aDVANCES IN SYSTEMS AND SYNTHETIC BIOLOGY 2018

Institute of Quantitative & Theoretical Biology

Introduction to Mathematical Modelling of Biological Systems

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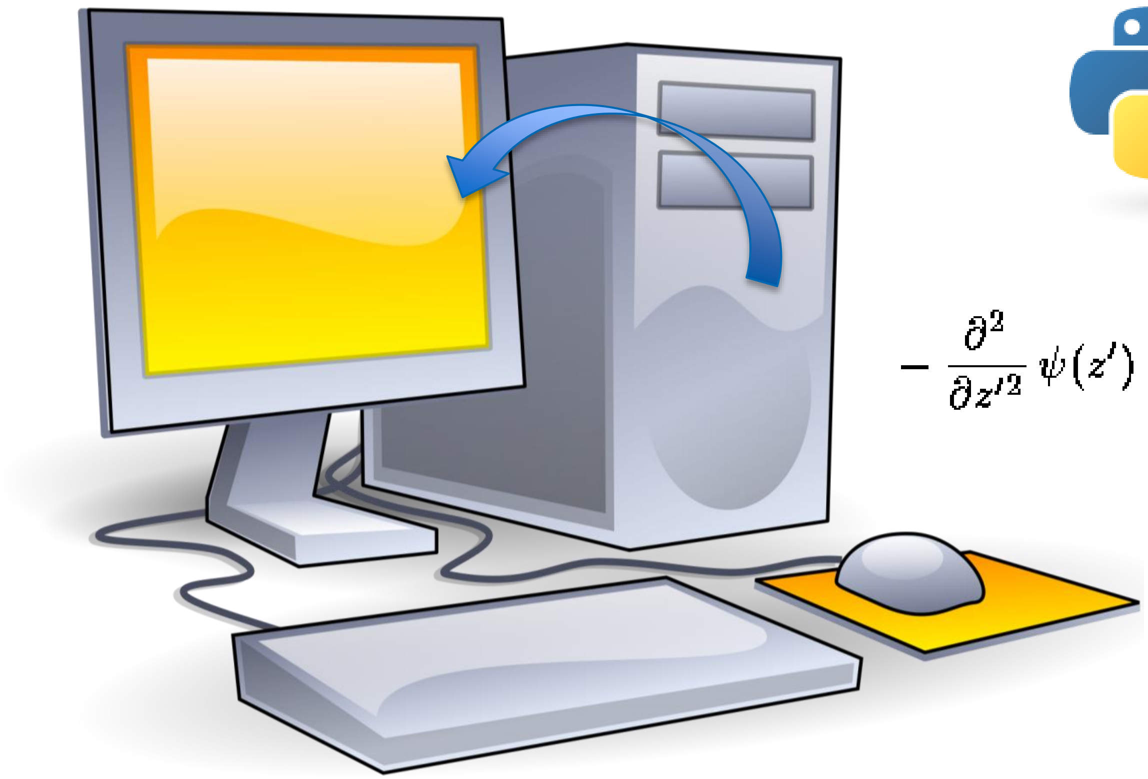
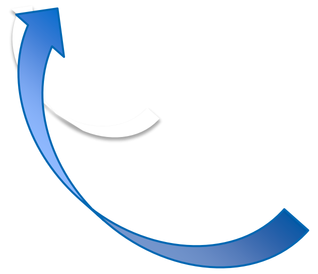
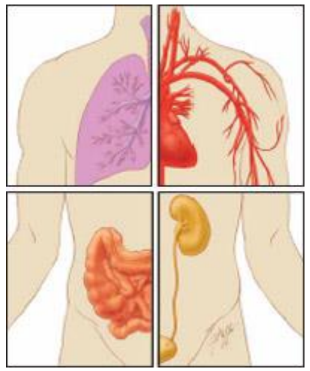


python™

$$-\frac{\partial^2}{\partial z'^2}\psi(z') + z'\,\psi(z') = E'\,\psi(z')$$





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SOLVING DIFFERENTIAL EQUATIONS

You can simulate simple dynamic systems

First differential equation

Simple Logistic Growth Equation

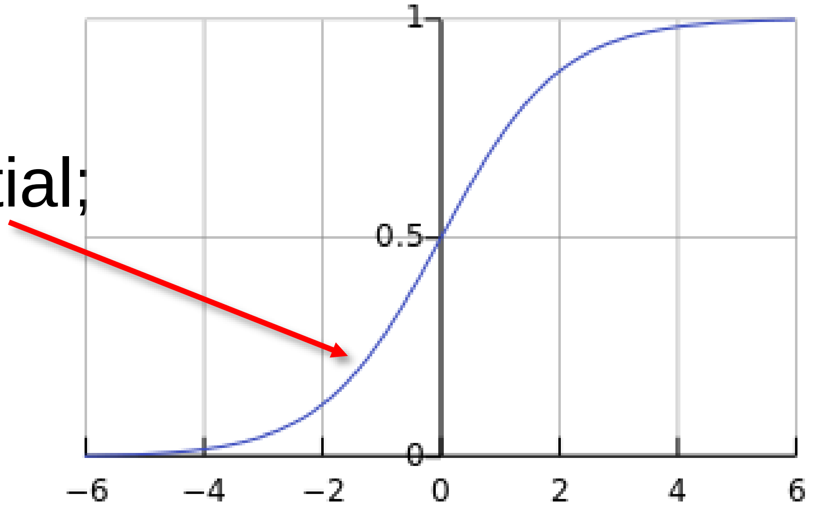
- Letting N represent population size and t represent time, this model is formalized by the differential equation:

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{k}\right)$$

N represents population size; r defines the growth rate; k is carrying capacity

- The function is a sigmoid curve.

The initial stage of growth is approximately exponential;
as saturation begins, the growth slows,
and at maturity, growth stops.



First differential equation

Tasks for today

- Goal: Your goal is to write two Python scripts to solve two one-dimensional problems: the logistic equation and the logistic equation with punishment for low population.

How to start:

- Mathematical description
- Initial conditions
- Parameter set
- Necessary tools for integration and plotting

Before we start

Import

```
import numpy as np
import scipy
import matplotlib.pyplot as plt
import pylab
```

We will be using functions that are not built in as a standard one. Therefore we need to import specific packages.

NumPy is a Python extension module that provides efficient operation on arrays.

SciPy is a set of open source (BSD licensed) scientific and numerical tools for Python.

Matplotlib is a python 2D plotting library which produces publication quality figures.

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GRAPHICAL PACKAGE

You can display the results graphically

Using graphical package

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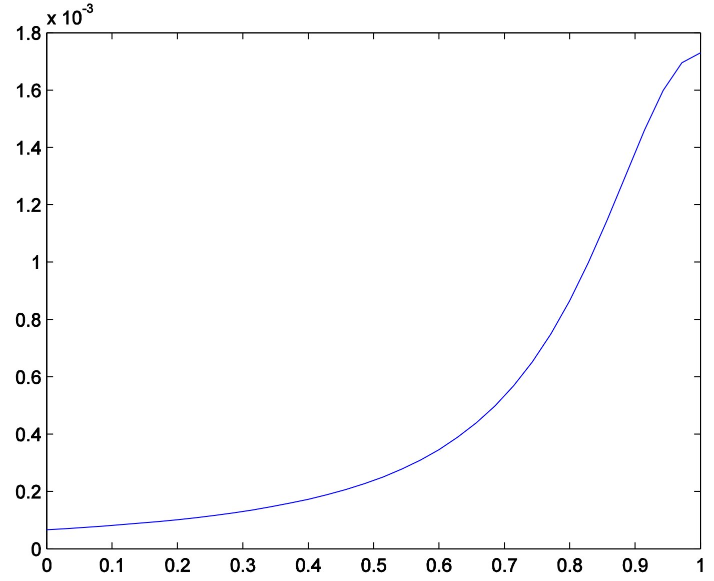
How to represent my data

```
~~from pylab import *~~
```



Create a figure.

Create your data. We need X and Y values.

```
X = [1,2,3]
X = range()
```

```
import numpy as np
X = np.linspace()
X = np.arange()
```

Use the pylab package to plot your results.

```
import pylab as pl
pl.plot()
```

Show results of screen

```
pl.show()
```

Using graphical package

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How to represent my data

1. Plot function f(x) = x.
2. Plot sine and cosine functions on the same plot.
3. Change the colours of the plot to red and blue.
4. Add legend, title and axes names.
5. Try to plot two plots next to each other.

scipy-lectures.github.io/intro/matplotlib/matplotlib.html

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SOLVING DIFFERENTIAL EQUATIONS

You can simulate simple dynamic systems

First differential equation

Simple Logistic Growth Equation

```
def logistic(y, t0, r, K):
        """ returns population  growth """
        dY = r * y[0] * (1 - y[0]/ float(K))
        return
```

Note that t0 is not used by the function. Why do we supply it as an argument?

First differential equation

Simple Logistic Growth Equation

```
def logistic(y, t0, r, K):
        """ returns population  growth """
        dY = r * y[0] * (1 – y[0]/ float(K))
        return
```

Note that t0 is not used by the function. Why do we supply it as an argument?

Provide values of r and K and starting population size.

```
params = (0.3, 10)
Y = [1]
```

What is the type of the params value?

First differential equation

Simple Logistic Growth Equation: integration

```
growth = scipy.integrate.odeint(func, y0, t, args=(), …)
```

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Simple Logistic Growth Equation: integration

```
growth = scipy.integrate.odeint(func, y0, t, args=(), …)
```

```
t = range(0,1000)
growth = scipy.integrate.odeint(logistic, y, t, args=params)

plt.plot(t, growth)
plt.show()
```

Second differential equation

Modified Verhulst Equation

```
def modifiedVerhulst(N, t0, c=5., g =3, d = 1.,r= 2., k = 40.):
        """ returns the population growth rate
        modified Verhulst equation with the factor
        governing population behaviour at small sizes    """
        dY = r * N * (g/r) * N/(N+c) – d/r – N/k

        return
```

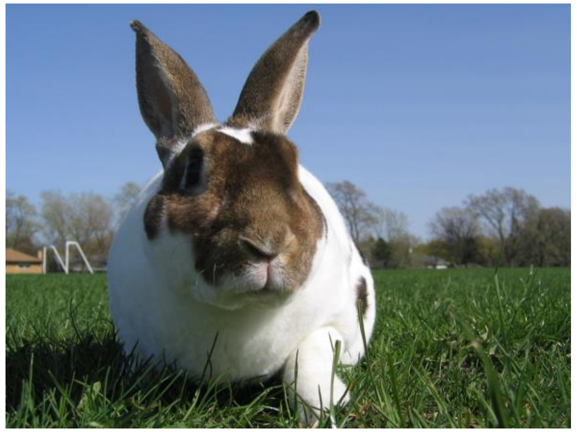
Tasks for today:

- Integrate the model over the time of 1 year, how the population evolves?
- Find the stationary states of the model. Are they stable?
- Plot the bifurcation diagram for the new bifurcation parameter c.

Coupled differential equations

Lotka-Voltera Model

- Lets consider population of two species that interact.
- One is a predator and second a prey.
- How to describe their dependent dynamics?



Coupled differential equations

Lotka-Voltera Model

- b is the natural growing rate of rabbits, when there are no wolfs
- d is the natural dying rate of rabbits, due to predation
- c is the natural dying rate of wolfs, when there are no rabbits
- f is the factor describing how many caught rabbits let create a new wolf

Coupled differential equations

Lotka-Voltera Model

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$$\text{rabbits} \longrightarrow \texttt{dr/dt = b*r - d*r*w}$$

$$\text{wolfs} \longrightarrow \texttt{dw/dt = -c*r + f*b*w*r}$$

Coupled differential equations

Task

- Solve the Lotka-Volterra model (also known as the predator-prey) and create plots of the evolution of the population for following cases:
  - a. r = d = c = f = 1 for variety of initial conditions
  - b. r = 1, d = 0.1, c = 1.5, f = 0.75 and t = 1000, for R = 10 and W = 5
- What does it mean that the population size is stable over the time?
- Play with parameters and initial conditions so different species will survive.

Coupled differential equations

Lotka-Voltera Model

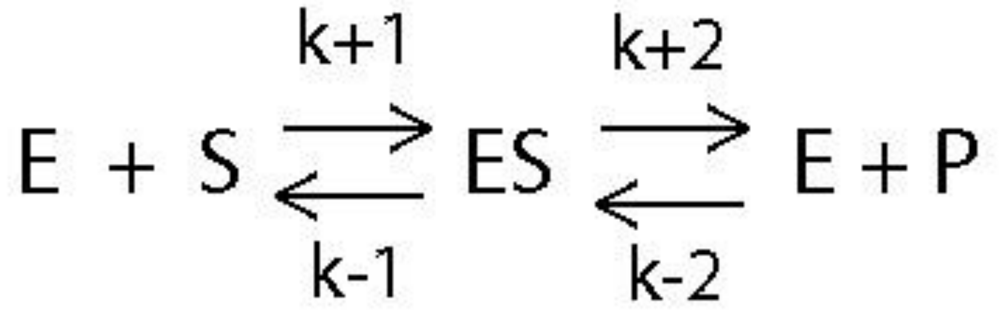
Use X = [r, w] to describe the state of both populations

```
from numpy import *
import pylab as p

# Set parameters
a = 1.
b = 0.1
c = 1.5
d = 0.75

def dX_dt(X, t=0):
    """ Return the growth rate
    of fox and rabbit populations. """
    return array([ a*X[0] - b*X[0]*X[1] ,

                  -c*X[1] + d*b*X[0]*X[1] ])
```

Modelling biochemical reactions

Simple biochemical network

- We will use differential-equation-based models for biological regulatory networks to ulitmately simulate the change in concentrations over the time of substrate (S), enzyme €, substrate-enzyme complex (ES) and the final product (P) in the following reaction:



FINAL PROJECT

You can do it! Prove it with your final project

Final Project

Your task

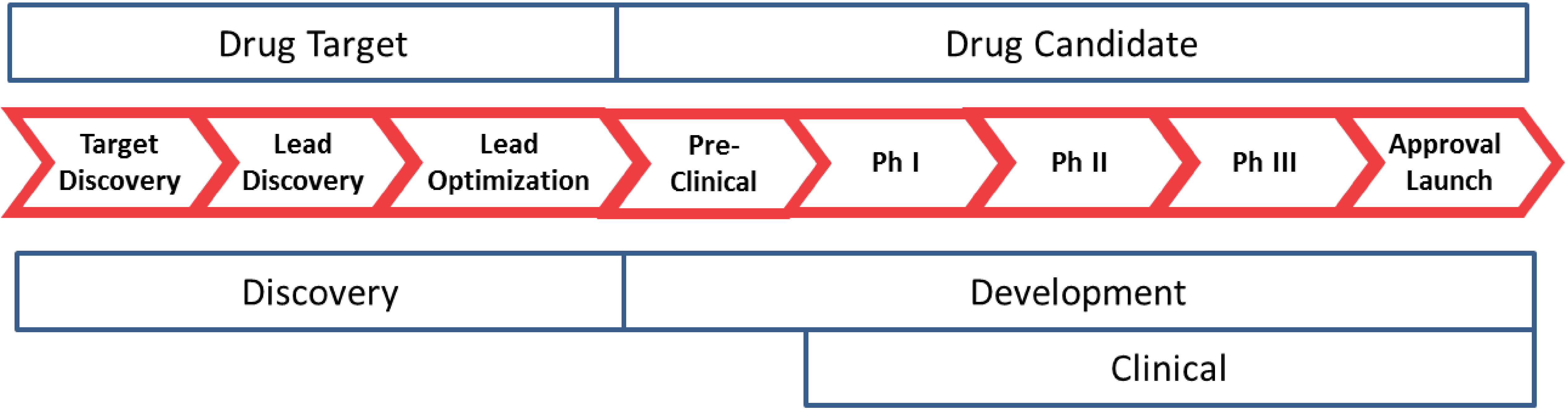
Using your knowledge about ordinary differential equations (ODE) and programming in Python, you are asked to build an n compartment model that will give a good approximation to the pharmacokinetics of a selected drug or its compound.

Introduction to pharmacokinetics

Drugs on the market

400 mg
Advil®
PER ZACHTE CAPSULE 400 mg IBUPROFEN
Liquid-Caps 400
20 stuks
Pijnstillend - Koortsverlagend - Ontstekingsremmend

Drug Discovery and Development



Introduction to pharmacokinetics

Pharmacokinetics

- the science of studying drugs in the body and how they are affected by different processes
- describes the behavior of an administered drug in the body over time
- uses mathematical equations to relate different variables to each other
- uses this to make predictions about drug behaviour in the body
- used to administer the drug appropriately and safely

Mathematical modeling of pharmacokinetics / pharmacodynamics (PKPD) is an important and growing field in drug development.

Introduction to pharmacokinetics

Vocabulary

- Compartment – a concept, it can be a tissue or organ or an entire body
- Dose – amount of drug administered
- Concentration – amount of the drug in a given volume of plasma
- Clearance –the volume of plasma cleared of the drug per unit of time
- Half-life – time it takes for a substance to lose half of its pharmacological activity

Example of a 2 compartment model

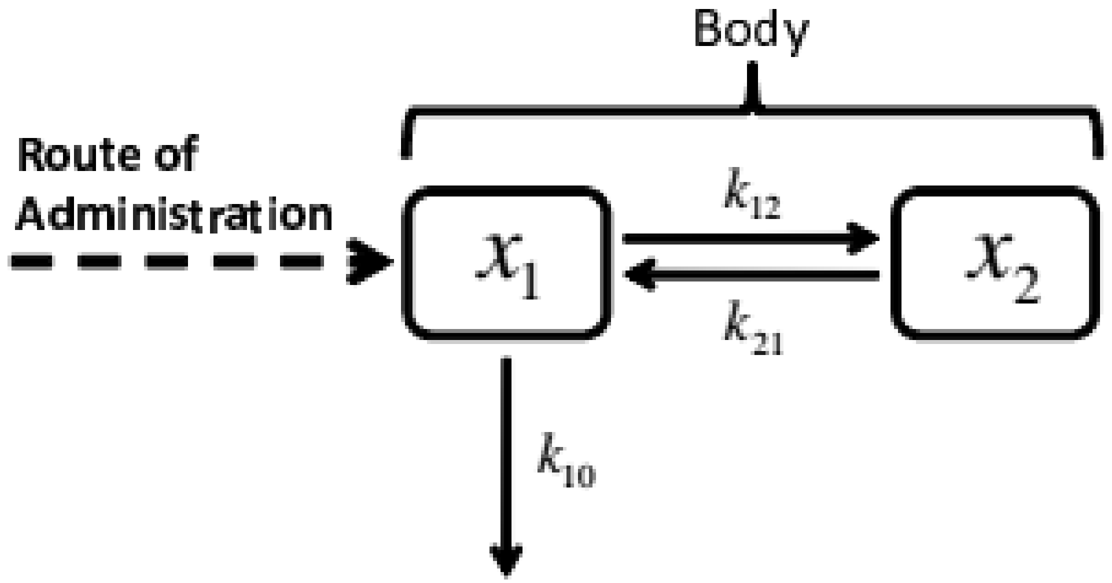


Figure 3.1: *General scheme of the two-compartment model.*

Source: Gilbert Koch, Modeling of Pharmacokinetics and Pharmacodynamics with Application to Cancer and Arthritis

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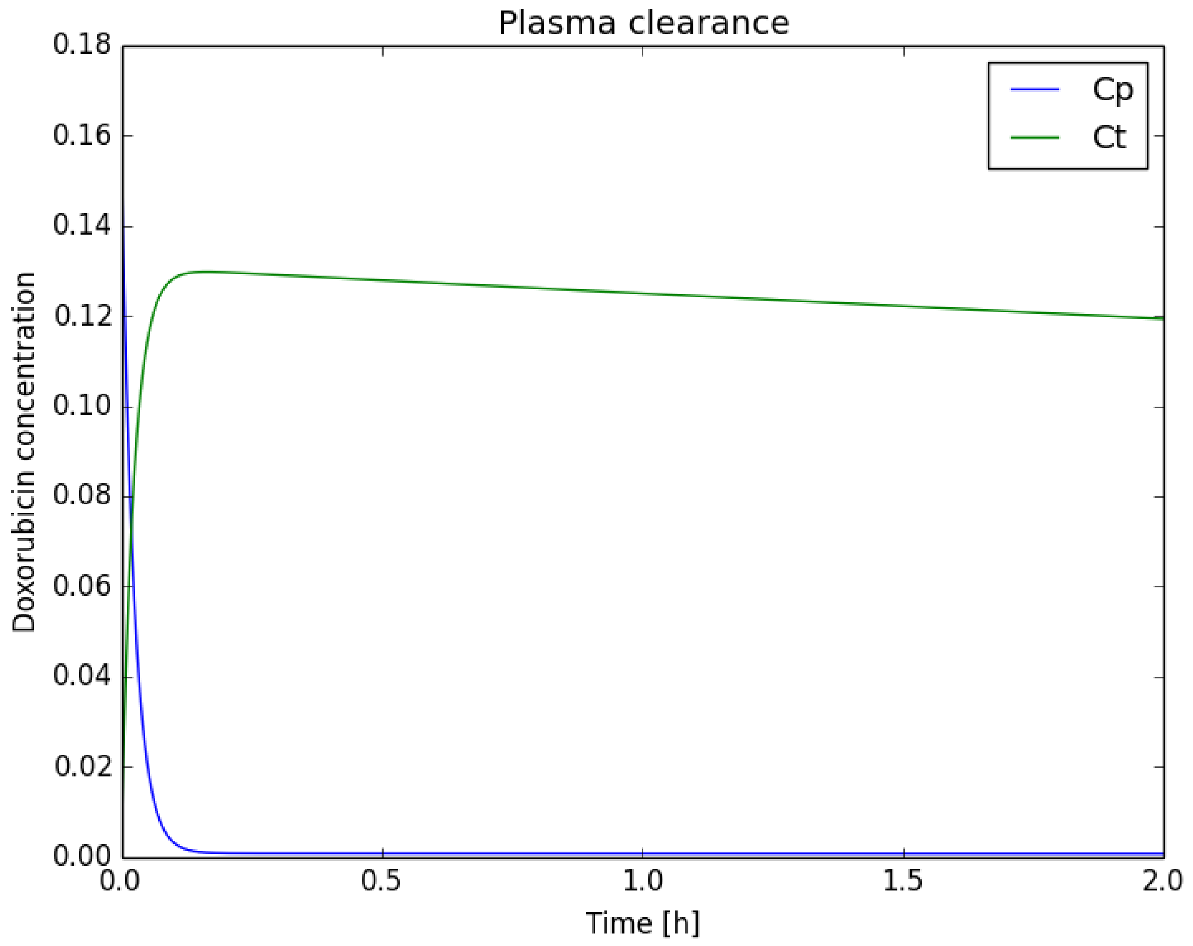
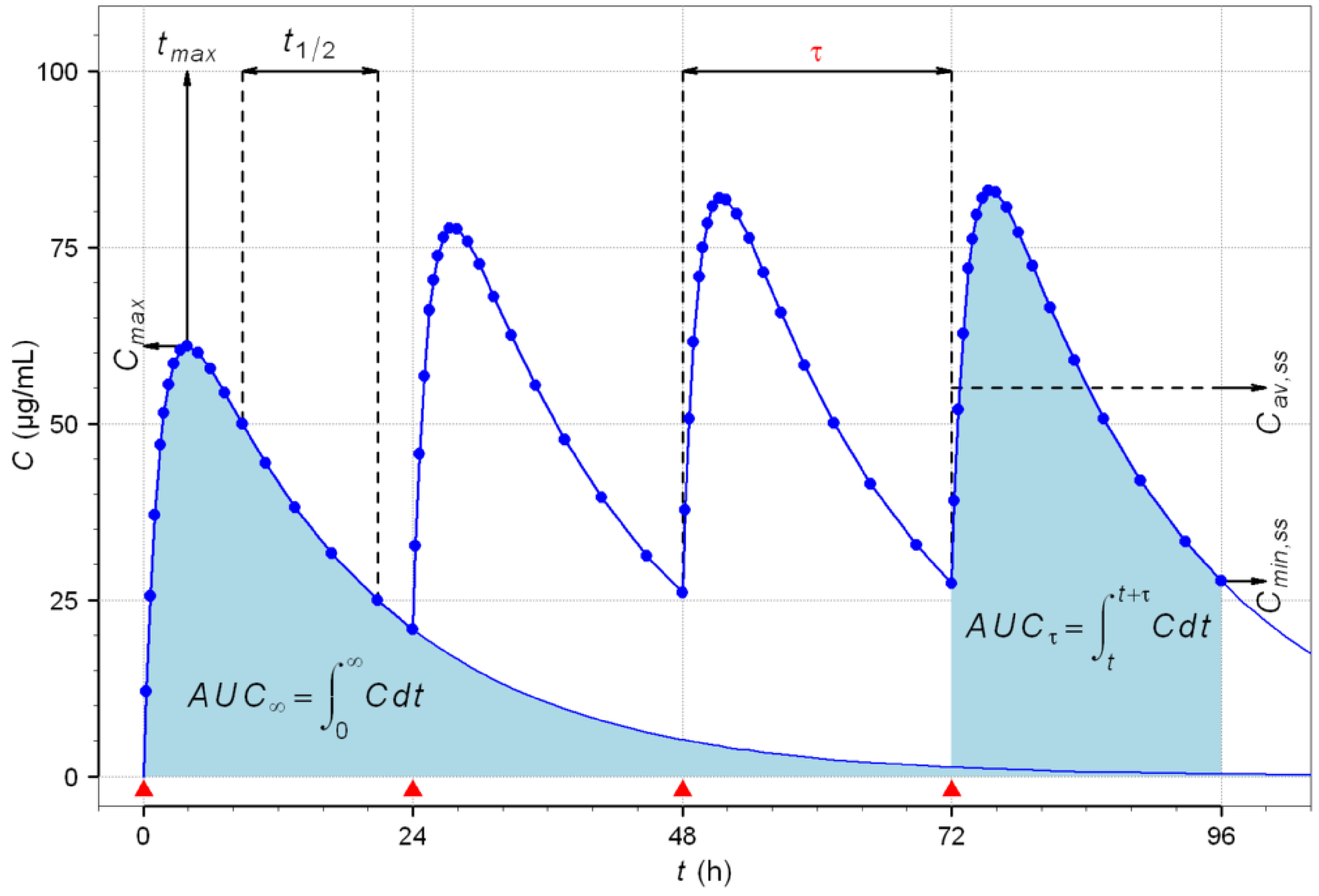
Single administration



Modelling Pharmacokinetics

Administration every 24 hours



GitLab

Collection of simple models in python

https://gitlab.com/ebenhoeh/models-for-teaching/tree/master