Copyrighted Material

Monographs on Statistics and Applied Probability 113

Mixed Effects Models for Complex Data



Lang Wu



Copyrighted Material

Mixed Effects Models For Complex Data

Lang Wu

____ |____

Contents

Preface							
1	Intr	Introduction					
	1.1	Introd	luction	1			
	1.2	Longi	tudinal Data and Clustered Data	3			
	1.3	Some	Examples	6			
		1.3.1	A Study on Mental Distress	6			
		1.3.2	An AIDS study	9			
		1.3.3	A Study on Students' Performance	12			
		1.3.4	A Study on Children Growth	13			
	1.4	Regre	ssion Models	14			
		1.4.1	General Concepts and Approaches	14			
		1.4.2	Regression Models for Cross-Sectional Data	16			
		1.4.3	Regression Models for Longitudinal Data	20			
		1.4.4	Regression Models for Survival Data	23			
	1.5	Mixed	l Effects Models	24			
		1.5.1	Motivating Examples	24			
		1.5.2	LME Models	27			
		1.5.3	GLMM, NLME, and Frailty Models	29			
	1.6	Comp	lex or Incomplete Data	30			
		1.6.1	Missing Data	31			
		1.6.2	Censoring, Measurement error, and Outliers	32			
		1.6.3	Simple Methods	33			
	1.7	Software					
	1.8	Outlin	ne and Notation	35			

iv			MIXED EFFECTS MODELS FOR COMPLEX D	ATA
2	Mix	ed Effe	cts Models	39
	2.1	Introdu	uction	39
	2.2	Linear	Mixed Effects (LME) Models	41
		2.2.1	Linear Regression Models	41
		2.2.2	LME Models	42
	2.3	Nonlir	near Mixed-Effects (NLME) Models	49
		2.3.1	Nonlinear Regression Models	49
		2.3.2	NLME Models	52
	2.4	Genera	alized Linear Mixed Models (GLMMs)	58
		2.4.1	Generalized Linear Models (GLMs)	58
		2.4.2	GLMMs	62
	2.5	Nonpa	rametric and Semiparametric Mixed-Effects Models	66
		2.5.1	Nonparametric and Semiparametric Regression Models	66
		2.5.2	Nonparametric and Semiparametric Mixed Effects Models	74
	2.6	Comp	utational Strategies	78
		2.6.1	"Exact" Methods	81
		2.6.2	EM Algorithms	83
		2.6.3	Approximate Methods	85
	2.7	Furthe	r Topics	89
		2.7.1	Model Selection and Further Topics	89
		2.7.2	Choosing A Mixed Effects Model and Method	93
	2.8	Softwa	are	94
3	Miss	sing Da	ta, Measurement Errors, Censoring, and Outliers	97
	3.1	Introdu	uction	97
	3.2	Missin	g Data Mechanisms and Ignorability	99
		3.2.1	Missing Data Mechanisms	99
		3.2.2	Ignorability	100
	3.3	Genera	al Methods for Missing Data	102

C	ONTE	ENTS		v	
		3.3.1	Naive Methods	102	
		3.3.2	Formal Methods	104	
		3.3.3	Sensitivity Analysis	107	
		3.3.4	Selection Models versus Pattern-Mixture Models	108	
		3.3.5	Choosing a Method for Missing Data	109	
	3.4	EM A	lgorithms	110	
		3.4.1	Introduction	110	
		3.4.2	An EM Algorithm for Missing Covariates	114	
		3.4.3	Properties and Extensions	115	
	3.5	Multi	ple Imputation	117	
		3.5.1	Introduction	117	
		3.5.2	Multiple Imputation Methods	118	
		3.5.3	Examples	122	
	3.6 General Methods for Measurement Errors				
		3.6.1	Covariate Measurement Errors	123	
		3.6.2	General Methods for Measurement Errors	125	
	3.7	Gener	al Methods for Outliers	126	
		3.7.1	Outliers	126	
		3.7.2	General Robust Methods	127	
	3.8	Softw	are	128	
4	Mix	ed Effe	ects Models with Missing Data	131	
	4.1	Introd	uction	131	
	4.2	Mixed	l Effects Models with Missing Covariates	133	
		4.2.1	Missing Data in Time-Independent Covariates	133	
		4.2.2	Non-ignorable Missing Covariates	139	
		4.2.3	Missing Data in Time-Dependent Covariates	141	
		4.2.4	Multivariate, Semiparametric, and Nonparametric Models	145	
	4.3	Appro	oximate Methods	147	

vi			MIXED EFFECTS MODELS FOR COMPLEX D	ATA		
		4.3.1	Linearization	148		
		4.3.2	Laplace Approximation	151		
	4.4	Mixed	Effects Models with Missing Responses	154		
		4.4.1	Exact Likelihood Inference	154		
		4.4.2	Approximate Likelihood Inference	157		
	4.5	Multip	ble Imputation Methods	159		
		4.5.1	Advantages and Issues of Multiple Imputation Methods	159		
		4.5.2	Multiple Imputation for Mixed Effects Models with Missing Data	160		
		4.5.3	Computational Issues and Other Methods	162		
	4.6	Comp	utational Strategies	163		
		4.6.1	Sampling Methods	163		
		4.6.2	Speed Up EM Algorithms	166		
		4.6.3	Convergence	167		
	4.7	Exam	ples	169		
5	Mixe	ed Effe	cts Models with Measurement Errors	177		
	5.1	Introd	uction	177		
	5.2	Measu	Measurement Error Models and Methods			
		5.2.1	Measurement Error Models	179		
		5.2.2	Measurement Error Methods	184		
		5.2.3	Bias Analysis	186		
	5.3	Two-S	tep Methods and Regression Calibration Methods	187		
		5.3.1	Two-Step Methods	187		
		5.3.2	A Two-Step Method for NLME Models with Measurement Errors	188		
		T :leal:	hood Methods	190		
	5.4	Likein				
	5.4	5.4.1	Joint Likelihood	190		
	5.4	5.4.1 5.4.2	Joint Likelihood Estimation Based on Monte-Carlo EM Algorithms	190 191		
	5.4	5.4.1 5.4.2 Appro	Joint Likelihood Estimation Based on Monte-Carlo EM Algorithms ximate Methods	190 191 192		

CC	ONTE	NTS	vii
		5.5.1 Linearization	193
		5.5.2 Laplace Approximation	194
	5.6	Measurement Error and Missing Data	196
		5.6.1 Measurement Errors and Missing Data in Covariates	197
		5.6.2 Measurement Errors in Covariates and Missing Data in Responses	199
6	Mix	ed Effects Models with Censoring	203
	6.1	Introduction	203
	6.2	Mixed Effects Models with Censored Responses	204
		6.2.1 LME Models	206
		6.2.2 GLMM and NLME Models	210
		6.2.3 Imputation Methods	211
	6.3	Mixed Effects Models with Censoring and Measurement Errors	214
		6.3.1 LME Models	214
		6.3.2 GLMM and NLME Models	217
	6.4	Mixed Effects Models with Censoring and Missing Data	221
	6.5	Appendix	224
7	Surv	vival Mixed Effects (Frailty) Models	229
	7.1	Introduction	229
	7.2	Survival Models	231
		7.2.1 Nonparametric Methods	232
		7.2.2 Semiparametric Models	234
		7.2.3 Parametric Models	236
		7.2.4 Interval Censoring and Informative Censoring	242
	7.3	Frailty Models	243
		7.3.1 Clustered Survival Data	243
		7.3.2 Models and Inference	245
	7.4	Survival and Frailty Models with Missing Covariates	246

_____|

| ____

|

viii		MIXED EFFECTS MODELS FOR COMPLEX DATA					
		7.4.1	Survival Models with Missing Covariates	246			
		7.4.2	Frailty Models with Missing Covariates	248			
	7.5	Frailty	y Models with Measurement Errors	249			
8	Join	nt Mode	eling Longitudinal and Survival Data	253			
	8.1	Introd	uction	253			
	8.2	Joint l	Modeling for Longitudinal Data and Survival Data	256			
		8.2.1	Joint Models with Right Censored Survival Data	256			
		8.2.2	Joint Models with Interval-Censored Survival Data	260			
	8.3	Two-S	Step Methods	263			
		8.3.1	Simple Two-Step Methods	263			
		8.3.2	Modified Two-Step Methods	265			
	8.4	Joint l	Likelihood Inference	266			
		8.4.1	Exact Likelihood Inference	266			
		8.4.2	Approximate Inference	268			
	8.5	Joint l	Models with Incomplete Data	270			
		8.5.1	Joint Models with Missing Data	271			
		8.5.2	Joint Models with Measurement Errors	278			
	8.6	Joint Modeling of Several Longitudinal Processes					
		8.6.1	Multivariate Mixed Effects Models with Incomplete Data	282			
		8.6.2	Other Joint Modeling Approaches	286			
		8.6.3	Joint Longitudinal Models with Incomplete Data: A Summary	289			
9	Rob	oust Miz	xed Effects Models	293			
	9.1	Introduction					
	9.2	Robus	st Methods	296			
		9.2.1	Robust Distributions	296			
		9.2.2	M-Estimators	298			
	9.3	Mixed	1 Effects Models with Robust Distributions	301			

|____

CC	ONTE	NTS		ix
		9.3.1	LME Models with Multivariate <i>t</i> -Distributions	301
		9.3.2	GLMM and NLME Models with Multivariate t -Distributions	305
		9.3.3	Robust Models with Incomplete Data	307
	9.4	M-esti	mators for Mixed Effects Models	308
		9.4.1	M-estimators for GLM	308
		9.4.2	M-estimators for Mixed Effects Models	310
		9.4.3	A Monte-Carlo Newton-Raphson Method	313
		9.4.4	A Robust Approximate Method	316
		9.4.5	Appendix	319
	9.5	Robus Data	t Inference for Mixed Effects Models with Incomplete	322
		9.5.1	Robust Inference with Covariate Measurement Errors	322
		9.5.2	A Robust Approximate Method	326
		9.5.3	Robust Inference with Non-ignorable Missing Data	328
		9.5.4	Appendix	330
10	Gen	eralized	l Estimating Equations (GEE)	333
	10.1	Introdu	action	333
	10.2	Margin	nal Models	336
		10.2.1	Quasi-Likelihood and GEE	336
		10.2.2	Marginal Models for Longitudinal Data or Cluster Data	341
		10.2.3	GEE for Marginal Models	344
	10.3	Estima	ting Equations with Incomplete Data	347
		10.3.1	Weighted GEE for Missing Data	347
		10.3.2	Weighted GEE for Measurement Errors and Missing Data	349
	10.4	Discus	sion	351

Х	MIXED EFFECTS MODELS FOR COMPLEX DA	ATA				
11	Bayesian Mixed Effects Models	353				
	11.1 Introduction	353				
	11.2 Bayesian Methods	354				
	11.2.1 General Concepts	354				
	11.2.2 Prior Distributions	356				
	11.3 Bayesian Mixed Effects Models	358				
	11.3.1 Bayesian LME Models	358				
	11.3.2 Bayesian GLMMs	361				
	11.3.3 Bayesian NLME Models	363				
	11.4 Bayesian Mixed Models with Missing Data	366				
	11.4.1 Bayesian Models with Missing Data	366				
	11.4.2 Bayesian Mixed Models with Missing Data	368				
	11.5 Bayesian Models with Covariate Measurement Errors	369				
	11.5.1 Bayesian Regression Models with Covariate Measure- ment Errors	369				
	11.5.2 Bayesian Mixed Models with Covariate Measurement Errors	370				
	11.6 Bayesian Joint Models of Longitudinal and Survival Data	372				
12	Appendix: Background Materials	375				
	12.1 Likelihood Methods	375				
	12.2 The Gibbs Sampler and MCMC Methods	380				
	12.3 Rejection Sampling and Importance Sampling Methods	383				
	12.4 Numerical Integration and the Gauss-Hermite Quadrature Method	385				
	12.5 Optimization Methods and the Newton-Raphson Algorithm	387				
	12.6 Bootstrap Methods	387				
	12.7 Matrix Algebra and Vector Differential Calculus	389				
References						
Index						
Abstract						