

---

# Contents

---

<b>1</b>	<b>Introduction</b>	<b>1</b>
1.1	Longitudinal studies	1
1.2	Examples	3
1.3	Notation	15
1.4	Merits of longitudinal studies	16
1.5	Approaches to longitudinal data analysis	17
1.6	Organization of subsequent chapters	20
<b>2</b>	<b>Design considerations</b>	<b>22</b>
2.1	Introduction	22
2.2	Bias	22
2.3	Efficiency	24
2.4	Sample size calculations	26
2.4.1	Continuous responses	28
2.4.2	Binary responses	30
2.5	Further reading	31
<b>3</b>	<b>Exploring longitudinal data</b>	<b>33</b>
3.1	Introduction	33
3.2	Graphical presentation of longitudinal data	34
3.3	Fitting smooth curves to longitudinal data	41
3.4	Exploring correlation structure	46
3.5	Exploring association amongst categorical responses	52
3.6	Further reading	53
<b>4</b>	<b>General linear models for longitudinal data</b>	<b>54</b>
4.1	Motivation	54
4.2	The general linear model with correlated errors	55
4.2.1	The uniform correlation model	55
4.2.2	The exponential correlation model	56
4.2.3	Two-stage least-squares estimation and random effects models	57
4.3	Weighted least-squares estimation	59
4.4	Maximum likelihood estimation under Gaussian assumptions	64
4.5	Restricted maximum likelihood estimation	66
4.6	Robust estimation of standard errors	70

<b>5 Parametric models for covariance structure</b>	81
5.1 Introduction	81
5.2 Models	82
5.2.1 Pure serial correlation	84
5.2.2 Serial correlation plus measurement error	89
5.2.3 Random intercept plus serial correlation plus measurement error	90
5.2.4 Random effects plus measurement error	91
5.3 Model-fitting	93
5.3.1 Formulation	94
5.3.2 Estimation	95
5.3.3 Inference	97
5.3.4 Diagnostics	98
5.4 Examples	99
5.5 Estimation of individual trajectories	110
5.6 Further reading	113
<b>6 Analysis of variance methods</b>	114
6.1 Preliminaries	114
6.2 Time-by-time ANOVA	115
6.3 Derived variables	116
6.4 Repeated measures	123
6.5 Conclusions	125
<b>7 Generalized linear models for longitudinal data</b>	126
7.1 Marginal models	126
7.2 Random effects models	128
7.3 Transition (Markov) models	130
7.4 Contrasting approaches	131
7.5 Inferences	137
<b>8 Marginal models</b>	141
8.1 Introduction	141
8.2 Binary responses	142
8.2.1 The log-linear model	142
8.2.2 Log-linear models for marginal means	143
8.2.3 Generalized estimating equations	146
8.3 Examples	148
8.4 Counted responses	160
8.4.1 Parametric modelling for count data	160
8.4.2 Generalized estimating equation approach	162
8.5 Sample size calculations revisited	165
8.6 Further reading	167

<b>9</b>	<b>Random effects models</b>	169
9.1	Introduction	169
9.2	Estimation for generalized linear mixed models	171
9.2.1	Conditional likelihood	171
9.2.2	Maximum likelihood estimation	172
9.3	Logistic regression for binary responses	175
9.3.1	Conditional likelihood approach	175
9.3.2	Random effects models for binary data	178
9.3.3	Examples of logistic models with Gaussian random effects	180
9.4	Counted responses	184
9.4.1	Conditional likelihood method	184
9.4.2	Random effects models for counts	186
9.4.3	Poisson–Gaussian random effects models	188
9.5	Further reading	189
<b>10</b>	<b>Transition models</b>	190
10.1	General	190
10.2	Fitting transition models	192
10.3	Transition models for categorical data	194
10.3.1	Indonesian children’s study example	197
10.3.2	Ordered categorical data	201
10.4	Log-linear transition models for count data	204
10.5	Further reading	206
<b>11</b>	<b>Likelihood-based methods for categorical data</b>	208
11.1	Introduction	208
11.1.1	Notation and definitions	209
11.2	Generalized linear mixed models	209
11.2.1	Maximum likelihood algorithms	212
11.2.2	Bayesian methods	214
11.3	Marginalized models	216
11.3.1	An example using the Gaussian linear model	218
11.3.2	Marginalized log-linear models	220
11.3.3	Marginalized latent variable models	222
11.3.4	Marginalized transition models	225
11.3.5	Summary	231
11.4	Examples	231
11.4.1	Crossover data	231
11.4.2	Madras schizophrenia data	234
11.5	Summary and further reading	243
<b>12</b>	<b>Time-dependent covariates</b>	245
12.1	Introduction	245
12.2	An example: the MSCM study	247

12.3	Stochastic covariates	253
12.3.1	Estimation issues with cross-sectional models	254
12.3.2	A simulation illustration	256
12.3.3	MSCM data and cross-sectional analysis	257
12.3.4	Summary	258
12.4	Lagged covariates	259
12.4.1	A single lagged covariate	259
12.4.2	Multiple lagged covariates	260
12.4.3	MSCM data and lagged covariates	261
12.4.4	Summary	265
12.5	Time-dependent confounders	265
12.5.1	Feedback: response is an intermediate and a confounder	266
12.5.2	MSCM data and endogeneity	268
12.5.3	Targets of inference	269
12.5.4	Estimation using $g$ -computation	273
12.5.5	MSCM data and $g$ -computation	275
12.5.6	Estimation using inverse probability of treatment weights (IPTW)	276
12.5.7	MSCM data and marginal structural models using IPTW	279
12.5.8	Summary	280
12.6	Summary and further reading	280
<b>13</b>	<b>Missing values in longitudinal data</b>	<b>282</b>
13.1	Introduction	282
13.2	Classification of missing value mechanisms	283
13.3	Intermittent missing values and dropouts	284
13.4	Simple solutions and their limitations	287
13.4.1	Last observation carried forward	287
13.4.2	Complete case analysis	288
13.5	Testing for completely random dropouts	288
13.6	Generalized estimating equations under a random missingness mechanism	293
13.7	Modelling the dropout process	295
13.7.1	Selection models	295
13.7.2	Pattern mixture models	299
13.7.3	Random effect models	301
13.7.4	Contrasting assumptions: a graphical representation	303
13.8	A longitudinal trial of drug therapies for schizophrenia	305
13.9	Discussion	316

<b>14 Additional topics</b>	<b>319</b>
14.1 Non-parametric modelling of the mean response	319
14.1.1 Further reading	326
14.2 Non-linear regression modelling	326
14.2.1 Correlated errors	328
14.2.2 Non-linear random effects	329
14.3 Joint modelling of longitudinal measurements and recurrent events	329
14.4 Multivariate longitudinal data	332
<b>Appendix Statistical background</b>	<b>337</b>
A.1 Introduction	337
A.2 The linear model and the method of least squares	337
A.3 Multivariate Gaussian theory	339
A.4 Likelihood inference	340
A.5 Generalized linear models	343
A.5.1 Logistic regression	343
A.5.2 Poisson regression	344
A.5.3 The general class	345
A.6 Quasi-likelihood	346
<b>Bibliography</b>	<b>349</b>
<b>Index</b>	<b>369</b>