DigiSem Wir beschaffen und digitalisteren



b UNIVERSITÄT BERN Universitätsbibliothek Bern

Dieses Dokument steht Ihnen online zur Verfügung dank DigiSem, einer Dienstleistung der Universitätsbibliothek Bern.

Kontakt: Gabriela Scherrer Koordinatorin digitale Semesterapparate E-Mail digisem@ub.unibe.ch, Telefon 031 631 93 26 José C. Pinheiro Douglas M. Bates

Mixed-Effects Models in S and S-PLUS

With 172 Illustrations





José C. Pinheiro
Department of Biostatistics
Novartis Pharmaceuticals
One Health Plaza
East Hanover, NJ 07936-1080
USA
jose.pinheiro@pharma.novartis.com

Douglas M. Bates Department of Statistics University of Wisconsin Madison, WI 53706-1685 USA bates@stat.wisc.edu

Series Editors:

J. Chambers Bell Labs, Lucent Technologies 600 Mountain Ave. Murray Hill, NJ 07974 USA W. Eddy Department of Statistics Carnegie Mellon University Pittsburgh, PA 15213 USA W. Härdle Institut für Statistik und Ökonometrie Humboldt-Universität zu Berlin Spandauer Str. 1 D-10178 Berlin Germany

S. Sheather Australian Graduate School of Management

University of New South Wales

Sydney NSW 2052 Australia L. Tierney School of Statistics University of Minnesota Vincent Hall Minneapolis, MN 55455

USA

Library of Congress Cataloging-in-Publication Data Pinheiro, José C.

Mixed-effects models in S and S-PLUS / José C. Pinheiro, Douglas M. Bates

Mixed-effects models in S and S-PLUS / Jose p. cm. — (Statistics and computing) Includes bibliographical references and index. ISBN 0-387-98957-9 (alk. paper) I. Bates, Douglas M. II. Title. III. Series. QA76.73.S15P56 2000 005.13'3—dc21

99-053566

Printed on acid-free paper.

© 2000 Springer Verlag New York, LLC

All rights reserved. This work may not be translated or copied in whole or in part without the written permission of the publisher (Springer-Verlag New York, LLC, 175 Fifth Avenue, New York, NY 10010, USA), except for brief excerpts in connection with reviews or scholarly analysis. Use in connection with any form of information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed is forbidden. The use of general descriptive names, trade names, trademarks, etc., in this publication, even if the former are not especially identified, is not to be taken as a sign that such names, as understood by the Trade Marks and Merchandise Marks Act, may accordingly be used freely by anyone.

Printed in the United States of America. (HAM)

9 8 7 6 5 SPIN 10995662

Springer Verlag is a part of Springer Science+Business Media

springeronline.com

References

- Abramowitz, M. and Stegun, I. A. (1964). Handbook of Mathematical Functions with Formulas, Graphs, and Mathematical Tables, Dover, New York.
- Bates, D. M. and Chambers, J. M. (1992). "Nonlinear models," in Chambers and Hastie (1992), Chapter 10, pp. 421–454.
- Bates, D. M. and Pinheiro, J. C. (1998). Computational methods for multilevel models, *Technical Memorandum BL0112140-980226-01TM*, Bell Labs, Lucent Technologies, Murray Hill, NJ.
- Bates, D. M. and Watts, D. G. (1980). Relative curvature measures of nonlinearity, *Journal of the Royal Statistical Society*, Ser. B 42: 1–25.
- Bates, D. M. and Watts, D. G. (1988). Nonlinear Regression Analysis and Its Applications, Wiley, New York.
- Beal, S. and Sheiner, L. (1980). The NONMEM system, American Statistician 34: 118–119.
- Becker, R. A., Cleveland, W. S. and Shyu, M.-J. (1996). The visual design and control of trellis graphics displays, *Journal of Computational and Graphical Statistics* **5**(2): 123–156.
- Bennett, J. E. and Wakefield, J. C. (1993). Markov chain Monte Carlo for nonlinear hierarchical models, *Technical Report TR-93-11*, Statistics Section, Imperial College, London.

- Boeckmann, A. J., Sheiner, L. B. and Beal, S. L. (1994). *NONMEM Users Guide: Part V*, NONMEM Project Group, University of California, San Francisco.
- Box, G. E. P., Hunter, W. G. and Hunter, J. S. (1978). Statistics for Experimenters, Wiley, New York.
- Box, G. E. P., Jenkins, G. M. and Reinsel, G. C. (1994). *Time Series Analysis: Forecasting and Control*, 3rd ed., Holden-Day, San Francisco.
- Brillinger, D. (1987). Comment on a paper by C. R. Rao, Statistical Science 2: 448–450.
- Bryk, A. and Raudenbush, S. (1992). Hierarchical Linear Models for Social and Behavioral Research, Sage, Newbury Park, CA.
- Carroll, R. J. and Ruppert, D. (1988). Transformation and Weighting in Regression, Chapman & Hall, New York.
- Chambers, J. M. (1977). Computational Methods for Data Analysis, Wiley, New York.
- Chambers, J. M. and Hastie, T. J. (eds) (1992). Statistical Models in S, Chapman & Hall, New York.
- Cleveland, W. S. (1994). Visualizing Data, Hobart Press, Summit, NJ.
- Cleveland, W. S., Grosse, E. and Shyu, W. M. (1992). "Local regression models," in Chambers and Hastie (1992), Chapter 8, pp. 309–376.
- Cochran, W. G. and Cox, G. M. (1957). Experimental Designs, 2nd ed., Wiley, New York.
- Cox, D. R. and Hinkley, D. V. (1974). *Theoretical Statistics*, Chapman & Hall, London.
- Cressie, N. A. C. (1993). Statistics for Spatial Data, Wiley, New York.
- Cressie, N. A. C. and Hawkins, D. M. (1980). Robust estimation of the variogram, Journal of the International Association of Mathematical Geology 12: 115–125.
- Crowder, M. and Hand, D. (1990). Analysis of Repeated Measures, Chapman & Hall, London.
- Davidian, M. and Gallant, A. R. (1992). Smooth nonparametric maximum likelihood estimation for population pharmacokinetics, with application to quinidine, *Journal of Pharmacokinetics and Biopharmaceutics* 20: 529–556.

- Davidian, M. and Giltinan, D. M. (1995). Nonlinear Models for Repeated Measurement Data, Chapman & Hall, London.
- Davis, P. J. and Rabinowitz, P. (1984). Methods of Numerical Integration, 2nd ed., Academic Press, New York.
- Dempster, A. P., Laird, N. M. and Rubin, D. B. (1977). Maximum likelihood from incomplete data via the EM algorithm, *Journal of the Royal Statistical Society, Ser. B* **39**: 1–22.
- Devore, J. L. (2000). Probability and Statistics for Engineering and the Sciences, 5th ed., Wadsworth, Belmont, CA.
- Diggle, P. J., Liang, K.-Y. and Zeger, S. L. (1994). Analysis of Longitudinal Data, Oxford University Press, New York.
- Dongarra, J. J., Bunch, J. R., Moler, C. B. and Stewart, G. W. (1979). Linpack Users' Guide, SIAM, Philadelphia.
- Draper, N. R. and Smith, H. (1998). Applied Regression Analysis, 3rd ed., Wiley, New York.
- Gallant, A. R. and Nychka, D. W. (1987). Seminonparametric maximum likelihood estimation, *Econometrica* **55**: 363–390.
- Geman, S. and Geman, D. (1984). Stochastic relaxation, Gibbs distributions and the Bayesian restoration of images, *IEEE Transactions on Pattern Analysis and Machine Intelligence* **6**: 721–741.
- Geweke, J. (1989). Bayesian inference in econometric models using Monte Carlo integration, *Econometrica* 57: 1317–1339.
- Gibaldi, M. and Perrier, D. (1982). Pharmacokinetics, Marcel Dekker, New York.
- Goldstein, H. (1987). Multilevel Models in Education and Social Research, Oxford University Press, Oxford.
- Goldstein, H. (1995). *Multilevel Statistical Models*, Halstead Press, New York.
- Golub, G. H. (1973). Some modified matrix eigenvalue problems, SIAM Review 15: 318–334.
- Golub, G. H. and Welsch, J. H. (1969). Calculation of Gaussian quadrature rules, *Mathematical Computing* **23**: 221–230.
- Grasela and Donn (1985). Neonatal population pharmacokinetics of phenobarbital derived from routine clinical data, *Developmental Pharmacology and Therapeutics* 8: 374–0383.

- Hand, D. and Crowder, M. (1996). Practical Longitudinal Data Analysis, Texts in Statistical Science, Chapman & Hall, London.
 - Harville, D. A. (1977). Maximum likelihood approaches to variance component estimation and to related problems, Journal of the American Statistical Association 72: 320-340.
- Hastings, W. K. (1970). Monte Carlo sampling methods using Markov chains and their applications, Biometrika 57: 97–109.
- Jones, R. H. (1993). Longitudinal Data with Serial Correlation: A Statespace Approach, Chapman & Hall, London.
- Joyner and Boore (1981). Peak horizontal acceleration and velocity from strong-motion records including records from the 1979 Imperial Valley, California, earthquake, Bulletin of the Seismological Society of America 71: 2011-2038.
- Kennedy, William J., J. and Gentle, J. E. (1980). Statistical Computing, Marcel Dekker, New York.
- Kung, F. H. (1986). Fitting logistic growth curve with predetermined carrying capacity, ASA Proceedings of the Statistical Computing Section pp. 340-343.
- Kwan, K. C., Breault, G. O., Umbenhauer, E. R., McMahon, F. G. and Duggan, D. E. (1976). Kinetics of indomethicin absorption, elimination, and enterohepatic circulation in man, Journal of Pharmacokinetics and Biopharmaceutics 4: 255-280.
- Laird, N. M. and Ware, J. H. (1982). Random-effects models for longitudinal data, Biometrics 38: 963-974.
- Lehmann, E. L. (1986). Testing Statistical Hypotheses, Wiley, New York.
- Leonard, T., Hsu, J. S. J. and Tsui, K. W. (1989). Bayesian marginal inference, Journal of the American Statistical Association 84: 1051-1058.
- Lindley, D. and Smith, A. (1972). Bayes estimates for the linear model, Journal of the Royal Statistical Society, Ser. B 34: 1-41.
- Lindstrom, M. J. and Bates, D. M. (1988). Newton-Raphson and EM algorithms for linear mixed-effects models for repeated-measures data (corr: 94v89 p1572), Journal of the American Statistical Association 83: 1014-1022.
- Lindstrom, M. J. and Bates, D. M. (1990). Nonlinear mixed-effects models for repeated measures data, Biometrics 46: 673–687.

- Littell, R. C., Milliken, G. A., Stroup, W. W. and Wolfinger, R. D. (1996). SAS System for Mixed Models, SAS Institute Inc., Cary, NC.
- Longford, N. T. (1993). Random Coefficient Models, Oxford University Press, New York.
- Ludbrook, J. (1994). Repeated measurements and multiple comparisons in cardiovascular research, *Cardiovascular Research* 28: 303–311.
- Mallet, A. (1986). A maximum likelihood estimation method for random coefficient regression models, *Biometrika* **73**(3): 645–656.
- Mallet, A., Mentre, F., Steimer, J.-L. and Lokiek, F. (1988). Nonparametric maximum likelihood estimation for population pharmacokinetics, with applications to Cyclosporine, *Journal of Pharmacokinetics and Biopharmaceutics* **16**: 311–327.
- Matheron, G. (1962). Traite de Geostatistique Appliquee, Vol. I of Memoires du Bureau de Recherches Geologiques et Minieres, Editions Technip, Paris.
- Milliken, G. A. and Johnson, D. E. (1992). Analysis of Messy Data. Volume 1: Designed Experiments, Chapman & Hall, London.
- Patterson, H. D. and Thompson, R. (1971). Recovery of interblock information when block sizes are unequal, *Biometrika* **58**: 545–554.
- Pierson, R. A. and Ginther, O. J. (1987). Follicular population dynamics during the estrus cycle of the mare, *Animal Reproduction Science* 14: 219–231.
- Pinheiro, J. C. (1994). *Topics in Mixed-Effects Models*, Ph.D. thesis, University of Wisconsin, Madison, WI.
- Pinheiro, J. C. and Bates, D. M. (1995). Approximations to the loglikelihood function in the nonlinear mixed-effects model, *Journal of Computational and Graphical Statistics* 4(1): 12–35.
- Potthoff, R. F. and Roy, S. N. (1964). A generalized multivariate analysis of variance model useful especially for growth curve problems, *Biometrika* 51: 313–326.
- Potvin, C., Lechowicz, M. J. and Tardif, S. (1990). The statistical analysis of ecophysiological response curves obtained from experiments involving repeated measures, *Ecology* **71**: 1389–1400.
- Ramos, R. Q. and Pantula, S. G. (1995). Estimation of nonlinear random coefficient models, *Statistics & Probability Letters* **24**: 49–56.

- Sakamoto, Y., Ishiguro, M. and Kitagawa, G. (1986). Akaike Information Criterion Statistics, Reidel, Dordrecht, Holland.
- Schwarz, G. (1978). Estimating the dimension of a model, *Annals of Statistics* **6**: 461–464.
- Searle, S. R., Casella, G. and McCulloch, C. E. (1992). Variance Components, Wiley, New York.
- Seber, G. A. F. and Wild, C. J. (1989). *Nonlinear Regression*, Wiley, New York.
- Self, S. G. and Liang, K. Y. (1987). Asymptotic properties of maximum likelihood estimators and likelihood ratio tests under nonstandard conditions, Journal of the American Statistical Association 82: 605–610.
- Sheiner, L. B. and Beal, S. L. (1980). Evaluation of methods for estimating population pharmacokinetic parameters. I. Michaelis-Menten model: Routine clinical pharmacokinetic data, *Journal of Pharmacokinetics* and *Biopharmaceutics* 8(6): 553-571.
- Snedecor, G. W. and Cochran, W. G. (1980). Statistical Methods, 7th ed., Iowa State University Press, Ames, IA.
- Soo, Y.-W. and Bates, D. M. (1992). Loosely coupled nonlinear least squares, *Computational Statistics and Data Analysis* 14: 249–259.
- Stram, D. O. and Lee, J. W. (1994). Variance components testing in the longitudinal mixed-effects models, *Biometrics* **50**: 1171–1177.
- Stroup, W. W. and Baenziger, P. S. (1994). Removing spatial variation from wheat yield trials: a comparison of methods, *Crop Science* **34**: 62–66.
- Thisted, R. A. (1988). Elements of Statistical Computing, Chapman & Hall, London.
- Tierney, L. and Kadane, J. B. (1986). Accurate approximations for posterior moments and densities, *Journal of the American Statistical Association* 81(393): 82–86.
- Venables, W. N. and Ripley, B. D. (1999). Modern Applied Statistics with S-PLUS, 3rd ed., Springer-Verlag, New York.
- Verme, C. N., Ludden, T. M., Clementi, W. A. and Harris, S. C. (1992). Pharmacokinetics of quinidine in male patients: A population analysis, *Clinical Pharmacokinetics* **22**: 468–480.
- Vonesh, E. F. and Carter, R. L. (1992). Mixed-effects nonlinear regression for unbalanced repeated measures, *Biometrics* 48: 1–18.

- Vonesh, E. F. and Chinchilli, V. M. (1997). Linear and Nonlinear Models for the Analysis of Repeated Measures, Marcel Dekker, New York.
- Wakefield, J. (1996). The Bayesian analysis of population pharmacokinetic models, *Journal of the American Statistical Association* **91**: 62–75.
- Wilkinson, G. N. and Rogers, C. E. (1973). Symbolic description of factorial models for analysis of variance, *Applied Statistics* **22**: 392–399.
- Wolfinger, R. D. (1993). Laplace's approximation for nonlinear mixed models, *Biometrika* 80: 791–795.
- Wolfinger, R. D. and Tobias, R. D. (1998). Joint estimation of location, dispersion, and random effects in robust design, *Technometrics* **40**: 62–71.
- Yates, F. (1935). Complex experiments, Journal of the Royal Statistical Society (Supplement) 2: 181–247.