

Contents

Contents	i
Nomenclature	v
1 Introduction and Outline	1
1.1 Mathematical formulation	4
1.2 Fitness criterion	5
1.3 Variational equations	5
1.4 Numerical solution of the model equations	7
1.5 Minimisation	8
1.6 Statistical background	9
1.7 Parameter constraints	12
1.8 A case study from biochemistry	13
1.9 A case study from population dynamics	14
1.10 Concluding remarks	16
Appendix 1.A	16
Appendix 1.B	16
Appendix 1.C	17
2 Parameter Estimation by Total Least Squares	21
2.1 Introduction	21
2.2 Mathematical description of TLS	22
2.3 Statistical background	25
2.4 Total least squares with parameter constraints	26
2.5 Conclusions	28
3 Maximum Likelihood Estimators	29
3.1 Introduction	29
3.2 Least squares criterion	29
3.3 Weighted least squares criterion	31
3.3.1 A priori known weights	31
3.3.2 Unknown weights	31
3.4 Numerical computation (independent case)	35
3.5 Dependent measurement errors	37
3.6 Numerical computation (dependent case)	39
3.7 MLE and total least squares	41

3.7.1	A priori known weights	41
3.7.2	Unknown weights (TLS)	42
3.7.3	Independent measurement errors	42
3.7.4	Dependent measurement errors	43
3.8	L_1 -optimisation and Laplace distribution	44
3.9	Conclusions	45
4	Nonlinear Regression, Bias and Curvature	47
4.1	Overview of the chapter	47
4.2	Linear Regression	48
4.3	Biased estimators	50
4.3.1	Analytic result	50
4.3.2	Monte Carlo	52
4.3.3	Bias measure of Box	53
4.4	Curvature measures	54
4.5	Investigation of levelsets	62
4.6	Parameter constraints and redundancy	63
4.7	Concluding remarks	64
5	Optimal Experiment Design	67
5.1	Introduction	67
5.2	Problem formulation	67
5.3	Parameter - state variable dependence	69
5.4	OED and improved confidence regions	72
5.4.1	Design criteria	72
5.4.2	Repeated design	73
5.4.3	Sequential design	75
5.5	OED and model discrimination	78
5.6	OED and nonlinearity	79
5.7	Concluding remarks	79
6	Case Studies	81
6.1	Production of resins	81
6.1.1	Introduction	81
6.1.2	Reaction mechanism	82
6.1.3	Experiments performed	83
6.1.4	Model equations	84
6.1.5	Treatment of the melamine concentrations	85
6.1.6	Parameter estimation	86
6.1.7	Reparametrisation and results	86
6.1.8	Conclusions	91
6.2	Modelling of blood coagulation	94
6.2.1	Introduction	94
6.2.2	Experimental data	95
6.2.3	Reaction mechanism	96

6.2.4	Model equations	98
6.2.5	Parameter estimation and model validation	100
6.2.6	Results	102
6.2.7	Conclusions	103
6.3	Production by plant cells in suspension	106
6.3.1	Introduction	106
6.3.2	Materials and methods	107
6.3.3	Model development	108
6.3.4	Experimental results and final model confirmation	111
6.3.5	Conclusions	116
6.4	ZLA-kinetics	119
6.4.1	Description of the chemical reactions	119
6.4.2	Problem description of ZLA-kinetics	120
6.4.3	Parameter estimation results for ZLA-kinetics	121
6.4.4	Conclusions and remarks for further research	123
6.5	Water penetration in an aramide yarn	124
6.5.1	Introduction to the problem	124
6.5.2	Proposed models	124
6.5.3	Numerical implementation	126
6.5.4	Model discrimination and parameter estimation	126
6.5.5	Conclusions	128
6.6	Macroeconomic time series	130
6.6.1	Introduction	130
6.6.2	Derivation of candidate models	130
6.6.3	Comparison of prediction results	132
6.6.4	Concluding remarks	133
6.7	The DOW problem	134
6.7.1	Introduction	134
6.7.2	Description of the problem	134
6.7.3	Data	136
6.7.4	Results	136
6.7.5	More general model equations	140
6.7.6	Concluding remarks	142
	Appendix 6.A	145
	Appendix 6.B	149
7	Software Design and Implementation	151
7.1	Introduction	151
7.2	Design principles of the application splds	152
7.3	Structure of the software	154
7.4	The modelfile	155
7.5	The datafile	160
7.6	Algebraic Engine	162
7.7	Filter	163

7.8 Numerical engine	163
7.9 Graphical user interface (GUI)	164
7.10 Database manager	165
7.11 Concluding remarks	166
Bibliography	167
Index	173