Cambridge University Press 978-0-521-68357-9 - Design of Comparative Experiments R. A. Bailey Frontmatter More information

Design of Comparative Experiments

This book should be on the shelf of every practising statistician who designs experiments.

Good design considers units and treatments first, and *then* allocates treatments to units. It does not choose from a menu of named designs. This approach requires a notation for units that does not depend on the treatments applied. Most structure on the set of observational units, or on the set of treatments, can be defined by factors. This book develops a coherent framework for thinking about factors and their relationships, including the use of Hasse diagrams. These are used to elucidate structure, calculate degrees of freedom and allocate treatment subspaces to appropriate strata. Based on a one-term course the author has taught since 1989, the book is ideal for advanced undergraduate and beginning graduate courses. Examples, exercises and discussion questions are drawn from a wide range of real applications: from drug development, to agriculture, to manufacturing.

R. A. BAILEY has been Professor of Statistics at Queen Mary, University of London since 1994. She is a fellow of the Institute of Mathematical Statistics and a past president of the International Biometric Society, British Region. This book reflects her extensive experience teaching design of experiments and advising on its application. Her book *Association Schemes* was published by Cambridge University Press in 2004.

Cambridge University Press 978-0-521-68357-9 - Design of Comparative Experiments R. A. Bailey Frontmatter More information

CAMBRIDGE SERIES IN STATISTICAL AND PROBABILISTIC MATHEMATICS

Editorial Board

R. Gill (Department of Mathematics, Utrecht University) B. D. Ripley (Department of Statistics, University of Oxford) S. Ross (Department of Industrial and Systems Engineering, University of Southern California) B. W. Silverman (St. Peter's College, Oxford) M. Stein (Department of Statistics, University of Chicago)

This series of high-quality upper-division textbooks and expository monographs covers all aspects of stochastic applicable mathematics. The topics range from pure and applied statistics to probability theory, operations research, optimization, and mathematical programming. The books contain clear presentations of new developments in the field and also of the state of the art in classical methods. While emphasizing rigorous treatment of theoretical methods, the books also contain applications and discussions of new techniques made possible by advances in computational practice.

Already published

- 1. Bootstrap Methods and Their Application, by A. C. Davison and D. V. Hinkley
- 2. Markov Chains, by J. Norris
- 3. Asymptotic Statistics, by A. W. van der Vaart
- 4. Wavelet Methods for Time Series Analysis, by Donald B. Percival and Andrew T. Walden
- 5. Bayesian Methods, by Thomas Leonard and John S. J. Hsu
- 6. Empirical Processes in M-Estimation, by Sara van de Geer
- 7. Numerical Methods of Statistics, by John F. Monahan
- 8. A User's Guide to Measure Theoretic Probability, by David Pollard
- 9. The Estimation and Tracking of Frequency, by B. G. Quinn and E. J. Hannan
- 10. Data Analysis and Graphics using R, by John Maindonald and John Braun
- 11. Statistical Models, by A. C. Davison
- 12. Semiparametric Regression, by D. Ruppert, M. P. Wand, R. J. Carroll
- 13. Exercises in Probability, by Loic Chaumont and Marc Yor
- 14. Statistical Analysis of Stochastic Processes in Time, by J. K. Lindsey
- 15. Measure Theory and Filtering, by Lakhdar Aggoun and Robert Elliott
- 16. Essentials of Statistical Inference, by G. A. Young and R. L. Smith
- 17. Elements of Distribution Theory, by Thomas A. Severini
- 18. Statistical Mechanics of Disordered Systems, by Anton Bovier
- 20. Random Graph Dynamics, by Rick Durrett
- 21. Networks, by Peter Whittle
- 22. Saddlepoint Approximations with Applications, by Ronald W. Butler
- 23. Applied Asymptotics, by A. R. Brazzale, A. C. Davison and N. Reid
- 24. Random Networks for Communication, by Massimo Franceschetti and Ronald Meester

Cambridge University Press 978-0-521-68357-9 - Design of Comparative Experiments R. A. Bailey Frontmatter <u>More information</u>

Design of Comparative Experiments

R. A. Bailey Queen Mary, University of London



Cambridge University Press 978-0-521-68357-9 - Design of Comparative Experiments R. A. Bailey Frontmatter <u>More information</u>

> CAMBRIDGE UNIVERSITY PRESS Cambridge, New York, Melbourne, Madrid, Cape Town, Singapore, São Paulo, Delhi

> > Cambridge University Press The Edinburgh Building, Cambridge CB2 8RU, UK

Published in the United States of America by Cambridge University Press, New York

www.cambridge.org Information on this title: www.cambridge.org/9780521683579

© R. A. Bailey 2008

This publication is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 2008

Printed in the United Kingdom at the University Press, Cambridge

A catalogue record for this publication is available from the British Library

Library of Congress Cataloguing in Publication data

ISBN 978-0-521-86506-7 hardback ISBN 978-0-521-68357-9 paperback

Cambridge University Press has no responsibility for the persistence or accuracy of URLs for external or third-party internet websites referred to in this publication, and does not guarantee that any content on such websites is, or will remain, accurate or appropriate.

Cambridge University Press 978-0-521-68357-9 - Design of Comparative Experiments R. A. Bailey Frontmatter <u>More information</u>

Contents

Pr	Prefacepa			
1	Forw	Forward look		
	1.1	Stages	in a statistically designed experiment	1
		1.1.1	Consultation	1
		1.1.2	Statistical design	2
		1.1.3	Data collection	2
		1.1.4	Data scrutiny	3
		1.1.5	Analysis	4
		1.1.6	Interpretation	5
	1.2	The ide	eal and the reality	5
		1.2.1	Purpose of the experiment	5
		1.2.2	Replication	5
		1.2.3	Local control	6
		1.2.4	Constraints	6
		1.2.5	Choice	7
	1.3	An exa	ample	7
	1.4	Definir	ng terms	8
	1.5	Linear	model	14
	1.6	Summa	ary	15
	Questions for discussion			16
2 Unst		ructured	l experiments	19
	2.1	Compl	etely randomized designs	19
	2.2	Why a	nd how to randomize	20
	2.3	The tre	eatment subspace	21
	2.4	Orthog	gonal projection	23
	2.5	Linear	model	24
	2.6	Estima	ition	24
	2.7	Compa	arison with matrix notation	26
	2.8	Sums o	of squares	26
	2.9	Variano	ce	28
	2.10	Replica	ation: equal or unequal?	30

CAMBRIDGE

Cambridge University Press	
78-0-521-68357-9 - Design of Comparative Experiments	
R. A. Bailey	
Frontmatter	
More information	

vi		Contents
	2.11 Allowing for the overall mean	30
	2.12 Hypothesis testing	33
	2.13 Sufficient replication for power	35
	2.14 A more general model	38
	Questions for discussion	41
3	Simple treatment structure	43
	3.1 Replication of control treatments	43
	3.2 Comparing new treatments in the presence of a control	44
	3.3 Other treatment groupings	47
	Questions for discussion	52
4	Blocking	53
	4.1 Types of block	53
	4.1.1 Natural discrete divisions	53
	4.1.2 Continuous gradients	55
	4.1.3 Choice of blocking for trial management	55
	4.1.4 How and when to block	56
	4.2 Orthogonal block designs	57
	4.3 Construction and randomization	59 50
	4.4 Models for block designs	59
	4.5 Analysis when blocks have random effects	01 67
	4.0 Analysis when blocks have random enects 4.7 Why use blocks?	68
	4.8 Loss of power with blocking	69
	Questions for discussion	71
5	Factorial treatment structure	75
	5.1 Treatment factors and their subspaces	75
	5.2 Interaction	77
	5.3 Principles of expectation models	84
	5.4 Decomposing the treatment subspace	87
	5.5 Analysis	90
	5.6 Three treatment factors	92
	5.7 Factorial experiments	97
	5.8 Construction and randomization of factorial designs	98
	5.9 Factorial treatments plus control	99
	Questions for discussion	99
6	Row–column designs	105
	6.1 Double blocking	105
	6.2 Latin squares	106
	6.3 Construction and randomization	108
	6.4 Orthogonal subspaces	110
	6.5 Fixed row and column effects: model and analysis	110

Сс	Contents vii				
	66	Rando	m row and column effects: model and analysis	112	
	Quest	tions for	discussion	112	
	-				
7	Expe	riments	on people and animals	117	
	7.1	Introdu	action	117	
	7.2	Histori	ical controls	118	
	7.3	Cross-o	over trials	118	
	7.4	Matche	ed pairs, matched threes, and so on	119	
	7.5	Compl	etely randomized designs	120	
	7.6	Body p	barts as experimental units	120	
	7.7	Sequer	ntial allocation to an unknown number of patients	121	
	7.8	Safegu	ards against bias	122	
	7.9	Ethical	issues	124	
	7.10	Analys	sis by intention to treat	126	
	Quest	tions for	discussion	127	
8	Smal	l units iı	nside large units	131	
	8.1	Experi	mental units bigger than observational units	131	
		8.1.1	The context	131	
		8.1.2	Construction and randomization	132	
		8.1.3	Model and strata	132	
		8.1.4	Analysis	132	
		8.1.5	Hypothesis testing	135	
		8.1.6	Decreasing variance	137	
	8.2	Treatm	nent factors in different strata	138	
	8.3	Split-p	lot designs	146	
		8.3.1	Blocking the large units	146	
		8.3.2	Construction and randomization	147	
		8.3.3	Model and strata	148	
		8.3.4	Analysis	149	
		8.3.5	Evaluation	152	
	8.4	The sp	lit-plot principle	152	
	Quest	tions for	discussion	154	
9	More about Latin squares				
	9.1	Uses of	f Latin squares	157	
		9.1.1	One treatment factor in a square	157	
		9.1.2	More general row–column designs	158	
		9.1.3	Two treatment factors in a block design	159	
		9.1.4	Three treatment factors in an unblocked design	161	
	9.2	Graeco	o-Latin squares	162	
	9.3	Uses of	f Graeco-Latin squares	166	
		9.3.1	Superimposed design in a square	166	
		9.3.2	Two treatment factors in a square	166	
		9.3.3	Three treatment factors in a block design	166	

CAMBRIDGE

viii			Contents
	934	Four treatment factors in an unblocked design	167
Oue	stions for c	liscussion	167
10 The	calculus o	of factors	169
10.1	Introduc	ction	169
10.2	Relatior	ns on factors	169
	10.2.1	Factors and their classes	169
	10.2.2	Aliasing	170
	10.2.3	One factor finer than another	171
	10.2.4	Two special factors	171
10.3	Operatio	ons on factors	171
	10.3.1	The infimum of two factors	171
	10.3.2	The supremum of two factors	172
10.4	10.3.3	Uniform factors	175
10.4	Hasse d	1agrams	175
10.5	Subspac	ces defined by factors	178
	10.5.1	One subspace per factor	178
	10.5.2	Fitted values and crude sums of squares	178
10.0	10.5.3	Relations between subspaces	1/8
10.6	Orthogo	Definition of orthogonality	1/8
	10.6.1	Definition of orthogonality	1/8
	10.6.2	Projection matrices commute	1/9
	10.0.5	Proportional meeting	180
	10.6.4	A shair of fastors	181
10.7	10.0.5 Orthese		181
10.7		A second subspace for each factor	182
	10.7.1	Effects and sums of squares	182
10.9	10.7.2	tions on the Usess diagram	104
10.8		Degrees of freedom	185
	10.0.1	Sume of squares	103
10.0	Orthogo	sums of squares	187
10.7	10.0.1	Conditions on treatment factors	189
	10.9.1	Collections of expectation models	109
10.1	0 Orthogo	anal nlot structures	193
10.1	10 10 1	Conditions on plot factors	193
	10.10.1	Variance and covariance	193
	10.10.2	Matrix formulation	195
	10.10.4	Strata	196
10.1	1 Random	nization	196
10.1	2 Orthogo	onal designs	197
10.1	10.12.1	Desirable properties	197
	10.12.2	General definition	198
	10.12.3	Locating treatment subspaces	198
	10.12.4	Analysis of variance	200
	10.12.1	J S	200

CAMBRIDGE

Contents			ix
	10.13	Further examples	202
	Ouest	tions for discussion	202
11	Incor	nplete-block designs	219
	11.1	Introduction	219
	11.2	Balance	219
	11.3	Lattice designs	221
	11.4	Randomization	223
	11.5	Analysis of balanced incomplete-block designs	226
	11.6	Efficiency	229
	11.7	Analysis of lattice designs	230
	11.8	Optimality	233
	11.9	Supplemented balance	234
	11.10	Row–column designs with incomplete columns	235
	Quest	tions for discussion	238
12	Facto	orial designs in incomplete blocks	241
	12.1	Confounding	241
	12.2	Decomposing interactions	242
	12.3	Constructing designs with specified confounding	245
	12.4	Confounding more than one character	249
	12.5	Pseudofactors for mixed numbers of levels	251
	12.6	Analysis of single-replicate designs	253
	12.7	Several replicates	257
	Quest	tions for discussion	258
13	Fract	tional factorial designs	250
15	13 1	Fractional replicates	259
	13.1	Choice of defining contrasts	257
	13.2	Weight	200
	13.5	Resolution	265
	13.4	Analysis of fractional replicates	205
	Ouest	tions for discussion	200
14	Back	ward look	271
	14.1	Randomization	271
		14.1.1 Random sampling	271
		14.1.2 Random permutations of the plots	272
		14.1.3 Random choice of plan	273
		14.1.4 Randomizing treatment labels	273
		14.1.5 Randomizing instances of each treatment	275
		14.1.6 Random allocation to position	275
		14.1.7 Restricted randomization	278
	14.2	Factors such as time, sex, age and breed	279
	14.3	Writing a protocol	282

Х			Contents
	14.3.1	What is the purpose of the experiment?	282
	14.3.2	What are the treatments?	282
	14.3.3	Methods	283
	14.3.4	What are the experimental units?	283
	14.3.5	What are the observational units?	283
	14.3.6	What measurements are to be recorded?	283
	14.3.7	What is the design?	283
	14.3.8	Justification for the design	284
	14.3.9	Randomization used	284
	14.3.10	Plan	284
	14.3.11	Proposed statistical analysis	284
14.4	The eigh	nt stages	285
14.5	A story		286
Quest	ions for d	liscussion	290
Exercises	5		291
Sources o	of exampl	les, questions and exercises	313
Further	reading		319
References			321
Index			327

Preface

This textbook on the design of experiments is intended for students in their final year of a BSc in Mathematics or Statistics in the British system or for an MSc for students with a different background. It is based on lectures that I have given in the University of London and elsewhere since 1989. I would like it to become the book on design which every working statistician has on his or her shelves.

I assume a basic background in statistics: estimation, variance, hypothesis testing, linear models. I also assume the necessary linear algebra on which these rest, including orthogonal projections and eigenspaces of symmetric matrices. However, people's exposure to these topics varies, as does the notation they use, so I summarize what is needed at various points in Chapter 2. Skim that chapter to see if you need to brush up your knowledge of the background.

My philosophy is that you should not choose an experimental design from a list of named designs. Rather, you should think about all aspects of the current experiment, and then decide how to put them together appropriately. Think about the observational units, and what structure they have before treatments are applied. Think about the number and nature of the treatments. Only then should you begin to think about the design in the sense of which treatment is allocated to which experimental unit.

To do this requires a notation for observational units that does not depend on the treatments applied. The cost is a little more notation; the gain is a lot more clarity. Writing Y_{24} for the response on the fourth unit with treatment 2 goes with a mindset that ignores randomization, that manages the experiment by treatment, and that does not see the need for blindness. I label observational units by lower-case Greek letters: thus $Y(\omega)$ is the response on observational unit ω and $T(\omega)$ is the treatment on that unit. This notation merely mimics good practice in data recording, which has a row for each observational unit: three of the columns will be the one which names the units, the one which shows the treatments applied, and the one showing the responses. In this book, randomization, blindness and management by plot structure are recurring themes.

Most structure on the set of observational units, or on the set of treatments, can be defined by factors. I have developed a method for thinking about factors and their relationships, including the use of Hasse diagrams, which covers all orthogonal designs. The method uses the *infimum* $F \land G$ of two factors (which almost everybody else, except Tjur [113], writes as F.G) and the dual concept, the *supremum* $F \lor G$, which almost nobody else (again apart from Tjur) sees the need for, until degrees of freedom mysteriously go wrong. Everyone that I have taught this method to has reacted enthusiastically and adopted it. However, you need to have some idea of simple structure before you can appreciate the generality of this approach, which xii

Preface

is therefore delayed until Chapter 10.

The Hasse diagrams, and the insistence on naming observational units, are two features of this book that do not appear in most other books on the design of experiments. The third difference, which is relatively minor, is my notation for models in factorial designs. Expressions such as $\mu + \alpha_i + \beta_j + (\alpha\beta)_{ij}$ are compact ways of parametrizing several models at once, but they do encourage the fitting of inappropriate models (what Nelder has called *the neglect of marginality* in [83]). I take the view, explained in Chapter 5, that when we analyse data we first choose which model to fit and then estimate the parameters of that model; we do not need to know how to parametrize any of the models that we did not fit. Also in Chapter 5 I spell out three principles of modelling. The first two (Sum and Intersection) are often implicit, but their neglect can lead to contradictions. The third is Orthogonality: not everyone will agree with this (see Mead [77], for example), but I believe that we should aim for orthogonality between treatment factors wherever possible.

Another relatively minor difference in my approach is that my analysis-of-variance tables always include the grand mean. This is partly to make all the calculations easier, especially when using the Hasse diagram. A more important reason is to demonstrate that fitting a larger model after a smaller one (such as a complete two-way table after an additive model) is in principle no different from fitting treatment effects after removing the grand mean.

Unlike some topics in mathematics, Design of Experiments can set out its stall early. Thus Chapter 1 introduces most of the issues, and points the way forward to where in the book they are covered in more detail. Read this chapter to see if this book is for you.

Chapter 2 covers the simplest experiments: there is no structure on either the observational units or the treatments. This gives an opportunity to discuss randomization, replication and analysis of variance without extra complications, as well as to revise prerequisite knowledge.

Structure on the observational units is developed in Chapters 4 (simple blocking), 6 (rowcolumn designs) and 8 (observational units smaller than experimental units). Structure on the treatments is developed in parallel, in two independent chapters. Chapter 5 deals with factorial treatments (crossed factors) while Chapter 3 covers control treatments and other ways of recursively splitting up the treatments (nested factors). Chapter 3 can be omitted in a short course, but there are some areas of application where Chapter 3 is more relevant than Chapter 5. The 'mixed' case of factorial treatments plus a control is covered in some detail in Chapters 1, 5 and 10; this occurs surprisingly often in practice, and is frequently misunderstood.

Chapter 8 deals with the situation when one or more of the treatment factors must be applied to something larger than observational units. This topic is often misunderstood in practice, as a glance at too many journals of experimental science shows. Every working statistician should be aware of the danger of false replication.

Chapters 7 and 9 are somewhat light relief from the main development, and could be omitted without making later chapters inaccessible. Chapter 7 applies the ideas so far to experiments on people; it also describes issues peculiar to such experiments. The reader who is concerned exclusively with such experiments is advised to continue with one of the more specialized texts, such as those recommended in the Further Reading. Chapter 9 takes a single combinatorial object—the Latin square—and uses it in several ways to design different types of experiment. This demonstrates that there is no such thing as a 'Latin-square design', or,

Preface

xiii

perhaps, that the phrase has many interpretations.

Chapter 10 is my favourite. It pulls all the preceding material together into a single general approach. Because it is so general, the proofs are more abstract than those in the earlier chapters, and you may want to omit them at the first reading.

Chapters 11–13 introduce three more advanced topics that a statistician needs to be aware of: incomplete-block designs, confounded factorial designs, and fractional factorial designs. Anyone who needs to use these techniques frequently should probably follow this with some more advanced reading on these topics: some suggestions are made in Further Reading.

Finally, Chapter 14 is a rerun of Chapter 1 in the light of what has been covered in the rest of the book. Confronted with an experiment to design, how should we think about it and what should we do?

Each chapter is followed by questions for discussion. Because so many aspects of designing an experiment have no single 'right' answer, I have used these discussion questions with my students rather than requiring written homework. Each student is required to lead the discussion at least once. Apart from the initial difficulty of persuading students that this is not a terrifying ordeal, this technique has worked remarkably well. Other students join in; they share ideas and offer helpful criticism. At the end, I comment on both the presenting student's work and the general discussion, commending what is good, correcting any outright mistakes, and pointing out any important features that they have all missed. Every year a new set of students finds new nuances in these questions.

Some instructors may want to supplement the discussion questions with written homeworks. The Exercises at the end are provided for this purpose. They are less closely linked to the individual chapters than the questions for discussion.

Acknowledgements

I should like to thank the following people. R.E. Waller taught me the basics at the Air Pollution Research Unit: careful data recording, meticulous verification at every stage, and the excitement of extracting patterns from data. H.D. Patterson taught me so much about designing experiments while I was working as a post-doctoral researcher under his guidance. D.J. Finney was bold enough to let me teach the course on Design of Experiments in the Statistics MSc at the University of Edinburgh within twelve months of my meeting the material. J. A. Nelder appointed me as a statistician at Rothamsted Experimental Station even though I had no formal statistical qualification. D. A. Preece introduced me to such practical matters as data sniffing. D. R. Cox has been gently nagging me to write this book for over twenty years.

Thanks, too, to all the scientists whose interesting experiments I have worked on and to all those statisticians who continue to bring me their interesting design problems. Many of these are named at the back of the book.

Finally, thanks to all those students, friends and colleagues, in the widest sense of the word, who have read drafts of part of the material and made helpful suggestions. Of course, all opinions and any remaining errors are my own.

R. A. Bailey December 2007