

Contents

1	Introduction	1
	References	4
2	Motivation	5
2.1	Introduction	5
2.2	Notation	6
2.3	Assumptions	7
2.4	On the Existence of Estimators	8
2.5	Fisher's Information Matrix	9
2.6	Linearization of the Model	11
2.6.1	Examples	11
	References	14
3	Locally Optimal Designs	15
3.1	Introduction	15
3.2	Formulation	16
3.3	Special Cases	17
3.4	Applications	18
3.5	Canonical Form of a Design ($c(\theta)$ -Optimality)	21
3.6	Designs for Subsets of Parameters	23
3.7	Geometrical Aspects	24
3.8	Partially Nonlinear Models	27
3.9	Discussion	29
	References	29
4	Static Design	31
4.1	Introduction	31
4.2	Locally Optimal Approach	32
4.3	Lauter's Approach	32
4.4	Stone and Morris Approach	33
4.5	Maxi-Min Criterion	34
4.6	Constant Information Designs	34
4.7	Applications from Chemical Kinetics	35
	References	37

5	Sequential Designs	39
5.1	Introduction	39
5.2	Background	40
5.3	Extensions	41
5.4	Binary Response Problems	43
5.5	Stochastic Approximation	44
5.6	Application to Cancer Problems	49
	References	50
6	Approximate Confidence Regions	51
6.1	Introduction	51
6.2	Background	51
6.3	Confidence Regions	52
6.4	Simulation Study	54
6.5	The Michaelis–Menten Model of Pharmacokinetics	55
	References	57
7	Simulation Studies	59
7.1	Introduction	59
7.2	The Dilution Series Assessment	59
7.3	The Strategy of Simulation I	62
7.4	Simulation Procedures	64
7.5	Discussion I	65
7.6	The First Order Growth Law	67
7.7	Strategy and Procedures of Simulation II	68
7.8	Discussion II	71
8	Optimal Design in Rythmometry	73
8.1	Introduction	73
8.2	Background	74
8.3	D-Optimal Design	75
8.4	c-Optimal Design	77
8.5	Restricted Design Space	79
8.6	Synopsis	80
8.7	Engineering Application	81
	References	83
9	Discussion	85
	Reference	87
	Appendix 1	89
	Appendix 2	91

Contents	ix
Appendix 3	93
Appendix 4	95
Appendix 5	99