Quantitative pharmacology modeling (QSP) using Python – pqsp

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This document support the use of the python code in
`https://github.com/kamaldeen91/qsp-modeling-with-python`

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QSP modeling with python – pqsp

pqsp is a Python object oriented programming software used for simulating, analyzing and visualizing ODE models of quantitative systems biology and pharmacology. ***pqsp*** can be used to simulate the ODE models for different single and multiple drug dose regimen.

Installation

This software requires Python 3.7 or previous versions, and the following prerequisite packages – numpy, pandas, and scipy. To install, first **clone** or **download** the repository. Depending on the computer OS: Windows – install the pqsp package using: **pip install -e /path/to/script/folder** in the command line OR navigate to the downloaded pqsp folder path in the command window and install pqsp using: **python setup.py install**. Mac OS – navigate to the downloaded pqsp folder path in the terminal window and install pqsp using: **python setup.py install** 👍

Getting started

To run a pharmacokinetic ODE model of your choice using any python IDE, follow example below:

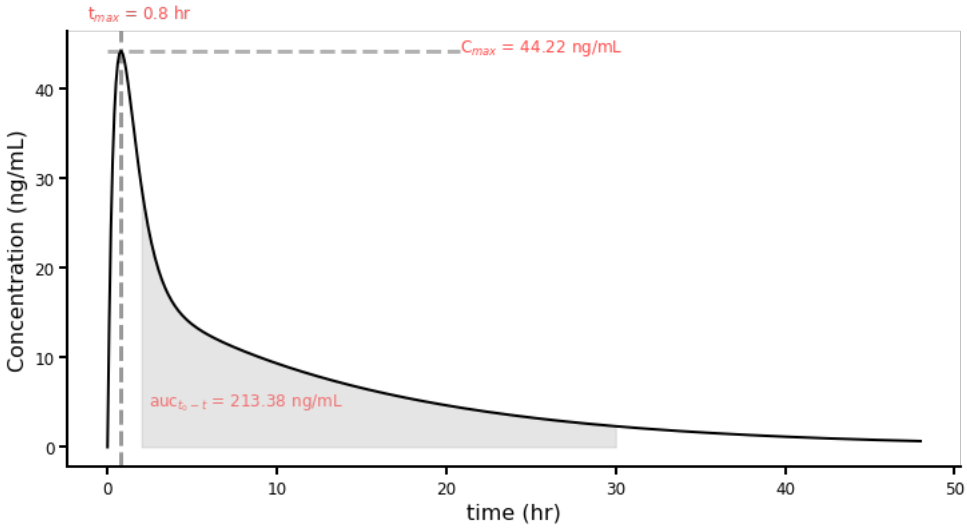
```
import pqsp

from pqsp.pqsp_single_dose_simulations import SingleDose
from pqsp.pqsp_multi_dose_simulations import MultipleDose
from pqsp.pqsp_multi_dose_delay_simulations import MultipleDoseDelay

from pqsp.pqsp_multi_bioav import MultipleDoseVaryBioav
from pqsp.pqsp_multi_bioav_delay import MultipleDoseVaryBioavDelay
```

```
def my_model(y, t, ka, F, K, K12, K21):

    G=y[0]; A1 = y[1]; A2 = y[2]

    dGdt = -ka*G
    dA1dt = F*ka*G + (K21*A2 - K12*A1) - K * A1
    dA2dt = K12*A1 - K21*A2

    return [dGdt, dA1dt, dA2dt]

##############################

ka = 1.8; F = 0.89; K = 0.28; K12 = 0.7; K21 = 0.3;
parameters = [ka, F, K, K12, K21]
```

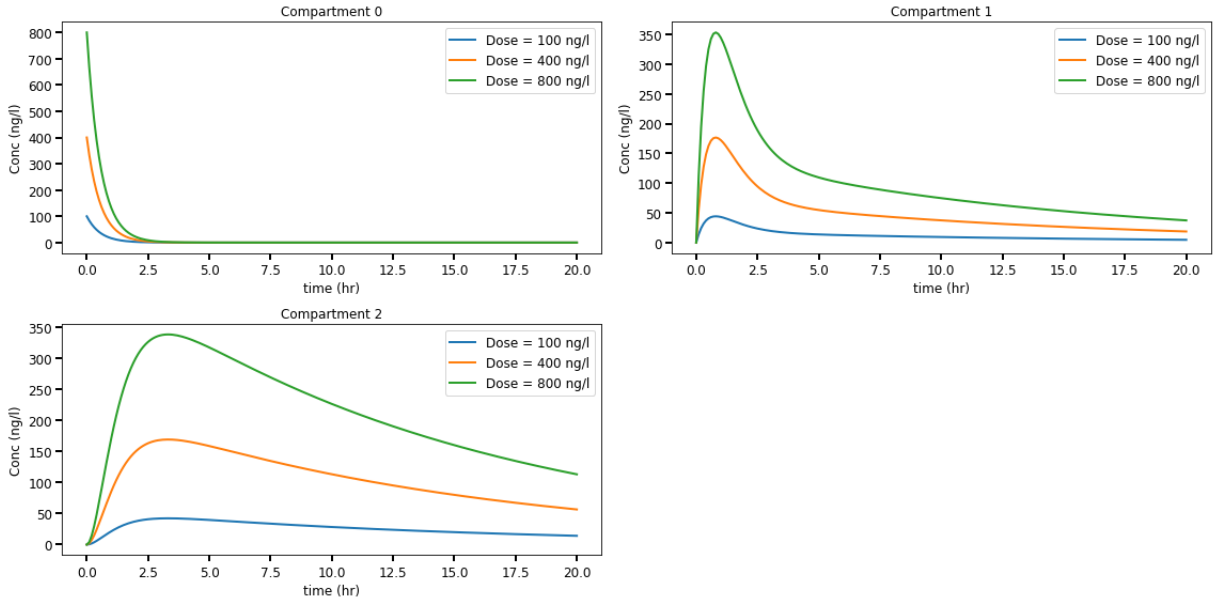
Single dose simulations and plots

```
mymodel = SingleDose(my_model, parameters, number_of_compartments=3)

t0, C0 = mymodel.simulation(simulation_time=2, time_unit='day', dose_mg=[100], compartment_pos=[1])

mymodel.plot_simulation(t0, C0, show_max=True, show_auc=True, auc_start=2, auc_end=30)
```

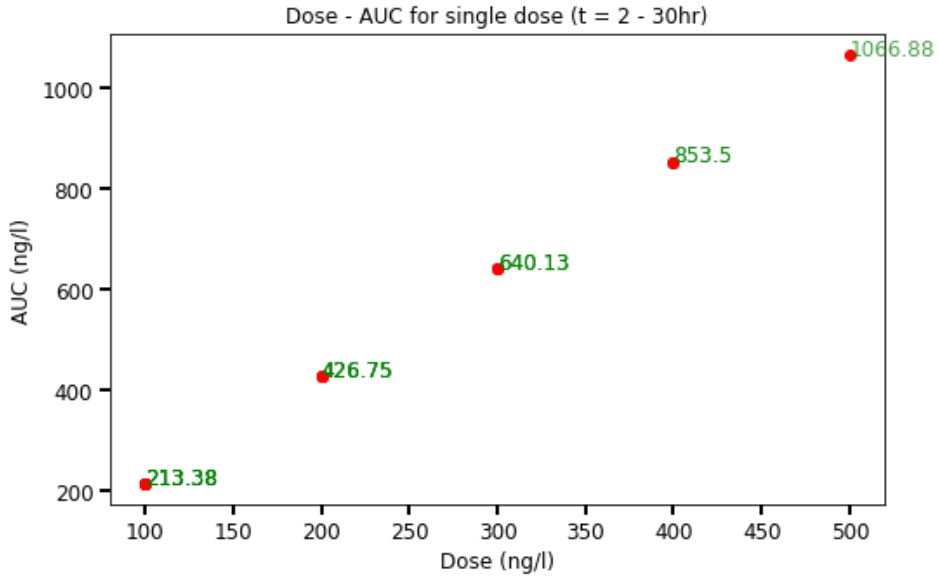
Note that, although the model is a two-compartment model with oral administration, the number of compartments in the simulaion is the number of ODE equations in the model. Also, a dataframe of t0 and c0 can be extracted and plotted using different plot format.




```
mymodel.single_dose_plot(simulation_time=20, time_unit='hrs', drug_doses=[100,400,800], compartment_pos=[0,1,2],
                         figsize=(16,8))
```



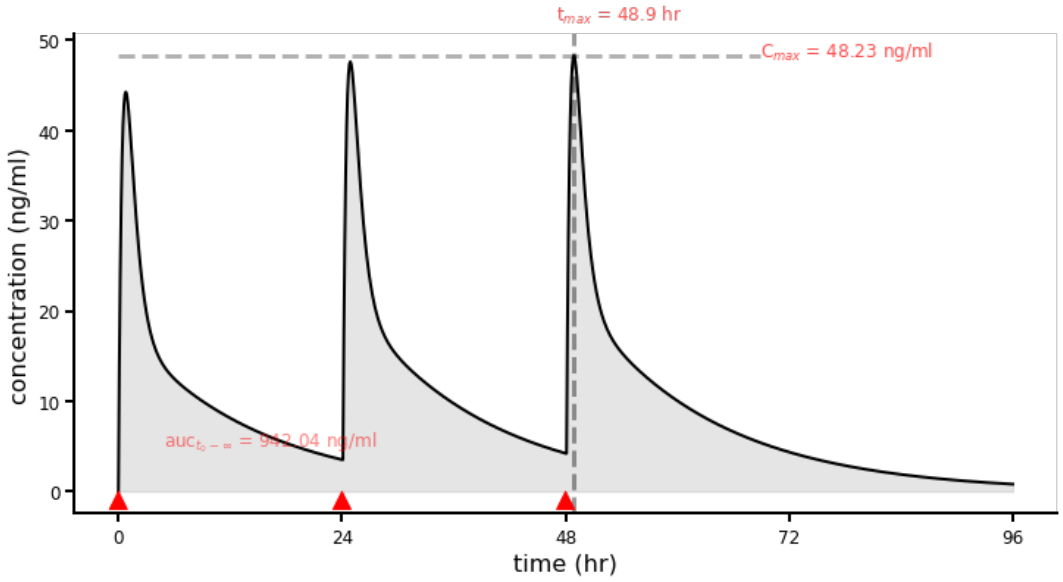
```
mymodel.dose_auc_plot(simulation_time=3, time_unit='days', drug_doses=[100,200,300,400,500], compartment_pos=[1],
                      auc_start=2, auc_end=30, figsize=(8,5))
```



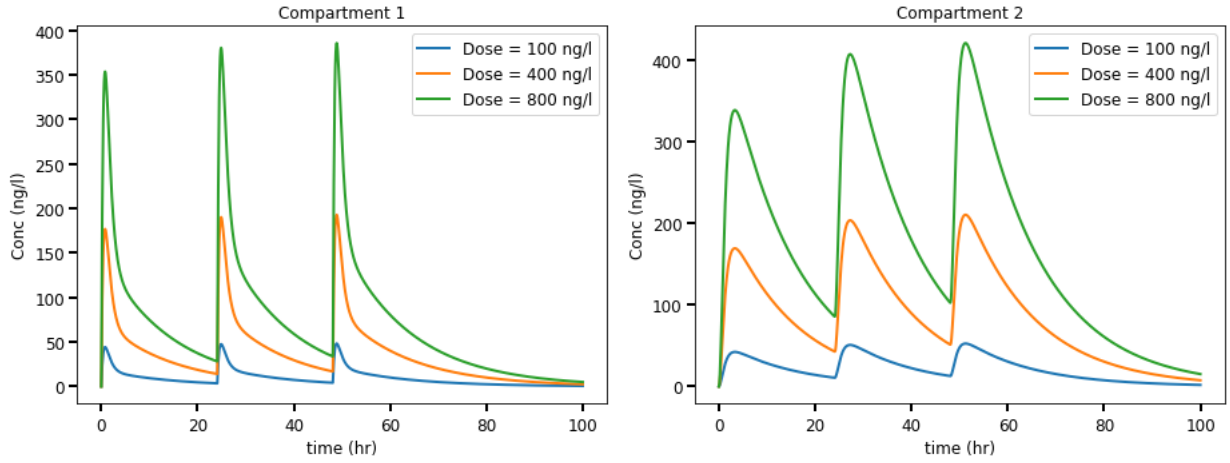
Multiple dose simulations and plots

```
mymultimodel = MultipleDose(my_model, parameters, number_of_compartments=3, number_of_dose=3, interval=24)

time_1, conc_1 = mymultimodel.simulation(simulation_time=4, time_unit='days', dose_mg=[100], compartment_pos=[1])

# time_1, conc_1 = mymultimodel.simulation(simulation_time=10, time_unit='days', dose_mg=[100, 100, 100],
#                  compartment_pos=[1])

mymultimodel.plot_simulation(time_1, conc_1, show_max=True, show_auc=True)
```

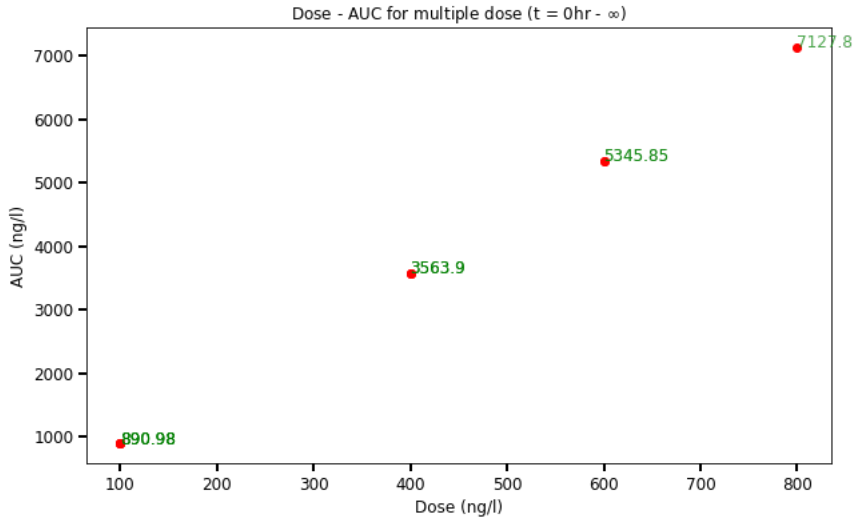
dose_mg can also be written as dose_mg = [100, 100, 100]. This allows for testing variation in dosage during therapy.



```
mymultimodel.multi_dose_plot(simulation_time=100, time_unit='hrs', drug_doses=[100,400,800], compartment_pos=[1,2],
                             figsize=(13,5))
```




```
mymultimodel.dose_auc_plot(simulation_time=3, time_unit='days', drug_doses=[100, 400, 600, 800], compartment_pos=[1])
```

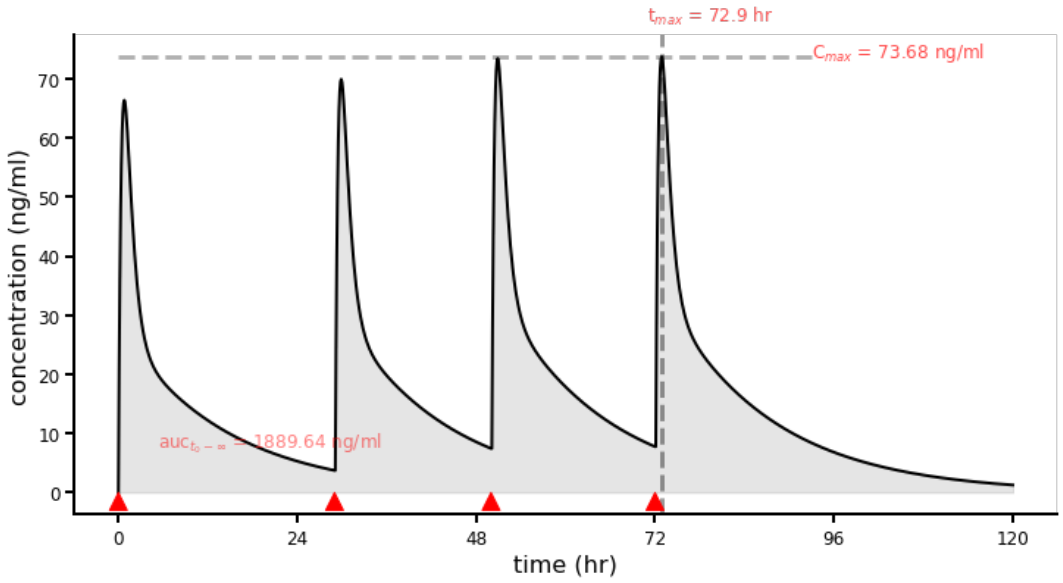


When auc_start and auc_end are not specified, the simulation runs for 0 to ∞.

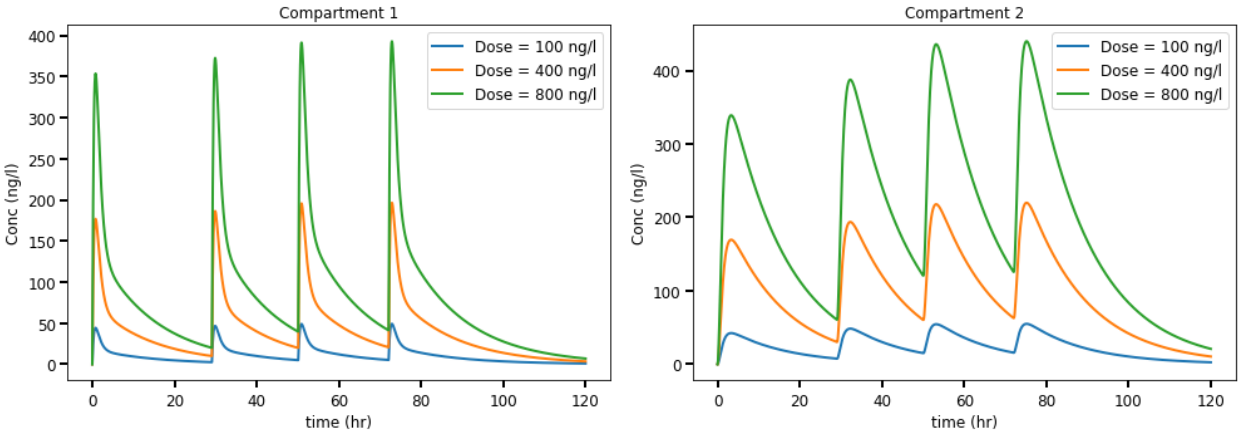
Multiple dose with delay simulations and plots

```
mydelaymodel = MultipleDoseDelay(my_model, parameters, number_of_compartments=3, number_of_dose=4, interval=24,
                                 delay=[5, 2, 0])

time_3, conc_3 = mydelaymodel.simulation(simulation_time=5, time_unit='days', dose_mg=[150], compartment_pos=[1])

# time, conc = mymodel_3.simulation(simulation_time=10, time_unit='days', dose_mg=[100, 150, 0, 100],
#                                                       compartment_pos=[1])
mydelaymodel.plot_simulation(time_3, conc_3, show_max=True, show_auc=True)
```

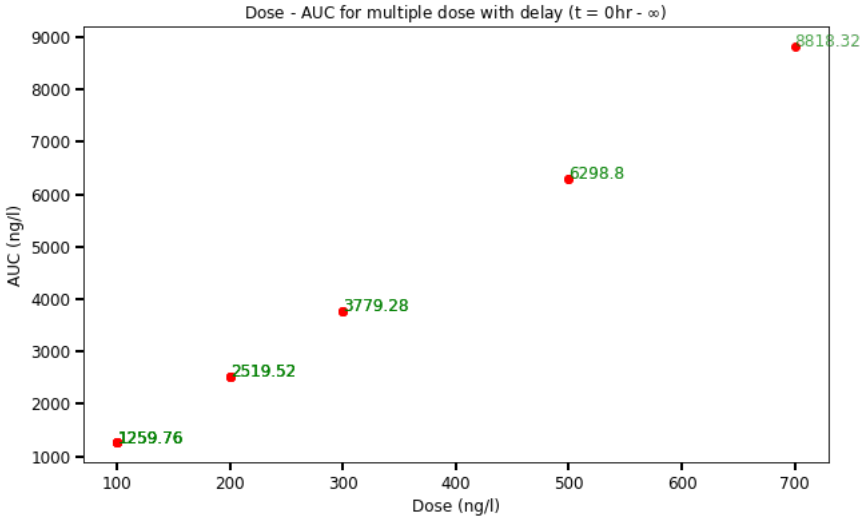
Note that number of entries in delay is one less than number of dose. This is because delay is assumed to occur in subsequent doses – after the first dose is taken.




```
mydelaymodel.multi_dose_delay_plot(simulation_time=5, time_unit='days', drug_doses=[100, 400, 800], compartment_pos=[1,2],
                                   figsize=(14,5))
```




```
mydelaymodel.dose_auc_plot(simulation_time=5, time_unit='days', drug_doses=[100,200,300, 500, 700], compartment_pos=[1])
```

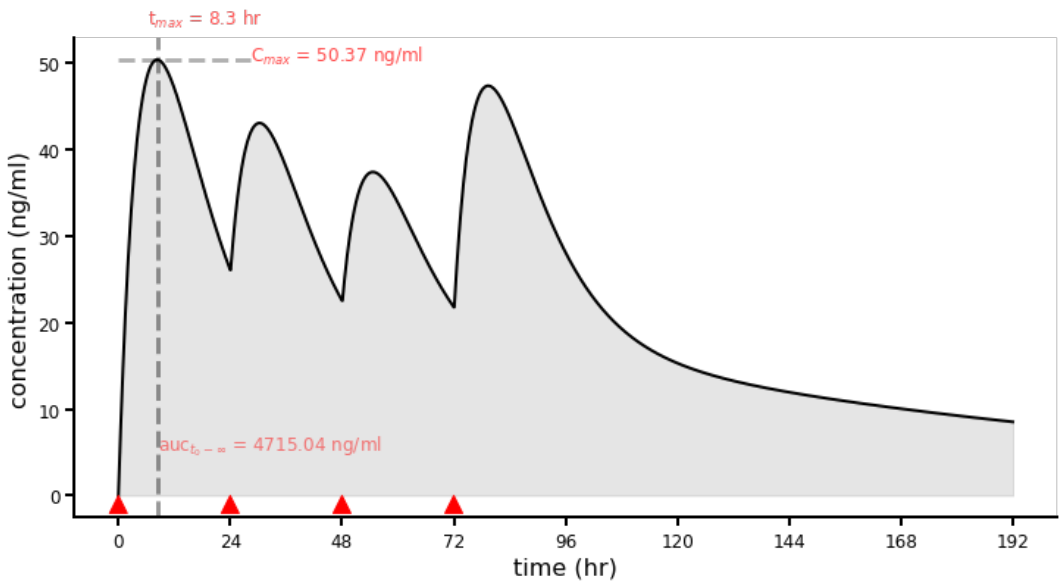


Multiple with varying bioavailability simulations and plots

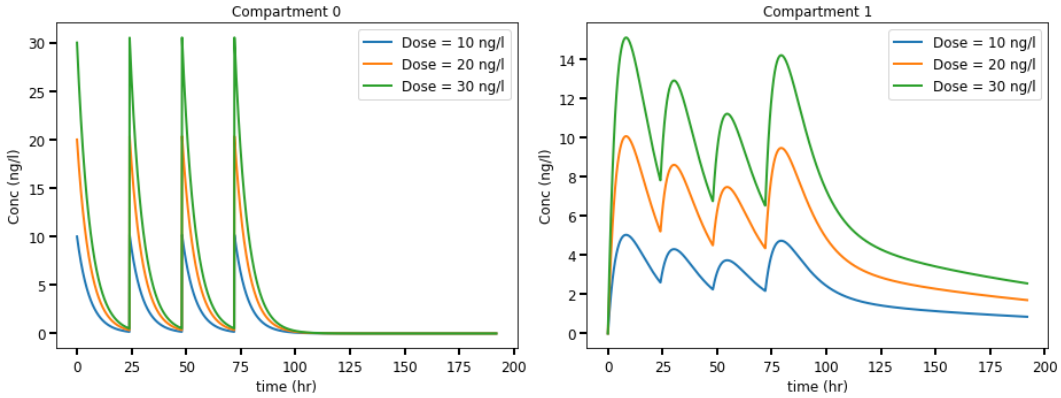
```
def two_c_model(y, t, ka, K, K12, K21, F):
    G = y[0]; A1 = y[1]; A2 = y[2]

    dGdt = -ka * G
    dA1dt = F * ka * G + K21 * A2 - K12 * A1 - K * A1
    dA2dt = K12 * A1 - K21 * A2

    return [dGdt, dA1dt, dA2dt]

ka = 0.17; Cl = 15.5; Vc = 368; Vd = 1060; Q = 16
K12 = Q / Vc; K21 = Q / Vd; K = Cl / Vc

par = [ka, K, K12, K21]
```

When defining model above, the bioavailability parameter F is listed as the last entry in the function. Always ensure this when executing the code for varied bioavailability.

```
mymulti_biov = MultipleDoseVaryBioav(two_c_model, par, number_of_compartments=3, number_of_dose=4, interval=24,
                                     bioav=[1, 0.51, 0.41, 0.6])

time_3, conc_3 = mymulti_biov.simulation(simulation_time=8, time_unit='days', dose_mg=[100], compartment_pos=[1])

mymulti_biov.plot_simulation(time_3, conc_3, show_auc=True, show_max=True)
```

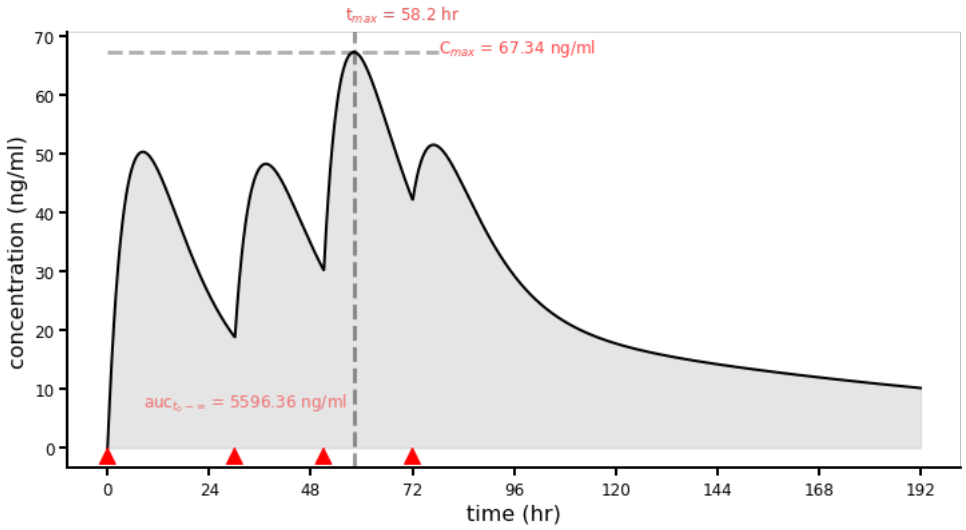



```
mymulti_biov.multi_dose_vary_bioav_plot(simulation_time=8, time_unit='days', drug_doses=[10,20,30], compartment_pos=[0,1],
                                        figsize=(13,5))
```

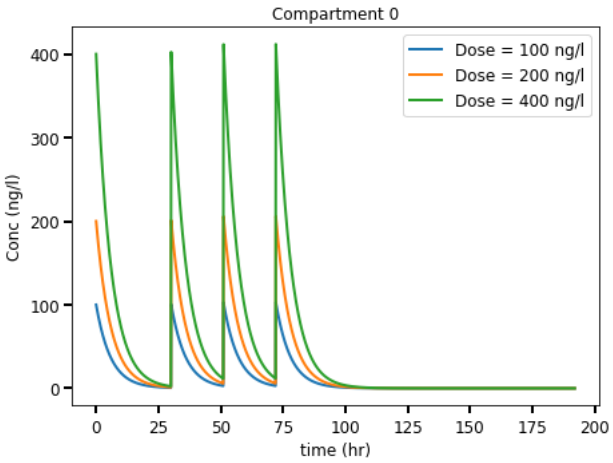


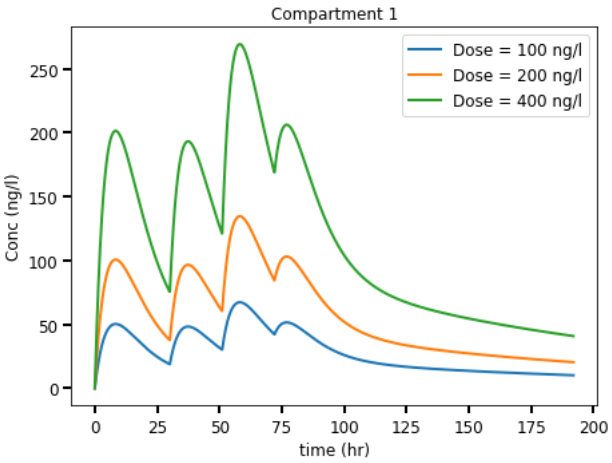
Model with delay and varying bioavailability simulations and plots

```
mymulti_biov_delay = MultipleDoseVaryBioavDelay(two_c_model, par, number_of_compartments=3, number_of_dose=4, interval=24,
                                                delay=[6,3,0], bioav=[1, 0.7, 0.9, 0.4])

tnn, cnn = mymulti_biov_delay.simulation(simulation_time=8, time_unit='days', dose_mg=[100])

mymulti_biov_delay.plot_simulation(tnn, cnn, show_auc=True, show_max=True)
```




```
mymulti_biov_delay.md_delay_vary_bioav_plot(simulation_time=8, time_unit='days', drug_doses=[100, 200, 400],
                                            compartment_pos=[0,1], figsize=(13,5))
```





Try this

1. Run a single and multiple does (with and without delay) simulations for an intravenous model given by

```
def my_intramodel(y, t, K, K12, K21):

    A1 = y[0]; A2 = y[1];

    dA1dt = (K21*A2 - K12*A1) - K * A1
    dA2dt = K12*A1 - K21*A2

    return [dA1dt, dA2dt]


############################

K = 0.28; K12 = 0.7; K21 = 0.3;
parameters = [K, K12, K21]
```

2. Run simulations for single, multiple does with and without delay, and with varied bioavaialabilty for any model(s) of your choice.

3. Reproduce some of the Figures 3 and 4 in [1] using ***pqsp***.

4. What are some of the errors you encountered when running the simulations and how did you correct them (eventually)?

👍👍👍

Bibliography

[1] Liu, G. S., Ballweg, R., Ashbaugh, A., Zhang, Y., Facciolo, J., Cushion, M. T., & Zhang, T. (2019). Correction to: A quantitative systems pharmacology (QSP) model for Pneumocystis treatment in mice. BMC systems biology, 13(1), 40.