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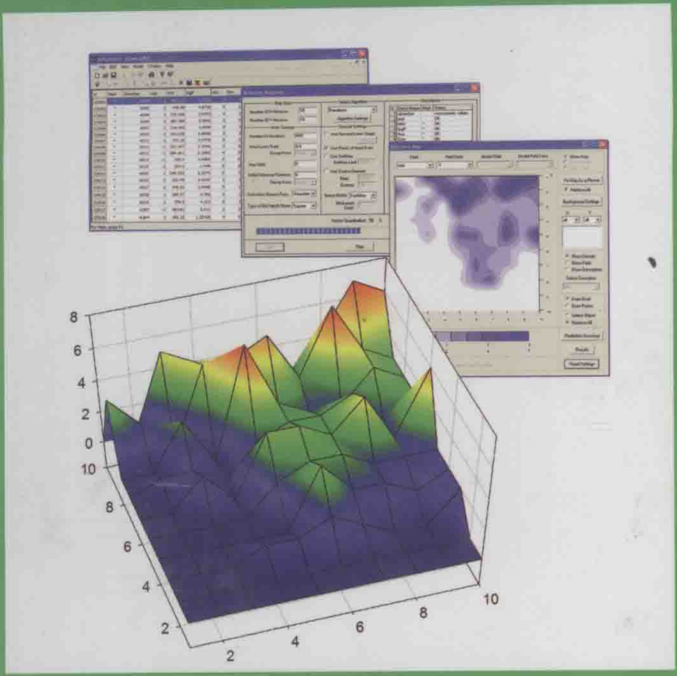
Pharmaceutical Data Mining

APPROACHES AND APPLICATIONS FOR DRUG DISCOVERY



EDITED BY
KONSTANTIN V. BALAKIN

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PHARMACEUTICAL DATA MINING

Approaches and Applications for Drug Discovery

Edited by

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PHARMACEUTICAL DATA MINING

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Edited by Konstantin V. Balakin

PREFACE

Pharmaceutical drug discovery and development have historically followed a sequential process in which relatively small numbers of individual compounds were synthesized and tested for bioactivity. The information obtained from such experiments was then used for optimization of lead compounds and their further progression to drugs. For many years, an expert equipped with the simple statistical techniques of data analysis was a central figure in the analysis of pharmacological information. With the advent of advanced genome and proteome technologies, as well as high-throughput synthesis and combinatorial screening, such operations have been largely replaced by a massive parallel mode of processing, in which large-scale arrays of multivariate data are analyzed. The principal challenges are the multidimensionality of such data and the effect of "combinatorial explosion." Many interacting chemical, genomic, proteomic, clinical, and other factors cannot be further considered on the basis of simple statistical techniques. As a result, the effective analysis of this information-rich space has become an emerging problem. Hence, there is much current interest in novel computational data mining approaches that may be applied to the management and utilization of the knowledge obtained from such information-rich data sets. It can be simply stated that, in the era of post-genomic drug development, extracting knowledge from chemical, biological, and clinical data is one of the biggest problems. Over the past few years, various computational concepts and methods have been introduced to extract relevant information from the accumulated knowledge of chemists, biologists, and clinicians and to create a robust basis for rational design of novel pharmaceutical agents.

Reflecting the needs, the present volume brings together contributions from academic and industrial scientists to address both the implementation of new data mining technologies in the pharmaceutical industry and the challenges they currently face in their application. The key question to be answered by these experts is how the sophisticated computational data mining techniques can impact the contemporary drug discovery and development.

In reviewing specialized books and other literature sources that address areas relevant to data mining in pharmaceutical research, it is evident that highly specialized tools are now available, but it has not become easier for scientists to select the appropriate method for a particular task. Therefore, our primary goal is to provide, in a single volume, an accessible, concentrated, and comprehensive collection of individual chapters that discuss the most important issues related to pharmaceutical data mining, their role, and possibilities in the contemporary drug discovery and development. The book should be accessible to nonspecialized readers with emphasis on practical application rather than on in-depth theoretical issues.

The book covers some important theoretical and practical aspects of pharmaceutical data mining within five main sections:

- *a general overview of the discipline*, from its foundations to contemporary industrial applications and impact on the current and future drug discovery;
- *chemoinformatics-based applications*, including selection of chemical libraries for synthesis and screening, early evaluation of ADME/Tox and physicochemical properties, mining high-throughput screening data, and employment of chemogenomics-based approaches;
- *bioinformatics-based applications*, including mining the gene expression data, analysis of protein–ligand interactions, analysis of toxicogenomic databases, and vaccine development;
- *data mining methods in clinical development*, including data mining in pharmacovigilance, predicting individual drug response, and data mining methods in pharmaceutical formulation;
- *data mining algorithms, technologies, and software tools*, with emphasis on advanced data mining algorithms and software tools that are currently used in the industry or represent promising approaches for future drug discovery and development, and analysis of resources available in special databases, on the Internet and in scientific literature.

It is my sincere hope that this volume will be helpful and interesting not only to specialists in data mining but also to all scientists working in the field of drug discovery and development and associated industries.

Konstantin V. Balakin

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My interest in data mining approaches for drug design and development was encouraged nearly a decade ago while at ChemDiv, Inc. by Dr. Sergey E. Tkachenko, Prof. Alexandre V. Ivashchenko, Dr. Andrey A. Ivashchenko, and Dr. Nikolay P. Savchuk. Collaborations with colleagues in both industry and academia since are also acknowledged. My anonymous proposal reviewers are thanked for their valuable suggestions, which helped expand the scope of the book beyond my initial outline. I would also like to acknowledge Elena V. Bovina for technical help.

I dedicate this book to my family and to my wife.

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