



Nonlinear Models for Repeated Measurement Data.

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is an index of these, giving Lemma 2.1 p.22, Lemma 2.2 p.26, . . . Proposition 1.1 p.7, . . . This is useful when trying to refer back to some previous result but otherwise is totally uninformative.)

Continuous-time Markov chains are the subject in Chapter 3. This begins by considering the soft component of cosmic radiation and continues via various well-known birth-death processes to queueing systems, statistical inference for continuous-time Markov chains (with an application to vital events in a baboon tribe), the modeling of neural activity, and the formation of blood in cats.

Chapters 4, 5 and 6 are concerned with Markov random fields, point processes, and Brownian motion and diffusion, respectively, always with much emphasis on applications and with many interesting and challenging exercises. As the book proceeds the amount of theory that is explained decreases. It does not really go very far into the underlying mathematics of stochastic processes; for that one needs back-ups such as Whittle's (1986) "Systems in Stochastic Equilibrium", Asmussen's (1987) "Applied Probability and Queues", and Guttorp's own (1991) "Statistical Inference for Branching Processes". Fortunately each chapter includes helpful bibliographic notes; there is a consolidated list of references at the end of the book. Beside the index of results, there are also useful indexes of applications and examples, of notation, and of terminology. The book ends with an explanation concerning ftp of the larger data sets.

Inevitably in a work of this kind, many topics are noticeable by their absence. These include renewal theory ("while renewal theory is a beautiful piece of probability, I have not found many interesting scientific applications"), martingales, and stationary time series ("in this area there are plenty of books containing both theory and data analysis"). The overriding emphasis is on Markov chain Monte Carlo methods. The importance of MCMC in present-day statistics makes any book with this emphasis a serious contender for space on one's bookshelves. The author's lucid presentation of his material, together with the very great number of applications from the life sciences, make this an excellent buy for only thirty pounds for every biometrician.

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DAVIDIAN, M. and GILTINAN, D. M. **Non-linear Models for Repeated Measurement Data**. Chapman & Hall, London, 1995. xv + 359 pp. £32.00/\$54.95. ISBN 0-412-98341-9.

This book gives an excellent introduction to an important field in applied statistics, a field in which the authors have a strong track record of research. The chapter contents are as follows.

In Chapter 1 four data sets from Biology are discussed in detail as a prelude to their use as examples later. There is some general scene-setting: the within-individuals model is

$$y_{ij} = f(x_{ij}, \beta_i) + e_{ij},$$

where y_{ij} is the j th measurement made on the i th individual ($j = 1, \dots, n_i$), e_{ij} is the error term, and f is some specified nonlinear function of parameter vector β_i and covariate vector x_{ij} ; the between-individuals model is usually taken to be a linear one, $\beta_i = A_i\beta + b_i$.

Chapter 2 gives a prerequisite account of nonlinear regression. There is detailed discussion of variance heterogeneity, serial correlation, and computation of least-squares estimates. The method referred to as 'iteratively reweighted least-squares', described on page 30 and used in various other places, should not be taken to mean the minimisation of $\sum (y_j - \mu_j)^2 / \sigma_j^2$, where μ_j and σ_j^2 are respectively the mean and variance of y_j , both functions of β : that method is well known to lead to a biased estimating equation and thence, in general, to inconsistent estimators. Also, the 'pseudo-likelihood' method (page 32) for estimating σ and θ , also called 'extended least-squares' (page 58), was proposed by Whittle back in 1961 under the name 'Gaussian estimation', being a method of estimation based on a Gaussian likelihood function. There is a quite a lot of discussion of the numerical implementation of least-squares, highlighting Newton-Raphson and Fisher scoring but not more recent methods for nonlinear optimization such as those following on from the original DFP algorithm (Fletcher and Powell, 1963). Inference is of the frequentist variety, relying on asymptotic (large-sample) theory. The chapter also reviews some other approaches to modelling and estimation.

Chapter 3 covers more prerequisite material, this time the Laird-Ware two-stage linear model. A number of aspects are discussed, including model misspecification and its consequences, the Bayesian approach, variance components, applications to simple cases, maximum likelihood, restricted maximum likelihood, best linear unbiased prediction, computation (EM algorithm, Newton-Raphson, software availability), and all well illustrated with some real-data examples.

Chapter 4 gets down to the business in hand, addressing two-stage nonlinear models. There is much illustrative discussion of examples describing how models are set up, etc., plus a way of accommodating more than one response variable. A topic appearing here, which is not covered in previous books on repeated measures to my knowledge, is non- and semi-parametric specification for between-individuals variation of the regression parameters. This appears in Section 4.3, based on an author's own research, and is described more fully later in chapter 7. There is sensible reiteration, here and elsewhere, of the danger of over-elaborate modelling when the data are not extensive.

Chapter 5 describes, at some length, two-stage estimation: this is feasible when there is enough data per individual to form reliable estimates of individual regression parameters; these can then be used as input data, accompanied by appropriate variability estimates, to fit the between-individuals model.

Chapter 6 addresses the case where the within-individuals data sets are not large. The main theme is linear approximation of the nonlinear functions in order to apply the numerical techniques associated with linear models. Many complicated and ingenious wheezes are described to get round the problem of nonlinearity and the integrations involved. However, it should be borne in mind that these approximations are in addition to the asymptotics relied upon for inference.

Chapter 7 describes certain non- and semi-parametric methods. Section 7.2 goes into some theoretical detail concerning non-parametric maximum likelihood. A method referred to as 'smooth non-parametric' is presented, taken from an author's own joint research. This chapter, in particular, presents material that has not appeared widely before. As pointed out by the authors, weaker distributional specifications rely on larger sample sizes.

Chapter 8 gives a nice overview of Bayesian MCMC, focussing mainly on Gibbs sampling since full conditionals of parameter-sets are readily available in the present context.

Chapter 9 presents three case studies in detail from pharmacology, after giving a general introduction to the models involved. The discussion of modelling, fitting and results for these data sets is careful and informative. However, the analyses performed in this chapter, which follows chapter 8, are set in the longer-established mould of previous chapters.

Chapter 10 examines some of the issues which arise in analyzing drug assay data. The treatment is detailed and looks comprehensive enough to form a useful introduction to the field for potential practitioners.

Chapter 11, Further Applications, describes three more case studies, one each in crop science, forestry and seismology. The account brings out further practical aspects of modelling, fitting and non-Bayesian inference.

Chapter 12, Open Problems and Discussion, is an agenda for further developments.

Overall, the book gives a very well-written account of the field over the past few decades, focussing mainly on US work and including much of the authors' own, plus a glimpse of the future. It fairly reflects that literature over the years in dwelling at length on certain computational methods for maximum likelihood estimation. There is a leaning towards biopharmaceutical applications, this being a field in which the authors are acknowledged authorities. There are no exercises, but enough detail of the methodology is given, together with helpful guidance on available software, to enable the keen novice to try his hand. Lastly, I hope I'll be forgiven for just adding a couple of citations to those given

in the book: a slightly different perspective on nonlinear regression models for repeated measures is described briefly in Crowder and Hand (1990, Section 9.4) and at greater length in Hand and Crowder (1995, chapter 8).

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CARROLL, R. J., RUPPERT, D., and STEFANSKI, L. A. **Measurement Error in Nonlinear Models**. Chapman & Hall, London, 1995. xxiv + 305 pp. £29.95/\$54.95. ISBN 0-412-04721-7.

It has been a pleasure to review this book, which provides both an accessible, carefully motivated account of a range of models, illustrated by real examples, and detailed discussion of the statistical theory.

Seven examples are given in the first chapter, including nutrition studies, bioassay in a herbicide study, lung function in children and the atom bomb survivors data. General models and issues in measurement error analysis are then reviewed: functional and structural models, and replicate measurements, validation studies and instrumental variables as methods for assessing error in covariates. A brief tour of the book is provided, which ensures that the reader can select material appropriate to their interests. The 'lovely and appealing folklore' that measurement error always results in attenuation is shown to be false in Chapter 2, which summarises methods for linear models. Readers are referred to Fuller (1987) for details of linear measurement error models, but are left with no illusions about the complexity which can arise in measurement error problems.

The next six chapters are structured so that readers with a particular applied problem to consider can read an overview and basic description of a method before being presented with a worked example. Those wishing greater understanding of the theory can read the remainder of the chapter.

Functional models, in which no or minimal assumptions are made about the distribution of variables measured with error, are described in Chapters 3 to 6. Regression calibration, in which