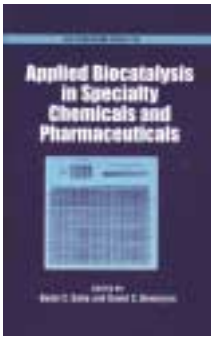
reproducibility. Of significant importance is the ease of replication, quality assurance and scalability.

PROfusion™ technology

Robert Kuimelis (Phylos, Lexington, MA, USA) described PROfusion™ technology, which covalently joins proteins to their encoding mRNA during *in vitro* translation, thus effectively linking phenotype and genotype. Massive protein libraries (10^{13} members) based on an 8.5 kDa single-domain antibody-mimic scaffold were subjected to directed protein evolution using PROfusion™ technology coupled with the PCR amplification of enriched binding sequences. After 8–10 rounds of selection and enrichment, a functional screen identified numerous high-affinity and specific binders against numerous protein targets. These binders were immobilized to a solid-phase in an oriented manner to generate affinity protein microarrays. These protein microarrays were stable for at least eight weeks, functioned in human serum, and detected subnanomolar levels of protein target. An example was shown using an immobilized binder in a microarray format to selectively capture a cytokine from serum followed by label-free detection using matrix-assisted laser desorption ionization time-of-flight MS (MALDI-TOF MS). The entire process of mRNA–protein fusion formation, *in vitro* selection, screening and protein production is currently being automated and 'industrialized' so that antibody-mimics can be prepared against a vast number of protein targets both quickly and cost-effectively.

Conclusion

Nucleic acid amplification, detection and screening is central to all molecular biological research. Emerging technologies are driven by the field's need for faster, easier, cheaper and more robust approaches. The Tucson meeting showcased the most recent advances in the field, primarily from the corporate sector, and emphasized real-world applications of these new technologies. Other topics presented at the meeting included sample preparation and nucleic acid purification, DNA probe design and bioinformatics.



Applied Biocatalysis in Specialty Chemicals and Pharmaceuticals

by Saha, B.C. and Demirjian, D.C., eds, ACS/Oxford University Press, 2000, 292 pages, hardback, £79.50, ISBN 0-8412-3679-8

The past several years have seen the continuing expansion of applied biocatalysis. As a result, more than two dozen commercial processes for the synthesis of fine chemicals and pharmaceuticals now use biological catalysts. The expanding role of biocatalysis has been clearly reflected by the growing number of publications on this subject – it has been estimated that 15% of papers on asymmetric synthesis use biological catalysts. This wealth of information was aptly summarized in two recent books: *Biocatalysis for Fine Chemical Synthesis* (published by J. Wiley & Sons in 1999) and *Industrial Biotransformations – A Comprehensive Handbook* (published by Weinheim: Wiley-VCH in 2000).

The book being reviewed here is based on a recent symposium on *Advances in Applied Biocatalysis* held at the *217th National Meeting of the American Chemical Society* in Anaheim in March 1999. The book represents a compilation of 16 manuscripts organized into three sections: biocatalyst discovery, characterization and engineering; applications: specialty chemicals; and applications: pharmaceuticals.

Content

It has been widely recognized that the current expansion of industrial biocatalysis is attributed to recent advancements in molecular biology, HTS and bioengineering. This notion is well reflected in the first section of the book. The screening of large collections of isolated enzymes or biocatalytic libraries requires the development of new and efficient HTS methods. In Chapter 3, Moris-Varas and co-authors present an effective tool for the rapid evaluation of enantioselectivity of hydrolytic enzymes. The method, developed for screening of a library of lipases against numerous substrates in a microplate format, is a general one and is applicable to screening of other hydrolases.

Directed evolution is undoubtedly the most powerful technique for improving the functional characteristics of an enzyme. The advantage of directed evolution over the more traditional protein engineering techniques is that it allows many characteristics of a protein to be improved without any knowledge of the protein's structure, function or mechanism of action. Chapter 6 of the book describes the application of this technique to β-glucosidase, lysozyme, xylanase and aminopeptidase resulting in the generation of mutants with improved thermostability.

Metabolic engineering has been successfully applied to the production

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optimization of a wide range of fine chemicals and pharmaceuticals including polyketides, steroids, vitamins and unnatural amino acids. Taylor and co-authors (Chapter 5), describe the application of this technique to the biosynthesis of D-phenylalanine. An alternative route to D-amino acids presented in Chapter 11 involves a whole-cell biotransformation with a recombinant *Escherichia coli* strain. Several D-amino acids including tyrosine, leucine and phenylalanine were synthesized with enantiomeric excesses of >95%. The use of a novel (*S*)-specific ω-transaminase for the production of various types of chiral amines via kinetic resolution and asymmetric synthesis is described in Chapter 16 by Shin and Kim.

Several chapters of the book are devoted to the use of alcohol dehydrogenases for the enantioselective reduction of ketones. To avoid the regeneration of the cofactor, the vast majority of enantioselective reductions is carried out by intact organisms. O'Neil and Woodward take issue with that in Chapter 8 by pointing out that the cost contribution of NADPH to the production of *sec*-phenethyl alcohol is reduced to <US$5 per kg if the cofactor is recycled 10,000 times. Several cost-effective methods of cofactor regeneration, and the use of macromolecular cofactor derivatives are also described. Chapter 13 describes the synthesis of vicinal aminoalcohols via alcohol dehydrogenase-catalyzed reduction of 2-substituted-β-ketoesters. Patel and Hanson (Chapter 15) present several excellent examples of enantioselective reductions practised in the synthesis of pharmaceutical intermediates.

The book also contains several miscellaneous applications of enzymes, including the generation of hydroxy fatty acids, synthesis of nucleoside analogs, production of galacto-oligosaccharides, and several examples of enantioselective hydrolysis of amides and esters.

Overall impression

On the whole, the book gives an unbiased picture of current developments in biocatalysis by covering major advances in biocatalyst discovery, optimization, and application. It is clearly written, well illustrated and contains an excellent subject index. However the uneven quality of chapters and the rather fragmented content is somewhat disappointing. For example, a personal and amusing Chapter 2 by Neidelman on historical perspectives in biocatalysis is followed by two specialized chapters on the bioconversion of fatty acids (Chapters 4 and 7) that, most likely, will be lost on many readers. Similarly, Chapter 13 on the preparation of vicinal aminoalcohols is rather limited in scope and references, but is followed by an excellent overview of the synthesis of chiral pharmaceuticals with oxidoreductases based on examples from Bristol-Myers Squibb (Chapter 15). There are also some inaccuracies, in particular in Chapter 1. For example, hydrolases are falsely defined as enzymes that 'catalyze the breakdown of larger biopolymers into smaller units'. The statement that 'enzymes increase the rate of chemical reaction by factors 10^9–10^{12}' is also misleading.

Despite these shortcomings, the book provides a broad picture of the contribution of biocatalysis to the development of specialty chemicals and pharmaceuticals. It should serve as a valuable resource for both students and professionals specializing in applied biocatalysis.

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