MODELLING AND SIMULATION

Lesson 13 - SS 2014 – Michel Kana

What do we do in today's lesson?

1. **Parameters Estimation**

Semester schedule

17ABBMS

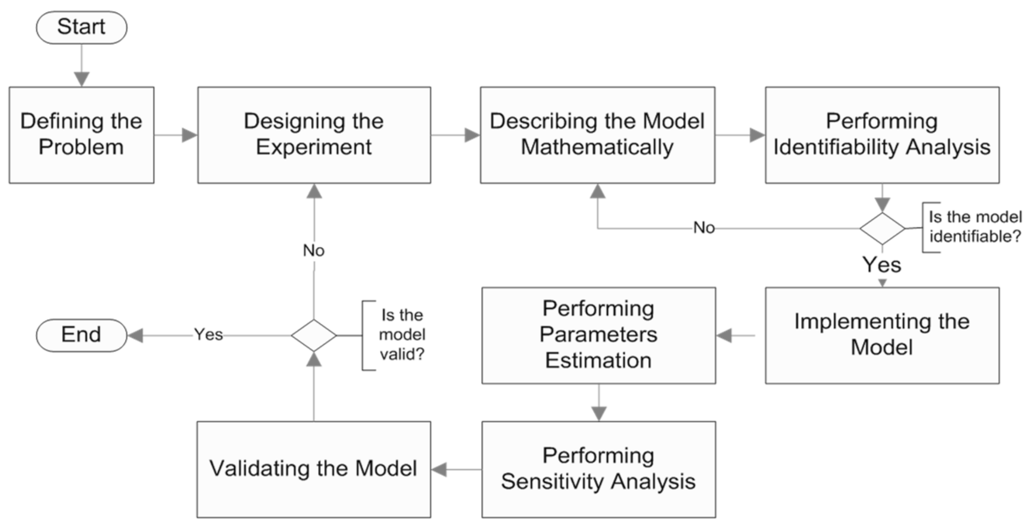
- **Population models**
  - 1th lecture
    Introduction to Mathematical Modeling
  - 2nd lecture
    Models for single specie populations
  - 3rd lecture
    Models for two species populations
  - 4th lecture
    Epidemiology models
- **Compartmental models**
  - 5th lecture
    1 - compartmental models
  - 6th lecture
    More - compartmental models
  - 7th lecture
    More - compartmental models
- **Advanced Topics**
  - 9th lecture Apr 15
    Identifiability analysis
  - 12th lecture May 6
    Identifiability analysis
  - 13th lecture May 13
    Identification of model parameters
  - 14th lecture May 20
    Sensitivity analysis

8th (Apr 8), 10th (Apr 22) and 11th (Apr 29) lessons are postponed
11th (May 1) and 12th (May 8) tutorials are postponed

May 27: final exam, May 29: correction of final exam
June 1: final presentations and grades

Purpose of parameters estimation

- **Performing parameters estimation**
  - estimate the values of unknown parameters using an identifiable model and experimental data
    - example
      - estimate the correct rate of elimination of glucose from the body (k_{11}) and apparent body volume (V_1) using the amount of glucose input (u_1) and the glucose concentration in urines (Y_1)



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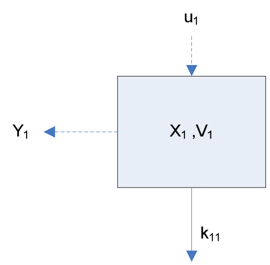

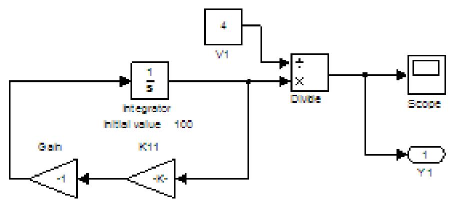

Simulink Model – model.mdl

Time (hour)	Concentration (mg/l)
0	19
0.5	10
1	7
1.5	5
2	4
...	...

Measured Data – t_i b_i

Matlab files optim.m & optimfun.m

Parameters values for V_1 and K_{11}

Methodology for parameters estimation

- Collecting experimental data
  - a specific drug dosage is given to subjects and drug concentrations are measured in certain compartments at regular time intervals
    - The measured data represent the **observed behavior** of the system
- Simulating the model with an initial guess of parameter values
  - For initial parameter values it would produce simulated values of drug concentration change in the compartment
    - The model output is called **simulated behavior**
- Fitting experimental data
  - Calculate the difference between simulated values and measured values
    - That difference is called **objective function** or **residuals**
- Estimate the perfect parameters values
  - Find the unique set of parameter values for which the difference between simulated and observed behavior is closed to zero
    - This is an optimization problem

Formal definition of parameters estimation

- There is a range of methods for parameters estimation including approaches based on non-linear least squares, maximum likehood, Bayesian estimation, simplex method.
- The nonlinear least squares optimization can be expressed as follows:
  - $Find\ x^*, a\ local\ minimizer\ of$

$$F(x) = \sum_{i=1}^{m} (f_i(x))^2$$

$$where\ f_i\colon \mathbb{R}^n \to \mathbb{R}\ are\ given\ functions$$

    - where, x is the parameters vector
    - f is the objective function
- Example of a 1-compartment model
  - the physiological process is modeled by a nonlinear function $M(x, t_i)$ that depends on a parameter vector x and time t_i.
    - $x = [k_{11}\ V_1]$ and $M(x, t_i) = Y_1(t_i)$
  - the measured drug concentration in blood at time t_i is given by b_i
  - the objective function is $f_i(x) = M(x, t_i) - b_i$

Linear regression

- Assuming a linear model of time $y = a.t + b$, where a, b are unknown parameters
- Assuming N pair of observations $(t_1, y_1), (t_2, y_2) \cdots (t_N, y_N)$
- We want to minimize the objective function $L(a,b) = \sum_{i=1}^{N} (y_i - (a.t_i + b))^2$
- For this purpose we solve
  - $\frac{\partial L}{\partial a} = 0$ and $\frac{\partial L}{\partial b} = 0$
- $\frac{\partial L}{\partial b} = \sum_{i=1}^{N} 2(-1)(y_i - (a.t_i + b)) = -2\left(\sum_{i=1}^{N} y_i \; - a\sum_{i=1}^{N} t_i \; - bN\right)$
  - $\frac{\partial L}{\partial b} = 0 \Longrightarrow \frac{1}{N}\sum_{i=1}^{N} y_i \; = \frac{a}{N}\sum_{i=1}^{N} t_i \; + b \Longrightarrow \bar{y} = a\bar{t} + b$
  - the best fitting straight line passes through the “average” of the data points $(\bar{y}, \bar{t})$
- $\frac{\partial L}{\partial a} = \sum_{i=1}^{N} -2t_i(y_i - (a.t_i + b)) = -2\left(\sum_{i=1}^{N} t_i y_i \; - a\sum_{i=1}^{N} {t_i}^2 \; - b\sum_{i=1}^{N} t_i \right)$
  - $\frac{\partial L}{\partial a} = 0 \Longrightarrow \frac{1}{N}\sum_{i=1}^{N} t_i y_i \; = \frac{a}{N}\sum_{i=1}^{N} {t_i}^2 + \frac{b}{N}\sum_{i=1}^{N} t_i \Longrightarrow \overline{ty} = a\overline{t^2} + b\bar{t}$
- $\begin{cases} a\bar{t} + b = \bar{y} \\ a\overline{t^2} + b\bar{t} = \overline{ty} \end{cases}$
  - $\Longrightarrow a = \frac{\overline{ty} - \bar{t}.\bar{y}}{\overline{t^2} - \bar{t}^2}$
  - $\Longrightarrow b = \bar{y} - a\bar{t}$