

Contents

I Prologue	1
1 Justification, objectives and contributions	3
1.1 Justification	4
1.2 Objectives	7
1.3 Contributions	9
1.3.1 Papers in peer-reviewed journals	9
1.3.2 Poster conference contributions	10
1.3.3 Oral conference contributions	10
1.3.4 Chapters of books	12
1.3.5 Software	12
1.3.6 Awards	12
2 On latent variable-based regression models	13
2.1 Introduction	14
2.2 Partial Least Square (PLS) Regression	14
2.2.1 Prediction uncertainty	16
2.2.2 Model inversion	17
2.2.3 Optimization problem formulation	21
2.3 Sequential Multi-block (SMB) PLS regression	22
Appendices	25
2.A SMB PLS regression	25
3 Materials	27

3.1	Hardware	28
3.2	Software	28
3.3	Datasets	28
II	Novel methodological contributions	29
4	On the properties of PLS for analyzing Design of Experiments	31
4.1	Introduction	32
4.2	Two-level factorial designs	34
4.2.1	Full factorial designs: 2^k	34
4.2.2	Fractional factorial designs: 2^{k-p}	39
4.3	Traditional approaches applied to two-level factorial designs with missing runs	40
4.4	PLS applied to two-level factorial designs with missing runs	41
4.4.1	Lack of resources to execute a factorial design (scenario i))	41
4.4.2	Unexpected problems in the execution of some runs (scenario ii)	44
4.5	Illustrative examples	45
4.5.1	First illustrative example: 2^4	45
4.5.2	Second illustrative example: 2^{6-2}	51
4.6	Discussion and conclusions	54
Appendices	56
4.A	Definition of PLS coefficients from NIPALS algorithm in a full factorial design	56
4.B	Definition of PLS coefficients from the criterion of maximum variance in a full factorial design	58
4.C	The second PLS component lacks predictive ability in a full factorial design	59
4.D	Illustrating the latent space in a full factorial design	60
4.E	Partitioning of the sum of squares for PLS in a full factorial design	61
4.F	Lists of recommended combinations of missing runs for the most popular designs	63
5	Defining multivariate raw materials specifications	67
5.1	Introduction	68
5.2	Data requirements	72
5.3	Defining the design space in the latent space by means of PLS	72
5.3.1	Design space with no uncertainty	72
5.3.2	High confidence design space	74
5.4	Exploiting the model	80
5.5	Industrial case studies	81
5.5.1	First industrial case study: cereal extraction process	81
5.5.2	Second industrial case study: blown film process	89
5.6	Conclusion	91

Appendices	93
5.A Specification confidence limits for the l -th critical quality attributes	93
6 Defining multivariate raw material specifications via SMB-PLS	97
6.1 Introduction	98
6.2 Data requirements	99
6.3 The SMB-PLS model in the raw material paradigm	100
6.4 Defining the design space in the latent space by means of SMB-PLS	101
6.5 Multivariate raw material specification region	102
6.5.1 Without improved control	102
6.5.2 Under improved control	104
6.6 Presence of known disturbances affecting control actions	105
6.7 Industrial case study	106
6.8 Conclusions	117
Appendices	118
6.A SMB-PLS weights transformed to be independent between components	118
7 Latent space-based multivariate capability index	121
7.1 Introduction	122
7.2 Data requirements	123
7.3 Supplier's raw material operating space (RMOS)	123
7.4 Latent space-based multivariate capability index	124
7.5 Diagnosing assignable causes	126
7.6 Proposed methodology	127
7.7 Industrial case study	128
7.8 Conclusions	132
III Novel applications	135
8 Health application: COVID-19 Pandemic	137
8.1 Introduction	138
8.2 Machine learning models for early estimation of COVID-19 mortality risk in hospitalized patients	138
8.3 Methods: Reformulation of the optimization problem	139
8.3.1 PLS customized optimization problem formulation	139
8.3.2 Nonlinear PLS customized optimization problem formulation	140
8.3.3 SMB-PLS customized optimization problem formulation	143
8.4 A Latent variable-based alternative to clinical trials upon new diseases	144
8.4.1 Simulated case study	146
8.4.2 Spanish society of hospital pharmacy case study	157

8.5 Conclusion	163
Appendices	164
8.A Function: H	164
9 Industrial application: Multivariate Six Sigma	165
9.1 Introduction	166
9.2 Methods	167
9.2.1 Six Sigma's DMAIC methodology	167
9.2.2 Optimization of the latent space-based multivariate capability index	167
9.3 Results	168
9.3.1 Define	168
9.3.2 Measure	169
9.3.3 Analyze	170
9.3.4 Improve	173
9.3.5 Control	174
9.4 Conclusion	176
IV Graphical user interface	177
10 Dragonet: a software for data analysis and process optimization	179
10.1 Introduction	180
10.2 Importing data	180
10.3 Building a model	182
10.4 Data analysis	184
10.5 Process optimization	187
10.6 Defining the high-confidence design space	190
10.7 Conclusions	192
V Epilogue	193
11 Conclusions	195
11.1 Meeting the objectives	196
11.2 Future research lines and transfer activities	199
Bibliography	201