

Contents

Preface	xi
1 Microbial Design	1
How to Read; Theoretical Background; The Design of Metabolism	
PART 1: THEORETICAL BACKGROUND	
2 Forces of Design	11
What Is Fitness?; The Difficulty of Measuring Fitness	
3 Comparison and Causality	17
Comparative Predictions; Evolutionary Response versus Organismal Response; Fundamental Forces and Partial Causes; Causal Inference; Structure and Notation of Comparative Predictions; Recap and Goal	
4 Brief Examples	29
Metabolism and Growth Rate; Support by Empirical Test; Patch Lifespan and Microbial Cancer; Heterogeneity in Public Goods; Stage-Dependent Growth; Summary	
5 Theory: Forces	43
Tragedy of the Commons; Similarity Selection and Kin Selection; Tradeoffs and Marginal Values; Repression of Competition; Heterogeneity in Vigor and Public Goods; Demography and Reproductive Value; Stage-Dependent Traits in Life Cycle; The Three Measures of Value; Scaling of Time and Space; Variable Environments	
6 Theory: Traits	83
Nature of Traits; Modification of Traits; Origin of Traits	

7 Theory: Control	95
Error-Correcting Feedback and Robustness; Principles of Control; Error Correction and Signal Amplification; Robustness to Process Uncertainty; Responsiveness versus Homeostasis; Sensors; Control Tradeoffs	
8 Studying Biological Design	115
PART 2: THE DESIGN OF METABOLISM	
9 Microbial Metabolism	121
10 Growth Rate	123
Comparative Hypotheses in the Study of Design; Testing Comparative Predictions; Comparative Predictions about Growth Rate; Comparative Predictions about Tradeoffs	
11 Thermodynamics: Biochemical Flux	141
Entropy Production; Force and Resistance Determine Flux; Mechanisms of Metabolic Flux Control	
12 Flux Modulation: Driving Force	155
Near-Equilibrium Glycolysis; Overflow Metabolism: Mechanisms; Overflow Metabolism: Design Puzzles; Evolutionary Timescale; Alternative Glycolytic Pathways	
13 Flux Modulation: Resistance	189
Resistance Impedes Flux; Mechanisms to Alter Resistance and Flux; Genetic Drift; Challenges in Control Design; Problems of Flux Modulation; Limitations and Prospects	
14 Variant Pathways	205
Glycolytic Yield; Final Electron Acceptors; Weak Redox Gradients; Electron Flow between Cells; Alternative Carbon Sources; Hierarchical Usage of Complex Carbohydrates; Puzzles of Design	

15 Tradeoffs	227
Biophysical Constraints and Cellular Allocation; Exploration versus Exploitation versus Regulation; Thermodynamics and Biochemical Flux; Fitness Components and Life History; Warfare versus Productive Traits; Cooperative Traits; Timescale Tradeoffs; Bet-Hedging Tradeoffs; Control Tradeoffs; Summary	
16 Predictions: Overflow Metabolism	253
Comparative Predictions and Partial Causes; Background; Proteome Limitation; Membrane Space Limitation; Response to Environmental Challenge; Summary	
17 Predictions: Diauxie, Electrons, Storage	291
Switching between Food Sources; Distributed Electron Flux; Storage When Resources Fluctuate; Challenges in the Study of Design	
18 Design Revisited	331
References	333
Index	369