Neural ODE meeting reading

For meeting in Data Analytics

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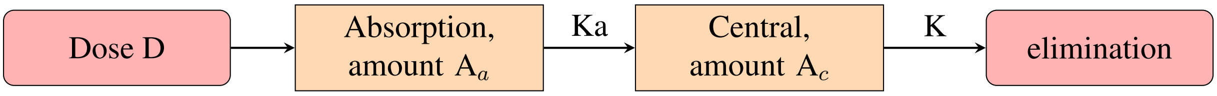
- two compartment model math derivation
- My code for two compartment model on github
- My code for one compartment model with gradient descent for optimization

One compartment, first order PO ODE derivation



First order, thus ODE:

$$\frac{\mathrm{d}A_a}{\mathrm{d}t} = -K_a A_a, \qquad \text{IC} : A_a = D \text{ when } t = 0;$$
$$\frac{\mathrm{d}A_c}{\mathrm{d}t} = K_a A_a - K A_c, \qquad \text{IC} : A_c = 0 \text{ when } t = 0;$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\begin{bmatrix} A_a \\ A_c \end{bmatrix} = \begin{bmatrix} -K_a & 0 \\ K_a & -K \end{bmatrix}\begin{bmatrix} A_a \\ A_c \end{bmatrix}$$

Solve for eigenvalues and eigenvectors and we obtain

$$\lambda_1 = -K_a, \qquad \mathbf{v}_1 = \begin{bmatrix} K - K_a \\ K_a \end{bmatrix}$$
$$\lambda_2 = -K, \qquad \mathbf{v}_2 = \begin{bmatrix} 0 \\ 1 \end{bmatrix}$$

Thus the equation is

$$\begin{bmatrix} A_a \\ A_c \end{bmatrix} = C_1 \mathbf{v}_1 \exp(-K_a t) + C_2 \mathbf{v}_2 \exp(-K t)$$

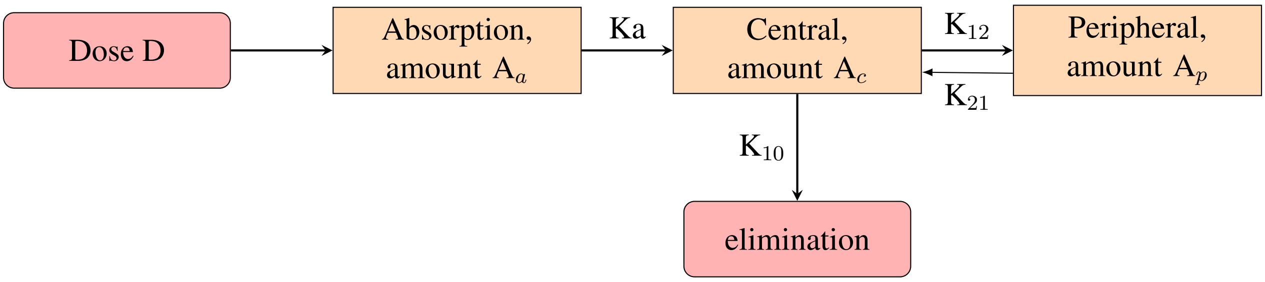
in which C_1 and C_2 are constants. Given the initial conditions, we could obtain $C_1 = \frac{D}{K-K_a}$ and $C_2 = \frac{-K_a D}{K-Ka}$, thus the final equation will be:

$$\begin{bmatrix} A_a \\ A_c \end{bmatrix} = \frac{D}{K - K_a}\begin{bmatrix} K - K_a \\ K_a \end{bmatrix} \exp(-K_a t) + \frac{-K_a D}{K - Ka}\begin{bmatrix} 0 \\ 1 \end{bmatrix} \exp(-K t)$$

We are interested in central compartment which could represent the plasma drug amount/concentration

$$A_c = \frac{K_a D}{K_a - K}(\mathrm{e}^{-Kt} - \mathrm{e}^{-K_a t})$$
$$Conc = \frac{A_c}{V_d} = \frac{K_a D}{(K_a - K) V_d}(\mathrm{e}^{-Kt} - \mathrm{e}^{-K_a t})$$

Two compartment, first order PO ODE derivation



First order, thus ODE:

$$\begin{aligned} \frac{\mathrm{d}A_a}{\mathrm{d}t} &= -K_a A_a, & \text{IC}: A_a = D \text{ when } t = 0; \\ \frac{\mathrm{d}A_c}{\mathrm{d}t} &= K_a A_a - (K_{10} + K_{12})A_c + K_{21}A_p, & \text{IC}: A_c = 0 \text{ when } t = 0; \\ \frac{\mathrm{d}A_c}{\mathrm{d}t} &= K_{12}A_c - K_{21}A_p, & \text{IC}: A_p = 0 \text{ when } t = 0; \end{aligned}$$

$$\frac{\mathrm{d}}{\mathrm{d}t}\begin{bmatrix} A_a \\ A_c \\ A_p \end{bmatrix} = \begin{bmatrix} -K_a & 0 & 0 \\ K_a & -K_{10} - K_{12} & K_{21} \\ 0 & K_{12} & -K_{21} \end{bmatrix} \begin{bmatrix} A_a \\ A_c \\ A_p \end{bmatrix}$$

Let $M = \begin{bmatrix} -K_a & 0 & 0 \\ K_a & -K_{10} - K_{12} & K_{21} \\ 0 & K_{12} & -K_{21} \end{bmatrix}$

Solve for eigenvalues and eigenvectors, we need to calculate $det(M - \lambda\mathbf{I}) = 0$ and we obtain

$$\det\left(\begin{bmatrix} -K_a - \lambda & 0 & 0 \\ K_a & -K_{10} - K_{12} - \lambda & K_{21} \\ 0 & K_{12} & -K_{21} - \lambda \end{bmatrix}\right) = 0$$

which is

$$(-K_a - \lambda)[(-K_{10} - K_{12} - \lambda)(-K_{21} - \lambda) - K_{12}K_{21}] = 0$$

We could observe that $\lambda_1 = -K_a$, we would solve the other 2 λs for

$$\begin{aligned} (-K_{10} - K_{12} - \lambda)(-K_{21} - \lambda) - K_{12}K_{21} &= 0 \\ \lambda^2 + (K_{10} + K_{12} + K_{21})\lambda + K_{10}K_{21} &= 0 \\ \text{Let } \alpha + \beta = K_{10} + K_{12} + K_{21}, \text{ and } \alpha\beta &= K_{10}K_{21} \\ \text{thus } \lambda^2 + (\alpha + \beta)\lambda + \alpha\beta &= 0 \\ (\lambda + \alpha)(\lambda + \beta) &= 0 \end{aligned}$$

Thus,

$$\lambda_2 = -\alpha, \lambda_3 = -\beta$$

Since two $\lambda = \frac{-(K_{10}+K_{12}+K_{21})\pm\sqrt{\Delta}}{2}$ in which $\Delta = (K_{10} + K_{12} + K_{21})^2 - 4K_{10}K_{21}$, we could obtain

$$\alpha, \beta = \frac{(K_{10} + K_{12} + K_{21}) \pm \sqrt{\Delta}}{2} \tag{1}$$

$$\lambda_1 = -K_a, \qquad \mathbf{v}_1 = \begin{bmatrix} \frac{(K_{10}-K_a)(K_{21}-K_a)}{K_a} - K_{12} \\ K_{21} - K_a \\ K_{12} \end{bmatrix}$$

$$\lambda_2 = -\alpha, \qquad \mathbf{v}_2 = \begin{bmatrix} 0 \\ K_{21} - \alpha \\ K_{12} \end{bmatrix}$$

$$\lambda_3 = -\beta, \qquad \mathbf{v}_3 = \begin{bmatrix} 0 \\ K_{21} - \beta \\ K_{12} \end{bmatrix}$$

Thus the equation is

$$\begin{bmatrix} A_a \\ A_c \\ A_p \end{bmatrix} = C_1 \mathbf{v}_1 \exp(-K_a t) + C_2 \mathbf{v}_2 \exp(-\alpha t) + C_3 \mathbf{v}_3 \exp(-\beta t)$$

in which C_1 and C_2 and C_3 are constants. Given the initial conditions $\begin{bmatrix} A_a \\ A_c \\ A_p \end{bmatrix} = \begin{bmatrix} D \\ 0 \\ 0 \end{bmatrix}$ at $t = 0$, we could obtain

$$C_1 = \frac{D K_a}{(K_{10} - K_a)(K_{21} - K_a) - K_{12} K_a}$$
$$C_2 = C_1 \frac{-K_a + \beta}{\alpha - \beta}$$
$$C_3 = C_1 \frac{K_a - \alpha}{\alpha - \beta}$$