Book Reviews

High-Throughput Screening in Drug Discovery. Methods and Principles in Medicinal Chemistry. Volume 35. Edited by J. Hüser. Wiley-VCH Verlag GmbH, Weinheim, Germany. 2007. xviii + 343 pp. 17.5 × 24.5 cm. ISBN 3527312838. $175.00.

This book covers four themes in high-throughput screening (HTS): the concepts of screening, the supporting hardware to run HTS, the bioassay technologies employed, and data analysis methods, all arranged into 10 chapters. The reader will gain an insight into the evolution of HTS through the multidisciplinary contributions to screening science from chemistry, biology, engineering, and informatics.

In the first part, Concept of Screening, for the essential elements of chemical genetics, provides an informative overview of the role of small molecules in the dissection of cellular pathways and how this approach is complemented by modern genetic techniques. This chapter is followed by a précis of more "traditional" HTS for lead discovery and discusses focused screening and molecular fragment screening, as well as serendipitous random screening. These chapters set the scene for the second part of the book that comprehensively catalogs the automation, miniaturization, and detection technology options that are required efficiently to prosecute HTS. For the reader who is considering setting up or upgrading an HTS infrastructure, this part of the book is informative.

After a discussion of approaches to screening together with the necessary hardware infrastructure, the reader is introduced to a critical component of screening: the assay. Assay Technologies in Part III focuses on commonly used methods for cellular and biochemical assays. The authors provide the reader with advice on the strengths and weaknesses of HTS assay technologies through a series of examples. For the experienced assay designer, the detail may be a bit superficial. However, for those who wish to understand the limitations of the data presented by these techniques, this is a very readable section.

Approximately 50% of the book (Part IV) is devoted to data analysis. In this HTS book, I was pleased to see significant descriptions of data analysis challenges. This is a very readable approach to a complex area of screening, covering theoretical considerations as well as cataloging commercial packages that are available to analyze screening data. Chapter 7 sets the scene for the visualization and scoring of hits within a statistical framework for the identification and correction of experimental artifacts. These discussions are complemented by descriptors defining "quality" measures of data from the assay design phase into the actual screening campaign. This is followed by chapters covering chemoinformatic tools with succinct discussion of commonly used descriptors, similarity metrics, clustering methods, principal component analysis, partitioning, and neural networks. Also buried in the Data Analysis part of the book is a perspective on the contribution of combinatorial chemistry to drug discovery. The overview of the techniques and applications is complemented by a discussion of the advantages and disadvantages of combinatorial chemistry in the lead identification and lead optimization phases of drug discovery. Importantly, given the controversial role of combinatorial chemistry in drug discovery, there are corresponding case studies describing the impact from these chemistry platforms.

Overall, I found this book to be very readable and informative and I would recommend it for HTS scientists as well as medicinal chemists. The descriptions and insights will help to put screening methods and data into context for drug discovery programs.

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