
CONTENTS

Motivation and Objectives	1
I State of the art	9
1 Parameter Estimation	11
1.1 Optimization and Intervals	11
1.2 Optimizing Identifiability	15
1.2.1 Methods based on FIM	15
1.2.2 Monte-Carlo methods	17
1.2.3 Practical Identifiability and Optimality	19
1.3 Identification with Uncertainty	22
1.3.1 Error-bounded Estimation	23
1.4 Software and optimization tools	25
1.4.1 Scatter search for Matlab	25
1.4.2 Covariance Matrix Adaptive Estimation	26

1.4.3	ϵ - MOGA Evolutionary Algorithm	26
2	Models for the artificial pancreas development	29
2.1	Introduction	29
2.2	Insulin absorption models	32
2.2.1	UVA model	33
2.2.2	Cambridge model	35
2.3	Glucose absorption models	37
2.3.1	UVA model	38
2.3.2	Cambridge model	39
2.4	Endogenous models	41
2.4.1	Bergman model	41
2.4.2	Panunzi model	43
2.4.3	UVA model	44
2.4.4	Cambridge model	46
2.5	Critical selection of models	49
3	Identification in Diabetes	57
3.1	Patient Identification	58
3.2	Experiment Design for Artificial Pancreas	61
3.3	Uncertainty and Interval Identification in Diabetes	64
Conclusions		67

II Issues in Continuous Glucose Monitoring for Patient

Identification	71
4 Optimal Experiment Design	73
4.1 Introduction	73
4.2 Experiments designed with Bergman's model	76
4.3 Experiments designed with modified Panunzi's model	85
4.4 Discussion and clinical protocol	94
5 CGM Statistical Modeling and Validation	99
5.1 Data and methodology	100
5.2 CGM Modelling	102
5.2.1 Analysis of delay	104
5.2.2 Analysis of Stationarity	105
5.2.3 Distribution fitting	109
5.3 Validation	111
Conclusions	117
III Interval identification	121
6 A New Paradigm for Model Individualization in T1DM	123
6.1 Optimization Set-up	124
6.2 Identification from reference glucose	128
6.3 Identification from CGM	130
6.4 Discussion	136
7 Identification From in-Patient Reference Data	139

7.1	Optimization and index definition	140
7.2	Validation Results	147
7.3	Best-case permutation	153
7.4	Discussion	156
8	Identification Under Domiciliary Conditions	159
8.1	Optimization settings and parameters	159
8.2	Influence of the Lack of Plasma Insulin Measurements	163
8.3	Identification from CGM data	171
8.4	Discussion	180
Conclusions		183
Final conclusions and future work		186