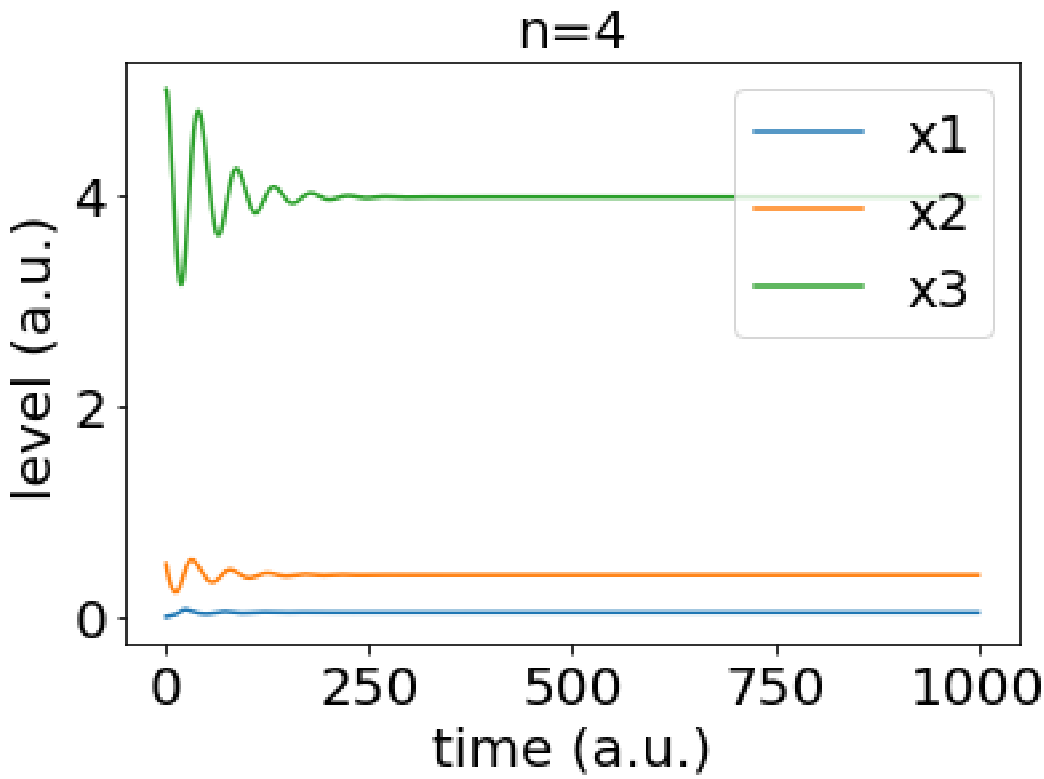
c) Now add a third variable x_3 that evolves according to: $\frac{dx_3}{dt} = x_2 - k_3\, x_3$, with k_3=0.1, and consider that x_1 is inhibited by x_3 instead of x_2.
Is there now a value of n for which the system shows sustained oscillations? (Make sure you integrate for sufficiently long time, it may help to plot the beginning and the final part of the simulation in different subplots.

In [5]:

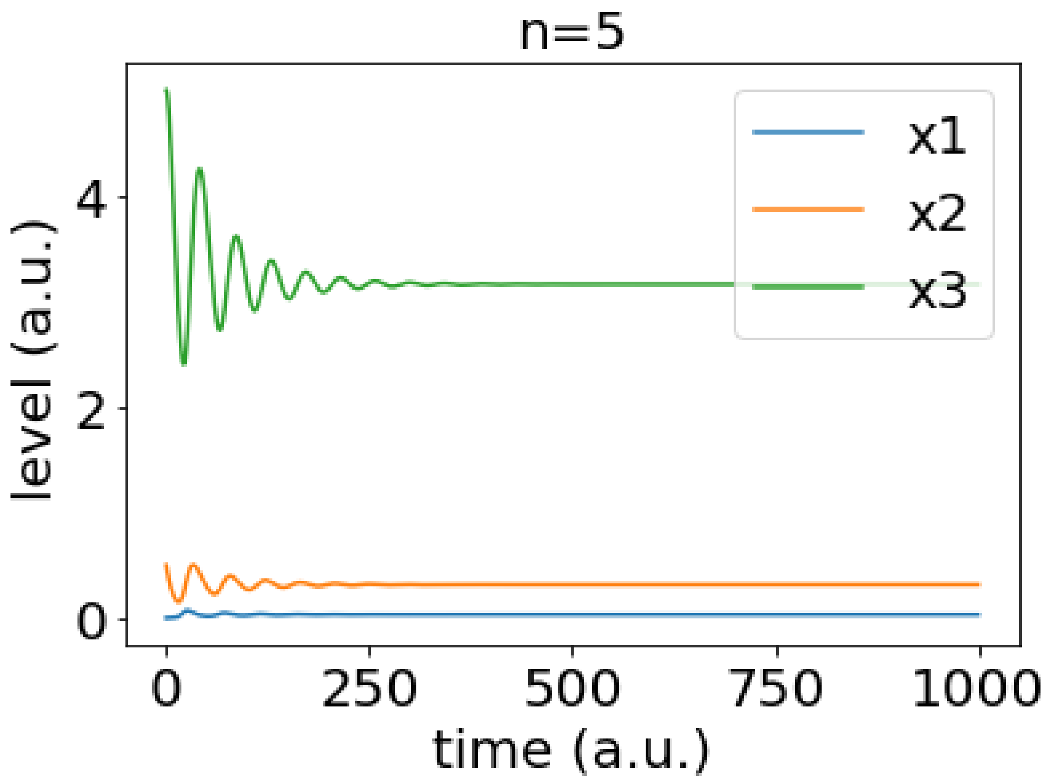


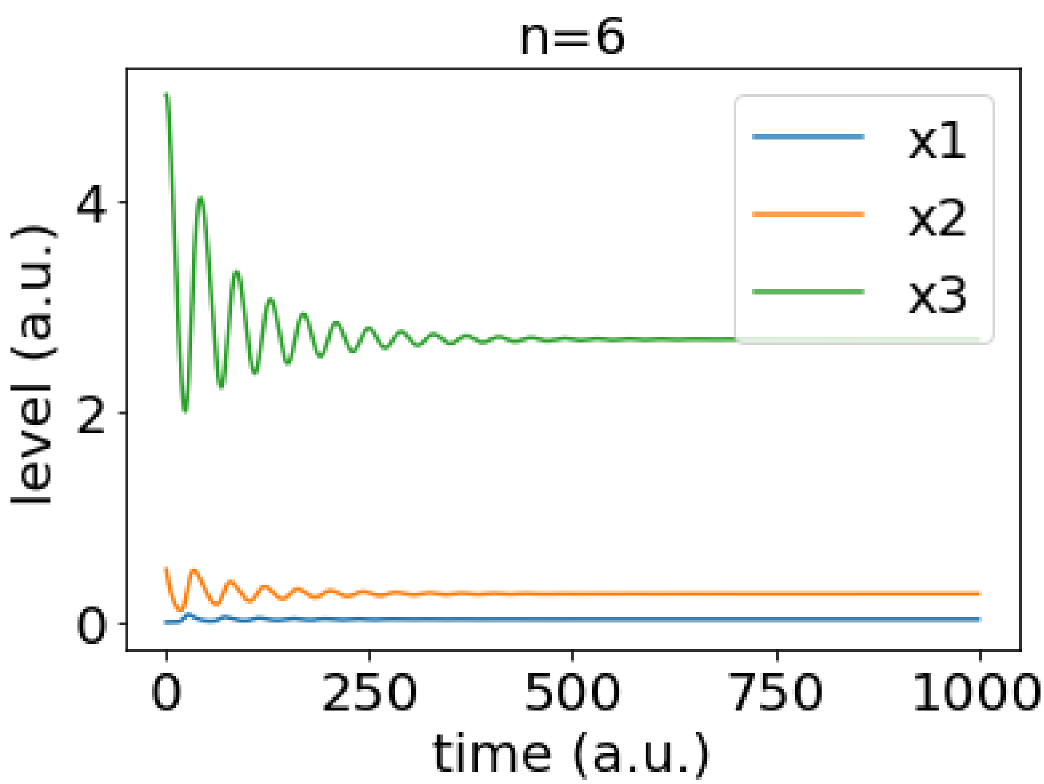

n=2
x1
x2
x3
10
5
0
0
250
500
750
1000
level (a.u.)
time (a.u.)

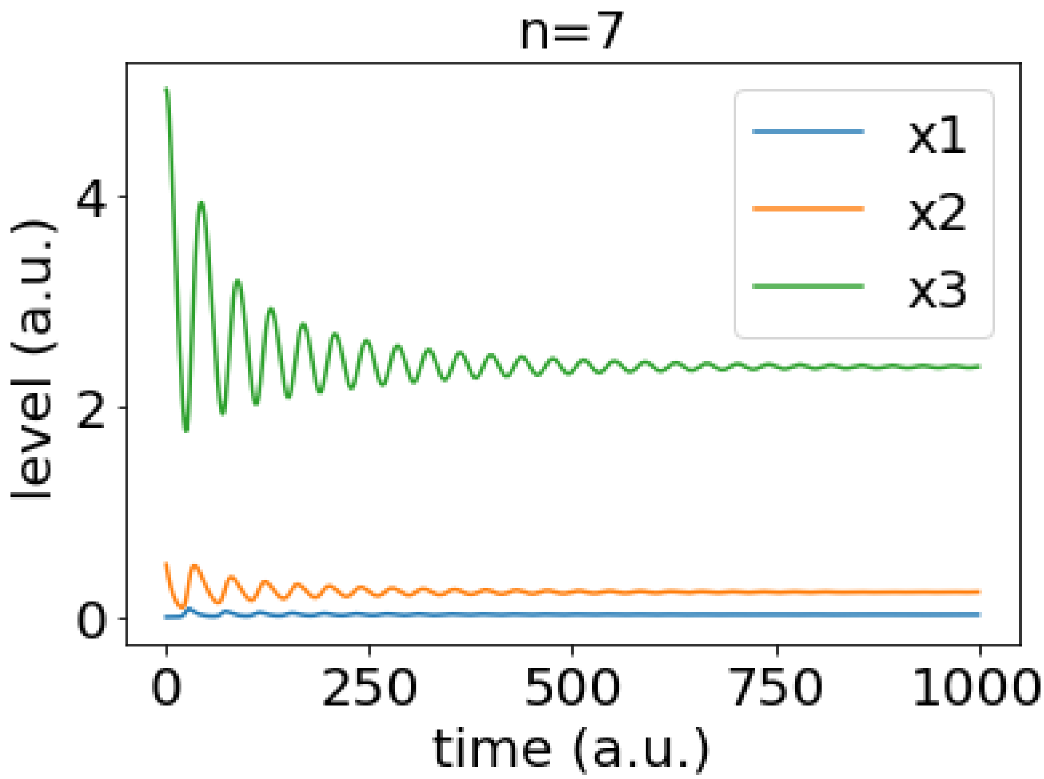

n=3
x1
x2
x3
6
4
2
0
0
250
500
750
1000
level (a.u.)
time (a.u.)

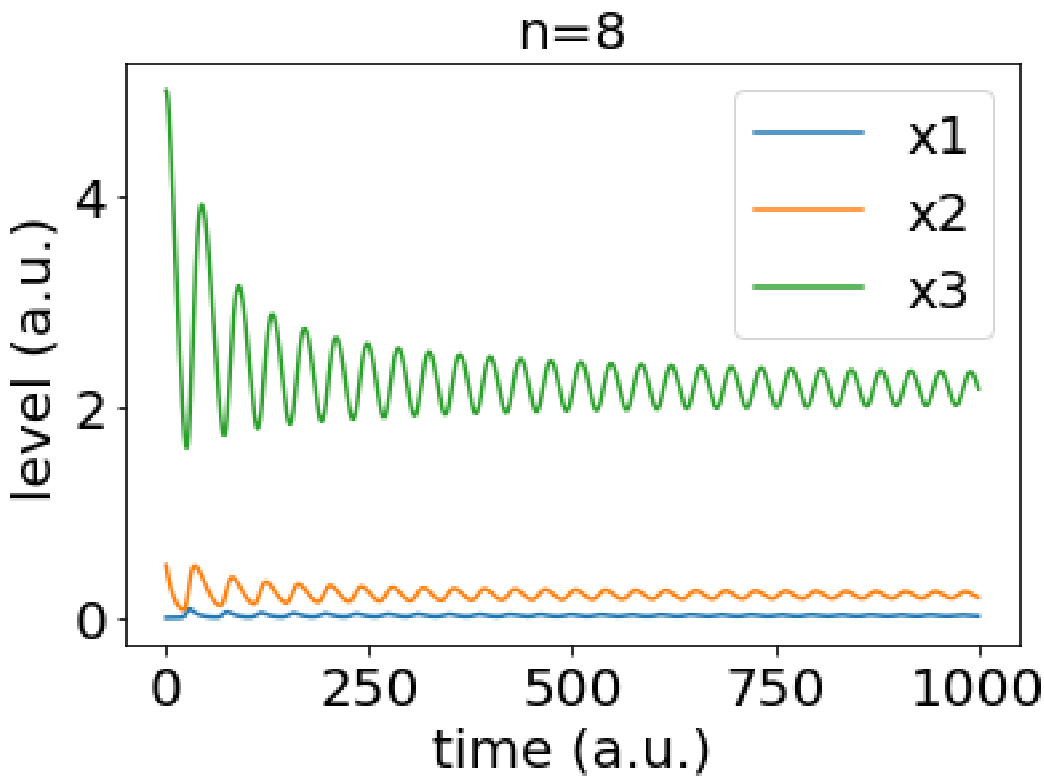


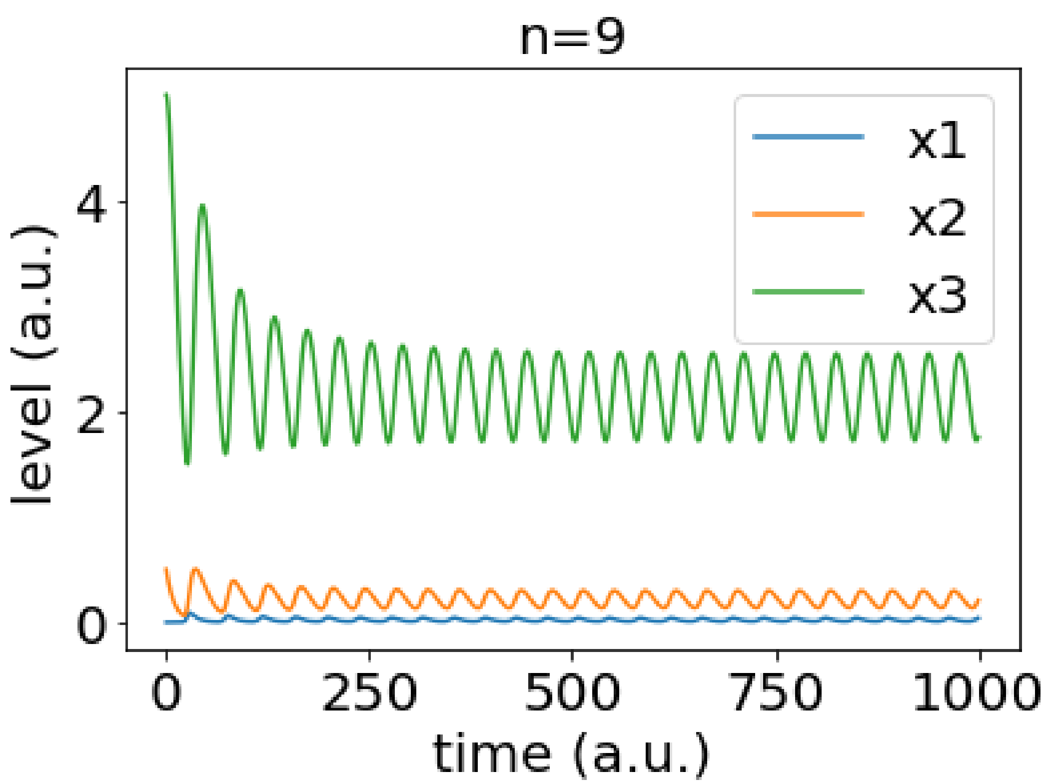
n=4
x1
x2
x3
level (a.u.)
time (a.u.)
0
2
4
0
250
500
750
1000

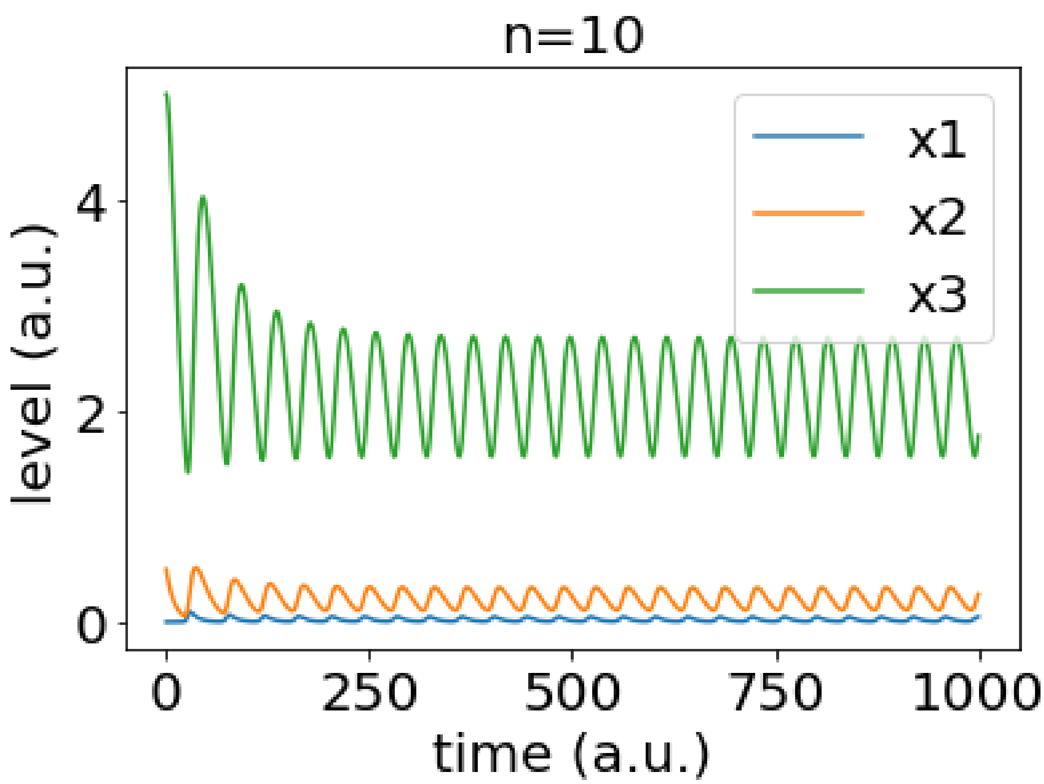

n=5
x1
x2
x3
level (a.u.)
0
2
4
0
250
500
750
1000
time (a.u.)


n=6
x1
x2
x3
level (a.u.)
0
2
4
0
250
500
750
1000
time (a.u.)


n=7
x1
x2
x3
level (a.u.)
0
2
4
0
250
500
750
1000
time (a.u.)


n=8
x1
x2
x3
level (a.u.)
time (a.u.)
0
2
4
250
500
750
1000


n=9
x1
x2
x3
level (a.u.)
time (a.u.)
0
2
4
250
500
750
1000



Comment your result here

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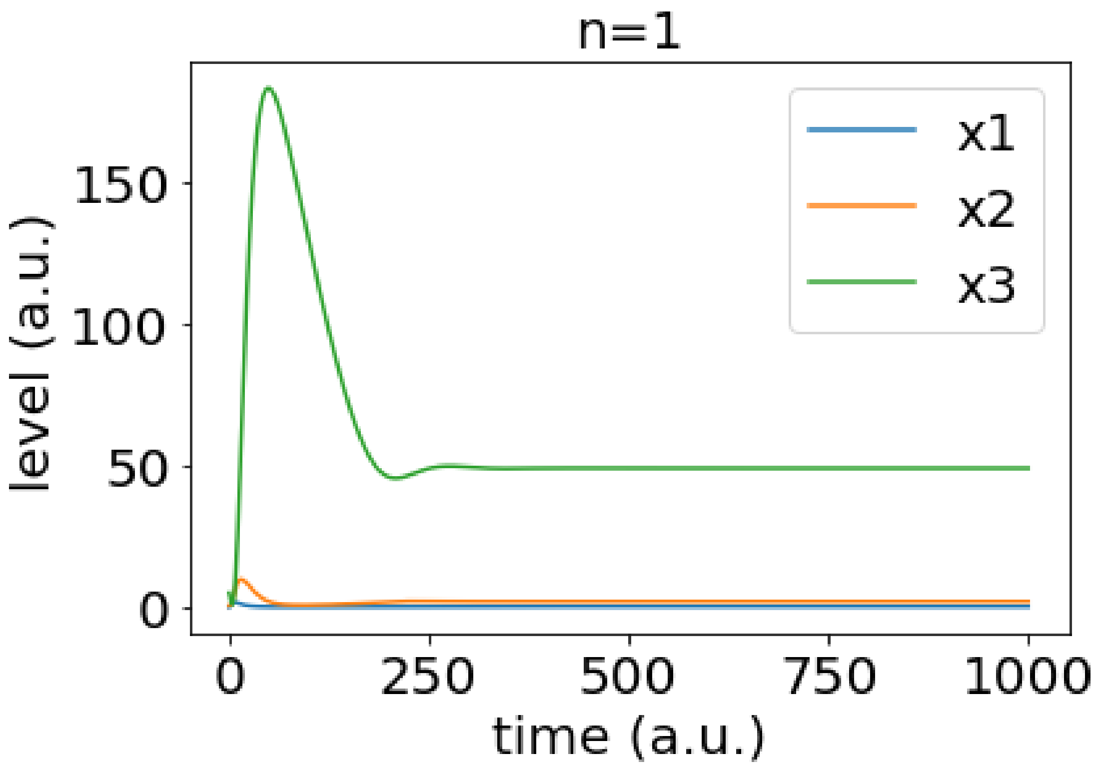
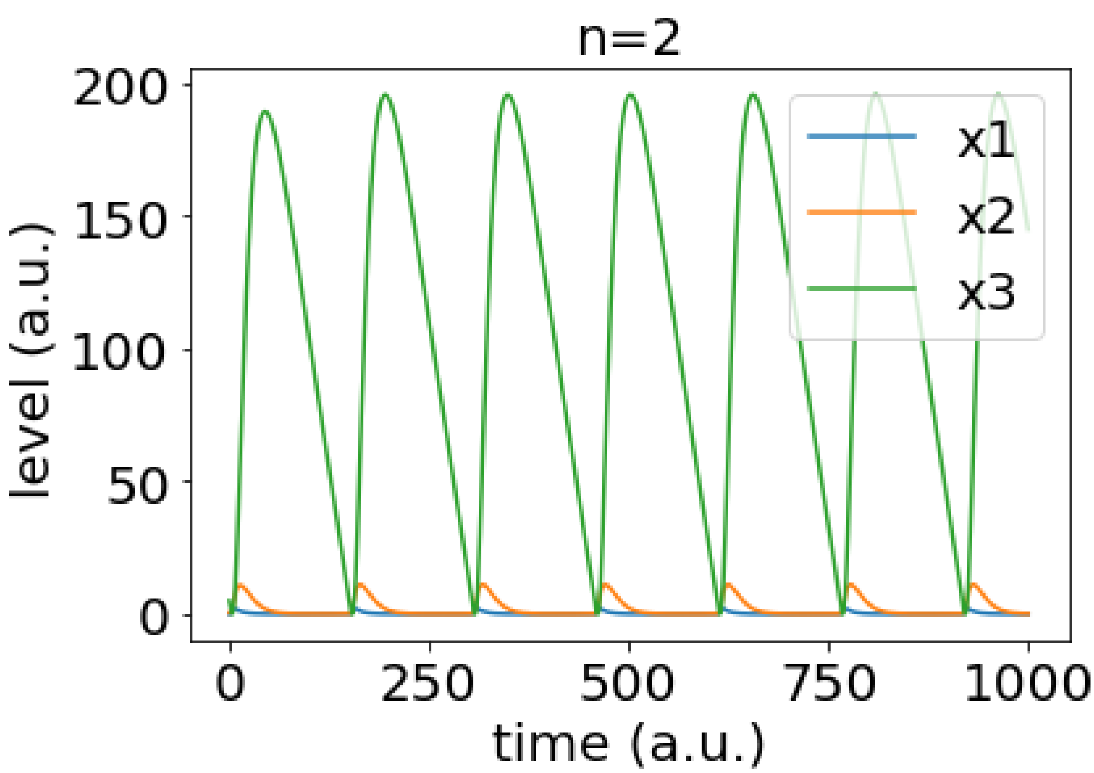
d) Add saturation to the degradation of x_3, with Michaelis constant K_d:

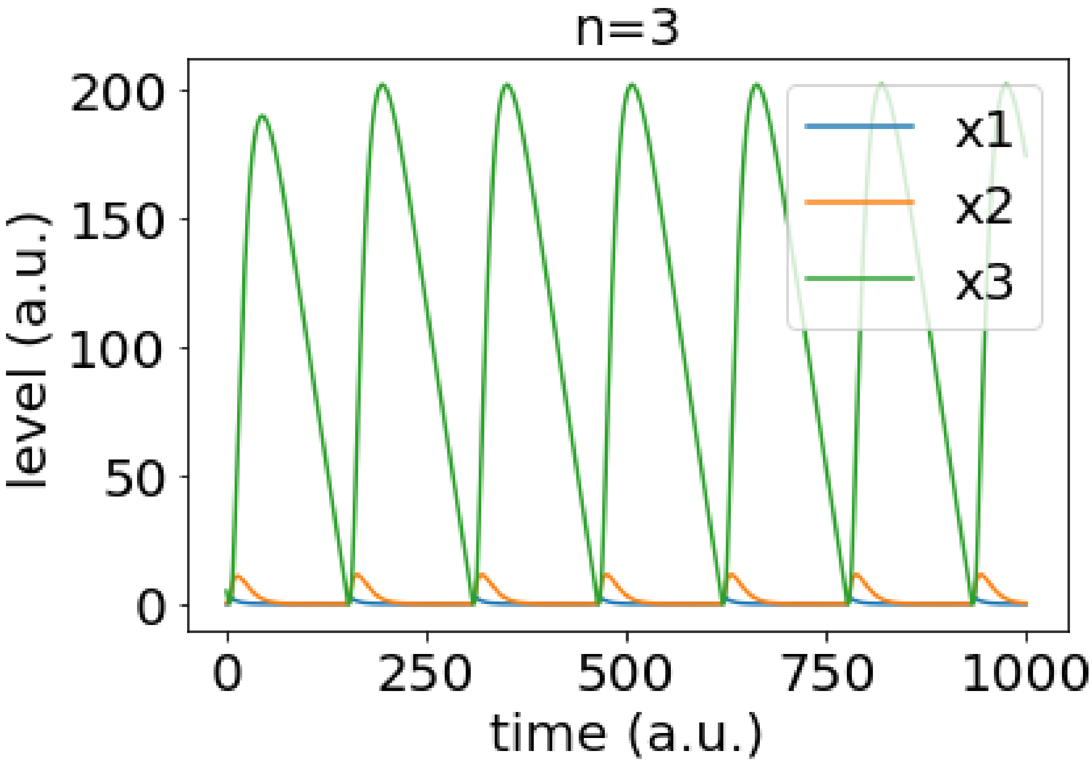
$$\frac{dx_3}{dt} = x_2 - \frac{k_3\, x_3}{K_d + x_3}$$

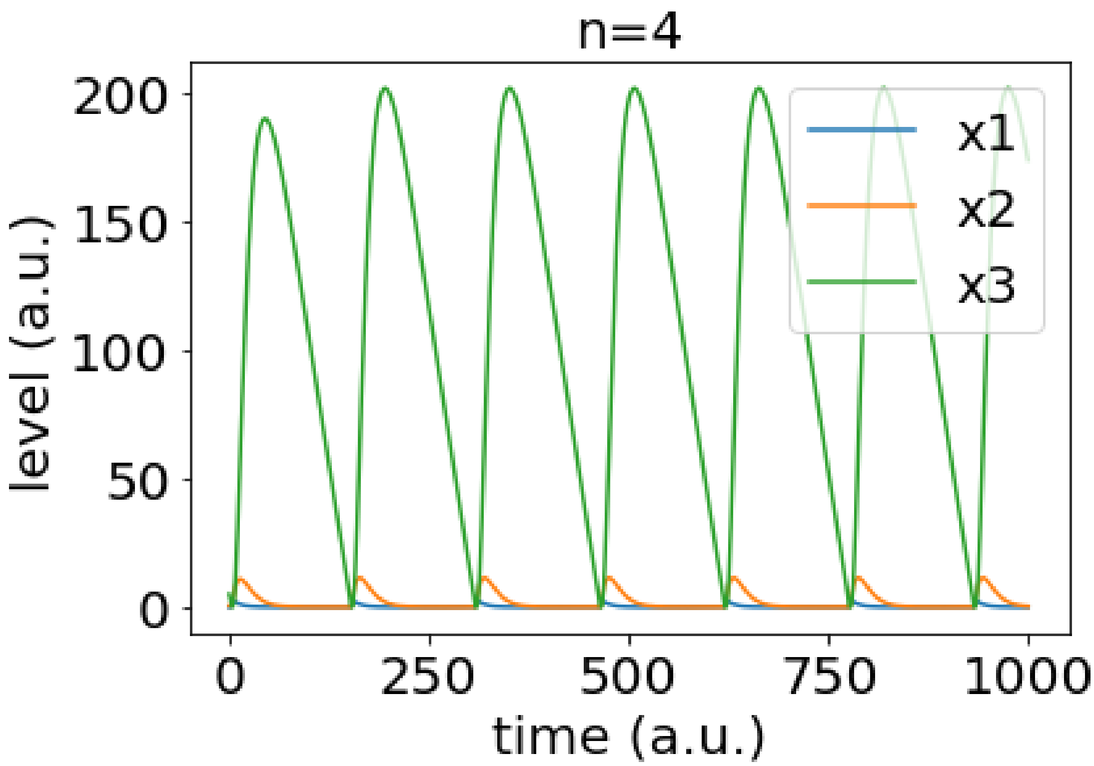
Consider that $k_1 = k_2 = 0.1$, $k_3 = 2$ and $K_d = 0.01$. What do you observe now as n increases?

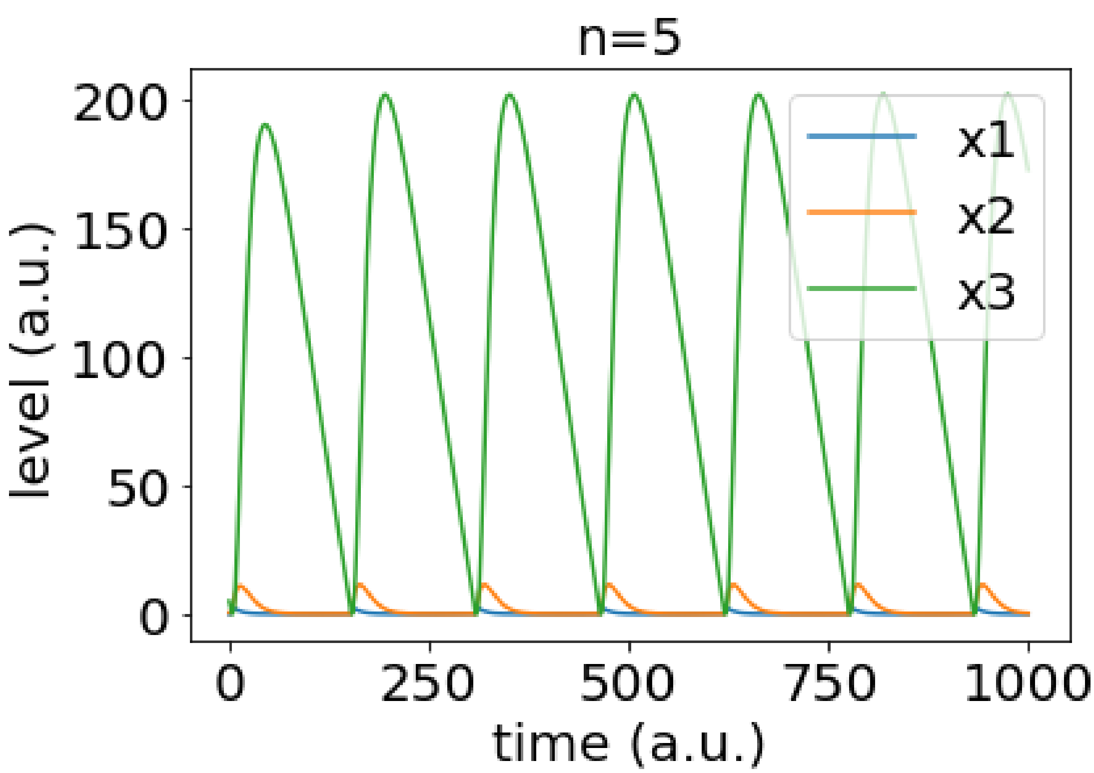
In [35]:


n=1
x1
x2
x3
level (a.u.)
150
100
50
0
250
500
750
1000
time (a.u.)


n=2
x1
x2
x3
level (a.u.)
200
150
100
50
0
250
500
750
1000
time (a.u.)


n=3
level (a.u.)
200
150
100
50
0
0
250
500
750
1000
time (a.u.)
x1
x2
x3


n=4
200
150
100
50
0
level (a.u.)
0
250
500
750
1000
time (a.u.)
x1
x2
x3


n=5
200
150
100
50
0
level (a.u.)
0
250
500
750
1000
time (a.u.)
x1
x2
x3

Comment your result here

B. **Oscillations from a single intermediate**

A negative feedback system can oscillate even with only one intermediate, if there are enough nonlinearities in the system. To see this, consider again the initial 2D system, but assume that there is an additional pathway of x_2 degradation that can saturate and whose activity is inhibited by high x_2 values. x_2 dynamics is now described by the following ODE:

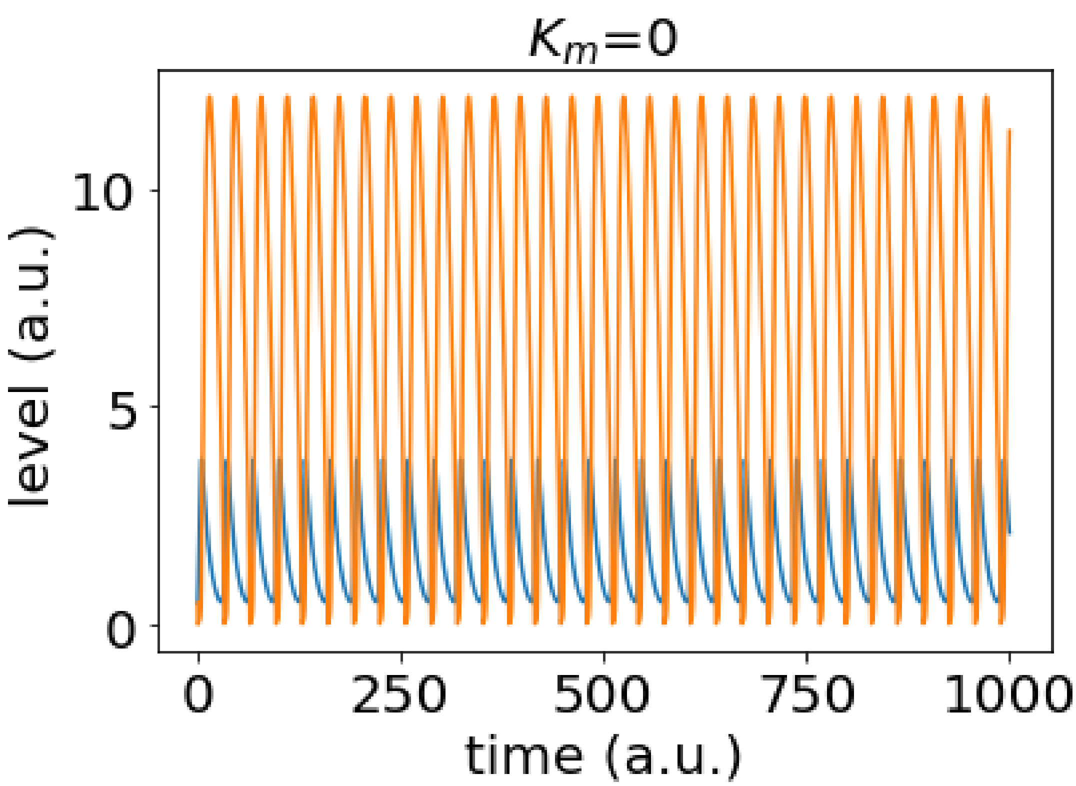
$$\frac{dx_2}{dt} = x_1 - k_2\,x_2 - \frac{k_3\,x_2}{K_m + x_2 + x_2^2}$$

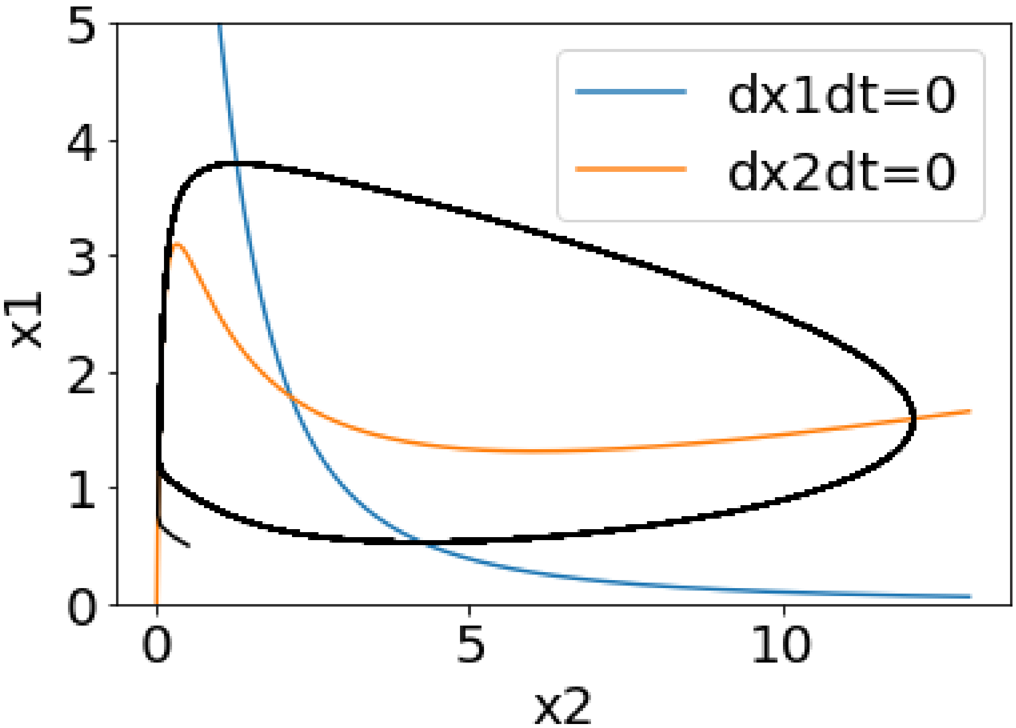
a) Plot the time evolution of the system for $k_1 = k_2 = 0.1$, $k_3 = 5$, $n = 2$, $K_m = 0.1$.

b) Increase K_m up to 10. What happens?

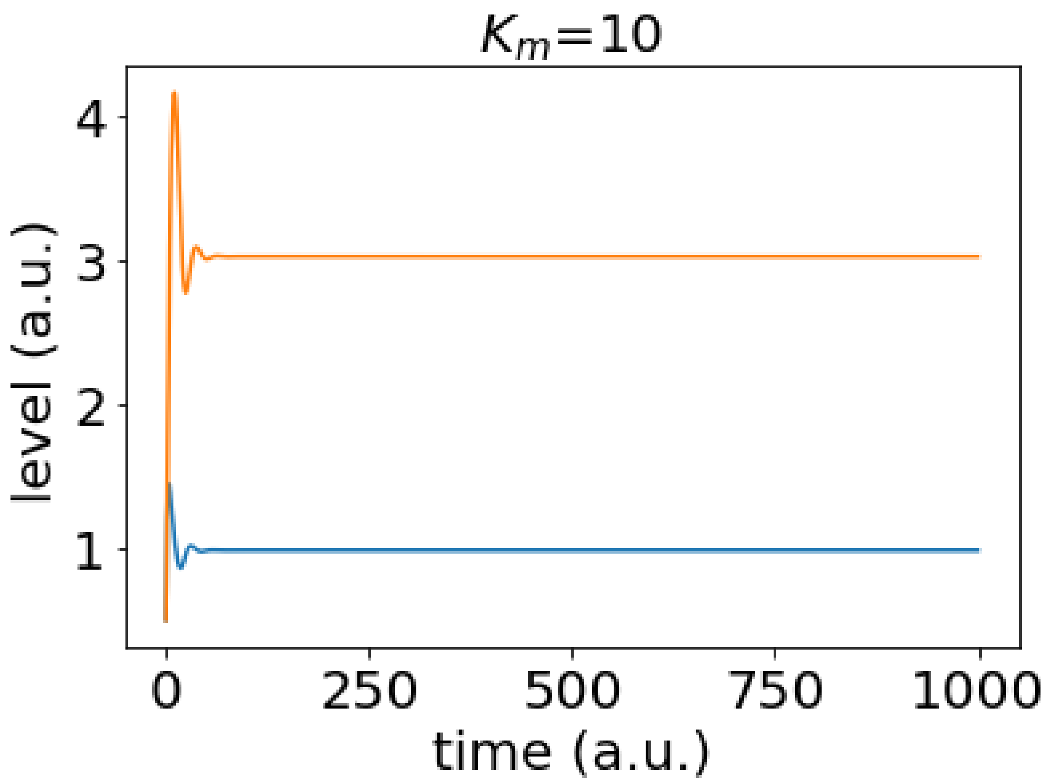
c) Plot the nullclines of the system and superimpose the corresponding trajectories. What do you observe?

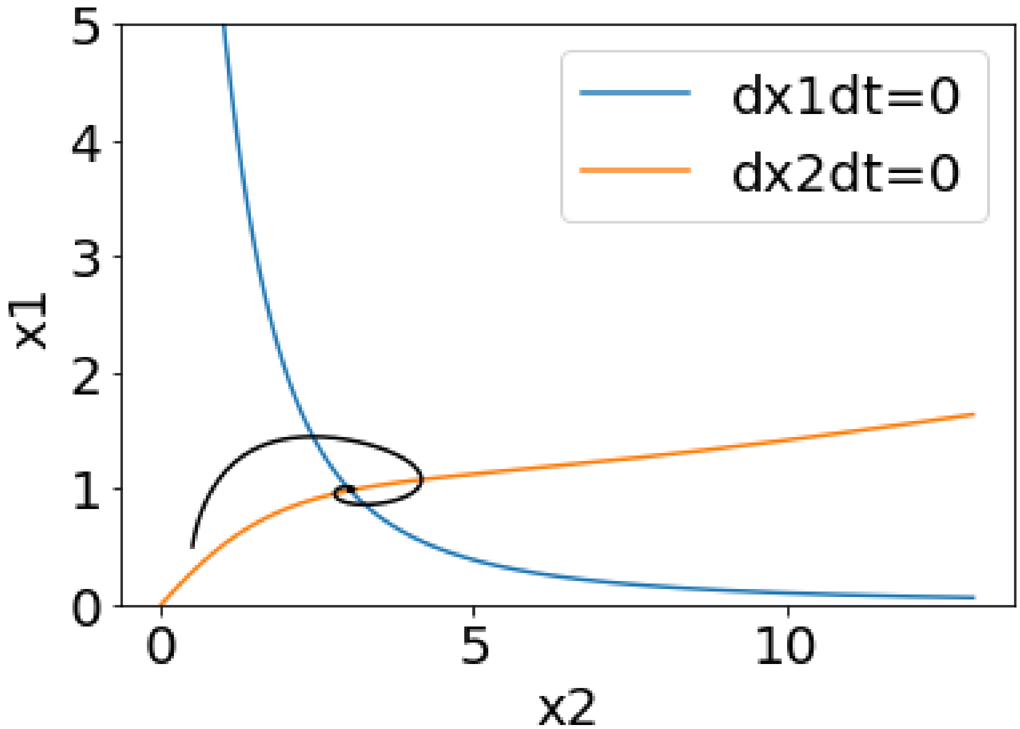
In [10]:





dx1dt=0
dx2dt=0
x1
x2
0
1
2
3
4
5
0
5
10


K_m=10
4
3
2
1
level (a.u.)
0
250
500
750
1000
time (a.u.)


dx1dt=0
dx2dt=0
5
4
3
2
1
0
x1
0
5
10
x2

Comment your result here

```
In [ ]:
```