

Contents

Abstract	i
Acknowledgements	iii
Introduction	1
1 Preliminaries	7
1.1 Notation and Abbreviations	7
1.2 Mathematical Prerequisites	8
1.3 Experimental Methodology	10
1.3.1 Hardware and Software, 10	
1.3.2 Averaging, 10	
1.3.3 Statistical Significance, 11	
1.4 Test Sets	13
1.4.1 Linear Programming, 13	
1.4.2 Metabolic Networks, 14	
1.4.3 Mixed-Integer Nonlinear Programming, 14	
2 Iterative Refinement for Linear Programming	15
2.1 Introduction to Linear Programming	16
2.1.1 Basic Concepts, 16	
2.1.2 Algorithms, 18	
2.1.3 Numerics, 19	
2.1.4 Iterative Refinement for Linear Systems of Equations, 22	
2.2 An Iterative Refinement Scheme for Linear Programs	23
2.2.1 The Basic Algorithm, 23	
2.2.2 Convergence, 28	
2.2.3 Oracle-Polynomial Running Time, 31	
2.2.4 Arithmetic Precision, 33	

2.3	Handling LPs of General Form	34
2.3.1	Variables with General Bounds, 34	
2.3.2	Inequality Constraints, 35	
2.4	Refining Infeasible and Unbounded LPs	37
2.4.1	Testing Feasibility, 38	
2.4.2	Approximate Proofs of Infeasibility, 40	
2.4.3	Testing Unboundedness, 44	
2.4.4	An Integrated Refinement Algorithm, 45	
2.5	Computational Study	47
2.5.1	Implementation, 47	
2.5.2	Experimental Setup, 50	
2.5.3	Computational Results, 51	
2.6	Conclusion	55
3	Exact Linear Programming over the Rational Numbers	57
3.1	Background and Previous Work	57
3.1.1	Edmonds' Q-Pivoting, 58	
3.1.2	Gärtner's Mixed-Precision Simplex Algorithm, 58	
3.1.3	QSOPT_EX's Incremental Precision Boosting, 59	
3.1.4	Diophantine Approximation Algorithms, 60	
3.1.5	Ellipsoid and Interior Point Methods, 62	
3.1.6	Rigorous Bounds, 63	
3.2	Exact Bases via Iterative Refinement	64
3.2.1	A First Experiment, 64	
3.2.2	Convergence to Optimal Bases, 65	
3.2.3	Iterative Refinement with Basis Verification, 73	
3.3	From Approximate to Exact Solutions	74
3.3.1	Convergence to an Optimal Solution, 74	
3.3.2	Interior Point Projections and Lattice Reduction, 76	
3.3.3	Reconstruction of Rational Limit Points, 76	
3.3.4	Exploiting Common Factors in Vector Reconstruction, 79	
3.4	Computational Study	81
3.4.1	Exact Solution of General Linear Programs, 81	
3.4.2	Implementation, 81	
3.4.3	Experimental Setup, 82	
3.4.4	Computational Results, 83	
3.5	Conclusion	88
4	Accurate Optimization over Multiscale Metabolic Networks	91
4.1	Background	91
4.1.1	Flux Balance Analysis, 92	
4.1.2	Integrated Models for Metabolism and Gene Expression, 93	

4.1.3	Increased Demand for Numerically Reliable LP Solvers, 93	
4.2	Iterative Refinement for Metabolic Networks	95
4.2.1	Experimental Setup, 95	
4.2.2	Computational Results, 97	
4.3	Conclusion	100
5	From Linear to Mixed-Integer Nonlinear Programming	101
5.1	Introduction to Mixed-Integer Nonlinear Programming	101
5.1.1	Basic Concepts, 102	
5.1.2	Algorithms, 104	
5.1.3	Solvers, 110	
5.2	Iterative Refinement for Quadratic Programming	113
5.2.1	Quadratic Programming, 113	
5.2.2	Optimality Conditions and Basic Solutions, 114	
5.2.3	Iterative Refinement for Quadratic Programs, 115	
5.2.4	Infeasibility and Unboundedness, 118	
5.2.5	Exact Solutions over the Rational Numbers, 119	
5.3	Conclusion	120
6	Three Enhancements for Optimization-Based Bound Tightening	121
6.1	Bound Tightening for Nonconvex MINLPs	121
6.1.1	Domain-Dependent Relaxations, 122	
6.1.2	Literature Review, 123	
6.1.3	Optimization-Based Bound Tightening, 125	
6.2	One-Row Relaxations by OBBT	126
6.2.1	Lagrangian Variable Bounds, 126	
6.2.2	OBBT via FBBT, 128	
6.2.3	The LVB Graph, 130	
6.3	Accelerating OBBT	132
6.3.1	Selecting Variables, 132	
6.3.2	Filtering Bounds, 132	
6.3.3	Ordering LP Solves, 135	
6.4	Computational Study	137
6.4.1	Implementation, 137	
6.4.2	Experimental Setup, 138	
6.4.3	Computational Results for Root Node Experiments, 140	
6.4.4	Computational Results for Tree Experiments, 144	
6.5	Conclusion	147

7	Branching on Nonlinear Integer Variables	149
7.1	Branching in Mixed-Integer Nonlinear Programming	149
7.1.1	Integer Branching, 150	
7.1.2	Spatial Branching, 152	
7.1.3	Interleaving Integer and Spatial Branching, 152	
7.2	Covers of Mixed-Integer Nonlinear Programs	153
7.2.1	A Discrete Measure of Nonlinearity, 153	
7.2.2	Computing Minimum Covers, 154	
7.2.3	Minimum Splitting Covers, 157	
7.3	Nonlinearity, Integrality, Covers	158
7.3.1	Implementation and Experimental Setup, 158	
7.3.2	Nonlinear Integer Variables, 159	
7.3.3	Minimum Covers, 161	
7.3.4	Minimum Splitting Covers, 162	
7.3.5	Summary, 163	
7.4	Three New Branching Rules for Mixed-Integer Nonlinear Programming	165
7.4.1	Variable Type Information in Spatial Branching, 165	
7.4.2	Minimum Splitting Covers in Integer Branching, 166	
7.4.3	Nonlinear Scores in Integer Branching, 168	
7.4.4	Computational Results, 168	
7.5	Conclusion	171
8	Conclusion	173
	List of Abbreviations and Names	174
	List of Algorithms	177
	List of Figures	179
	List of Tables	182
	Bibliography	200
A	Experimental Data and Results	201
A.1	Linear Programming	201
A.1.1	Problem Statistics, 201	
A.1.2	Iterative Refinement, 218	
A.1.3	Exact Linear Programming, 235	
A.1.4	Accurate Flux Balance Analysis, 279	

- A.2 Mixed-Integer Nonlinear Programming 283
 - A.2.1 Optimization-Based Bound Tightening, 283
 - A.2.2 Experiments with New Branching Rules, 338