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

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Preface

Rapid advances in computer science, biology, chemistry, and other disciplines are enabling powerful new computational tools and models for toxicology and pharmacology. These computational tools hold tremendous promise for advancing applied and basic science, from streamlining drug efficacy and safety testing to increasing the efficiency and effectiveness of risk assessment for environmental chemicals. These approaches also offer the potential to improve experimental design, reduce the overall number of experimental trials needed, and decrease the number of animals used in experimentation.

Computational approaches are ideally suited to organize, process, and analyze the vast libraries and databases of scientific information and to simulate complex biological phenomena. For instance, they allow researchers to (1) investigate toxicological and pharmacological phenomena across a wide range of scales of biological organization (molecular $\rightarrow$ cellular $\rightarrow$ organism), (2) incorporate and analyze multiple biochemical and biological interactions, (3) simulate biological processes and generate hypotheses based on model predictions, which can be tested via targeted experimentation in vitro or in vivo, (4) explore the consequences of inter- and intra-species differences and population variability on the toxicology and pharmacology, and (5) extrapolate biological responses across individuals, species, and a range of dose levels.

Despite the exceptional promise of computational approaches, there are presently very few resources that focus on providing guidance on the development and practice of these tools to solve problems and perform analyses in this area. This volume was conceived as part of the Methods in Molecular Biology series to meet this need and to provide both biomedical and quantitative scientists with essential background, context, examples, useful tips, and an overview of current developments in the field. To this end, we present a collection of practical techniques and software in computational toxicology, illustrated with relevant examples drawn principally from the fields of environmental and pharmaceutical sciences. These computational techniques can be used to analyze and simulate a myriad of multi-scale biochemical and biological phenomena occurring in humans and other animals following exposure to environmental toxicants or dosing with drugs.

This book (the first in a two-volume set) is organized into four parts each covering a methodology or topic, subdivided into chapters that provide background, theory, and illustrative examples. Each part is generally self-contained, allowing the reader to start with any part, although some knowledge of concepts from other parts may be assumed. Part I introduces the field of computational toxicology and its current or potential applications. Part II outlines the principal elements of mathematical and computational modeling, and accepted best practices and useful guidelines. Part III discusses the use of computational techniques and databases to predict chemical properties and toxicity, as well as the use of molecular dynamics. Part IV delineates the elements and approaches to pharmacokinetic and pharmacodynamic modeling, including non-compartmental and compartmental modeling, modeling of absorption, prediction of pharmacokinetic parameters, physiologically based pharmacokinetic modeling, and mechanism-based pharmacodynamic modeling; chemical mixture and population effects, as well as interspecies extrapolation, are also described and illustrated.
Although a complete picture of toxicological risk often involves an analysis of environmental transport, we believe that this expansive topic is beyond the scope of this volume, and it will not be covered here; overviews of computational techniques in this area are contained in a variety of excellent references [1–4].

Computational techniques are increasingly allowing scientists to gain new insights into toxicological phenomena, integrate (and interpret) the results from a wide variety of experiments, and develop more rigorous and quantitative means of assessing chemical safety and toxicity. Moreover, these techniques can provide valuable insights before initiating expensive laboratory experiments and into phenomena not easily amenable to experimental analysis, e.g., detection of highly reactive, transient, or trace-level species in biological milieu. We believe that the unique collection of explanatory material, software, and illustrative examples in Computational Toxicology will allow motivated readers to participate in this exciting field and undertake a diversity of realistic problems of interest.

We would like to express our sincere thanks to our authors whose enthusiasm and diverse contributions have made this project possible.

Colorado, USA

Brad Reisfeld
Arthur N. Mayeno

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List of Contributors

HERVÉ ABDI • School of Behavioral and Brain Sciences, The University of Texas at Dallas, Richardson, TX, USA

BILLY AMZAL • LA-SER Europe Ltd, London, UK

MELVIN E. ANDERSEN • The Hamner Institutes for Health Sciences, Research Triangle Park, NC, USA

JAMES B. BASSINGTHWAIGHTE • Department of Bioengineering, University of Washington, Seattle, WA, USA

FRÉDÉRIC Y. BOIS • Royallieu Research Center, Technological University of Compiegne, Compiegne, France; INERIS, DRC/VIVA/METO, Verneuil en Halatte, France

MICHAEL B. BOLGER • Simulations Plus, Inc., Lancaster, CA, USA

ERIK BUTTERWORTH • Department of Bioengineering, University of Washington, Seattle, WA, USA

JERRY L. CAMPBELL JR. • The Hamner Institutes for Health Sciences, Research Triangle Park, NC, USA

DANIEL T. CHANG • National Exposure Research Laboratory, US Environmental Protection Agency, Research Triangle Park, NC, USA

XIAOLIN CHENG • Oak Ridge National Laboratory, UT/ORNL Center for Molecular Biophysics, Oak Ridge, TN, USA; Department of Biochemistry and Cellular and Molecular Biology, University of Tennessee, Knoxville, TN, USA

HARVEY J. CLEWELL III • The Hamner Institutes for Health Sciences, Research Triangle Park, NC, USA

REBECCA A. CLEWELL • The Hamner Institutes for Health Sciences, Research Triangle Park, NC, USA

JEAN PAUL COMET • I3S laboratory, UMR 6070 CNRS, University of Nice-Sophia Antipolis, Sophia Antipolis, France

RORY CONOLLY • National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC, USA

AMÉLIE CREPET • French Agency for Food, Environment and Occupational Health Safety (ANSES), Maisons-Alfort, France

CURTIS C. DARY • National Exposure Research Laboratory, US Environmental Protection Agency, Research Triangle Park, NC, USA

LISETTE G. DE PILLIS • Department of Mathematics, Harvey Mudd College, Claremont, CA, USA

JEAN LOU DORNE • Emerging Risks Unit, European Food Safety Authority, Parma, Italy

STEPHEN B. DUFFULL • School of Pharmacy, University of Otago, Otago, New Zealand

HARISH DUREJA • M. D. University, Rohtak, India
SEAN EKINS • Collaborations in Chemistry, Fuquay Varina, NC, USA; Department of Pharmaceutical Sciences, University of Maryland, Baltimore, MD, USA; Department of Pharmacology, University of Medicine & Dentistry of New Jersey (UMDNJ)-Robert Wood Johnson Medical School, Piscataway, NJ, USA

MELANIE A. FELMLEE • Department of Pharmaceutical Sciences, University at Buffalo, State University of New York, Buffalo, NY, USA

JOHAN GABRIELSSON • Division of Pharmacology and Toxicology, Department of Biomedical Sciences and Veterinary Public Health, Swedish University of Agricultural Sciences, Uppsala, Sweden

P. ROBINAN GENTRY • Environ International Corporation, Monroe, LA, USA

MICHAEL R. GOLDSMITH • National Exposure Research Laboratory, US Environmental Protection Agency, Research Triangle Park, NC, USA

JANNA HASTINGS • European Bioinformatics Institute, Hinxton, UK

GEOFFREY K. ISBISTER • Department of Clinical Toxicology and Pharmacology, Calvary Mater Newcastle, University of Newcastle, Newcastle, NSW, Australia; Discipline of Clinical Pharmacology, University of Newcastle, Newcastle, NSW, Australia

IVAYLO IVANOV • Department of Chemistry, Georgia State University, Atlanta, GA, USA

BARTHOLOMEW JARDINE • Department of Bioengineering, University of Washington, Seattle, WA, USA

ZARA JOSEPHS • European Bioinformatics Institute, Hinxton, UK

MUTHUKUMARASAMY KARTHIKEYAN • National Chemical Laboratory, Digital Information Resource Centre & Centre of Excellence in Scientific Computing, Pune, India

ELAINA KENYON • Pharmacokinetics Branch, Integrated Systems Toxicology Division, MD B105-03, National Health and Environmental Effects Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC, USA

JOHN KERRIGAN • Cancer Institute of New Jersey, Robert Wood Johnson Medical School, New Brunswick, NJ, USA

SANDHYA KORTAGERE • Department of Microbiology and Immunology, Drexel University College of Medicine, Philadelphia, PA, USA

MATTHEW D. KRASOWSKI • Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City, IA, USA

MARKUS LUKACOVA • Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University, West Lafayette, IN, USA

VIERA LUKACOVA • Simulations Plus, Inc., Lancaster, CA, USA

A.K. MADAN • Pt. B.D. Sharma University of Health Sciences, Rohtak, India

DONALD E. MAGER • Department of Pharmaceutical Sciences, University at Buffalo, State University of New York, Buffalo, NY, USA

ARTHUR N. MAYENO • Department of Chemical and Biological Engineering, Colorado State University, Fort Collins, CO, USA

Marilyn E. Morris • Department of Pharmaceutical Sciences, University at Buffalo, State University of New York, Buffalo, NY, USA
SHANE D. PETERSON • National Exposure Research Laboratory, US Environmental Protection Agency, Research Triangle Park, NC, USA
AMI E. RADUNSKAYA • Department of Mathematics, Pomona College, Claremont, CA, USA
GARY M. RAYMOND • Department of Bioengineering, University of Washington, Seattle, WA, USA
BRAD REISFELD • Department of Chemical and Biological Engineering, Colorado State University, Fort Collins, CO, USA
OLA SJJUTH • Department of Pharmaceutical Biosciences, Uppsala University, Uppsala, Sweden; Swedish e-Science Research Center, Royal Institute of Technology, Stockholm, Sweden
CHRISTOPH STEINBECK • European Bioinformatics Institute, Hinxton, UK
YU-MEI TAN • National Exposure Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC, USA
ROGELIO TORNERO-VELEZ • National Exposure Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC, USA
THOMAS R. TRANSUE • Lockheed Martin Information Technology, Research Triangle Park, NC, USA
JESSICA TRESSOU • National Institute for Agronomic Research (INRA), Paris, France
PAYAN VAJJAH • School of Pharmacy, University of Otago, Otago, New Zealand; Systems Pharmacology Group, Simcyp Ltd, Sheffield, UK
PHILIPPE VERGER • Department of Food Safety and Zoonoses, World Health Organization, Geneva, Switzerland
RENU VYAS • Department of Bioinformatics and Computer Science, Dr. D.Y. Patil Biotechnology and Bioinformatics Institute, Pune, India
DANIEL WEINER • Division of Certara, Pharsight Corporation, Cary, NC, USA
ANTONY J. WILLIAMS • Royal Society of Chemistry, Wake Forest, NC, USA
EGON L. WILLIGHAGEN • Department of Pharmaceutical Biosciences, Uppsala University, Uppsala, Sweden; Division of Molecular Toxicology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; Department of Bioinformatics - BiGaT, Maastricht University Universiteitssingel 50, Maastricht, The Netherlands
WALTER S. WOLTOSZ • Simulations Plus, Inc., Lancaster, CA, USA