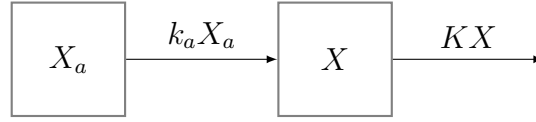


We model the absorption via the following cascading compartmental decay model.



The initial amounts are given by $X_a(0) = FX_0$ and $X(0) = 0$, where F is the fraction of the drug absorbed by the mouse and X_0 is the amount administered. So, we have the following system of differential equations

$$\begin{aligned}\frac{dX_a}{dt} &= -k_a X_a(t), \\ \frac{dX}{dt} &= k_a X_a(t) - KX(t), \\ X_a(0) &= FX_0, \quad X(0) = 0.\end{aligned}$$

We wish to estimate F , the fraction of drug absorbed, k_a the rate of absorption into the blood, and K the rate of dispersion from the blood.

The data recorded are in terms of concentration of the drug in the cell, if V is the average volume of the cell, is introduced and then we can reparameterize X , $C(t) = X(t)/V$, and the parameter.

Note that this system can be solved analytically, as it is linear,

$$\frac{d}{dt} \begin{pmatrix} X_a \\ X \end{pmatrix} = \begin{pmatrix} -k_a & 0 \\ k_a & -K \end{pmatrix} \begin{pmatrix} X_a \\ X \end{pmatrix}, \quad \begin{pmatrix} X_a(0) \\ X(0) \end{pmatrix} = \begin{pmatrix} FX_0 \\ 0 \end{pmatrix}.$$

The solution for the absorption into the blood is given by

$$\begin{aligned}X_a(t) &= FX_0(k_a e^{-k_a t}), \\ X(t) &= \frac{k_a F X_0}{k_a - K}(e^{-Kt} - e^{-k_a t}).\end{aligned}$$

1 Methods

We must first fit the model. Note that We fit the parameters of the model by optimizing the function that returns a numerical solution to the differential equation.

$$C(t) = \frac{X(t)}{V} = \frac{F}{V} \cdot X_0 \cdot \frac{k_a}{k_a - K}(e^{-Kt} - e^{-k_a t}).$$

by least squares with respect to the parameters F/V , k_a , and K . However the factor $k_a - K$ in the denominator makes this optimization step unstable. Instead we optimize the system of differential equations, with the added scaling factor $1/V$ to X .

2 Results

95% Confidence Interval for $K_1 - K_2 : [-0.3101, -0.2296]$.

```
>> CI95_diff_K
```

```
CI95_diff_K =
```

```
    -0.3101    -0.2296
```

```
>> CI95_diff_FV
```

```
CI95_diff_FV =
```

```
    -0.1187     0.0353
```

```
>>
```