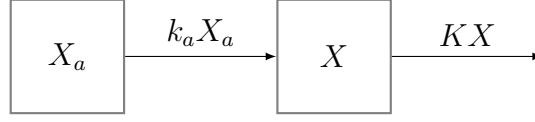


We model the absorbtion via the following cascading compartmental decay model.



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 absobed,  $k_a$  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 absoption 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 denomonator 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  $K_1 - K_2$  :  $[-0.3101, -0.2296]$ .