practical_3_negative_feedback_solved

October 19, 2022

1 SYSTEMS AND NETWORK BIOLOGY - PRACTICAL 3

2 Negative feedback

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 objectives of this practical are: - to become familiar with numerical integration of dynamical systems using scipy's odeint function. - to become familiar with the basic models of gene regulation for basal expression and transcriptional repression. - to understand the differences between unregulated gene expression and negative autoregulation. - to explore the effects of saturation in the controller of an integral feedback control system

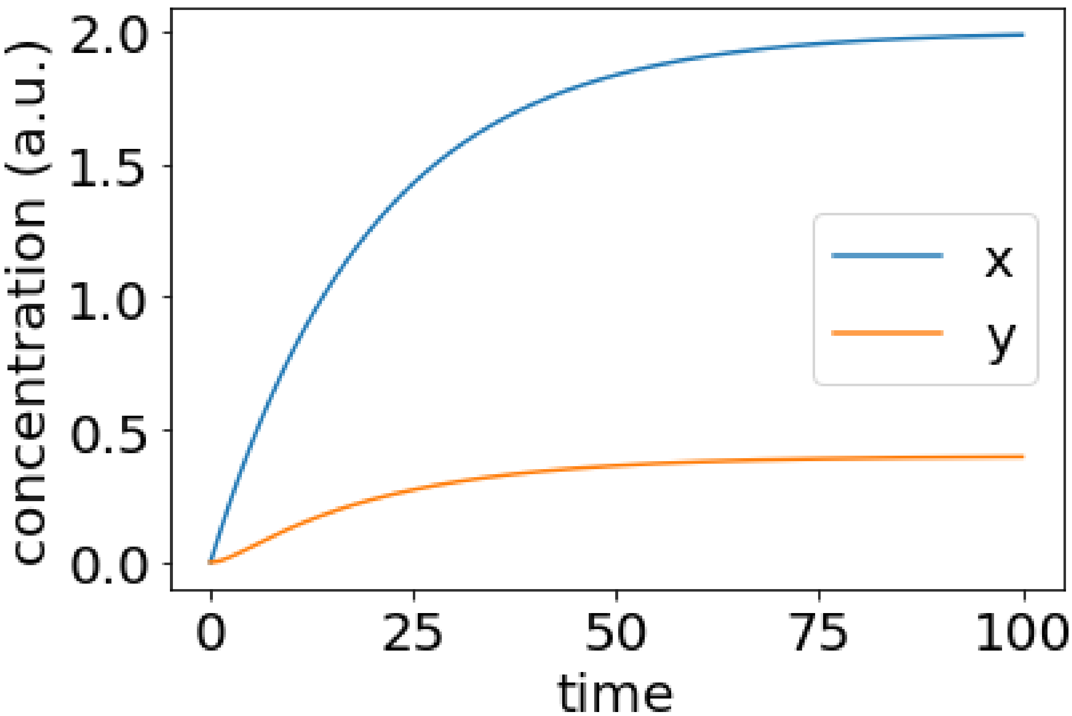
[1]:
```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt
%matplotlib inline
```

2.1 Numerical integration

We will use scipy's odeint function to numerically integrate ODEs. Here is an example:

[2]:
```
def test(xy,t):
    x,y=xy
    dx=alpha1-delta1*x
    dy=alpha2*x-delta2*y
    return [dx,dy]
```

```
alpha1 = 0.1
alpha2 = 0.1
delta1 = 0.05
delta2 = 0.5
tvec = np.arange(0,100,0.01)
x0 = [0,0]
y = odeint(test,x0,tvec)
plt.figure()
plt.rc('font', size=20)
plt.plot(tvec,y[:,0],label='x')
plt.plot(tvec,y[:,1],label='y')
plt.legend()
plt.xlabel('time')
plt.ylabel('concentration (a.u.)')
plt.show()
```



3 Constitutive expression

The following equation can be used to model the constitutive expression of a gene:

$$\frac{dP}{dt} = \alpha - \delta P$$

1. Consider $\alpha = 10$ and $\delta = 1$.
    1. What is the analytic expression for the steady state of the system?
    2. Plot the time evolution of the system starting from $P_0 = 0$ using scipy's odeint function.
    3. Does the final value of the trajectory in b) coincide with the analytical steady state?
    4. At what time does P reach half the steady state value? Plot a vertical line at that point.

** Write your answer here **

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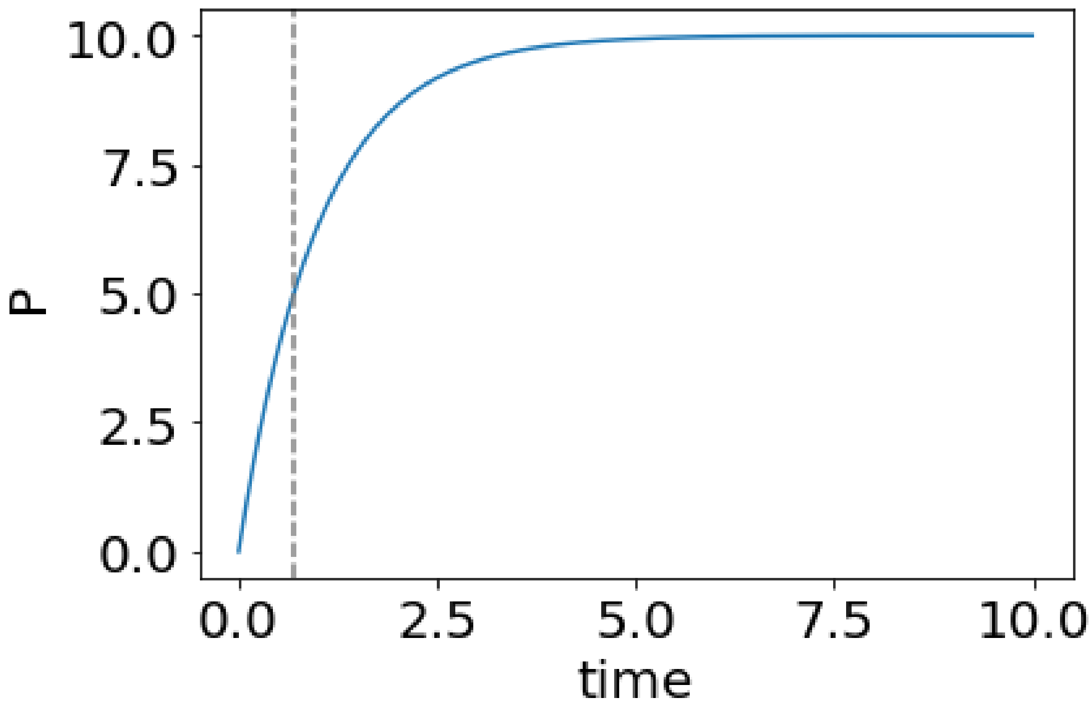
[3]:



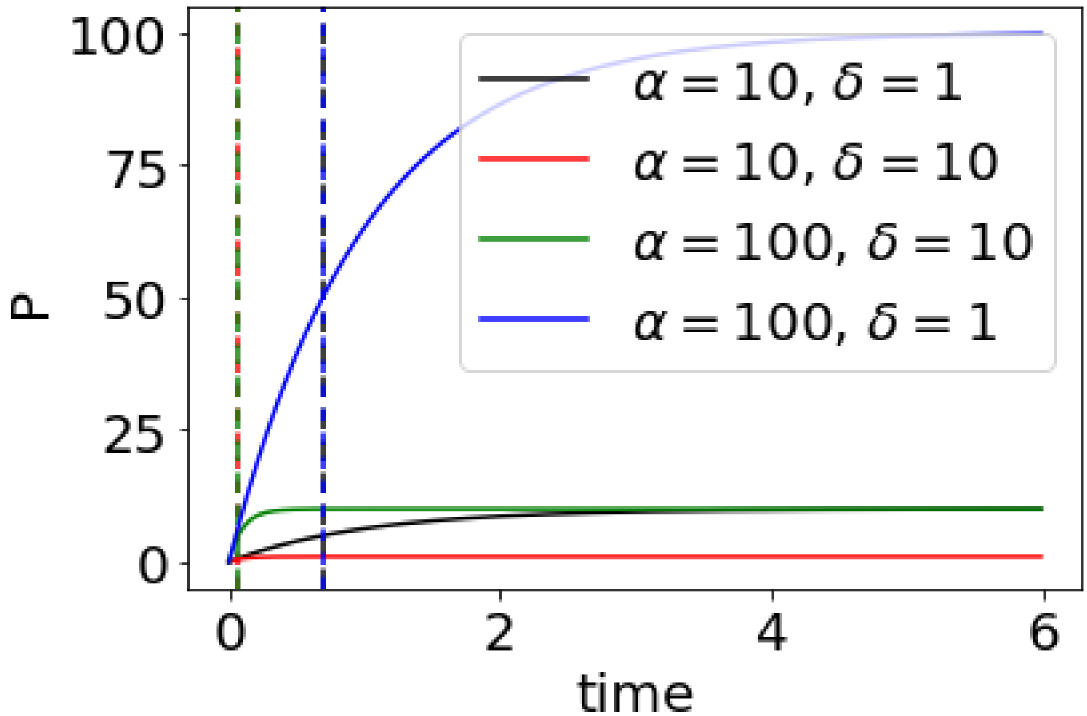

```
The final value of the protein concentration is 9.999541435840129
The time at which the protein concentration reaches half its steady state is 0.7
```

2. What happens for the following parameter sets, in comparison with the previous one? Plot the four of them in the same plot and compare them.
    1. alpha=10, delta=10
    2. alpha=100, delta=10
    3. alpha=100, delta=1

---

[4]:

```
For alpha=10, delta=1, the time to reach half of the steady state concentration
is 0.7
For alpha=10, delta=10, the time to reach half of the steady state concentration
is 0.07
For alpha=100, delta=10, the time to reach half of the steady state
concentration is 0.07
For alpha=100, delta=1, the time to reach half of the steady state concentration
is 0.7
```



** Write your answer here **

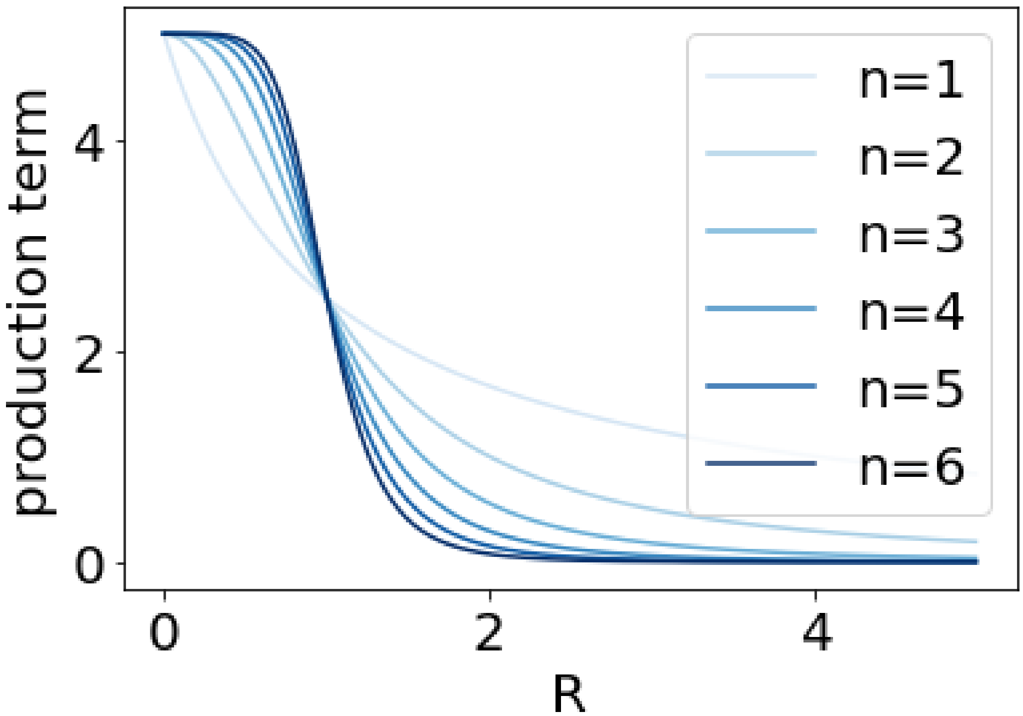
4 Negative feedback

Now consider the following negative autoregulation system:

$$\frac{dR}{dt} = \frac{\alpha}{1 + \left(\frac{R}{K}\right)^n} - \delta R$$

1. Plot the production term for alpha=5, K=1, and n ranging from 1 to 6, for a range of R values from 0 to 5. What is the effect of increasing n?

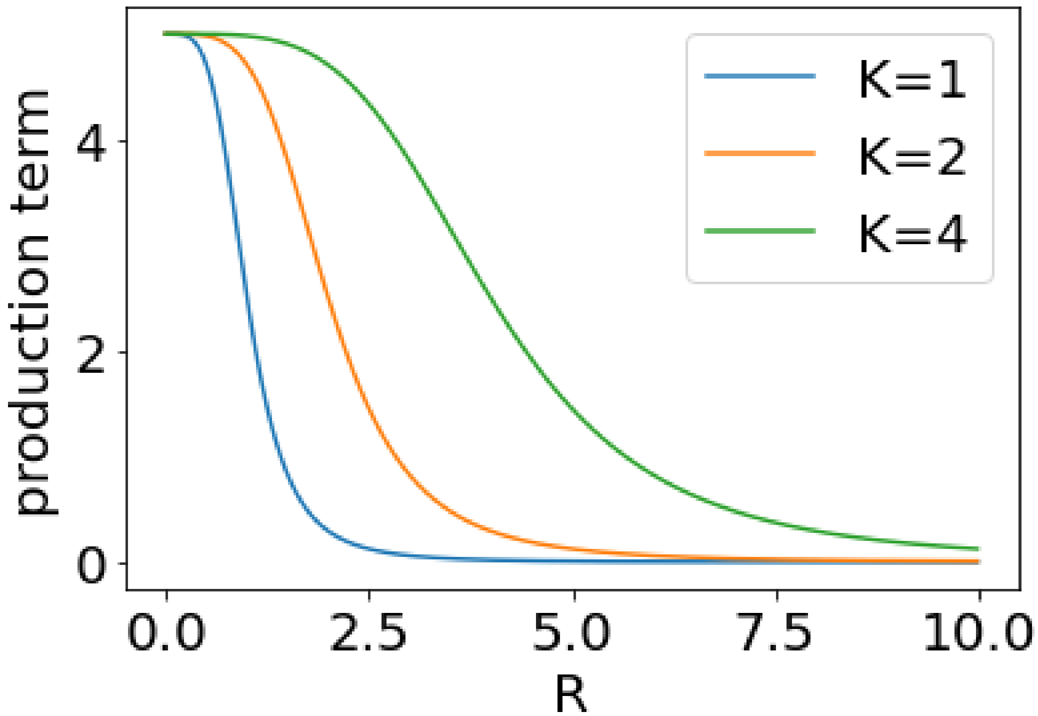
[5]:



** Write your answer here **

2. Now fix n to 4, and plot the production term for K = 1, 2, and 4. What is the effect?

[6]:



** Write your answer here **

3. If you wanted to build a repression system that is highly repressed at low values of repressor, how would you choose K and n? (in terms of low/high values)

** Write your answer here **

5 Study the response timescale of the system:

1. We will now compare how quickly the two models introduce above generate their product. To that end:
   1. Integrate the negative feedback model for $n = 4$, $K = 1$, $\alpha = 10$ and $\delta = 1$, starting from $R = 0$ and compute the time to reach half the steady state concentration.
   2. Integrate the constitutive expression model with $\alpha = 1.5$ and $\delta = 1$ starting from $R = 0$ and compute the time to reach half the steady state concentration.
   3. Compare the results of B) and C).

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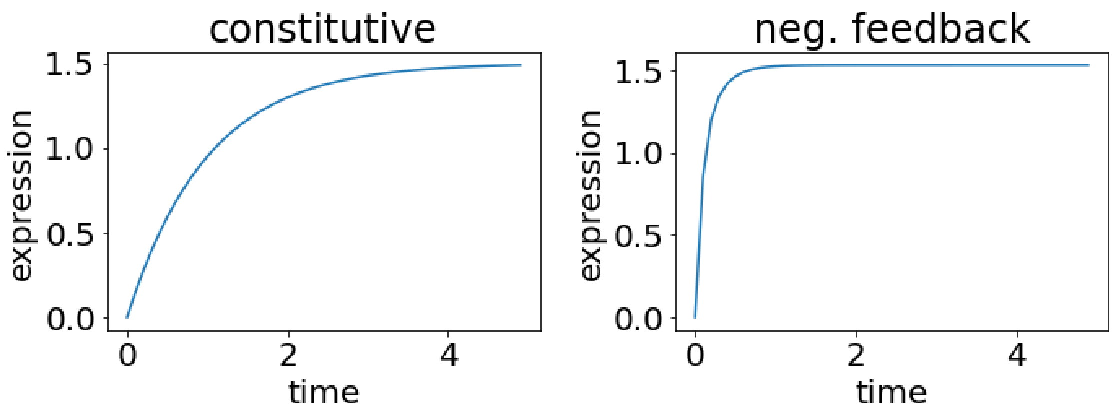
[7]:
```
Time to reach half the steady state for the constitutive model 0.7
Time to reach half the steady state for the neg. feedback model 0.1
```

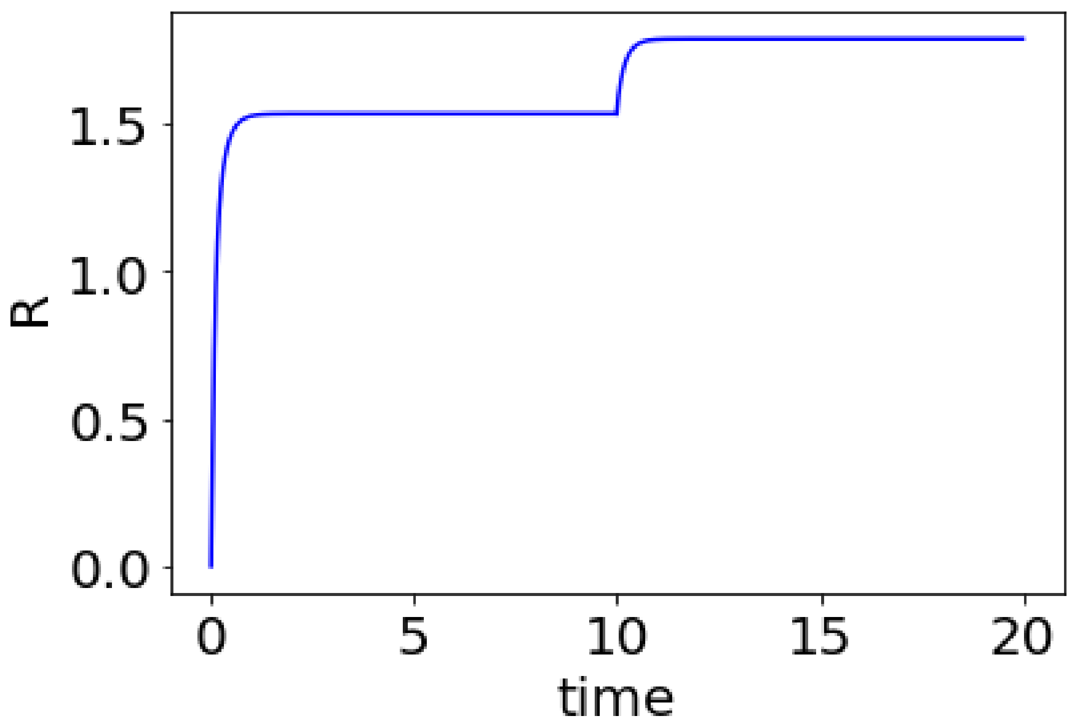


** Write your answer here **

6 Adaptation to perturbations

Integrate the negative feedback model for n=4, K=1, $\alpha = 10$ and $\delta = 1$, starting from R=0, for 10 time units. At that point, double the value of α and integrate for another 10 time units. Does the system return to the same steady state as before?

[8] :



** Write your answer here **

Do the same for the constitutive expression model.

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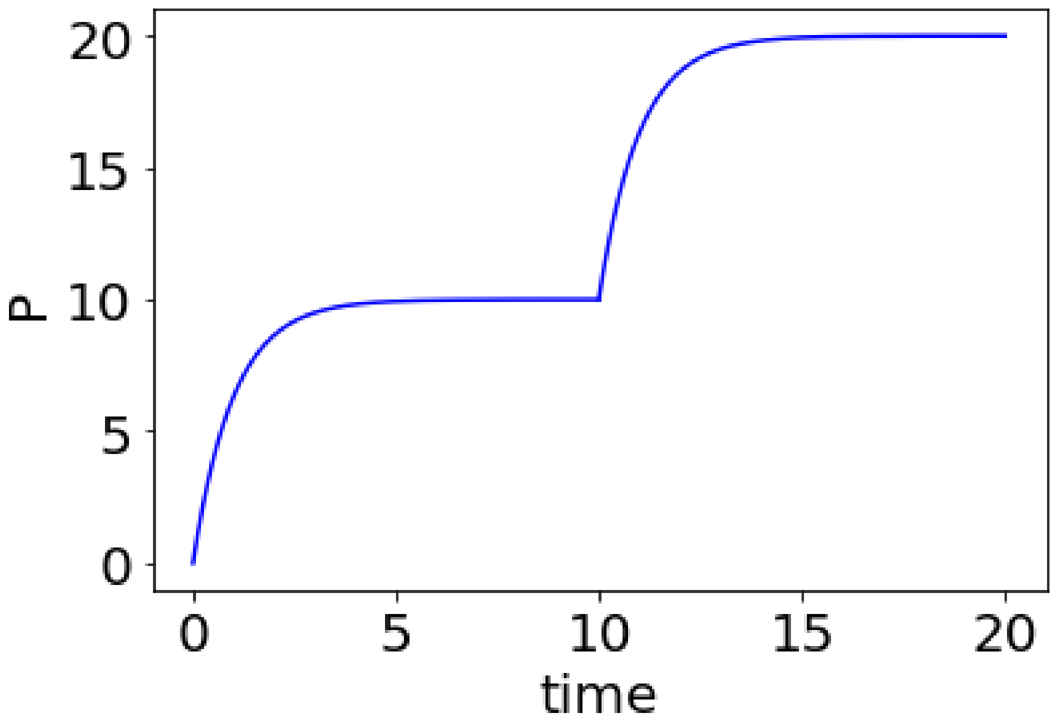
[9]:



** Write your answer here **

Interpret the results above in terms of the difference in robustness between the two models.

** Write your answer here **