Modeling Dose-Response Microarray Data in Early Drug Development Experiments Using R: Order-Restricted Analysis of Microarray Data (Use R!)

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This book focuses on the analysis of dose-response microarray data in pharmaceutical settings, the goal being to cover this important topic for early drug development experiments and to provide user-friendly R packages that can be used to analyze this data. It is intended for biostatisticians and bioinformaticians in the pharmaceutical industry, biologists, and biostatistics/bioinformatics graduate students.

Part I of the book is an introduction, in which we discuss the dose-response setting and the problem of estimating normal means under order restrictions. In particular, we discuss the pooled-adjacent-violator (PAV) algorithm and isotonic regression, as well as inference under order restrictions and non-linear parametric models, which are used in the second part of the book.

Part II is the core of the book, in which we focus on the analysis of dose-response microarray data. Methodological topics discussed include:

- Multiplicity adjustment
- Test statistics and procedures for the analysis of dose-response microarray data
- Resampling-based inference and use of the SAM method for small-variance genes in the data
- Identification and classification of dose-response curve shapes
- Clustering of order-restricted (but not necessarily monotone) dose-response profiles
- Gene set analysis to facilitate the interpretation of microarray results
- Hierarchical Bayesian models and Bayesian variable selection
- Non-linear models for dose-response microarray data
- Multiple contrast tests
- Multiple confidence intervals for selected parameters adjusted for the false coverage-statement rate

All methodological issues in the book are illustrated using real-world examples of dose-response microarray datasets from early drug development experiments.

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