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BOOK REVIEWS
Editor: Niels Keiding

1. *Shayne C. Gad*, Statistics and Experimental Design for Toxicologists.
2. *Chi-Lun Cheng and John W. Van Ness*, Statistical Regression with Measurement Error.

1. STATISTICS AND EXPERIMENTAL DESIGN FOR TOXICOLOGISTS. 3rd edition. Shayne C. Gad, CRC Press, U.S.A. 1999. No. of pages: 437. Price: $79.95. ISBN 0-8493-3132-8

Statistics and Experimental Design for Toxicologists (3rd edition) by Shayne C. Gad is designed as a source book and textbook for both practising and student toxicologists, with the central objective of equipping them for the regular statistical analysis of experimental data.

Good laboratory practice and detailed protocols are well incorporated in the daily work practice of toxicologists. However, these practices and protocols mostly do not include detailed plans for the statistical analysis. Prior selection of statistical methodologies is, however, essential for an overall proper design. Moreover, as statistical packages become more powerful and easier to use, the probability of misuse of these powerful methods increases.

The book covers all steps in the cascade of statistical checks and analyses usually encountered in the analysis of experimental data. The steps are illustrated by examples and SAS command codes. Much attention is given to the description of methods that can be used. However, only limited statistical background information is provided for the presented methodologies. As a result the book becomes a kind of 'cockbook' for statistical analysis and experimental design for toxicologists. Therefore, it might be recommendable to check the statistical background in an appropriate handbook for biostatistics. Assumptions and limitations of the proposed methods are carefully enumerated, but are unfortunately not explained in detail.

The statistical analyses proposed for most presented examples are sound and have been used in toxicology for many decades. No attention is given to more novel statistical techniques such as the application of mixed models for the analysis of variance or the application of Monte Carlo simulations. The latter method is widely used for assessing uncertainty in the output function, based on the collective uncertainty of the model's input.

Some minor errors and mistakes are still present in this edition (for example, Table 1.1 has too many digits in the given significance levels: 0.005 and 0.001 instead of 0.05 and 0.01; Chapter 4 has a different name in the contents).

In conclusion, the book describes statistical methods that can be used in toxicology research. It enables students and practitioners in the field to select appropriate methodologies easily. However, students and practitioners interested in the background of the applied statistics will not gain very much from this book.

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2. STATISTICAL REGRESSION WITH MEASUREMENT ERROR. Chi-Lun Cheng and John W. Van Ness, Kendall's Library of Statistics 6, Arnold, London, 1999. No. of pages: xiv+262. Price: £35. ISBN: 0-340-61461-7

This book is intended to replace and extend the treatment of functional and structural relationship models in the classical work *Kendall's Advanced Theory of Statistics*. The relevant part, the earlier Chapter 29 of Kendall and Stuart [1] has been deleted from the fifth edition (by Stuart and Ord).

The basic setting given in the book is that the ordinary simple linear regression model is replaced by an assumed relation $\eta_i = \beta_0 + \beta_1 \xi_i$ in the 'true' unobservable variables (ξ_i, η_i), and that one observes $x_i = \xi_i + \delta_i$ and $y_i = \eta_i + \varepsilon_i$, where the errors are uncorrelated with finite variances. If the ξ_i's are fixed unknown constants, this is called a functional model; if they are random variables with a constant expectation, it is called a structural model; a general set of assumptions covering both cases is called an ultrastructural model.

For many users of statistical methods, it may seem to be a very relevant supplement to their

toolbox to be able to include errors in the explanatory variables of the regression equation. The serious user will indeed find a very thorough and readable introduction to these models and the corresponding estimation methods in this book, together with a discussion of the strengths and the weaknesses of the methods.

However, before such potential users abandon their simple regression framework altogether, it may be appropriate to give a few brief warnings:

1. The structural model is unidentifiable in the Gaussian case (Reiersøl [2]), and the corresponding functional model, while identifiable, lacks consistent estimators. Thus extra assumptions have to be introduced in the measurement error models in order that decent estimators can be found, and these assumptions may be difficult to jusify. The only simple case seems to be when one can assume $\sigma_\varepsilon^2/\sigma_\delta^2 = 1$; then the solution is orthogonal regression, found by minimizing distances perpendicular to the regression line.
2. If the purpose is prediction, it is important to distinguish between two cases: (a) The future x-values for which prediction shall be made are of the same kind x as those used in estimating the regression line (that is, with errors), or (b) they are ideal error-free variables ξ. In the former case, which may be quite common, the ordinary linear regression line is optimal (exactly so in the normal structural model, approximately more generally). It is only in the latter case that the measurement error methods are appropriate.
3. The ordinary least squares estimates are also appropriate for the so-called Berkson model (x is fixed at certain values, which may be measured with errors.)
4. Finally, if the errors in the x-variable are small enough (a statement which can be made more precise by looking at sums of squares), the bias in the least squares estimates may be small enough to be tolerable.

A user who, still feels after having thought through the above points, that the measurement error methods are of interest, will find the monograph by Cheng and Van Ness to contain an almost encyclopaedic treatment of various aspects of these models and methods. The models themselves and the corresponding maximum likelihood estimation are introduced in Chapter 1. In Chapter 2 asymptotic properties of the estimators are discussed under various assumptions, with applications to confidence intervals and confidence regions. The joint confidence set for (β_0, β_1) turns out to be unbounded quite generally.

In Chapter 3 we find more discussion of the identifiability conditions, and of the estimation methods generalized least squares and modified least squares. Chapter 4 contains a discussion of instrument variables, in particular grouping variables, of which the authors are rather sceptical. Chapter 5 gives the necessary generalization to the multiple regression case, while Chapter 6 treats polynomial regression, which turns out to be quite complicated for measurement error models. Robust estimation for measurement error models is treated in Chapter 7, starting with a general survey of robust estimation theory, and ending up with computational methods illustrated on a simulated example. Finally, Chapter 8 briefly treats some additional topics, most notably the relation to other latent variable settings like factor analysis models.

Each chapter is well organized; in most cases they conclude with a very informative discussion session together with a set of exercises. Of particular interest are the 'exercises' that are formulated as open research problems, a special feature that shows that the authors are in close touch with the research frontier attached to their subject. This should also be clear from the comprehensive bibliography included. One may miss a few of the central references on calibration, though, but here the book may be supplemented by the recent review paper by Sundberg [3].

In summary, this is a very thorough and well-written book on nearly all aspects of the use of measurement error models in regression. The serious user of these methods who consults this book will probably find an impartial discussion of most topics of interest. For somebody interested in doing methodological research on a subject related to measurement error models, the book is a must.

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