MODELLING AND SIMULATION

Lecture 1 - SS 2014 – Michel Kana

What do we do in today's lecture?

1. Organization of the course
2. Entrance test
3. Semester Schedule
4. Requirements for a grade
5. Why modeling and simulation?
6. Modeling guidelines
7. Review of some mathematical concepts
8. Summary

How is the course organized?

Biomedical Technician BMT (17ABBMS)

- **1 group**
- **2 students**
- **13 lectures x 1.5 hours**
- **13 tutorials x 1.5 hours**

17ABBMS - Modelling and Simulation WWW pages (2+2) - even and odd week												
hour	1	2	3	4	5	6	7	8	9	10	11	12
time	8:00 - 8:50	9:00 - 9:50	10:00 - 10:50	11:00 - 11:50	12:00 - 12:50	13:00 - 13:50	14:00 - 14:50	15:00 - 15:50	16:00 - 16:50	17:00 - 17:50	18:00 - 18:50	19:00 - 19:50
Monday												
Tuesday	KL:A-12 - Lec M. Kana 1(1 stud.)											
Wednesday												
Thursday	KL:B-505 - Pra D. Müllerová 1(1 stud.)											
Friday												

Lectures	Practice	Laboratory	Other

What you should already know

Biomedical Technician BMT (17ABBMS)

- **Linear Algebra and Differential Calculus**
- **Integral Calculus**
- **Programming in Matlab**
- **Introduction to Signals and Systems**

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**
  - 8th lecture
    Identifiability analysis
  - 9th lecture
    Identifiability analysis
  - 10th lecture
    Identification of model parameters
  - 11th lecture
    Sensitivity analysis
  - 12th lecture
    Final exam
  - 11th lecture
    Final presentations

Requirements for grade

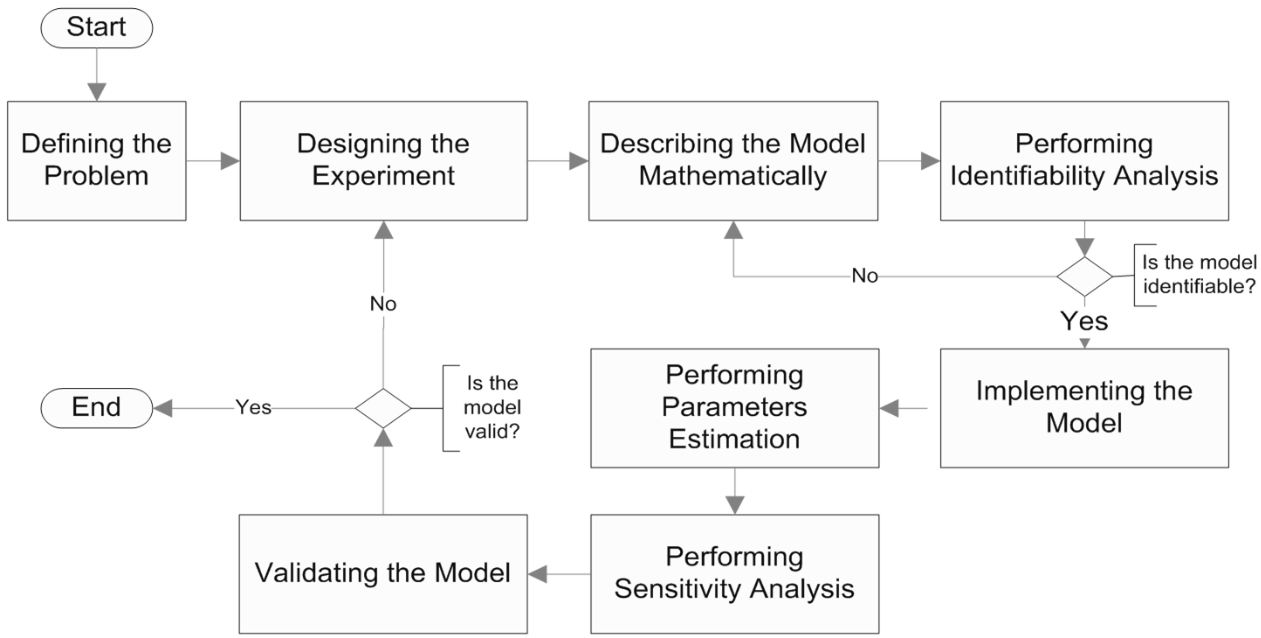
- Attendance to ALL tutorials
  - In case of non-attendance, provide a valid reason
- 12 points from tutorials
  - 1 point per week for each attendance
- 28 points from practical projects
  - 10 points for designing your project
  - 13 points for implementing your project
  - 5 points for presenting your project
  - Guidelines will be given in lesson 8
- 60 points from final exam
  - 40 points about the lectures
  - 20 points about the tutorials

Entrance test

Motivation for Modeling and Simulating

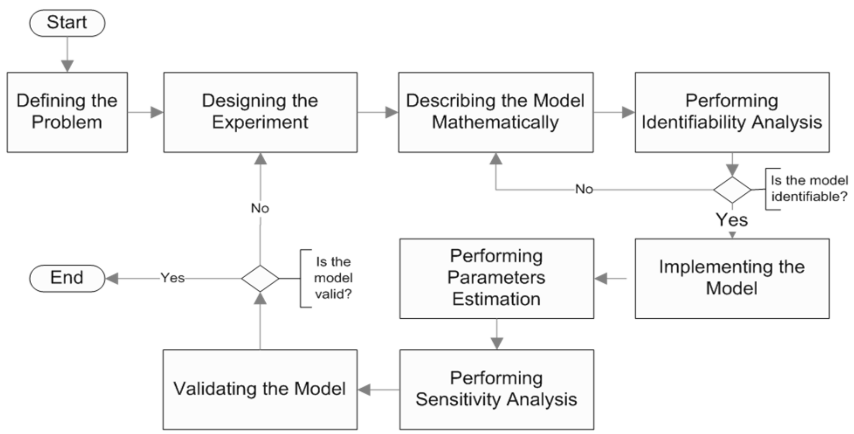
- Goal: gain knowledge about complex physiological and pathophysiological behavior
  - understanding and testing hypothesis
  - measuring inferences
  - teaching
  - simulating and designing experiments
- A model is an approximated representation of the real system using mathematical tools
  - data-driven or black box models
  - physiologically-based models
- Examples of applications:
  - study the liberation, absorption, distribution and elimination of drugs in the body
  - estimate quantities of a substrate or hormone that are not directly measurable because they are in non-accessible portion of the body
  - predict the most possible time when a patient with renal failure should undergo haemodialysis
  - understand heart failure, which is a leading cause of death in humans
  - estimates the tone of sympathetic and parasympathetic discharge on the cardiovascular system

Guidelines for Modeling



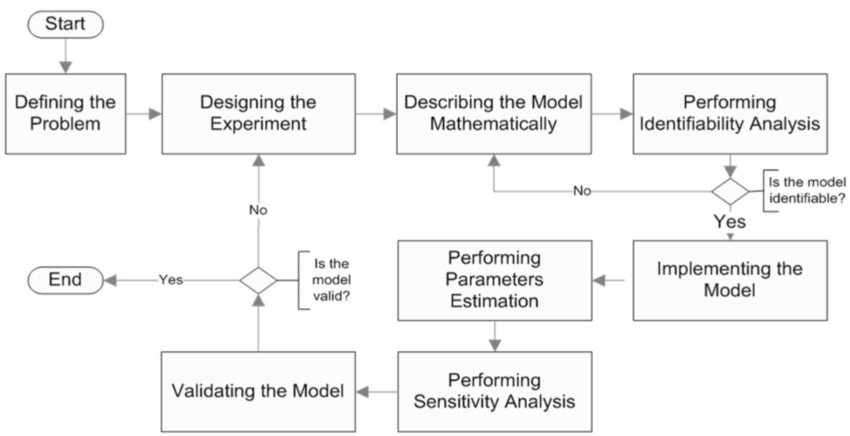
Guidelines for Modeling

- **Defining the problem**
  - define the biological or physiological background of the process or problem we aim to model
    - example
      - study the extraction rate of glucose from the body into urines in order to understand glucosuria
  - make assumptions
    - examples
      - the body is considered as an homogeneous compartment system with blood as solvent and glucose as solute
      - glucose is extracted from the body using urines as a medium
  - set the focus to some processes and eliminate others
    - example
      - we do not consider insulin and glucagon regulation



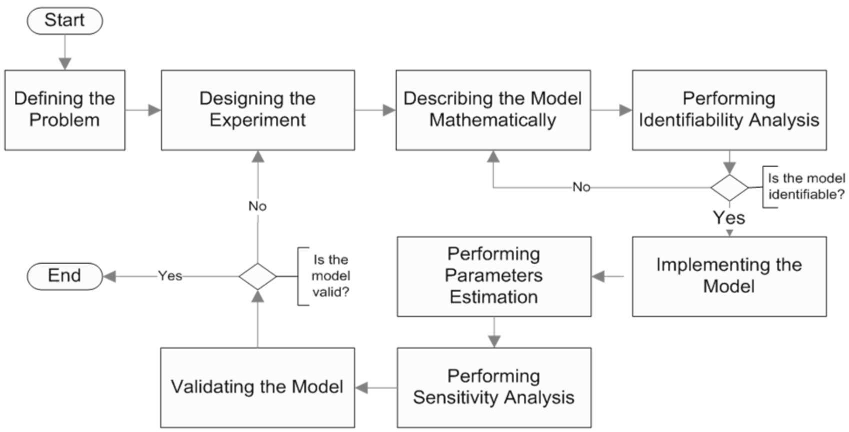
Guidelines for Modeling

- **Designing the experiment**
  - build an experimental setup for making observations in order to validate the model later on
  - define inputs
    - example
      - one-time 100 mg intra-venous glucose intake
  - define outputs
    - example
      - glucose amount in urines in mg, measured per hour over 12 hours



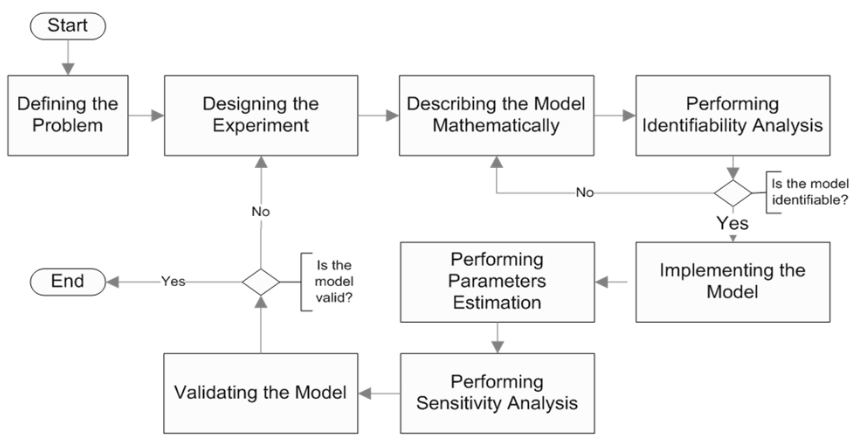
Guidelines for Modeling

- **Describing the model mathematically**
  - describe the static and dynamic properties of the system using mathematical notations:
    - differential equations, phase plane analysis, stability theory, bifurcation theory, linear transformation theory, linear systems theory, complex variable techniques, partial differential equations, asymptotic methods, perturbation theory
  - define input variables and constants
    - example
      - one-time glucose input as a constant with value 100 mg
  - define state variables
    - example
      - glucose amount in the urines in mg
  - define parameters
    - examples
      - rate of extraction of glucose into urines



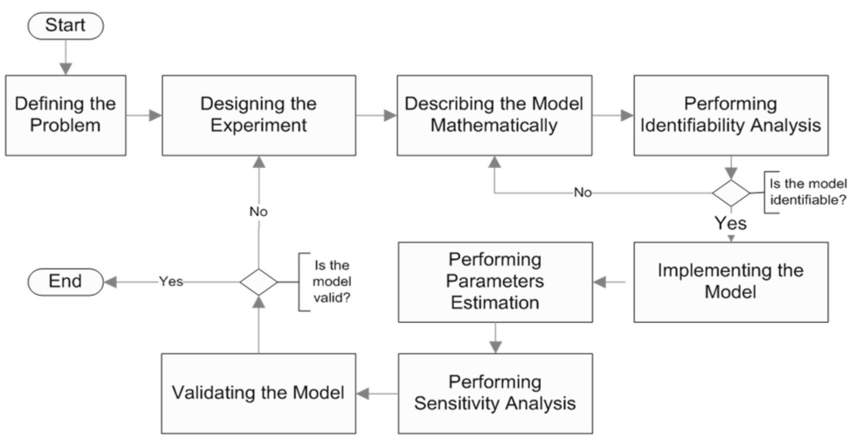
Guidelines for Modeling

- **Performing identifiability analysis**
  - answers the question if the hidden model parameters are calculable given perfect input-output data
    - example
      - can the rate of elimination of glucose into urines can be estimated if we know the amount of glucose intake and the glucose amount in urines?
  - if we cannot identify parameters it is advisable to return to the previous stage and readjust the mathematical model



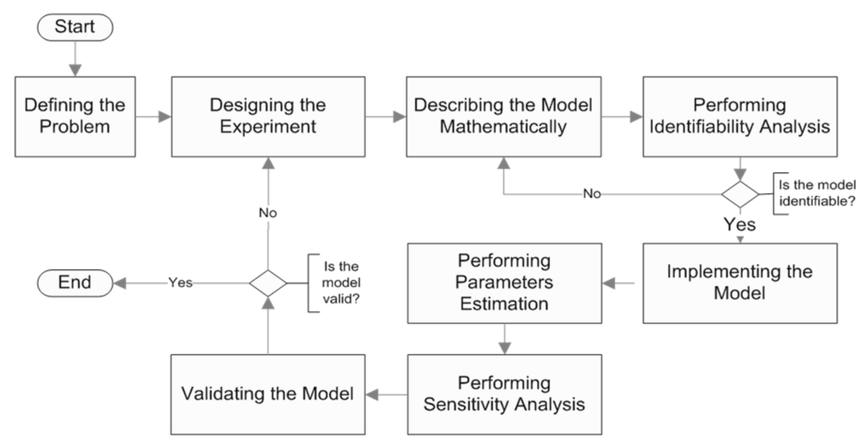
Guidelines for Modeling

- **Implementing the model**
  - solve the model on a computer
    - example
      - Simulink implementation of the model of glucose extraction to urines
  - visually observe how the computer model is predicting physiological variables
    - example
      - the change of glucose amount in urines over time
  - the computer model produces predictive values of the output vector, also called **simulated behavior**



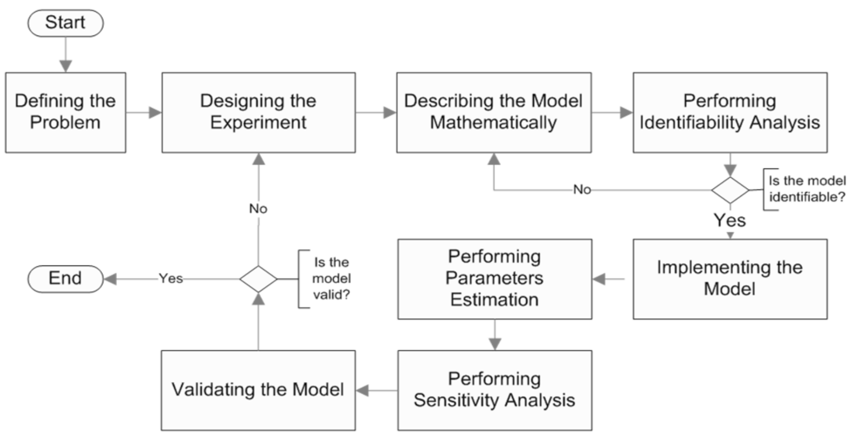
Guidelines for Modeling

- **Performing parameters estimation**
  - perform experiments and collect real life measurements of the observable variables
    - example
      - 100 mg glucose is given to subjects orally, urine samples are taken every hour and glucose amount is measured
  - the measured data represent the **observed behavior** of the system
  - the difference between simulated and observed behavior is called **residual**
  - find the unique set of parameter values for which the residual is closed to zero
    - example
      - find the extraction rate for which the computer model will simulated the same glucose amounts that were measured



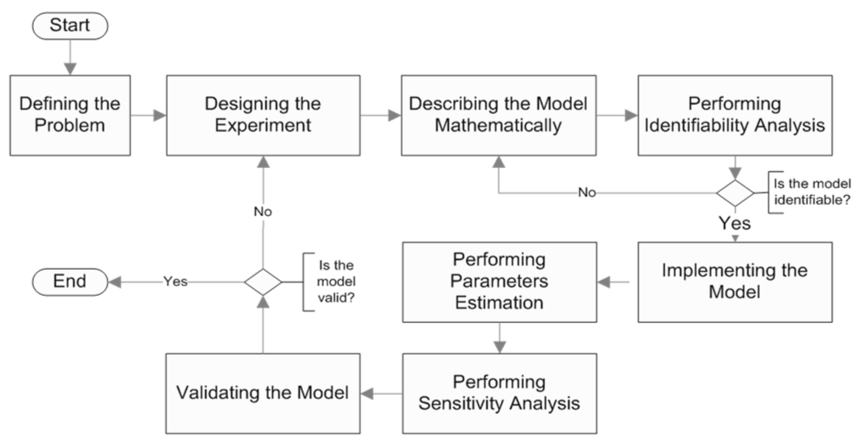
Guidelines for Modeling

- **Performing sensitivity analysis**
  - check if the quality of the measurement data is sufficient for identifying the model parameters
    - example
      - should urine samples be taken every 30 min instead?
  - finding the optimal experimental design that helps finding the best possible parameter estimate
  - usually by performing partial differentiation of model outputs with regards to the parameters



Guidelines for Modeling

- **Validating the model**
  - validate the model performance against known physiological behaviour
    - example
      - study residuals from the parameters estimation activity and the plausibility of the estimates
  - evaluate the variances and correlation of parameter estimates



Review of some mathematical concepts

- **Polynomial**
  - $f(x) = a_n x^n + a_{n-1} x^{n-1} + \cdots + a_2 x^2 + a_1 x + a_0$
  - coefficients of polynomial, order of polynomial, roots of polynomial
- **Equations**
  - equation with one variable
  - linear system of equations
  - non - linear system of equations
- **Matrices**
  - square schema of numbers, row and column
  - row matrices, column matrices
  - square matrices, main diagonal of matrix, identity matrix
  - matrix operations: sum, difference, product, determinant, transpose of matrix, inverse matrix
- **Differential equations**
  - mathematical equation which contains derivative of function
  - linear differential equation and system of equations

Summary of today's lecture

[Organization of practices]
13 hours with modeling guidelines, population modeling, compartmental modeling, and the creation of own models.
To obtain the credit you need 50 points.
12 points can be obtained for active participation in the practices. 60 points can be obtained for the final exam, which will take place in the 12th lesson, 28 points can be obtained from final presentations that will take place in the 13th lesson.

[Mathematical concepts]
Polynomials, equations, matrices

[Modeling guidelines]
Defining the Problem, Designing the Experiment, Describing the Model Mathematically, Performing Identifiability Analysis, Implementing the Model, Performing Parameters Estimation, Performing Sensitivity Analysis, Validating the Model

[What comes next?]
Next week we will study single specie population models