Modelling and simulation

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Transfer function of the system

- State space notation of Linear time invarinat dynamic system LTI system

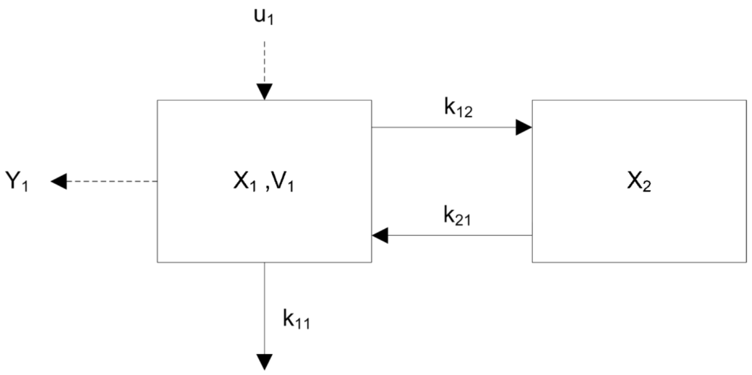
$$\dot{\mathrm{X}} = \mathrm{A.X} + \mathrm{B.U}$$

$$\mathrm{Y} = \mathrm{C.X}$$

- Transfer function is the dependence between output and input LTI system

$$\frac{\boldsymbol{L}\{\boldsymbol{Y}\}}{\boldsymbol{L}\{\boldsymbol{U}\}} = C.(s.I - A)^{-1}.\mathrm{B}$$

Transfer function of 2-compartmental model



State space notation

$$X = \begin{bmatrix} X_1 \\ X_2 \end{bmatrix} \quad Y = \begin{bmatrix} Y_1 \\ Y_2 \end{bmatrix} \quad U = \begin{bmatrix} u_1 \\ 0 \end{bmatrix}$$

$$A = \begin{bmatrix} (-k_{11} - k_{12}) & k_{21} \\ k_{12} & -k_{21} \end{bmatrix}$$

$$\mathrm{B} = \begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix}$$

$$C = \begin{bmatrix} \dfrac{1}{V_1} & 0 \\ 0 & 0 \end{bmatrix}$$

Differential equation

$$\begin{aligned} \dot{X}_1 &= (-k_{11} - k_{12}) \cdot X_1 + k_{21} \cdot X_2 + u_1 \\ \dot{X}_2 &= k_{12} \cdot X_1 + (-k_{21}) \cdot X_2 + 0 \end{aligned}$$

$$Y_1 = \frac{1}{V_1} \cdot X_1 + 0 \cdot X_2$$

$$Y_2 = 0 \cdot X_1 + 0 \cdot X_2$$

Transfer function

$$\frac{L\{Y\}}{L\{U\}} = C \cdot (s.I - A)^{-1} \cdot \mathrm{B}$$

$$\begin{bmatrix} \dfrac{\boldsymbol{L}\{Y_1\}}{\boldsymbol{L}\{u_1\}} & \dfrac{\boldsymbol{L}\{Y_1\}}{\boldsymbol{L}\{u_2\}} \\ \dfrac{\boldsymbol{L}\{Y_2\}}{\boldsymbol{L}\{u_1\}} & \dfrac{\boldsymbol{L}\{Y_2\}}{\boldsymbol{L}\{u_2\}} \end{bmatrix} = \begin{bmatrix} \frac{1}{V_1} & 0 \\ 0 & 0 \end{bmatrix} \cdot \begin{bmatrix} (-k_{11} - k_{12}) & k_{21} \\ k_{12} & -k_{21} \end{bmatrix}^{-1} \cdot \begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix}$$

$$\boldsymbol{\frac{L\{Y_1\}}{L\{u_1\}} = \frac{\frac{1}{V_1} s + \frac{1}{V_1} k_{21}}{s^2 + (k_{11} + k_{12} + k_{21}) s + k_{21} k_{11}}}$$

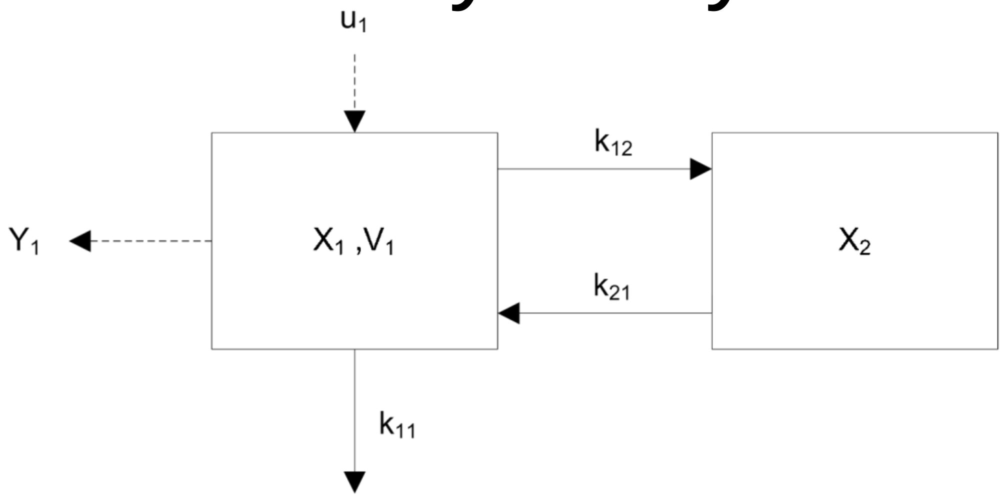
Idetifiability analysis

- The model parameters are usually unknown, such $k_{11}, k_{12}, k_{21}, V_1$
- Doctors are only able to dose input u_1 and measure drug concentrations Y_1.
- determine whether the measured variables are sufficient to estimate the unknown parameters.
  - YES, the model is identifiable**.**
  - NO, the model is unidentifiable**.**

$$\frac{\boldsymbol{L\{Y\}}}{\boldsymbol{L\{U\}}} = \frac{\boldsymbol{a_{n-1} \cdot s^{n-1} + a_{n-2} \cdot s^{n-2} + \cdots + a_1 \cdot s + a_0}}{\boldsymbol{b_n \cdot s^n + b_{n-1} \cdot s^{n-1} + \cdots + b_1 \cdot s + b_0}}$$

- Identifiability can be determined using the transfer function:
  - The transfer function is a fraction of two polynomials.
  - Polynomial coefficients a_i, b_i are called observational parameters.
  - Observational parameters are nonlinear functions of the model parameters.
  - If the model parameters can be uniquely calculated using the observation parameters, then the model is identifiable.
  - Therefore, the analysis of identifiability equals number of solution of the system of nonlinear algebraic equations.

Idetifiability analysis of 2-compartmental model



$$\frac{L\{Y_1\}}{L\{u_1\}} = \frac{\frac{1}{V_1}s + \frac{1}{V_1}k_{21}}{s^2 + (k_{11} + k_{12} + k_{21})s + k_{21}k_{11}}$$

transfer function

$$a_1 = \frac{1}{V_1}$$
$$a_0 = \frac{1}{V_1}k_{21}$$
$$b_1 = k_{11} + k_{12} + k_{21}$$
$$b_0 = k_{21}k_{11}$$

observational parameters

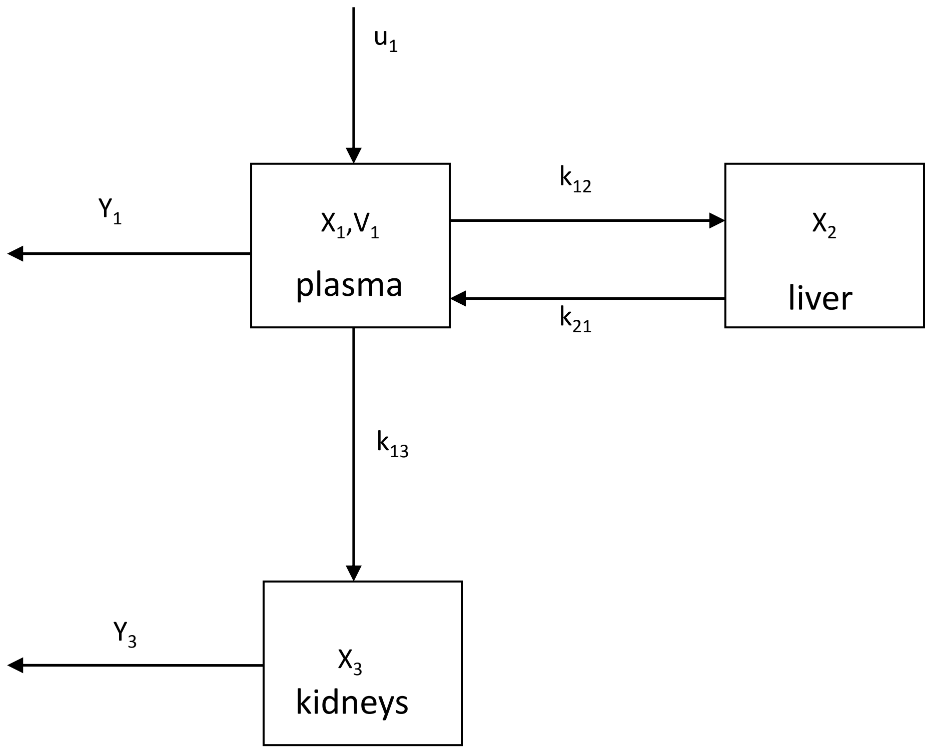
$$V_1 = \frac{1}{a_1}$$
$$k_{21} = \frac{a_0}{a_1}$$
$$k_{11} = \frac{b_0 a_1}{a_0}$$
$$k_{12} = b_1 - \frac{a_0}{a_1} - \frac{b_0 a_1}{a_1}$$

solving a system of equations

model parameters can be uniquely calculated using the observational parameters → the model identifiable

Practice 2 - assignment

- 3-compartmental model



Practice 2 - assignment

- Compose idetifiability analysis
  - Define differential equations of the model
  - Define matrix A, B, C, D
  - Define transfer function
  - Define observational parameters
  - Define model parameters
- Compose model in Simulink
  - Model parameters (k12=0.5 mg/h, k13=0.3 mg/h, k21=0.4 mg/h,V1=5l, u(0)=200 mg)

Practice 2 – desired output

- Model file *. mdl with correctly described blocks
- Short paper in *. pdf containing
  - Block diagram of the model
  - Definition equation model
  - Matrices A, B, C, D
  - Transfer function
  - Observational parameters
  - Model parameters defined by observational parameters
  - Graphical output (amount) of the simulation.