MODELLING AND SIMULATION

Lesson 5- SS 2014 – Michel Kana

What do we do in today's lesson?

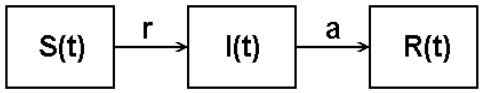
1. **Summary of the previous practice**
2. **Epidemiology models**
3. **Compartmental modeling**
4. **Summary**

Summary of the previous practice

[Population models]
Models of structured populations

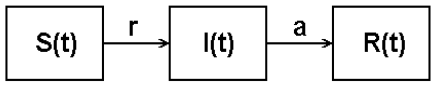
Epidemiology models - SIR

- We assume to have an epidemic with the following characteristics
  - The disease spreads through contact or close proximity between infected and healthy individuals
  - The probability for two individuals to come to contact is the same within the population
  - There is no incubation period and the disease becomes effective immediately after contact
  - The population is closed with constant size (no births neither deaths)
- SIR is a simple model for many infectious diseases, including measles , mumps and rubella
  - $S(t)$ represents the number of individuals susceptible to infection
  - $I(t)$ represents the number of infected individuals, i.e. those who show signs of illness and spreads disease further.
  - $R(t)$ represents the number of removed individuals, i.e. those in a period of isolation or resistant individuals who were previously infected and have recovered with immunity.
  - r represents the average spreading rate of infection, i.e. the adequate number of contacts sufficient for the transmission of infection between individuals.
  - a represents the removal rate, the speed of isolation or treatment of infected individuals.

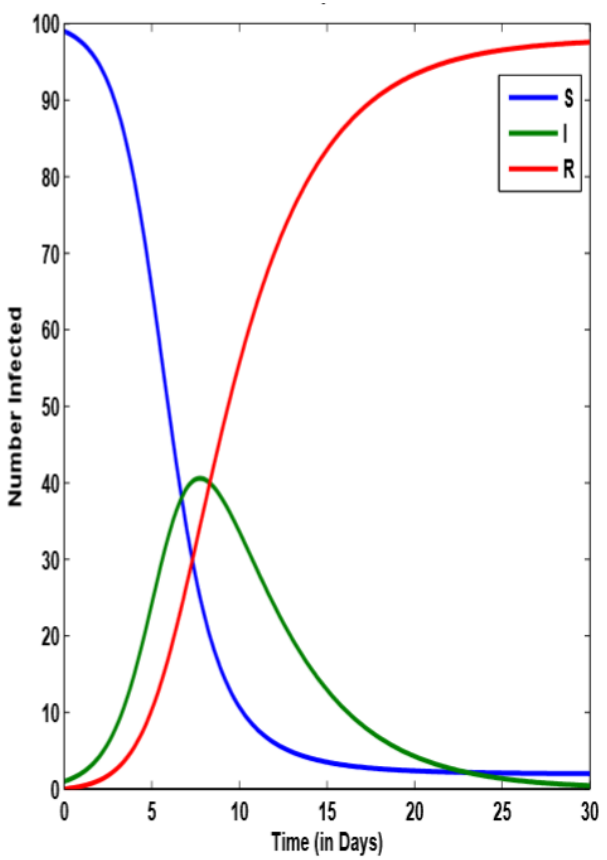


Epidemiology models - SIR

- N is the total number of individuals in the population.
- $\frac{I(t)}{N}$ represents the proportion of infected individuals in the population.
- $\frac{r \cdot I(t)}{N}$ represents the rate infected individual gives rise to new infections.
- $\frac{r \cdot I(t)}{N} \cdot S(t)$ represents the rate at which susceptible individuals encounter infected individuals and become infected.
- $a \cdot I(t)$ is the rate at which infected individuals are removed from the infective class



$$\frac{dS\ (t)}{dt} = -r \cdot S(t) \cdot I(t)$$
$$\frac{dI\ (t)}{dt} = r \cdot S(t) \cdot I(t) - a \cdot I(t)$$
$$\frac{dR\ (t)}{dt} = a \cdot I(t)$$
$$S(t) + I(t) + R\ (t) = N$$



Epidemiology models - SIR

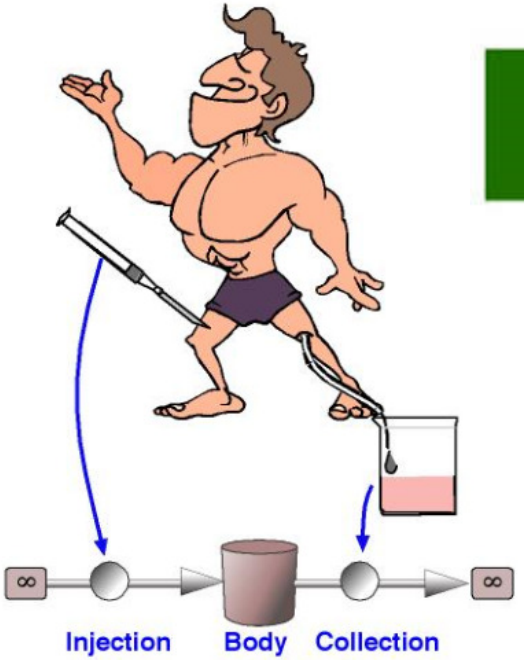
- Equilibrium occurs
  - Before disease begins spreading $S(0) = N$ and $R(0) = 0$
  - Disease begins to spread if $\frac{dI\,(t)}{dt} > 0$
    - $r \cdot S(0) \cdot I(t) - a \cdot I(t) > 0$
    - $(r \cdot S(0) \cdot -a) \cdot I(t) > 0$
    - $r \cdot S(0) \cdot -a > 0$
    - $\frac{r}{a} \cdot S(0) > 1$
      - $\frac{r}{a} \cdot S(0)$ is the basic contact number
      - $\frac{r}{a} \cdot S(0) > 1$: infection will be established in the population. Infection peaks and then disappears.
      - $\frac{r}{a} \cdot S(0) < 1$: the infection dies out and there is no epidemic.
  - After disease has moved through the entire population $S = 0$ and $R = N$

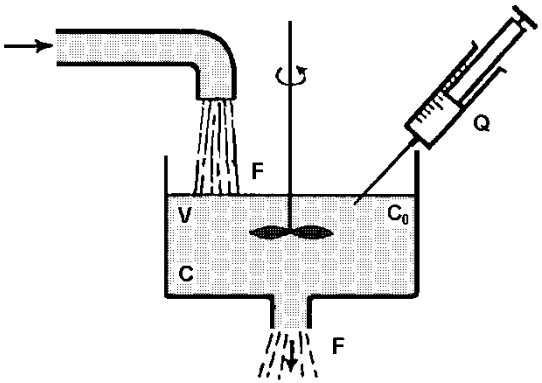
$$\frac{dS\,(t)}{dt} = -r \cdot S(t) \cdot I(t)$$
$$\frac{dI\,(t)}{dt} = r \cdot S(t) \cdot I(t) - a \cdot I(t)$$
$$\frac{dR\,(t)}{dt} = a \cdot I(t)$$
$$S(t) + I(t) + R\,(t) = N$$

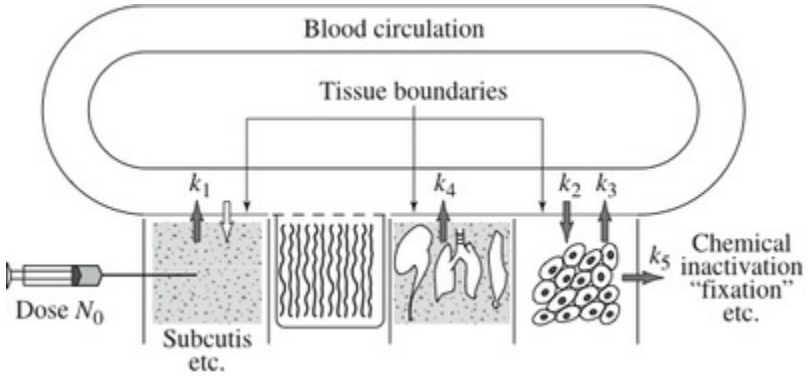
Introduction to compartment models

- Compartment models are often used to describe transport of material in biological systems
  - Material could be energy, substance, individuals of a population
  - Compartments can represent organs, species of animal and plants
  - Material can either
    - flow from one compartment to another,
    - or it can be added from the outside through a source
    - or it can be removed through a drain or a sink
- We assume that
  - all material in the compartment is homogeneous
  - The system is closed in some sense. In other words the compartments may not include un-accounted for sources or sinks
  - All transport channels are known and the equation of mass balance can be applied

Example of compartment models

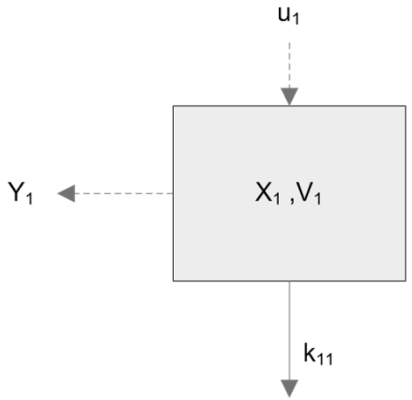






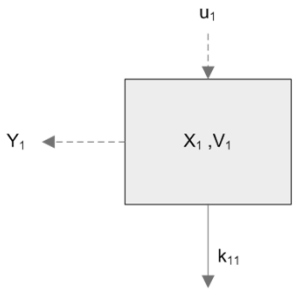
Pharmacokinetic model with 1 compartment

- A one-compartment model is a simplified view of a homogeneous body where drug quantity u_1 is input as bogus
- The amount of drug X_1 is distributed over the hypothetical volume V_1.
- An experimental setup measures the concentration of drug in the body $Y_1 = X_1/V_1$.
- The rate of extraction of drug k_{11} from the body is proportional to the amount of drug inside the body.



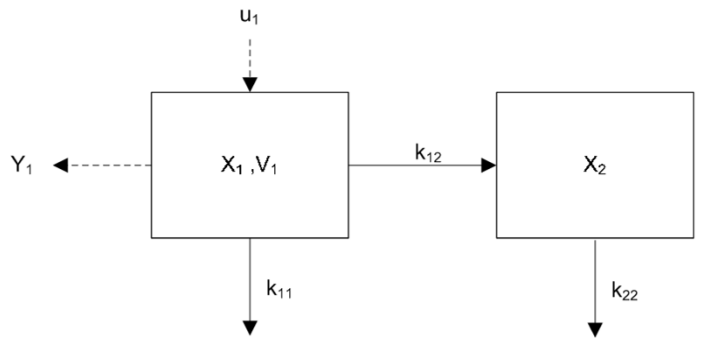
Pharmacokinetic model with 1 compartment

- The change of drug amount over the time in the compartment is equal to the drug input minus drug output
  - $\frac{dX_1}{dt} = \dot{X}_1 = u_1 - k_{11}X_1$
- Observation or measurements of drug concentration in the body is equal to the drug amount in the body divided by the hypothetical volume
  - $Y_1 = \frac{1}{V_1}X_1$
- The observation function shows the change of concentration of drug in the compartment over the time and can be visualized for given parameter values
  - $\mathbf{Y_1(t) = \left(\frac{1}{V_1} e^{-k_{11}t}\right) u_1}$



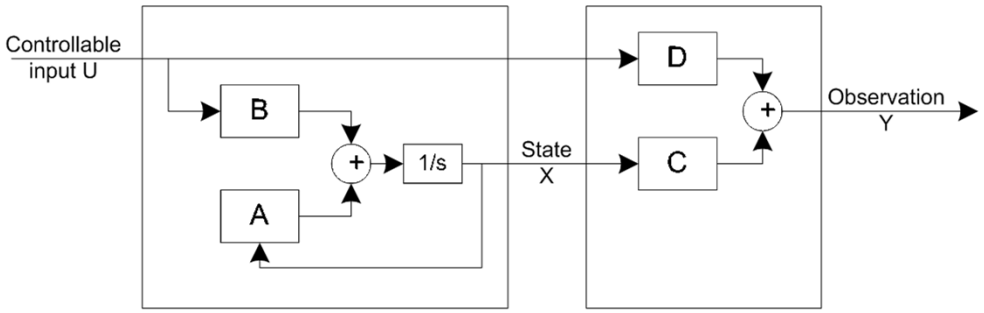
Pharmacokinetic model with 2 compartments

- The change of drug amount (input minus output) in the compartments is given by the following differential equations:
  - $\dot{X}_1 = (-k_{11} - k_{12})X_1 + 0.X_2 + u_1$
  - $\dot{X}_2 = k_{12}X_1 + (-k_{22})X_2 + 0$
- Observation or measurements of drug concentration in the body is equal to the drug amount in the body divided by the hypothetical volume
  - $Y_1 = \frac{1}{V_1}X_1 + 0.X_2$



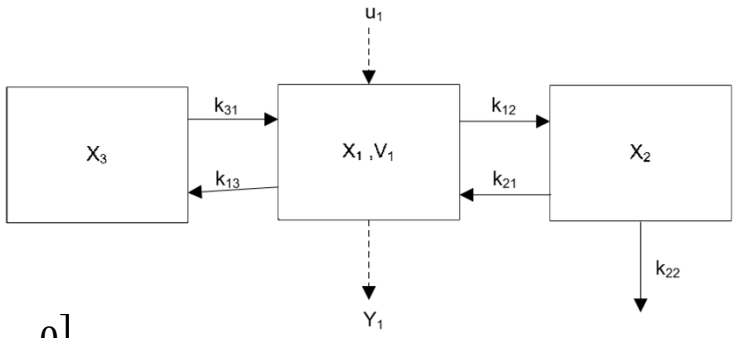
Pharmacokinetic model with 2 compartments

- We rewrite this differential equation using matrixes, we obtain the so called **state-space notation** of the **Linear Time Invariant Lumped Parameters Dynamic System**
  - $\dot{\mathrm{X}} = \mathrm{A}.\mathrm{X} + \mathrm{B}.\mathrm{U}$
  - $\mathrm{Y} = \mathrm{C}.\mathrm{X} + D.U$
    - $X = \begin{bmatrix} X_1 \\ X_2 \end{bmatrix}$ is the state vector
    - $U = [u_1]$ is the input vector
    - $A = \begin{bmatrix} (-k_{11} - k_{12}) & 0 \\ k_{12} & -k_{22} \end{bmatrix}$ is the system or parameter matrix
    - $B = \begin{bmatrix} 1 \\ 0 \end{bmatrix}$ is the input matrix
    - $Y = [Y_1]$ is the observation vector
    - $C = \begin{bmatrix} \frac{1}{V_1} & 0 \end{bmatrix}$ is the output matrix



Pharmacokinetic model with 3 compartments

$$\dot{X}_1 = (-k_{12} - k_{13}) \cdot X_1 + k_{21} \cdot X_2 + k_{31} \cdot X_3 + u_1$$
$$\dot{X}_2 = k_{12} \cdot X_1 + (-k_{21} - k_{22}) \cdot X_2 + 0.X_3 + 0$$
$$\dot{X}_3 = k_{13} \cdot X_1 + 0.X_2 + (-k_{31}) \cdot X_3 + 0$$
$$Y_1 = \frac{1}{V_1} \cdot X_1 + 0 \cdot X_2 + 0 \cdot X_3$$



$$X = \begin{bmatrix} X_1 \\ X_2 \\ X_3 \end{bmatrix} \quad Y = [Y_1]$$
$$U = [u_1]$$
$$A = \begin{bmatrix} -k_{12} - k_{13} & k_{21} & k_{31} \\ k_{12} & -k_{21} - k_{22} & 0 \\ k_{13} & 0 & -k_{31} \end{bmatrix} \quad B = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} \quad C = \begin{bmatrix} \frac{1}{V_1} & 0 & 0 \end{bmatrix}$$

Summary of today's lesson

[Population models]
Epidemiology models
Pharmacokinetic models

[What is next?]
Pharmacokinetic model.