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1: Classical Strain Improvement; 1.0 Introduction; 1.1 The Approach Defined; 1.2 Mutagenesis; 1.2.1 Numerical Considerations in Screen Design; 1.2.2 Random Genetic Drift; 1.2.3 Forced Mutagenesis; 1.2.4 Strain Mating; 1.3 Genotypic Landscapes; 1.4 Screening; 1.4.1 Rational Screens; 1.4.2 Random Screens; 1.4.3 Screening Platforms; 1.5 Conclusions; References; 2: Tracer-Based Analysis of Metabolic Flux Networks; 2.0 Introduction; 2.1 Setting Up a Stoichiometric Network Model; 2.2 Small-Scale Models versus Genome Scale Models; 2.3 Network Analysis: Maximum Theoretical Yield; 2.4 (Stoichiometric) Metabolic Flux Analysis; 2.5 Carrying Out a Labeling Experiment; 2.6 MEASURING ISOTOPE LABELING PATTERNS; 2.7 Tracer-Based MFA; 2.8 Validating Metabolic Flux Networks; 2.9 Conclusions; Acknowledgments; References; 3: Integration of "Omics" Data with Genome-Scale Metabolic Models; 3.0 Introduction; 3.1 Genome-Scale Metabolic Networks; 3.2 Constraint-Based Modeling Theory; 3.3 Current Analysis of Omics Data; 3.4 New Approaches to Developing Model Constraints; 3.5 Use of Gene Expression Data in Metabolic Models; 3.6 Use of Metabolomics Data in Metabolic Models: TMFA Example; 3.7 Integration of Multiple Omics Data Sets; 3.8 Future Directions and Applications to Strain Engineering; References; 4: Strain Improvement via Evolutionary Engineering; 4.0 Introduction; 4.1 Methodologies for Evolutionary Engineering; 4.1.1 Adaptive Evolution; 4.1.2 Genome Shuffling; 4.1.3 Global Transcriptional Machinery Engineering; 4.1.4 Transposon Insertion Mutagenesis; 4.1.5 Multiplex Automated Genome Engineering; 4.1.6 Tractable Multiplex Recombineering; 4.1.7 Chemically Induced Chromosomal Evolution; 4.1.8 Multiscale Analysis of Library Enrichment (SCALE); 4.1.9 Screening and Selection; 4.2 Examples of Evolutionary Engineering; 4.2.1 Enhancement of Product Yield and Productivity; 4.2.2 Extension of Substrate Range; 4.2.3 Improvement of Cellular Properties; 4.3 Conclusions and Future Prospects; Acknowledgments; References; 5: Rapid Fermentation Process Development and Optimization; 5.0 Introduction; 5.1 Overview of Classical Fermentation Process Development Methodology; 5.1.1 Noninvasive Sensor Technologies; 5.2 Fermentation Process Development and Optimization; 5.2.1 Medium Design and Optimization; 5.2.2 Optimization of Growth Conditions; 5.3 Rapid Process Development and Optimization Using Conventional Fermentation System; 5.3.1 Dynamic DO Control to Determine Optimal Feed Rate for Carbon Source-Limited Fermentation; 5.3.2 Feed Forward Control for Carbon Source Excess Fermentation; 5.4 Strain Evaluation and Process Optimization under Scale-Down Conditions; 5.4.1 Identify Scale-Down Parameters; 5.4.2 Scale-Down of Mixing Related Parameters; 5.4.3 Oxygen Uptake Rate (OUR) Clipping; 5.4.4 Dissolved CO<sub>2</sub>; 5.5 Control and Sensor Technologies for Minibioreactor

## Sommario/riassunto

This book highlights current trends and developments in the area of engineering strains. The book details the current and future tools used in the production of bulk chemicals and biofuels from renewable biomass using green technologies. Complex phenotypes are traits in a microbe that requires multiple genetic changes to be modulated simultaneously in the microorganism's DNA. Knowing what those genetic changes are for a given trait and how to make those changes in the most efficient way forms the motivation behind writing this book. This book explains the newer tools to develop and enable engi