Statistical Techniques in Bioassay
Z. Govindarajulu

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2nd, revised and enlarged edition

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Fellow of the Institute of Mathematical Statistics, American Statistical Association, Royal Statistical Society (England), and the American Association for the Advancement of Science; member of the Bernoulli Society; member of the International Statistical Institute and member of the National Academy of Sciences (India).
Dedicated to the memory of my parents-in-law,
Dr. and Mrs. Mahanand Gupta
‘Sound and sufficient reason falls, after all, to the share of but few men, and those few men exert their influence in silence.’

*Johann Wolfgang von Goethe*

‘Every man should use his intellect, not as he uses his lamp in the study, only for his own seeing, but as the lighthouse uses its lamps, that those after off on the sea may see the shining, and learn their way.’

*Henry Ward Beecher*
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I am happy indeed to write this foreword. Raju and I were two of Richard Savage’s first thesis students at the University of Minnesota. My thesis was on certain aspects of quantal assay. Raju was interested and helpful. We have kept in touch and I am gratified to see this product of an interest partially fostered by me then and encouraged in the succeeding years.

This is a book that has been needed for a long time. Every biostatistical consultant is faced, now and again, with a question on the design or analysis of a quantal assay. Quantal assays will always be an important tool in experimental biomedicine. This book presents the statistical aspects of quantal assay and analysis in a mathematically concise, rigorous and modern format. Coverage includes some material found at the present only in periodicals and technical reports. It will be a useful addition to the armamentarium of the biostatistical consultant, whether fledgling or veteran. I believe the book will also serve well as a text for a course that focuses on quantal assay, for students of statistics interested in biomedical consulting, or as a supplementary text for a more generally applied statistics course for such students.

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Foreword to the Second Edition

The second edition of Professor Govindarajulu’s book on statistical aspects of biological assay will be of interest to students of this experimental area, to professional statisticians with an interest in research in this topic, to teachers in statistics and biology and to investigators in the biological and medical sciences who use bioassay in their work. Raju’s first edition was a valuable contribution to the topic and the second edition is a timely event. There is a fair amount of new material stemming from the recent statistical literature, some of it based on the author’s personal work. The material reflects recent modern trends in general applied statistical research and the efforts of statisticians to bring this work into practice in the biological and medical sciences. Examples are discussions of generalized logistic models, a response model using non-linear kinetics, additional discussion on design and planning, e.g. choices of dose levels, an additional section in the chapter on Bayes methods, and a new chapter on sequential estimation for the logistic model. The literature citations will also be of value to student, teacher, bioassayist and statistician. The book will have a proper place in the library of all applied statisticians and biologists who have a continuing interest in the subject of bioassay.

Stanford, Calif., May 2000

Byron Wm. Brown, Jr.

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Since the beginning of the 20th century, there has been a lot of activity in developing statistical methods for analyzing biological data. The development of the probit method is originally due to Gaddum and Bliss. The two important methods of analyzing biological data are: (1) the probit method, and (2) the logit method. Finney [1971] has written an exhaustive treatise on the probit method; Ashton [1972] a short monograph on the logit approach. Here we give equal importance to both the probit and the logit approaches and deal with other approaches to bioassay. Chapters first deal with direct and indirect assays. The logit approach is then covered. Further chapters focus on the angular response curve and other methods, while other chapters consider sequential methods. Readers will also find chapters devoted to estimation of low doses, Bayesian methods, and radioimmunoassays. There have been recent developments, especially in robust estimation methods in bioassay; however, these are not included in this book. More than 200 references are cited and given in a list at the end; this list is by no means complete. A basic course in statistical inference is all that is required of the readers.

I shall appreciate readers drawing my attention to any shortcomings or errors found in this book. This book grew out of my lecture notes based on a course in bioassay given at the University of Kentucky during several summers. A quarter or semester’s course on bioassay can be taught out of this book. Selection of the appropriate chapters depends upon the emphasis of the course and the interests of the audience.

I give special thanks to my students who were the involuntary ‘guinea pigs’ in the course I taught. I am thankful to Vicki Kenney, Debra Arterburn, Brian Moses and Susan Hamilton for the excellent typing of the manuscript. I thank the Department of Statistics for its support and other help. It is also a pleasure to thank the staff of S. Karger AG for generous help and excellent cooperation throughout this project. I thank Professors Byron Brown of Stanford University, Charles Bell of San Diego State University and Bartholomew Hsi of the University of Texas.
at Houston for reading the manuscript in its early stages and making very helpful comments and suggestions. For generous permission to reproduce tables and/or to use material, my special thanks go to Dr. Margaret Wesly, American Association for the Advancement of Science, Association of Applied Biologists, the American Statistical Association, the Biometric Society, the Biometrika Trustees, the Biochemical Society, the Institute of Mathematical Statistics, the Royal Statistical Society, the Society for Industrial and Applied Mathematics, Charles Griffin Publishers, the Methuen Company, Cambridge University Press, the MacMillan Publishing Company, Freeman and Company, the Longman House (United Kingdom), Marcel Dekker Inc., MIT Press, and the University of California Press.

Z. Govindarajulu
Addendum to the Preface

The present form constitutes a revision of the first edition of this book published in 1988. Among the changes, numerous typographical errors have been corrected, helpful elaborations have been provided wherever necessary in order to enhance the readability of the book, new sections, namely 3.12, 3.13, 5.7, 6.9, 7.5, 10.10, and 11.9 have been included in order to reflect the current developments in this area. Further, a new Chapter 12 entitled “Sequential Estimation of the Mean Logistic Response Function” has been added. 53 additional references that are cited in the book have been added to the list at the end.

In addition to the people whom I thanked in the first edition, I would like to include the following people to the list: Mr. Rolf Steinebrunner, Product Manager of S. Karger Publishers and Ms. Esther Bernhard, Production Editor, S. Karger Publishers, for their patience and encouragement and cooperation in bringing out the second edition, Professor Byron Brown for writing a new foreword, Brian Moses for an excellent typing of all the revisions, and Yuhua Su for his assistance in preparing the subject index.

Lexington, Ky., April 2000

Z. Govindarajulu