Preface

Metabolic engineering has always been focused on using a systems-level view to analyze cellular metabolism and predict optimal rewiring of metabolic networks. Since its inception, significant advances have been made in our capacity to obtain high-resolution details about cellular state. In response to this newfound capacity, Systems Metabolic Engineering emerges as a paradigm that connects the area of systems biology with metabolic engineering goals. Specifically, this field incorporates large-scale data collection/high-throughput biology and in silico modeling efforts along with new capacities for genome-wide engineering to accomplish the goal of improving a cellular phenotype or pathway flux. These technologies and efforts continue to expand the global systems-level view of metabolic engineering by shifting focus away from individual pathways and toward the collective, interconnected nature of metabolism and regulation. The advances of systems biology enable high-throughput collection of genomic, transcriptomic, proteomic, metabolomic, and fluxomic data. However, this immense snapshot of cells brings about a large challenge for data collection, integration, interpretation, synthesis, and ultimately perturbation to the cell. Moreover, the rate of data generation is also being matched by our rate of multiplexed engineering of pathways and genomes.

The ultimate goal of a Systems Metabolic Engineering approach is to systematically and robustly define the specific perturbations necessary to alter a cellular phenotype. The tangible outcome of such an approach would be a complete cell model capable of (1) simulating cell and metabolic function and (2) predicting phenotypic response to changes in media, gene knockouts/overexpressions, or incorporation of heterologous pathways. While the field is not yet at this point, it is clearly on a trajectory toward such capacity. The field of Systems Metabolic Engineering has already proven to be a successful paradigm for improving pathway performance for small molecules in both the laboratory and industrial setting. As techniques continue to improve, the design cycle for engineering a cell will be greatly reduced.

As stated above, great strides have been made in advancing the key aspects of a Systems Metabolic Engineering approach. Thus, the aim of this book is to describe the methodologies and approaches in the area of Systems Metabolic Engineering and provide a step-by-step guide for their implementation. In particular, four major tenants of this approach will be discussed: (1) modeling and simulation, (2) multiplexed genome engineering, (3) 'omics technologies, and (4) large data-set incorporation and synthesis. Each of these four capacities plays an important role in the design cycle for strain improvement. Tools and protocols within each of these tenets will be described to enable facile implementation of a Systems Metabolic Engineering approach using model host organisms. This book is designed especially for metabolic engineers, molecular biologists, and microbiologists who are proficient in the genetic manipulation of organisms. The coverage of this material is quite broad to allow for accessibility by novices and experts alike. It is hopeful that this book will serve as a guide to implementing the most recent approaches in Systems Metabolic Engineering.

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