DDT Vol. 7, No. 1 January 2002

Combinatorial Library Design and Evaluation: Principles, Software Tools and Applications in Drug Discovery

Edited by Arup K. Ghose and Vellarkad N. Viswanadha, Marcel Dekker, 2001, 648 pages, hardback, US$195.00, ISBN 0-8247-0487-8

This book is an attempt to describe, in significant depth, the range of approaches to combinatorial library design. As such, it sets itself a tough challenge, which is acknowledged in the preface where the editors describe the partitioning of the book into four sections. The first three sections sequentially describe the field, starting from targeting a relative novice researcher through to experienced practitioners capable of using complex computational tools on a daily basis. The final section draws together many of the earlier discussions with illustrated applications. For this reviewer, mainly an end user of design elements (preferably 'shrink wrapped' and idiot proof), this meant approaching the book from a viewpoint somewhere in the middle of this target range.

The first section aims, in a single chapter, to introduce background concepts, and details significant milestones in the development of combinatorial chemistry. This is a good introduction but is unlikely to be needed by any other than complete novices to the area and the material is better covered by other introductory texts (for example, Terrett's *Combinatorial Chemistry* and in many undergraduate courses). The discussion on library construction strategies could have included greater reference to ongoing trends in the area (such as the general move away from pooled synthesis) and there is a surprising lack of discussion over the use of radiofrequency encoded approaches. However, other sections looking at compound design and the target of particular libraries provide good comprehensive coverage.

The second section of the book provides a more comprehensive overview of various library-design principles, covering pharmacophore approaches, QSAR, binding and docking approaches, and other aspects of ligand design. There are six chapters in this section, each providing a historical and present day review of a particular methodology. Each chapter provides a comprehensive reference list. The editors identify this section of the book as being valuable to chemists who are attempting to understand the various methods, and these chapters do succeed in providing that understanding. Each chapter can be read on its own, or sequentially, in a process of building understanding of the models being applied.

The third section, written by various practitioners and developers of computational design methods, explains in detail the methods they employ. Each topic is constructed to give an overview and rationale for the approach before going into a fairly detailed description of the methods and algorithms that are exploited. This section is targeted at the computational and/or design chemist, but also provides a useful level of information about these approaches for synthetic chemists.

The final section of the book attempts to draw together the methodologies through a series of chapters describing real applications of the methods described. Each chapter retains a focus on a specific approach, which aligns the studies well with the format of the rest of the book. However, it would have been valuable to also have some illustrated approaches, such as the description of specific therapeutic programmes, where the application of a range of different methods could then be carefully examined and the benefits and drawbacks of each approach could have been highlighted.

The content of this book is comprehensive and, as such, it will have many potential users. It is a pity that there are a few points of detail that could have added to the value of this book. For example, many chapters use graphical depiction of results; however, by producing the book in monochrome the subtleties are hard to see and colour would have added greatly to the illustrations. The structuring of the book described in the introduction is not clearly identified throughout its whole. It is not evident to a casual 'browser' whether they are reading sections associated with background information or technical detail, although it is this separation that the editors draw attention to. Finally the index is poor, with few links to other reference material.

So who is this book aimed at? Not withstanding the comments above, this is a valuable book with a large amount of useful background and current information. However, the decision to cover all the areas of combinatorial chemistry limits the potential individual target reader, as I suspect any reader will find some areas useful, whereas other areas are too simple or too complex. This would be an excellent addition to library shelves supporting a combinatorial chemistry research group, where many people could find numerous reasons to refer to these pages.

Andy Merritt
Director
High Throughput Chemistry
GlaxoSmithKline
Gunnels Wood Road
Stevenage
UK SG1 2NY
e-mail: atm8930@glaxowellcome.co.uk

  PII: S1359-6446(02)02103-1