Statistics in Toxicology I (Modelling)
Statistics in Toxicology II (Testing)

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Organization

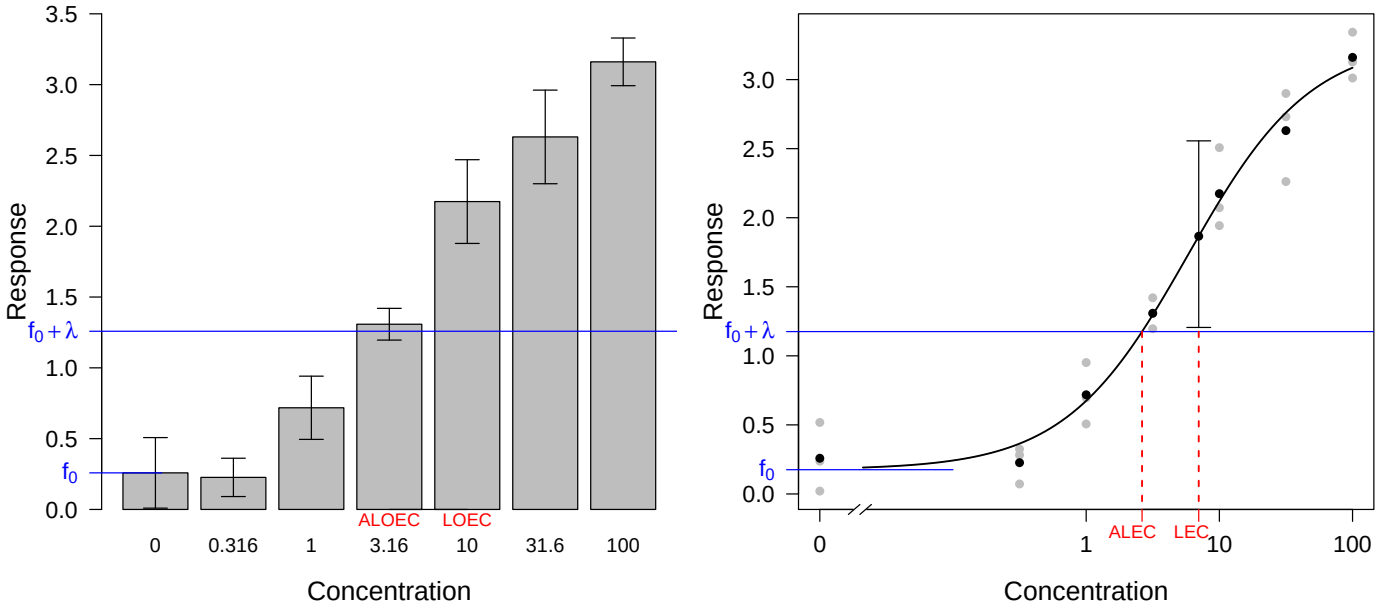
- Suitable modules: MS 6-7 / MD Applications
- Two separate modules with separate exams, 4.5 ECTS each
- In the first seven weeks, Tox I will be given with 4 weekly hours of lecture and 2 weekly hours of exercises
- In the last seven weeks, Tox II will be given with 4 weekly hours of lecture and 2 weekly hours of exercises
- Participation in only one part or in both parts is possible
- Statistics in Toxicology I (Modelling)
  - Lecturer: Franziska Kappenberg
  - Takes place in the first half of the semester, i.e. 9.10.-1.12.
  - Exam on 12.12., retry exam in the end of March
- Statistics in Toxicology II (Testing)
  - Lecturer: Jörg Rahnenführer
  - Takes place in the second half of the semester, i.e. 4.12.-2.2.
  - Exam in February, retry exam in the end of March

Organization

- Lecturer (part II): Prof. Dr. Jörg Rahnenführer, 'Statistical Methods in Genetics and Chemometrics'
  - Contact: rahnenfuehrer@statistik.tu-dortmund.de
- Lecturer (part I) and exercises: Dr. Franziska Kappenberg, research associate of Prof. Rahnenführer
  - Contact: kappenberg@statistik.tu-dortmund.de
- Moodle: individual Moodle courses for each part
  - Will be linked via the LSF
- The grade will be determined via a written exam for each part separately
- Admission to the written exam will be gained via one corrected exercise sheet for each part, in addition there will be voluntary weekly exercise sheets
- Lecture dates: Monday, 10.15-11.45 and Thursday, 12.30-14.00
- Times for exercises: to be announced

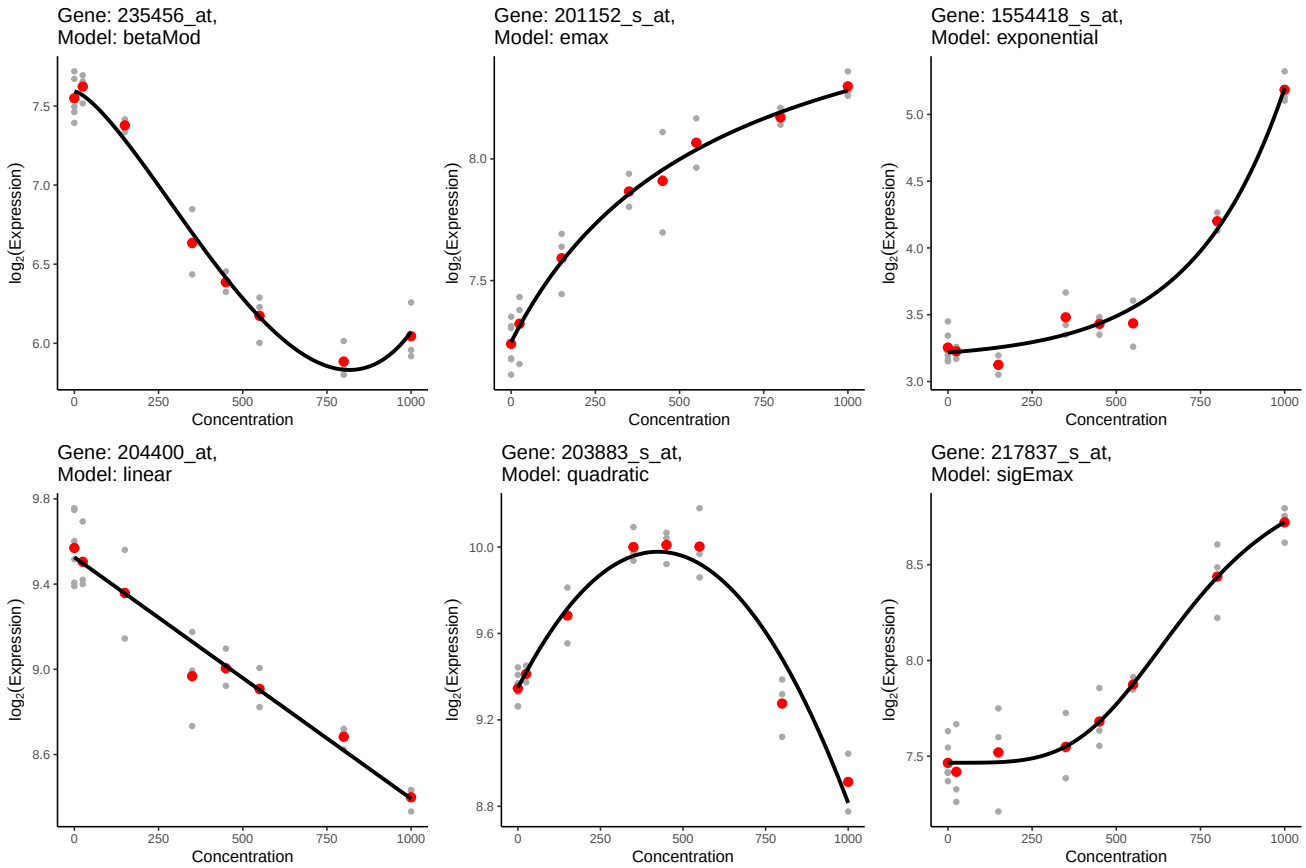
Stats in Tox I - Modelling: Motivation

- Different approaches to analyzing dose-response data: Consider only the actually measured doses (left) or perform interpolation by a modelling approach
- Often, the goal is to determine 'alerts', where a pre-specified effect level is attained



Stats in Tox I - Modelling: Motivation

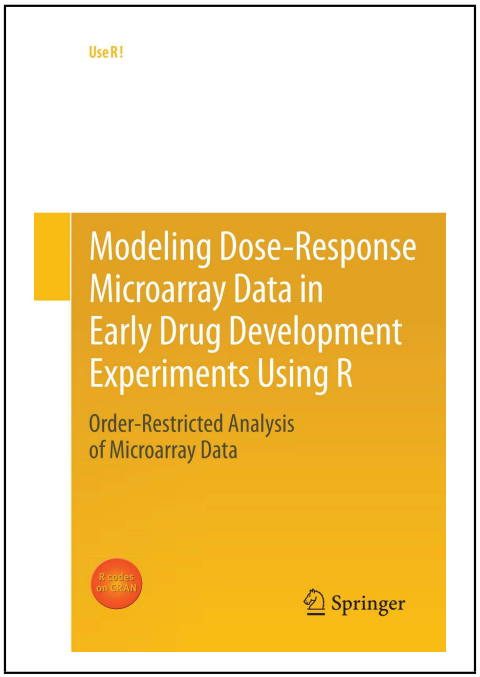
Different profiles can be observed, thus a variety of concentration-response models need to be taken into account:



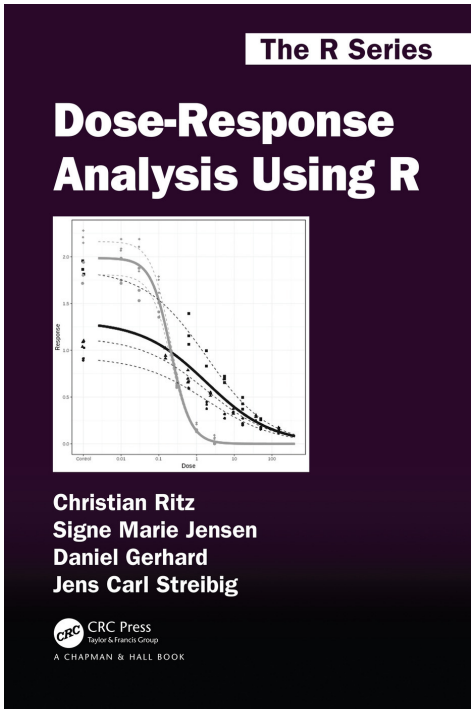
Stats in Tox I - Modelling: Contents

- Isotonic regression
  - Estimation under order-restrictions
- Basics of concentration-response modelling
  - Overview over different models
  - Models for different types of data
  - Calculation of alert concentrations
  - Modelling vs. testing
  - Optimal design considerations
- Model selection and model averaging
  - The MCP-Mod methodology
  - Model averaging
- Genomic concentration-response data
  - Multiple testing
  - Bi- and order-restricted clustering

Stats in Tox I - Modelling: Literature



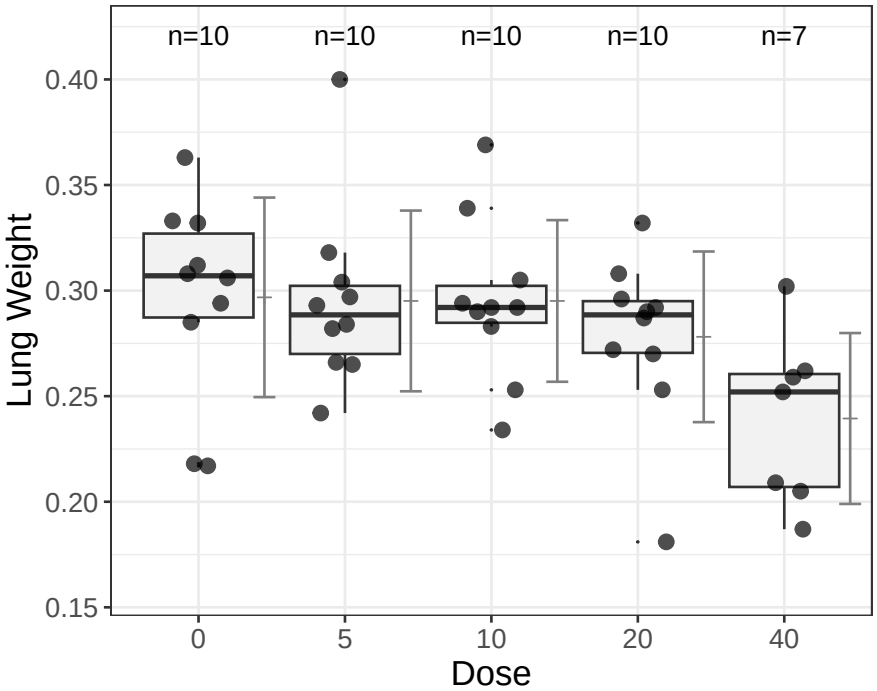
- Lin, D., Shkedy, Z., Yekutieli, D., Amaratunga, D., Bijnens, L. (Eds.)
- Isotonic regression and order-restricted clustering are based on this book

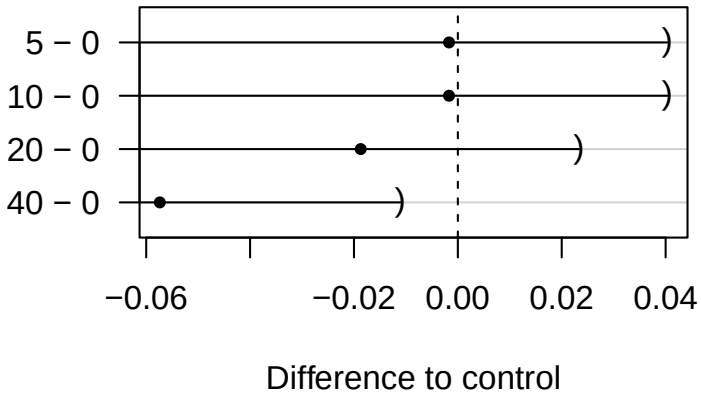


- Christian Ritz, Signe Marie Jensen, Daniel Gerhard, Jens Carl Streibig
- Introduction of the `drc`-package used for modelling

Stats in Tox II - Testing: Motivation

Consider the effect of a compound on the weight of mices' lungs for increasing doses of a compound. Multiple comparisons against the negative control, significant result only for the highest dose.

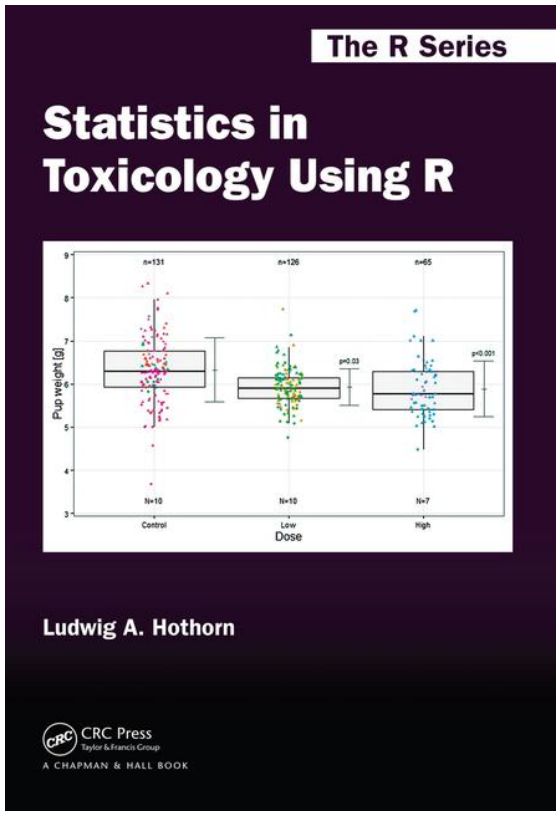




Stats in Tox II - Testing: Contents

- Proof of hazard using multiple comparisons with negative control
  - Multiple testing
  - Tests for normally distributed endpoints and for proportions
- Trend tests
  - Analysis of long-term effects in cancer studies
  - Survival analysis, tests for survival endpoint
- Analysis of effects in mutagenicity assays
  - Mixture distributions
  - EM algorithm
- Dose-finding in Phase I clinical trials

Stats in Tox II - Testing: Literature



- Ludwig A. Hothorn
- associated R-package on github with example datasets