
Preface

Infectious diseases caused by viruses, parasites, bacteria, and fungi are the number one cause of death worldwide. In addition to treatment costs, the social and economic challenges faced by governments, individuals, and families in managing these diseases and in preventing epidemics present an enormous burden to society. Although new technologies have improved diagnosis of infectious diseases, treatment remains a challenge. The efficacy of all known current anti-infective agents is threatened by the spread of drug-resistant forms of the pathogens. Hence the need remains urgent to develop anti-infective agents that target drug-resistant pathogens.

This book presents a comprehensive discussion of the role of *in silico* models in understanding infectious diseases and in developing novel therapeutics to treat them. This includes the role of *in silico* methods in vaccine development as well as small molecule development against known and new drug targets. Each chapter is written by a leading expert and addresses a unique aspect of *in silico* methods in drug design. The book is divided into two main sections, with the first ten chapters providing an overview of the methods and techniques used in drug design and the later six chapters detailing applications of these methods to real-world drug discovery problems. Chapter 1 provides an overview of the *in silico* models used in virtual screening, and Chapters 2 and 3 describe techniques to derive novel antimicrobial targets. One of the major problems associated with curing infectious diseases is the ability of the pathogen to acquire drug resistance. Chapter 4 provides an excellent overview and describes methods of predicting drug resistance using *in silico* models. Current trends in drug discovery have shifted towards developing novel therapeutics with systemic effects. Chapter 5 details methods of interpreting these polypharmacology based drug target networks. Chapter 6 addresses the modeling techniques involved in building structure–activity relationships of molecules. These techniques can be used for optimization of drug candidates. Chapter 7 highlights the molecular dynamics techniques used to compute binding energies of drugs to their target proteins. Chapters 8 and 9 address *in silico* immunology and describe the tools and databases that aid in B-cell epitope prediction and vaccine design. Chapter 10 explores a unique concept in drug design that features collaborative efforts between scientists in academia and in the biotechnology or pharmaceutical industries working under an integrated platform of drug design. Chapters 11 through 16 describe various applications of *in silico* models to real-world problems of drug design. These include using nontrivial homology models to derive functional relationships in *Helicobacter pylori* and designing novel inhibitors of anthrax toxin, HIV-1, malaria parasite kinase proteins, *Trypanosoma brucei*, and tuberculosis-causing agents, respectively.

The contribution of *in silico* models to vaccine development comprises algorithms for accelerated *in silico* identification of relevant protein candidates; *in silico* design of novel immunogens with improved expression, safety, and immunogenicity profiles; and *in silico* design of nucleic acid-based, vectored, or live attenuated vaccines. In small molecule development, *in silico* models play a major role in comparative genomics, whole genome analysis,

pathway analysis, delineation of novel protein–protein interactions, explication of systems and network biology, target identification, virtual screening, and identification of multidrug targets for combination therapy.

The contribution of *in silico* models to the field of drug discovery for infectious diseases has not previously been comprehensively reviewed in the literature. Hence we think this book should be of interest to all those involved in the study and treatment of infectious diseases, including academic researchers, students, industrial and pharmaceutical scientists, and other healthcare professionals. In addition, each chapter in the book covers a unique *in silico* technique and hence the book could also be used in the microbiology and immunology curricula in medical and graduate schools.

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