Foreword

Here is my stamp of approval for this book. I give it unreservedly.

This book has expertly assembled a diverse set of researchers to cover all aspects of Molecular Docking. The book will find favour with all comers, starting with those new to the area, but the specifics also ensure important lessons for all. Part of the secret of the approach is to have significant coverage of both methodologies as well as application and case studies.

Dastmalchi, who most credibly leads the editors of this book, is with the Medicinal Chemistry Department at the School of Pharmacy, at the Tabriz University of Medical Sciences, Tabriz and also has been Director of the Biotechnology Research Centre at the University. He is co-located with his co-editors Hamzeh-Mivehroud and Sokouti. The Centre encompasses Biochemistry, Genetics, Molecular Biology, Structural Biology and Molecular Design. The Molecular Design remit of the Centre has spawned an active and well balanced interest in all aspects of pharmaceutical biotechnology and computational biology including Molecular Docking and bioinformatics, just to mention these specific aspects. Also, at least some of Dastmalchi and Hamzeh-Mivehroud’s interests have been supported by interludes at the University of Sydney.

The analogies of the discovery of new drug activities with the approaches taken to searches for valuable land by the explorers and navigators of the western world of the 17 and 18th Century I attribute to Richard (Dick) Cramer. Cramer, one of the doyens of the area, started working on the relationship between shape and biological activity in 1975, on a programme that became Comparative Molecular Field Analysis, the technique more often going by the name “CoMFA” alone. Mostly the “finds” of the explorers and navigators of 3 and 4 centuries ago were to be of small islands which had great import, although there are also some sizeable islands out there. So the mission in drug discovery becomes something akin to seeking and developing the “islands of activity” in “chemistry space”. Of course land mass is valuable for different reasons, as there are also different drug activities.

The game changers in computation are now fast becoming algorithms that are termed artificial intelligence or machine learning. So, an important component is to accumulate the data from which the algorithms can learn, but the underlying assumption is fast computing. In principle all the required processing power exists…in the last 10 years supercomputers have broken the petaflop (10 to the power 15 floating operations per second) barrier, but now over 80 supercomputers have a performance over 1 petaflop. Biological applications can increasingly take advantage not only of clusters of multi-core processors, but also GPGPUs (general-purpose graphical processing units) and highly parallel coproces-
Foreword

ors. Research teams can use local servers, shared High Performance Computer (HPC) centres, or turn to private cloud providers to create their own virtual computing environment. This volume has within it the clues about the algorithms that will be providing information on drug activity.

In the context of this book, there is no better way to point out recognition of the role of closely related areas than to point to the award of the 2013 Nobel Prize for Chemistry to Martin Karplus, Michael Levitt, and Arieh Warshel “for the development of multiscale models for complex chemical systems”. They have contributed to computational chemistry at many levels for many years, and for those unfamiliar with all their work, be assured that many of their contributions are captured in much existing software. By all means seek the individual published works of researchers, but also be reassured that the output of researchers the calibre of these Nobel Prize winners has undergone much scrutiny. Remember that in science, there should be no obligation to fully trust any dogma. Helping one’s faith can be important, and this is often achieved by great communicators and their willingness to communicate. I have crossed paths with Michael Levitt, none of the times more notable than in 1984, at the start of my career in research, when he was briefly in-house at the University of Sydney as a guest of the Inorganic Chemistry Department. He gave a series of lectures speaking about Protein Structure and Dynamics - to chemists, albeit primarily to structural chemists and biochemists and protein chemists. A willingness to communicate can easily kick off a career, but communication takes the form of both the spoken and written word. The written word is amply on display and accessible in this volume.

Computational fields have generally blossomed due to the advances in computer architecture, but so too have areas of endeavour using three-dimensional structure. While I might ask you to assume for the moment that methods in small molecule structure determination have improved, it is a simple matter to cite the growth of the protein database, itself a protein structure database, and therefore representing a significant source of information on target structures of interest… after its establishment in 1972 it hit 114,697 entries at the end of 2015. It is a more simple matter to cite the protein structure numbers as there is really only the one database for protein structure, and hopefully there is nothing like a simple statistic to be convincing. Be aware that the depositions can represent structures with a different ligand or mutant proteins, rather than solely a new protein structure, but they can also merely represent a protein solved in different conditions. Unsurprisingly over the period of the accrual of these database entries all methodological aspects of protein structure determination have developed, and as these entries themselves are models, this is also an important consideration relevant to achieving a true comprehension of our biological world.

This book is a “has it all” volume for those wanting entry into the field of Structure-based Drug Design, with coverage from the theoretical to practical, and also from the here-and-now to the possible in the near future. The pedigree is right for these editors to produce a volume on Molecular Docking-Based Drug Design and Discovery. While the techniques discussed in the book are crucial, so too is the fundamental knowledge of the Drug Discovery field, including the interplay with biology, medicinal and pharmacetics. The requisite requirements we want to design into a therapeutic dictate that multi-disciplinary approaches are a necessity. Let there be no mistake: let’s have strong computational input in all the disciplines that feed into our studies, but clearly positive clinical studies are the ultimate- the clinic is the endpoint which ever way you look at it, but there can and should be a leading role for computational effort and algorithms at every point along the path of discovery.
Let me end by ensuring I clearly commend this book to you. The editors are most ably led by my colleague and friend Siavoush Dastmalchi, and the result is a wonderfully comprehensive achievement. The principles and learnedness of Siavoush are very worthy- a not so veiled reference to the Siavoush, another Prince of Persia!

W. Bret Church  
*University of Sydney, Australia*