

Contents

Objectives 17

1 Introduction 19

Bibliography 23

2 Designability of transcription regulatory networks 25

2.1 Assembly of networks 26
2.2 Mathematical modeling and optimization method ... 28
2.3 Network design and modularity 31
2.4 Functional diversity and designability 36
2.5 Discussion 41
Bibliography 47

3 Network design to identify robustness principles 53

3.1 Gradient-driven pattern formation 53
3.2 Mathematical modeling 55
3.3 Optimal FFL circuits for pattern formation 57
3.4 Robustness of FFLs: adaptiveness, parameter
sensitivity and noise tolerance 62
3.5 Discussion 65
Bibliography 69

4 Integral control networks: a natural design 73

4.1 The case of plant gravitropism 73
4.2 Modeling at molecular and physiological levels 75
4.3 Integral control and stochasticity 82
4.4 Discussion 86
Bibliography 89

5 Balance of integral and derivative control strategies 93

5.1 The case of RNA silencing 93
5.2 Mathematical modeling 96
5.3 Strategies for bypassing RNA silencing 97
5.4 Discussion 101
Bibliography 103

6 Design of riboregulatory networks 107

6.1 Riboregulation in bacteria 107
6.2 Computational method for sequence design 109
6.3 Design of synthetic riboregulators 114
6.4 Theoretical model for activity 118
6.5 Discussion 122
Bibliography 125

7 Designability of metabolic pathways 129

7.1 Metabolic engineering 129
7.2 Computational method 131
7.3 Metabolic designability 134
7.4 Molecular hydrogen bioproduction 136
7.5 Discussion 138
Bibliography 141

8 Hierarchical regulatory networks: a natural design 145

8.1 The case of plant viruses 145

8.2 Genetic profile targeted by plant viruses	148
8.3 Biological functions triggered by plant viruses	154
8.4 Viruses preferentially alter highly connected genes . .	156
8.5 Discussion	160
Bibliography	165

9 General conclusion 169

Acknowledgements 175