Preface

Based upon a few principle folding paradigms, proteins have evolved to carry out a vast number of highly tuned, interactive functions within the metabolic web. The process of natural selection, using a limited set of amino acids, a few basic mechanisms for mutation and recombination, and the functional output of the resultant three dimensional architecture, is able to parse a nearly infinite variety of amino acid sequences and lengths to optimize phenotypic parameters and protein functions in the context of the cell, the organism, and sometimes the organism's environmental niche. The results of this selection process are a testament to the plasticity of protein folds and the underlying chemistry associated with a particular three dimensional arrangement of amino acids, which together validate the efficiency of Nature's evolutionary process perfected over several billion years.

Within the last decade, a confluence of new technologies in molecular biology, biochemistry, and automation engineering has revolutionized our ability to understand, harness, and ultimately accelerate the evolutionary process. Using comprehensive mutagenesis, large libraries of gene sequences and their associated variants can be rapidly created and, with intelligent, targeted assays, screened for the acquisition and optimization of any intensive or extensive phenotypic variable. Substrate and enantiomeric selectivity, catalytic activity, relief from inhibition, temperature, or oxidant stability, operating optima as well as efficiency of gene expression in native and heterologous hosts, are a few of the parameters that have been optimized in a laboratory setting. Nearly all general protein classes have been targeted for engineering and found to be amenable to the rapid acquisition of adaptive changes necessary for new applications. Those of us who may have thought that Nature had already reached seeming perfection in the form of optimized gene products were surprised by the seemingly unlimited potential for phenotypic enhancement and *ex situ* application of proteins. These new technologies have engendered the exploration of many new medical, agricultural, and industrial opportunities.

We have divided this volume into five sections to best highlight particularly inventive and effective laboratory evolution techniques, some high throughput and ultra high throughput screening technologies, and some results of the application of these technology developments in the fields of industrial catalysis, pathway engineering, protein therapeutics, and device design. We hope to present a balanced picture of the current state of the art as it exists in 2004.

We thank all of the contributing authors for sharing their knowledge with the scientific community. This field is in its infancy and it is by the application and extension of efforts like these that new knowledge and new technologies will be built upon this already firmly rooted foundation.

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