Preface

In drug discovery pipeline, one can have a feeling much like a “finding a needle in the haystack”. Undoubtedly, computational approaches have evolved as a pivotal component to rationalize the drug design and development processes. Molecular docking, a crucial tool in computer-assisted drug design, has secured its position in modern structure-based drug discovery. Molecular docking tries to predict predominant intermolecular interactions between ligands and the target macromolecules with known (or predicted) three-dimensional structures. Orientation and conformational geometry of the ligand in its docked position are determined through defined force fields. Information obtained from docking studies in conjunction with biophysical experiments can provide a framework for engineering bioactive molecules with controlled interaction profile toward the target of interest. Methods and Algorithms for Molecular Docking-Based Drug Design and Discovery is a book with total of 15 chapters. It aims to provide comprehensive coverage and in-depth description of the basic concepts of molecular docking with special emphasis on search algorithms, scoring functions, validation methods, and applications of the docking studies taking into account the recent advances in the field. The case studies mostly presented in chapters included in the second volume give the readers demonstrated examples of the application of docking methods on specific problems. These volumes are useful for researchers both in academia and industry as well as the students working in the field of theoretical and computational chemistry. The current volume contains fifteen chapters focusing on basic concepts, algorithms and techniques in molecular docking, although the methodological aspects were also touched in couple of chapters in second volume.

The introductory chapter, chapter 1 titled “Molecular Docking at a Glance”, is authored by Maryam Hamzeh-Mivehroud, Babak Sokouti and Siavoush Dastmalchi has tried to give a light overview on docking algorithms and studies. In this chapter, the overall view of a molecular docking approach by considering its different stages including different methods, search algorithms, scoring functions, validation of the methods, and their applications in some case studies is discussed. Moreover, some of the limitations faced in the docking studies are categorized.

The molecular docking has emerged to shorten the process of developing novel drugs in drug discovery field. AA T Naqvi and Md Imtaiyaz Hassan are the authors of Chapter 2 titled “Methods for Docking and Drug Designing: Docking Methods”. The authors in this chapter have discussed various recent docking developments along with some useful known tools for docking studies. Different classification of scoring function has also been discussed with some recent examples. The need for more improvements of the developed techniques in terms of performance and hardware has also been emphasized.

“Scoring Functions in Docking Experiments” constitutes the chapter 3 of this book in which Pravin Ambure and Kunal Roy have contributed. The in-depth discussion on various types of scoring functions, and whether they are used in isolation or in combination in the docking studies for finding the
relevant pose of the ligands on the receptors are the issues put forward in this chapter. Their theoretical background has also been given special consideration by discussing the challenges and limitations faced by these functions.

The authors Marjana Novič, Tjaša Tibaut, Marko Anderluh, Jure Boršek, and Tihomir Tomašič have presented Chapter 4; “The Comparison of Docking Search Algorithms and Scoring Functions: An Overview and Case Studies”. The chapter is organized in two sections including the basic overview on molecular docking and case studies. Application of docking tools including AutoDock, FRED, CDOCKER, FlexX, and GOLD are demonstrated on two target systems, namely DC-SIGN and cathepsin K proteins. The differences in the results of these methods in terms of scoring functions and search algorithms are also discussed.

Chapter 5 titled “Protein Ligand Interaction Fingerprints” is authored by Ali HajEbrahimi, Hamioreza Ghafoori, Mohsen Ranjbar, and Amirhossein Sakhteman. Scoring functions are regarded as the most important part of a docking-based virtual screening study. It has also been outlined that the affinity values measured for structure-based virtual screening require additional post-docking filters for achieving better results. Based on diversity of PLIF algorithms in the literature, comparison of the methods and their advantages and disadvantages, as well as their classifications considering the future trends are also discussed.

“Different Types of Molecular Docking Based on Variations of Interacting Molecules: Variations of Molecular Docking” have been contributed by Amit Das and Simantu Bhattacharya in Chapter 6. In this chapter, by considering the types of diseases, a detailed discussion on various docking methodologies including protein-protein, protein-DNA, protein-small molecule, and DNA-small molecule is covered. Also, the relevant tools and software are listed and their applications in terms of molecular docking in drug discovery with some useful examples are highlighted.

Chapter 7 “Protein-Protein Docking: Are We There Yet?” presented by Horia Jalily Hasani and Khaled Barakat demonstrates the current position of protein-protein docking studies at the atomic level. In this chapter, various methodologies used for search and scoring techniques along with their pros and cons, and their related case studies are discussed. Additionally, incorporation of the term “protein flexibility” in docking studies has received a considerable attention. Authors provided informative future directions for attaining more improvements on flexible protein docking.

In Chapter 8 titled “Protein-Ligand Docking Methodologies and Applications in Drug Discovery”, the authors Sanchita Rajkhowa and Ramesh C. Deka have provided diverse details on types of docking methods by considering the receptor’s side chain flexibility as a major problem. In this chapter, an ensemble set of proteins is selected and local move Monte Carlo method (LMMC) is used for ligand sampling. In a situation that there is no known docking and scoring algorithm method covering all requirements for obtaining better results, and also the relationship between accuracy and computational cost is not fully understood, the authors have emphasized that still virtual screening is so fast and less expensive compared to experimental high throughput screening methods, which justifies its routine application in drug discovery projects.

Scoring functions are playing important roles in predicting the binding affinity by selecting the active molecules from non-active ones which have had many progresses in recent decades. Chapter 9 “Scoring Functions of Protein-Ligand Interactions” authored by Zhiqiang Yan and Jin Wang discusses the promising role of these functions in achieving good results in terms of selecting optimized binding affinity values in the pool of various binding poses of ligands. It has also been noted that several factors including the solvation, entropic effects, and binding specificity can be fused for further optimization of the results gained from the scoring functions to make a balance between accuracy and computational costs.
Preface

Kailas Dashrath Sonawne and Maruti Kayram Dhanavade describe identifying the enzyme-ligand interactions using the docking techniques in Chapter 10. This helps the researchers to get a brief mind map on the docking process and its algorithms by joining the experimental outcomes to understand the interactions between several enzymes and amyloid beta peptide and find out the cause of Alzheimer disease at the molecular level.

Chapter 11 by Vijay Kumar Srivastav, Vineet Singh, and Meena Tiwari, discusses the latest progresses achieved in various stages of molecular docking in terms of ligand sampling, scoring functions, and algorithms. Besides, two case studies based on inverse docking for identifying the anti-cancer targets and predicting the homology models for dopamine and CCR2 receptors have been demonstrated by considering their thermodynamic aspects.

Chapter 12 focuses on the recent advancements in docking methodologies. In this chapter Ashwani Kumar, Ruchika Goyal and Sandeep Jain have covered recent advances in the docking methodologies such as fragment docking, covalent docking and inverse docking. Moreover, the progress in scoring functions and searching methods are highlighted.

Chapter 13 titled “Current Trends in Docking Methodologies” contributed by Shubhandra Tripathi, Akhil Kumar, Amandeep Kaur Kahlon and Ashok Sharma describes the role of molecular docking in high throughput screening as well as virtual screening. In addition, molecular dynamics simulation as a tool for validation of docking results is explained. The importance of Relaxed Complex Scheme (RCS) as a new methodology considering receptor flexibility is also reviewed.

To do the molecular docking, availability of the three dimensional (3D) structure of the target protein is a priori knowledge. Homology modeling can serve as a valuable tool for the prediction of 3D structure for the proteins. This strategy is extensively used where there is no experimentally solved structure for the protein of interest. Chapter 14 authored by Akanksha Gupta, Pallavi Mohanty, and Sonika Bhatnagar gives a brief overview on homology modeling based protein structure prediction. Different steps involved in homology modeling are discussed.

In the last chapter of this volume, i.e. Chapter 15, Adriana Isvoran introduces the available online molecular docking resources along with many useful illustrative and practical examples.

In conclusion, the current volume, which consists of fifteen chapters, reviews various aspects of molecular docking technique and covers computational algorithms for searching and scoring the diverse pool of ligands poses along with many experimental and theoretical examples. Moreover, many useful online and stand alone software are introduced. We hope that the topics included in this volume will be of benefit for the researchers working in the field of molecular docking, however, by all means, we don’t intend to give the impression that the book provides the full coverage of all possible topics.

Siavoush Dastmalchi  
Tabriz University of Medical Sciences, Iran

Maryam Hamzeh-Mivehroud  
Tabriz University of Medical Sciences, Iran

Babak Sokouti  
Tabriz University of Medical Sciences, Iran

December 30, 2015