METHODS IN MOLECULAR BIOLOGY

Series Editor
John M. Walker
School of Life and Medical Sciences
University of Hertfordshire
Hatfield, Hertfordshire, AL10 9AB, UK

For further volumes:
http://www.springer.com/series/7651

Computational Drug Discovery and Design

Edited by

Mohini Gore

Department of Basic and Applied Sciences, Dayananda Sagar University, Bangalore, KA, India

Umesh B. Jagtap

Department of Biotechnology, Shivaji University, Kolhapur, MH, India;
Department of Botany, Government Vidarbha Institute of Science and Humanities, Amaravati, MH, India

Humana Press

Editors
Mohini Gore
Department of Basic and Applied Sciences
Dayananda Sagar University
Bangalore, KA, India

Umesh B. Jagtap
Department of Biotechnology
Shivaji University
Kolhapur, MH, India

Department of Botany
Government Vidarbha Institute of Science and Humanities
Amaravati, MH, India

ISSN 1064-3745 ISSN 1940-6029 (electronic)
Methods in Molecular Biology
ISBN 978-1-4939-7755-0 ISBN 978-1-4939-7756-7 (eBook)
https://doi.org/10.1007/978-1-4939-7756-7

Library of Congress Control Number: 2018935920

Printed on acid-free paper

This Humana Press imprint is published by the registered company Springer Science+Business Media, LLC part of Springer Nature.
The registered company address is: 233 Spring Street, New York, NY 10013, U.S.A.

Preface

Computer-aided drug design is an indispensable approach for accelerating and economizing the costly and time-consuming process of drug discovery and development. In the recent years, there has been a spurt in the protein and ligand structure data. This has led to a surge in the number of databases and bioinformatics tools to manage and process the available data. Optimal application of the vast array of available computational tools is crucial for the discovery and design of novel drugs.

The aim of this volume on *Computational Drug Discovery and Design* is to provide methods and techniques for identification of drug target, binding sites prediction, high-throughput virtual screening, lead discovery and optimization, and prediction of pharmacokinetic properties using computer-based methodologies. This volume includes an overview of the possible techniques of the available computational tools, developing prediction models for drug target prediction and de novo design of ligands. Structure-based drug designing, fragment-based drug designing, molecular docking, and scoring functions for assessing protein-ligand docking protocols have been outlined with practical examples. Phylogenetic analysis for protein functional site prediction has been described. Virtual screening and microarray studies for identification of potential compounds for drug discovery have been described using examples. The use of molecular dynamics simulation for virtual ligand screening, studying the protein-ligand interaction, estimating ligand binding free energy, and calculating the thermodynamic properties of bound water has been presented with stepwise protocols. In silico screening of pharmacokinetic and toxicity properties of potential drugs has been demonstrated. The currently available algorithms and software for protein-protein docking have been discussed with latest examples. Protocols for quantitative structure-activity relationship have been described. Computational approaches for the prediction of protein dynamics and protein aggregation have been presented with relevant protocols. The important methods of enhanced molecular dynamics have been analyzed with the help of practical procedure description. In silico analysis for inclusion of solvent in docking studies has been described with detailed methodology. We have also included a chapter on data analytics protocol, which is useful to summarize independent studies on drug designing.

There is abundant literature available on bioinformatics. However, there is very limited literature which will provide a step-by-step approach to utilize the various bioinformatics tools. In this volume, we present a stepwise description of the protocols for the use of bioinformatics tools in drug discovery and design. This volume will assist graduate and postgraduate students, researchers, and scholars working in the fields of drug discovery and design, pharmacology, bioinformatics, chemoinformatics, computational biology, medicinal chemistry, molecular biology, and systems biology to effectively utilize computational methodologies in the discovery and design of novel drugs.

We would like to express our heartfelt gratitude to the series editor John Walker for his valuable advice and support during every stage of development of this book. We thank all the authors who contributed to this book in a timely manner and shared their practical knowledge by providing stepwise methodology for the utilization of bioinformatics tools for drug discovery and design. We hope that this volume will be helpful to both novice in the field of bioinformatics and scientists actively engaged in drug discovery research.

Bangalore, KA, India ***Mohini Gore***
Kolhapur, MH, India ***Umesh B. Jagtap***

Contents

Contributors

Amr H. A. Abdallah • *Department of Medicinal Chemistry and Molecular Pharmacology, College of Pharmacy, Purdue University, West Lafayette, IN, USA*

Samia Aci-Sèche • *Institut de Chimie Organique et Analytique (ICOA), UMR7311 CNRS-Université d'Orléans, Université d'Orléans, Orléans Cedex 2, France*

Matteo Aldeghi • *Structural Bioinformatics and Computational Biochemistry, Department of Biochemistry, University of Oxford, Oxford, UK; Department of Theoretical and Computational Biophysics, Max Planck Institute for Biophysical Chemistry, Göttingen, Germany*

Adriano D. Andricopulo • *Laboratório de Química Medicinal e Computacional, Centro de Pesquisa e Inovação em Biodiversidade e Fármacos, Instituto de Física de São Carlos, Universidade de São Paulo (USP), São Carlos, SP, Brazil*

David B. Ascher • *Department of Biochemistry and Molecular Biology, University of Melbourne, Parkville, VIC, Australia; Department of Biochemistry, University of Cambridge, Cambridge, UK*

Heval Atas • *Department of Health Informatics, Graduate School of Informatics, METU, Ankara, Turkey; Cancer Systems Biology Laboratory (CanSyL), METU, Ankara, Turkey*

Khaled Barakat • *Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, Canada*

Damian Bartuzi • *Department of Synthesis and Chemical Technology of Pharmaceutical Substances with Computer Modelling Lab, Medical University of Lublin, Lublin, Poland*

Shaherin Basith • *National Leading Research Laboratory (NLRL) of Molecular Modeling & Drug Design, College of Pharmacy and Graduate School of Pharmaceutical Sciences, Ewha Womans University, Seoul, Republic of Korea*

Philip C. Biggin • *Structural Bioinformatics and Computational Biochemistry, Department of Biochemistry, University of Oxford, Oxford, UK*

Joseph P. Bluck • *Structural Bioinformatics and Computational Biochemistry, Department of Biochemistry, University of Oxford, Oxford, UK*

Pascal Bonnet • *Institut de Chimie Organique et Analytique (ICOA), UMR7311 CNRS-Université d'Orléans, Université d'Orléans, Orléans Cedex 2, France*

Abdennour Braka • *Institut de Chimie Organique et Analytique (ICOA), UMR7311 CNRS-Université d'Orléans, Université d'Orléans, Orléans Cedex 2, France; Centre de Biophysique Moléculaire (CBM), CNRS, UPR 4301, Orléans Cedex 2, France*

Yang Cao • *Center of Growth, Metabolism and Aging, Key Lab of Bio-Resources and Eco-Environment of Ministry of Education, College of Life Sciences, Sichuan University, Chengdu, People's Republic of China*

Ishwar Chandra • *Computer Aided Drug Design and Molecular Modelling Lab, Department of Bioinformatics, Alagappa University, Karaikudi, Tamil Nadu, India*

Radha Chaube • *Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi, Uttar Pradesh, India*

Sun Choi • *National Leading Research Laboratory (NLRL) of Molecular Modeling & Drug Design, College of Pharmacy and Graduate School of Pharmaceutical Sciences, Ewha Womans University, Seoul, Republic of Korea*

Benjamin P. Cossins • *Computer-Aided Drug Design and Structural Biology, UCB Pharma, Slough, UK*
Georges Czaplicki • *Institute of Pharmacology and Structural Biology, UMR 5089, University of Toulouse III, Toulouse, France*
Wentao Dai • *Shanghai Center for Bioinformation Technology, Shanghai, People's Republic of China*
Julien Diharce • *Institut de Chimie Organique et Analytique (ICOA), UMR7311 CNRS-Université d'Orléans, Université d'Orléans, Orléans Cedex 2, France*
Tunca Doğan • *Department of Health Informatics, Graduate School of Informatics, METU, Ankara, Turkey; Cancer Systems Biology Laboratory (CanSyL), METU, Ankara, Turkey; European Molecular Biology Laboratory, European Bioinformatics Institute (EMBL-EBI), Cambridge, UK*
Tianhua Feng • *Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, Canada*
Leonardo G. Ferreira • *Laboratório de Química Medicinal e Computacional, Centro de Pesquisa e Inovação em Biodiversidade e Fármacos, Instituto de Física de São Carlos, Universidade de São Paulo (USP), São Carlos, SP, Brazil*
Francis Gaudreault • *National Research Council Canada, Ottawa, Canada*
Jodi A. Hadden • *Department of Chemistry and Biochemistry, University of Delaware, Newark, DE, USA*
Mar Huertas • *Department of Fisheries and Wildlife, Michigan State University, East Lansing, MI, USA; Department of Biology, Texas State University, San Marcos, TX, USA*
Agnieszka A. Kaczor • *Department of Synthesis and Chemical Technology of Pharmaceutical Substances with Computer Modelling Lab, Medical University of Lublin, Lublin, Poland; School of Pharmacy, University of Eastern Finland, Kuopio, Finland*
Lisa M. Kaminskas • *School of Biomedical Sciences, University of Queensland, St. Lucia, QLD, Australia*
Shashank P. Katiyar • *Department of Biochemical Engineering and Biotechnology, DBT-AIST International Laboratory for Advanced Biomedicine (DAILAB), Indian Institute of Technology Delhi, New Delhi, India*
Daisuke Kihara • *Department of Biological Science, Purdue University, West Lafayette, IN, USA; Department of Computer Science, Purdue University, West Lafayette, IN, USA*
Leslie A. Kuhn • *Department of Biochemistry and Molecular Biology, Michigan State University, East Lansing, MI, USA; Department of Fisheries and Wildlife, Michigan State University, East Lansing, MI, USA; Department of Computer Science and Engineering, Michigan State University, East Lansing, MI, USA*
Anjani Kumari • *Department of Biochemical Engineering and Biotechnology, DBT-AIST International Laboratory for Advanced Biomedicine (DAILAB), Indian Institute of Technology Delhi, New Delhi, India*
Priyanka Kumari • *Department of Biotechnology, Delhi Technological University, Delhi, India*
Alastair D. G. Lawson • *Computer-Aided Drug Design and Structural Biology, UCB Pharma, Slough, UK*
Yoonji Lee • *National Leading Research Laboratory (NLRL) of Molecular Modeling & Drug Design, College of Pharmacy and Graduate School of Pharmaceutical Sciences, Ewha Womans University, Seoul, Republic of Korea*

Siu-wai Leung • *State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao, China; School of Informatics, University of Edinburgh, Edinburgh, UK*
Weiming Li • *Department of Fisheries and Wildlife, Michigan State University, East Lansing, MI, USA*
Markus A. Lill • *Department of Medicinal Chemistry and Molecular Pharmacology, College of Pharmacy, Purdue University, West Lafayette, IN, USA*
Vidhi Malik • *Department of Biochemical Engineering and Biotechnology, DBT-AIST International Laboratory for Advanced Biomedicine (DAILAB), Indian Institute of Technology Delhi, New Delhi, India*
Dariusz Matosiuk • *Department of Synthesis and Chemical Technology of Pharmaceutical Substances with Computer Modelling Lab, Medical University of Lublin, Lublin, Poland*
Laurent Maveyraud • *Institute of Pharmacology and Structural Biology, UMR 5089, University of Toulouse III, Toulouse, France*
Grégory Menchon • *Laboratory of Biomolecular Research, Paul Scherrer Institute, Villigen PSI, Switzerland*
Zhichao Miao • *European Molecular Biology Laboratory, European Bioinformatics Institute, Cambridge, UK; Wellcome Trust Sanger Institute, Cambridge, UK*
Louis-Philippe Morency • *Department of Pharmacology and Physiology, Faculty of Medicine, Université de Montréal, Montréal, QC, Canada*
Rafael Najmanovich • *Department of Pharmacology and Physiology, Faculty of Medicine, Université de Montréal, Montréal, QC, Canada*
Abhigyan Nath • *Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi, Uttar Pradesh, India*
Umesh Panwar • *Computer Aided Drug Design and Molecular Modelling Lab, Department of Bioinformatics, Alagappa University, Karaikudi, Tamil Nadu, India*
Samuel Peña-Díaz • *Institut de Biotecnologia i Biomedicina, Universitat Autònoma de Barcelona, Bellaterra, Spain; Departament de Bioquímica i Biologia Molecular, Universitat Autònoma de Barcelona, Bellaterra, Spain*
Juan R. Perilla • *Department of Chemistry and Biochemistry, University of Delaware, Newark, DE, USA*
Douglas E. V. Pires • *Centro de Pesquisas René Rachou, FIOCRUZ, Belo Horizonte, Brazil*
Jordi Pujols • *Institut de Biotecnologia i Biomedicina, Universitat Autònoma de Barcelona, Bellaterra, Spain; Departament de Bioquímica i Biologia Molecular, Universitat Autònoma de Barcelona, Bellaterra, Spain*
Sebastian Raschka • *Department of Biochemistry and Molecular Biology, Michigan State University, East Lansing, MI, USA*
Sergey A. Samsonov • *Laboratory of Molecular Modeling, Department of Theoretical Chemistry, Faculty of Chemistry, University of Gdańsk, Gdansk, Poland*
Ricardo N. dos Santos • *Departamento de Físico-Química, Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil*
Anne M. Scott • *Department of Fisheries and Wildlife, Michigan State University, East Lansing, MI, USA*
Jana Selent • *GPCR Drug Discovery Group, Research Programme on Biomedical Informatics (GRIB), Universitat Pompeu Fabra (UPF)-Hospital del Mar Medical Research Institute (IMIM), Parc de Recerca Biomèdica de Barcelona (PRBB), Barcelona, Spain*
Jiye Shi • *Computer-Aided Drug Design and Structural Biology, UCB Pharma, Slough, UK*

Woong-Hee Shin • *Department of Biological Science, Purdue University, West Lafayette, IN, USA*

Kamya Singh • *Department of Biochemical Engineering and Biotechnology, DBT-AIST International Laboratory for Advanced Biomedicine (DAILAB), Indian Institute of Technology Delhi, New Delhi, India*

Sanjeev Kumar Singh • *Computer Aided Drug Design and Molecular Modelling Lab, Department of Bioinformatics, Alagappa University, Karaikudi, Tamil Nadu, India*

Tomasz Maciej Stępniewski • *GPCR Drug Discovery Group, Research Programme on Biomedical Informatics (GRIB), Universitat Pompeu Fabra (UPF)-Hospital del Mar Medical Research Institute (IMIM), Parc de Recerca Biomèdica de Barcelona (PRBB), Barcelona, Spain*

Durai Sundar • *Department of Biochemical Engineering and Biotechnology, DBT-AIST International Laboratory for Advanced Biomedicine (DAILAB), Indian Institute of Technology Delhi, New Delhi, India*

Venkatesan Suryanarayanan • *Computer Aided Drug Design and Molecular Modelling Lab, Department of Bioinformatics, Alagappa University, Karaikudi, Tamil Nadu, India*

Alan Talevi • *Laboratorio de Investigación y Desarrollo de Bioactivos (LIDeB), Faculty of Exact Sciences, National University of La Plata (UNLP), Buenos Aires, Argentina; Argentinean National Council of Scientific and Technical Research (CONICET), Buenos Aires, Argentina*

Nurcan Tuncbag • *Department of Health Informatics, Graduate School of Informatics, METU, Ankara, Turkey; Cancer Systems Biology Laboratory (CanSyL), METU, Ankara, Turkey*

Salvador Ventura • *Institut de Biotecnologia i Biomedicina, Universitat Autònoma de Barcelona, Bellaterra, Spain; Departament de Bioquímica i Biologia Molecular, Universitat Autònoma de Barcelona, Bellaterra, Spain*

Ying Yang • *Department of Medicinal Chemistry and Molecular Pharmacology, College of Pharmacy, Purdue University, West Lafayette, IN, USA*

Sze Chung Yuen • *State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao, China*

Hongmei Zhu • *State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao, China*

Sonia Ziada • *Institut de Chimie Organique et Analytique (ICOA), UMR7311 CNRS-Université d'Orléans, Université d'Orléans, Orléans Cedex 2, France*