

Contents

List of Figures	11	
List of Tables	13	
Abbreviations	15	
1 Introduction	19	
1.1 Introduction to synthetic biology	19	Has snippets from
1.2 System design in synthetic biology	19	other documents
1.3 Introduction to Biochemical Modelling	21	but must be re-
1.3.1 Graphical representation of biochemical systems	21	written
1.3.2 Deterministic and Stochastic modelling	21	
1.3.3 Steady state and stability	22	
1.4 The genetic toggle switch	22	
1.4.1 Importance in natural systems	23	
1.4.2 Uses in synthetic biology	23	
1.4.3 Modelling the genetic toggle switch	24	
1.5 Introduction to Bayesian statistics	27	
1.5.1 Bayes' theorem	27	
1.5.2 Bayesian inference	27	
1.5.3 Model checking	27	
1.5.4 Model comparison	27	
1.5.5 Prior selection	27	
2 Bayesian model selection	29	
2.1 Introduction to ABC-SysBio	29	Re-run all 7
2.2 Methods	29	models, check
2.2.1 ABC for parameter estimation	29	that results still
		stand

8 CONTENTS

2.2.2	ABC for model selection	29	
2.3	Models of the genetic toggle switch	29	
2.4	Results	29	
2.4.1	Genetic toggle switch model selection	29	
2.5	Conclusions	29	
3	Toggle switch stability	31	
3.1	Parameter scan	31	
3.1.1	Background	31	
3.1.2	Methods	31	
3.1.3	Results	31	
3.2	Bayesian approach to model stability	31	
3.2.1	Background	31	
3.2.2	Methods	33	
3.2.3	Testing StabilityFinder	35	
3.2.4	Calculating robustness	37	
3.2.4.1	Normal distribution	39	
3.2.4.2	Uniform distribution	42	
3.2.5	Lu toggle switch models	44	
3.2.6	Mass Action switches	48	
3.3	Conclusions	49	
4	Characterising the genetic toggle switch	59	
4.1	Circuit overview	59	
4.2	Growth rate investigation	59	not done
4.2.1	Methods	59	
4.2.2	Results	59	
4.3	Flipping the switch - promoter sensitivity	59	Complete
4.3.1	Methods	59	
4.3.2	Results	59	
4.4	Time course data	59	Run experiment again in our FACS
4.4.1	Methods	59	
4.4.2	Results	59	
4.5	Model fitting	59	Not done
4.6	Conclusions	59	
5	ABC-Flow	61	

Complete, how does it compare to SF?

Have to re-run some of the models:
1)Gardner with high V_{tot}
2)MA-dp-stoch full asymmetric
3)MA symmetric models

5.1	Introduction	61	
5.2	Methods	61	
5.3	Results	63	
5.3.1	Distance Calculations	63	Complete
5.3.2	Comparing 1D and 2D distances	63	
5.3.2.1	Normal distribution	64	
5.3.2.2	Uniform distribution	70	Also add the acceptance rate subsection
5.3.2.3	Comparing uniform and normal distributions	70	
5.3.2.4	Bimodal distributions	72	
5.3.2.5	Comparing bimodal and normal distributions	74	
5.3.3	Applying ABC-Flow to simulated Gardner data	74	Complete
5.3.4	Applying ABC-Flow to experimental toggle switch data	77	
5.3.4.1	ATc induction	77	
5.3.4.2	IPTG induction	78	Not done
5.3.5	Conclusions	78	
6	Designing new switches	79	Complete? it is now future work
6.1	Circuit overview	79	
6.2	Parts	79	
7	Conclusions	81	Not done
7.1	Evaluation	81	
7.2	Future work	81	
	Bibliography	83	
A	Appendix	87	
A.1	Ordinary Differential Equations	87	
A.1.1	CS-MA	87	
A.1.2	DP-MA	88	
A.2	Sequences	89	
A.2.1	pKDL071	89	
A.3	Algorithms	89	
A.3.1	Clustering algorithms	89	
A.3.1.1	Deterministic case	89	
A.3.1.2	Stochastic case	89	