Parameter Estimation for Dynamic Biological Systems I (PE I)

Lecturer:

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Room: to be announced

Usability: Master of Mathematics

Prerequisites: Bachelor in mathematics, bioinformatics, statistics or related fields.
Basic MATLAB programming skills.

Exercises: Computer exercises and small homework assignments.

ECTS: 6 (SWS 2+2)

Number of participants: < 20

Language: english

Topic: Mathematical models are nowadays essential for the quantitative assessment of technical, physical, chemical, and biological processes. While a broad class of models is used in the different field, almost all models share one common property: the need for accurate parameter values. Due to experimental constraints, many parameters cannot be measured directly, but have to be estimated from the available experimental data.

In this course, we will introduce deterministic modeling approaches for biochemical reaction networks. These modeling approaches can be used to describe, e.g., signal transduction and metabolic processes. For these models the respective parameter estimation problem will be formulated and methods will be presented to solve these problems. As parameter estimates carry uncertainties due to limited amounts of data and measurement noise, we furthermore provide methods for a rigorous analysis of parameter uncertainties. This is crucial to evaluate the model uncertainties as well as the predictive power of models.

The participants will gather hands-on experiences with parameter estimation and uncertainty analysis, including the implementation of own models and estimation procedures in MATLAB. The estimation methods are presented in the context of biological processes, but the approaches are applicable in many other fields.

Aims:

After the course, the participants can:

1. model biochemical reaction networks using ODEs.
2. solve parameter estimation problems for ODEs using MATLAB.
3. analyze the uncertainty of parameter estimates using MATLAB.
4. critically evaluate parameter estimation procedures.

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Topic 1 **Modeling of biochemical reaction networks in a nutshell ……..…. 2 lectures**

1) Introduction of biochemical reaction networks (including several examples)
2) Mass action and Michaelis-Menten kinetics
3) Reaction rate equation (RRE)

   (The RRE is a system of ordinary differential equations which can be used describe the dynamics of reaction networks. It is widely used in chemistry, biochemistry and biology. In this lecture we develop methods for systems of ordinary differential equations and illustrate them using different RRE models.)

Topic 2 **Maximum likelihood estimation for RREs ……..……..…. 4 lectures**

1) Likelihood function
2) Maximum likelihood estimation as optimization problem
3) Local and global optimization
   a. Gradient descent and interior point methods
   b. Multi-start optimization

Topic 3 **Identifiability and uncertainty analysis for RREs ……..……..…. 3 lectures**

1) Structural and practical identifiability
2) Uncertainty analysis of and confidence intervals for parameters
   a. Asymptotic confidence intervals
   b. Bootstrapping confidence intervals
   c. Profile likelihoods

Topic 4 **Bayesian parameter estimation for RREs ……..……..……..…. 3 lectures**

1) Bayes' theorem and Bayesian statistics
2) Markov chain Monte-Carlo sampling
3) Bayesian confidence intervals for parameter estimates and predictions

Topic 5 **Properties of estimators (e.g. bias and variance) ……..……..……..…. 1 lectures**

Topic 6 **Summary and Outlook ……..……..……. 1 lectures**