
Preface

Over the past decade there has been an explosion of developments in mixed effects models and their applications. This book concentrates on two major classes of mixed effects models, linear mixed models and generalized linear mixed models, with the intention of offering an up-to-date account of theory and methods in the analysis of these models as well as their applications in various fields.

The first two chapters are devoted to linear mixed models. We classify linear mixed models as Gaussian (linear) mixed models and non-Gaussian linear mixed models. There have been extensive studies in estimation in Gaussian mixed models as well as tests and confidence intervals. On the other hand, the literature on non-Gaussian linear mixed models is much less extensive, partially because of the difficulties in inference about these models. However, non-Gaussian linear mixed models are important because, in practice, one is never certain that normality holds. This book offers a systematic approach to inference about non-Gaussian linear mixed models. In particular, it has included recently developed methods, such as partially observed information, iterative weighted least squares, and jackknife in the context of mixed models. Other new methods introduced in this book include goodness-of-fit tests, prediction intervals, and mixed model selection. These are, of course, in addition to traditional topics such as maximum likelihood and restricted maximum likelihood in Gaussian mixed models.

The next two chapters deal with generalized linear mixed models. These models may be regarded as extensions of the Gaussian mixed models. They are useful in situations where responses are correlated as well as discrete or categorical. McCullagh and Nelder (1989) introduced one of the earlier examples of such models, a mixed logistic model, for the infamous salamander mating problem. Since then these models have received considerable attention, and various methods of inference have been developed. A major issue regarding generalized linear mixed models is the computation of the maximum likelihood estimator. It is known that the likelihood function under these models may involve high-dimensional integrals that cannot be evaluated analytically.

Therefore, the maximum likelihood estimator is difficult to compute. We classify the methods of inference as likelihood-based, which include the Bayesian methods, and nonlikelihood-based. The likelihood-based approaches focus on developing computational methods. Markov chain Monte Carlo methods have been used in both the likelihood and the Bayesian approaches to handle the computations. The nonlikelihood-based approaches try to avoid the computational difficulty by considering alternative methods. These include approximate inference and estimating equations. Another challenging problem in this area is generalized linear mixed model selection. A recently developed method, called *fence*, is shown to be applicable to selecting an optimal model from a set of candidate models.

There have been various books on mixed effects models and related topics. The following are the major ones published in the last ten years.

1. Demidenko (2004), *Mixed Models—Theory and Applications*
2. McCulloch and Searle (2001), *Generalized, Linear and Mixed Models*
3. Sahai and Ageel (2000), *Analysis of Variance: Fixed, Random and Mixed Models*
4. Verbeke et al. (2000), *Linear Mixed Models for Longitudinal Data*
5. Pinheiro and Bates (2000), *Mixed-Effects Models in S and S-Plus*
6. Brown and Prescott (1999), *Applied Mixed Models in Medicine*
7. Rao (1997), *Variance Components Estimation: Mixed Models, Methodologies and Applications*
8. Littell et al. (1996), *SAS System for Mixed Models*

The latest publication, book 1, provides a quite comprehensive introduction on Gaussian mixed models and applications in problems such as tumor regrowth, shape, and image. Book 2 emphasizes application of the maximum likelihood and restricted maximum likelihood methods for estimation. Book 3 intensively studies the ANOVA type models with examples and computer programs using statistical software packages. Books 4, 5, 6 and 8 are mainly application-oriented. Many examples and case studies are available, and computer programs in SAS and S-Plus as well. Book 7 presents a comprehensive account of the major procedures of estimating the variance components, and fixed and random effects. These books, however, do not discuss non-Gaussian linear mixed models, neither do they present model diagnostics and model selection methods for mixed models. As mentioned, non-Gaussian linear mixed models, mixed model diagnostics, and mixed model selection are among the main topics of this book.

The application of mixed models is vast and expanding so fast as to preclude any attempt at exhaustive coverage. Here we use a number of selected real-data examples to illustrate the applications of linear and generalized linear mixed models. The areas of application include biological and medical research, animal and human genetics, and small area estimation. The latter has evolved quite rapidly in surveys. These examples of applications are considered near the end of each chapter.

The text is supplemented by numerous exercises. The majority of the problems are related to the subjects discussed in each chapter. In addition, some further results and technical notes are given in the last section of each chapter. The bibliography includes the relevant references. Three appendices are attached. Appendix A lists the notation used in this book. Appendix B provides the necessary background in matrix algebra. Appendix C gives a brief review of some of the relevant results in probability and statistics.

The book is aimed at students, researchers, and other practitioners who are interested in using mixed models for statistical data analysis or doing research in this area. The book is suitable for a course in a MS program in statistics, provided that the sections of further results and technical notes are skipped. If the latter sections are included, the book may be used for two courses in a PhD program in statistics, perhaps one on linear models and the other on generalized linear models, both with applications. A first course in mathematical statistics, the ability to use a computer for data analysis and familiarity with calculus and linear algebra are prerequisites. Additional statistical courses, such as regression analysis, and a good knowledge of matrices would be helpful.

A large portion of the material in this book is based on lecture notes from two graduate courses, “Linear Models” and “Generalized Linear Models”, that the author taught at Case Western Reserve University between 1996 and 2001. The author would like to thank Prof. Joe Sedransk for initiating these courses. Grateful thanks are also due, in particular, to Prof. Partha Lahiri for his role in drawing the author’s attention to application of mixed models to small area estimation, and to Prof. Rudy Beran for his advice and encouragement. My special thanks also go to Prof. J. N. K. Rao, who reviewed an earlier version of this book and made valuable suggestions. A number of anonymous reviewers have reviewed the earlier drafts of this book, or chapters of this book. Their comments led to major changes, especially in the organization of the contents. The author wishes to thank them for their time and effort that have made the book suitable for a broader audience. Two graduate students have helped with the data analyses that are involved in this book. In this regard, my sincere thanks go to Ms. Zhonghua Gu and Ms. Thuan Nguyen. In addition, the author thanks Ms. Qiuyan Xu and Ms. Zhonghua Gu for proofreading the book and providing solutions to some of the exercises. Finally, the author is grateful for Dr. Sean M. D. Allan for his comments that helped improve the presentation of this preface.

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