Preface

The ultimate goal of medicinal chemistry is designing new drugs effective in alleviating disease states using most rational approaches. It seems that drug design process without application of computational techniques is unimaginable, and *in silico* approaches help developing potent, bioavailable, safe and well tolerated therapeutic agents. In this regard, molecular docking has been known as a valuable technique in modern structure-based drug design and become a first line technique in early phase of hit and lead identification. Location, conformation, and orientation of a molecule at the binding site of a target biomacromolecule is predicted through molecular docking techniques. This volume continues to discuss methodologies and importance of Molecular Docking in drug design, but with more emphasis on different applications of the technique presented in the following chapters aiming to familiarize the reader with different aspects of the molecular docking technique.

The first chapter, authored by Subhabrata Sen, Rahul Agarwal, and Ashutosh Singh, has overviewed most of docking methodologies along with some case studies related to the corresponding methods. This will provide the readers a comprehensive application-based chapter entitled "Role of Molecular Docking in Computer-Aided Drug Design and Development".

In Chapter 2 titled "Application of Docking Methodologies in QSAR-Based Studies", Omar Deeb, Heidy Martinez-Pachecho, Guillermo Ramirez-Galicia, and Ramon Garduno-Juarez have discussed the important role of docking methodologies in the QSAR studies in which molecular descriptors are important properties of the target compounds. Furthermore, the relationships between 3D-QSAR studies carried out by molecular docking are presented which have also been included by a case study for providing the readers more comprehensive content.

Although the molecular docking has passed the infancy period and tremendous advances have been achieved, however, accuracy and speed of docking calculation are still challenging issues. Jahan B. Ghasemi, Azizeh Abdolmaleki, and Fereshteh Shiri contributed a chapter titled "Molecular Docking Challenges and Limitations" (Chapter 3). In this chapter, different aspects of molecular docking processes such as receptor flexibility, ligand conformation and sampling, entropy in biomolecular interaction, and role of structural water molecules in docking are reviewed. At the end solutions and recommendations are suggested.

Natural products constitute a significant portion of pharmaceuticals. Moreover, they are in most cases the main source of lead identification for drug design and discovery. Flavonoids and coumarins are a group of plant secondary metabolites found in many dietary sources of foods and beverages. These compounds exhibit broad pharmaceutical activities and wide variety of the enzymes are influenced by these nutraceuticals. Chapter 4 titled "Application of Molecular Docking in Studies on the Binding Mechanism of Three Enzymes with Natural Products" contributed by Hua-jin Zeng, Ran Yang and

Ling-bo Qu, reveals the inhibitory activity and binding of flavonoids and coumarins to the enzymes like pepsin, hyaluronidase and acetylcholinesterase using molecular docking and fluorescence spectroscopy.

Nucleic acids can be a suitable target for many therapeutics available in the market. Understanding the molecular interactions between biologically active compounds and nucleic acid is of great importance especially in designing anticancer drugs. Kateryna V. Miroshnychenko and Anna V. Shestopalova applied different docking programs such as Vina, and different versions of AutoDock for the prediction of the structures of 50 DNA-ligand complexes taken from the Nucleic Acid Database. The results were analyzed using RMSD and demonstrated in Chapter 5.

G protein-Coupled Receptors (GPCRs) are very important receptors which are widely distributed in cell surface. These receptors are the target for approximately 30% of marketed drugs. Lack of specificity observed for GPCR targeted drugs can be a major obstacle leading to undesirable side effect. Chapter 6 titled "Molecular Docking-Based Drug Design and Discovery: Rational Drug Design for the Subtype Selective GPCR Ligands" authored by Soo-Kyung Kim and William A Goddard III, focuses on the molecular docking based design of subtype-selective GPCR ligands. The interactions of the ligands with 5-HT2B (5-Hydroxytryptamine, 5-HT) serotonin receptor (HT2BR), H3 histamine receptor (H3HR) and A3 adenosine receptor (A3AR) at the atomic level using molecular docking studies are discussed in this chapter. Understanding the mode of interactions between these subtype selective ligands and GPCR subtypes would be helpful in designing of novel classes of compounds with minimum level of undesirable side effects.

Chapter 7 with the title of "Molecular Modelling, Dynamics, and Docking of Membrane Proteins: Still a Challenge" contributed by Nanda Kumar Yellapu addresses the challenging issues regarding molecular modeling, dynamics and docking of membrane proteins. Since there are difficulties associated with membrane proteins purification and crystallization, there is a great tendency toward the use of molecular modeling techniques for determining the three dimensional structures of these proteins required for docking studies and investigation of the interactions between membrane proteins and related ligands.

Ebola Virus Disease (EVD) is caused by a fatal viral hemorrhagic fever in human, which is recognized by Toll-Like Receptor-4 (TLR4) in the body. Chapter 8 contributed by Sujay Ray and Arundhati Banerjee, presents the interactions between Ebola glycoprotein and human TLR4 using molecular docking studies. The chapter starts with an introduction on Ebola virus and TLR4. Then the homology based modeling of the TLR4 along with its mutated form is presented. Moreover, the result of docking studies of Ebola glycoprotein into the modeled TLR4 and mutated form are described.

Allergens can stimulate allergic reactions mediated by different cytokines leading to production of antibodies. Antiallergic drugs reduce the signs and symptoms of the allergic reactions. The major class of the allergens belongs to grass pollens. Chapter 9, "Molecular-Docking-Based Antiallergic Drug Design," contributed by Anamika Basu, Piyali Basak, and Anasua Sarkar, explains the design of antiallergic agent against the Zea m 1 pollen allergen using molecular docking study. In this chapter, a sense siRNA is introduced as antiallergen drug against homo sapiens STAT6 mRNA as target.

As Protein-Protein Interactions (PPIs) are the source of many cellular functions and are important in wide array of signal transduction processes. This makes them a suitable target for intervention in many pathological conditions such as cancer. Among which protein kinases are important targets for pharmaceuticals such as kinase inhibitors. In Chapter 10 authored by Sailu Sarvagalla and Mohane Selvaraj Coumar, an explanation is given to highlight the important proteins involved in PPIs. Then, authors provide some practical examples related to structure-based drug design of PPI inhibitors using in silico studies such as molecular docking.

Apart from drug design and discovery, molecular docking has been applied in other fields of science. Chapter 11 titled "Applications of Molecular Docking: Its Impact and Importance Outside the Purview of Drug Discovery" contributed by Josephine Anthony, Vijaya Raghavan Rangamaran, Kumar T Sivashankarasubbiah, Dharani Gopal and Kirubagaran Ramalingam, presents the other application of the molecular docking. The authors first give a brief explanation about structure based drug design and peptidomimetic designing, then other applications of molecular docking studies in bioremediation process, fatty acid biosynthesis, nutraceuticals and nanomaterial interactions are described by providing case studies.

Taken together, we hope that the chapters in this volume are useful for newcomers as well as those in the field and provide practice-oriented applications for the molecular docking and provide thought-provoking ensemble for the readers with recipes for an appropriate application of the algorithms.

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
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