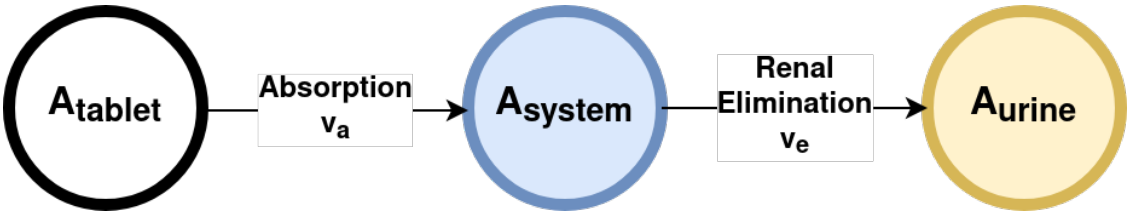
04_simple_absorption

June 6, 2023

1 Simple absorption models

In the following we study a simple model for absorption and elimination. A can be absorbed from the tablet in the systemic circulation ($A_{tablet} \rightarrow A_{system}$) which can be eliminated in the urine via renal excretion ($A_{system} \rightarrow A_{urine}$).

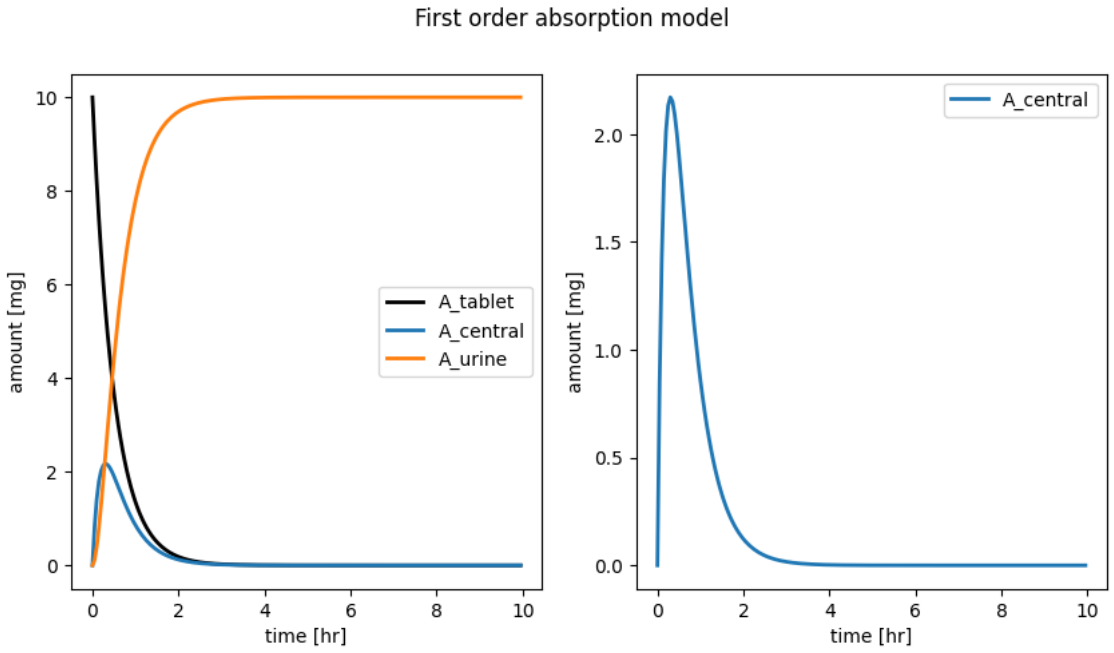


Elimination and absorption are assumed to be Mass-Action, i.e., depending on a rate constant k and the amount or concentration of the respective substance.

The ordinary differential equation system (ODE) results in:

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

def dxdt_absorption_first_order(x, t, ka, ke):
    """
    First order absorption model
    """
    # state variables
    A_tablet = x[0]  # [mg]
    A_central = x[1] # [mg/l]
    A_urine = x[2] # [mg]

    # rates
    va = ka * A_tablet  # [mg/hr]
    ve = ke * A_central # [mg/hr]

    # odes (stoichiometric equation)
    return [
        -va,            # dA_tablet/dt  [mg/hr]
```

```
        va - ve,        # dA_central/dt [mg/hr]
        ve,             # dA_urine/dt  [mg/hr]
    ]


# initial condition and time span
t = np.arange(0, 10, 0.05) # [hr]
Dose_A = 10.0  # [mg]
x0 = [
    Dose_A,  # A_tablet  [mg]
    0.0,   # A_central [mg]
    0.0,   # A_urine [mg]
]

# parameters
ka = 2.0  # [1/hr]
ke = 5.0  # [1/hr]

x = odeint(dxdt_absorption_first_order, x0, t, args=(ka, ke))
names = ["A_tablet", "A_central", "A_urine"]
colors = ["black", "tab:blue", "tab:orange"]

# plot results
f, (ax1, ax2) = plt.subplots(nrows=1, ncols=2, figsize=(10,5))
f.suptitle("First order absorption model")
# all species
for k, name in enumerate(names):
    ax1.plot(t, x[:, k], linewidth=2, label=name, color=colors[k])

# only A_central
ax2.plot(t, x[:, 1], linewidth=2, label=names[1], color=colors[1])

for ax in (ax1, ax2):

    ax.legend()
    ax.set_xlabel("time [hr]")
    ax.set_ylabel("amount [mg]")

plt.show()
```

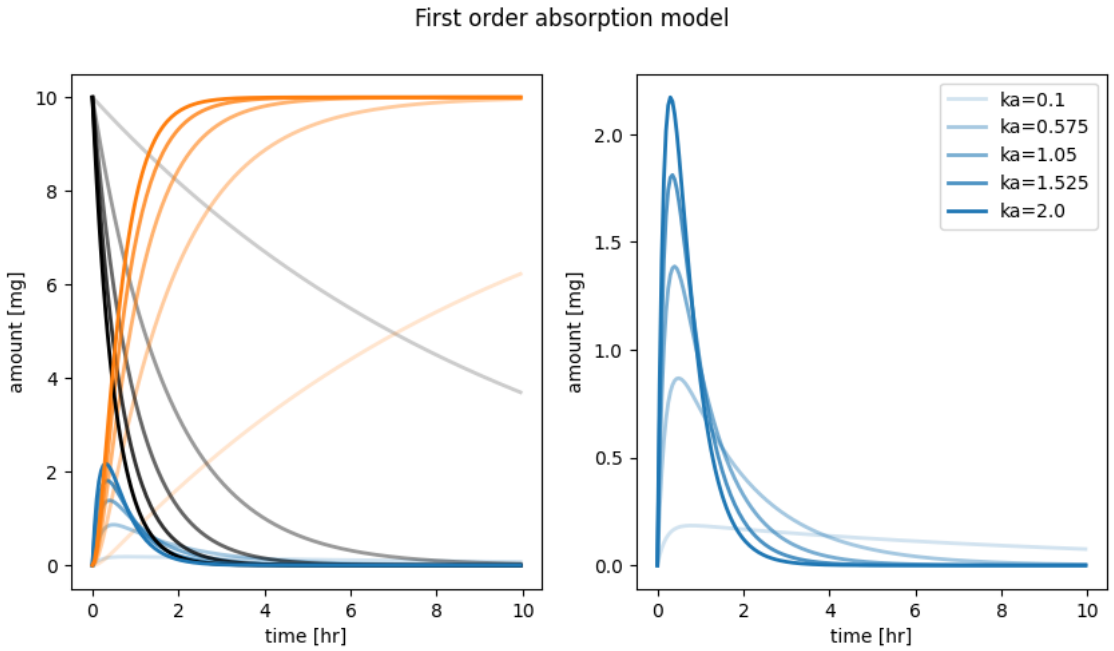


When `va = ve` the peak concentration in the central compartment is reached.

1.1 Effect of absorption parameter

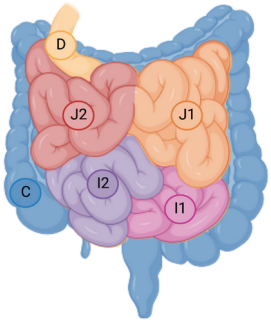
[2]:
```
# parameters
ka = 2.0  # [1/hr]
ke = 5.0  # [1/hr]

n_samples = 5
kas = np.linspace(0.1, 2.0, num=n_samples)  # [1/hr]

# plot results
f, (ax1, ax2) = plt.subplots(nrows=1, ncols=2, figsize=(10,5))
f.suptitle("First order absorption model")

for kp, ka in enumerate(kas):
    x = odeint(dxdt_absorption_first_order, x0, t, args=(ka, ke))

    # all species
    for k, name in enumerate(names):
        ax1.plot(t, x[:, k], linewidth=2, color=colors[k], alpha=(kp+1)/
↪n_samples, label=f"{ka=}")

    # only A_central
    ax2.plot(t, x[:, 1], linewidth=2, color=colors[1], alpha=(kp+1)/n_samples,␣
↪label=f"{ka=}")
```

```
    for ax in (ax1, ax2):
        ax.set_xlabel("time [hr]")
        ax.set_ylabel("amount [mg]")
    ax2.legend()

plt.show()
```



2 Lag absorption models

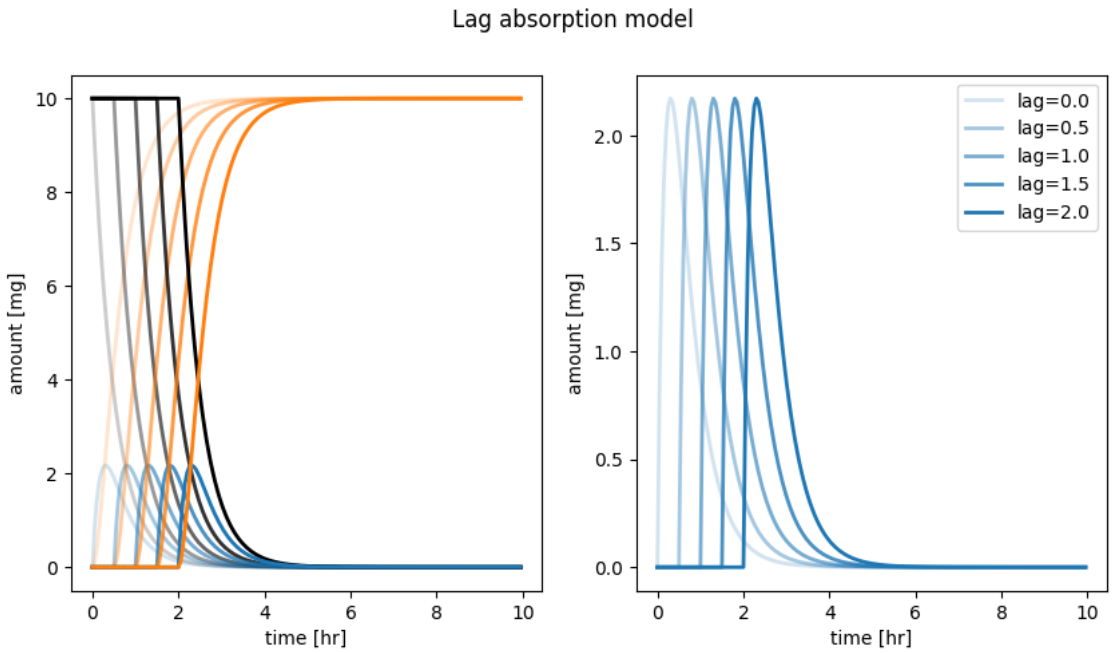
Absorption can show a time lag due stomach passage or absorption in later regions of the intestine (e.g. ileum, jejunum). Such lags can be introduced either directly in absorption equations or via so called transit chains (i.e. chains of absorption reactions).



First we have a look at models with an explicit delay in form of a lag time.

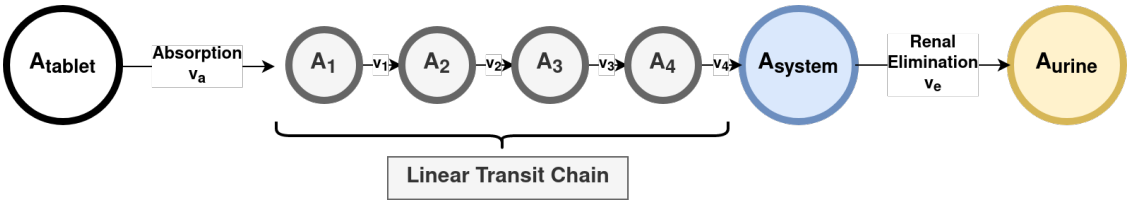
[3]:
```
import numpy as np
from scipy.integrate import odeint
from matplotlib import pylab as plt

def dxdt_absorption_lag(x, t, ka, ke, lag=0.0):
    """
    First order absorption model with lag time
    """
    # state variables
    A_tablet = x[0]  # [mg]
    A_central = x[1] # [mg/l]
    A_urine = x[2] # [mg]

    # rates
    if t >= lag:
        va = ka * A_tablet  # [mg/hr]
    else:
        va = 0
    ve = ke * A_central # [mg/hr]

    # odes (stoichiometric equation)
    return [
        -va,            # dA_tablet/dt  [mg/hr]
         va - ve,       # dA_central/dt [mg/hr]
         ve,            # dA_urine/dt   [mg/hr]
    ]

ka = 2.0  # [1/hr]
ke = 5.0  # [1/hr]

n_samples = 5
lags = np.linspace(0.0, 2.0, num=n_samples)  # [hr]

# plot results
f, (ax1, ax2) = plt.subplots(nrows=1, ncols=2, figsize=(10,5))
f.suptitle("Lag absorption model")

for kp, lag in enumerate(lags):
    x = odeint(dxdt_absorption_lag, x0, t, args=(ka, ke, lag))

    # all species
    for k, name in enumerate(names):
        ax1.plot(t, x[:, k], linewidth=2, color=colors[k], alpha=(kp+1)/
↪n_samples, label=f"{lag=}")

    # only A_central
```

```
    ax2.plot(t, x[:, 1], linewidth=2, color=colors[1], alpha=(kp+1)/n_samples,␣
↪label=f"{lag=}")

    for ax in (ax1, ax2):

        ax.set_xlabel("time [hr]")
        ax.set_ylabel("amount [mg]")
    ax2.legend()

plt.show()
```



3 Transit chain absorption models

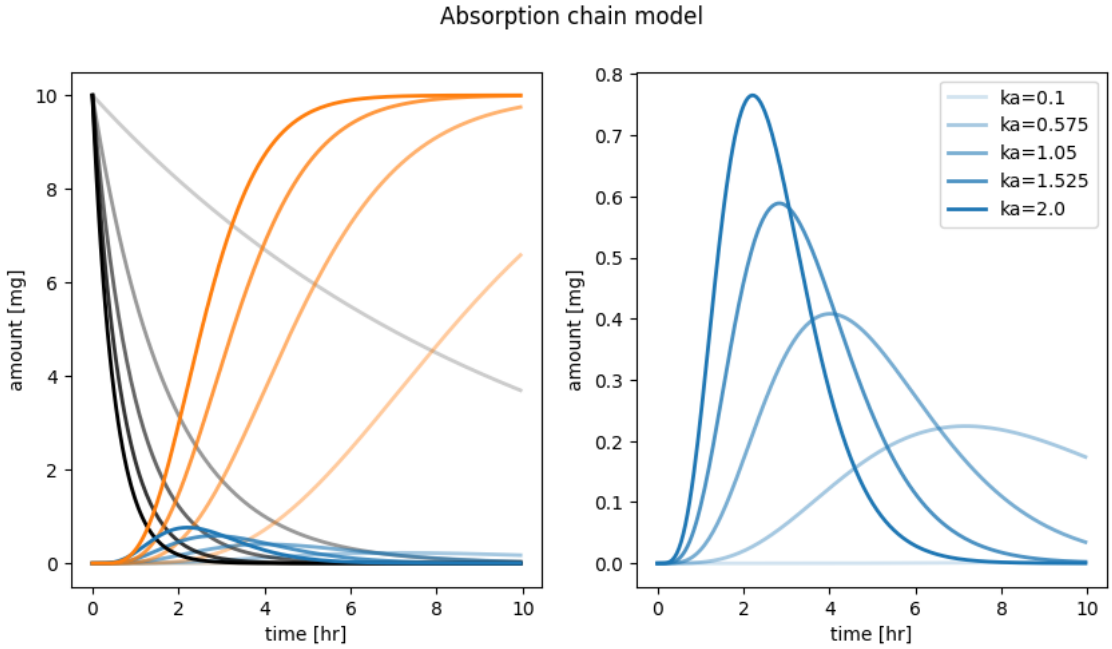
Now we have a look at the example of a transit chain. By coupling a set of reactions delays can be introduced and curves are smoothend.



Due to the transit chain the substance appears delayed in the systemic circulation (central compartment).

[4]:
```
def dxdt_absorption_chain(x, t, ka, ke):
    """
    First order absorption model for transit chain.
    """
    # state variables
    A_tablet = x[0]  # [mg]
    A_central = x[1] # [mg/l]
    A_urine = x[2] # [mg]
    A1 = x[3]
    A2 = x[4]
    A3 = x[5]
    A4 = x[6]

    # rates
    va = ka * A_tablet  # [mg/hr]
    ve = ke * A_central # [mg/hr]
    v1 = ka * x[3]
    v2 = ka * x[4]
    v3 = ka * x[5]
    v4 = ka * x[6]

    # odes (stoichiometric equation)
    dxdt = np.zeros(7)

    dxdt[0] = -va            # dA_tablet/dt  [mg/hr]
    dxdt[1] =  v4 - ve     # dA_central/dt [mg/hr] (end of chain)
    dxdt[2] =  ve            # dA_urine/dt  [mg/hr]
    dxdt[3] = va - v1
    dxdt[4] = v1 - v2
    dxdt[5] = v2 - v3
    dxdt[6] = v3 - v4

    return dxdt

# initial condition and time span
t = np.arange(0, 10, 0.05) # [hr]
Dose_A = 10.0  # [mg]
x0 = [
    Dose_A,  # A_tablet  [mg]
    0.0,   # A_central [mg]
    0.0,   # A_urine [mg]
    0.0,   # A1 [mg]
    0.0,   # A2 [mg]
    0.0,   # A3 [mg]
    0.0,   # A4 [mg]
]
```

```
names = ["A_tablet", "A_central", "A_urine"]
colors = ["black", "tab:blue", "tab:orange"]

# parameters
ka = 2.0  # [1/hr]
ke = 5.0  # [1/hr]

n_samples = 5
kas = np.linspace(0.1, 2.0, num=n_samples)  # [1/hr]

# plot results
f, (ax1, ax2) = plt.subplots(nrows=1, ncols=2, figsize=(10,5))
f.suptitle("Absorption chain model")

for kp, ka in enumerate(kas):
    x = odeint(dxdt_absorption_chain, x0, t, args=(ka, ke))

    # all species
    for k, name in enumerate(names):
        ax1.plot(t, x[:, k], linewidth=2, color=colors[k], alpha=(kp+1)/
↪n_samples, label=f"{ka=}")

    # only A_central
    ax2.plot(t, x[:, 1], linewidth=2, color=colors[1], alpha=(kp+1)/n_samples,␣
↪label=f"{ka=}")

    for ax in (ax1, ax2):
        ax.set_xlabel("time [hr]")
        ax.set_ylabel("amount [mg]")
    ax2.legend()

plt.show()
```


Absorption chain model
amount [mg]
time [hr]
amount [mg]
time [hr]
ka=0.1
ka=0.575
ka=1.05
ka=1.525
ka=2.0

[ ]: