Computational drug design – A Guide for Computational and Medicinal Chemists; a book review

David C. Young. John Wiley & Sons, Inc. Hoboken, New Jersey. 2009. 307 p. ISBN: 978-0-470-12685-1.

Molecular modeling used to be restricted to a small number of scientists. They wrote their own programs, managed their own computer systems and mended them when they broke down. Today´s computer workstations are much more powerful than that old computers and they can be purchased relatively cheaply. It is no longer necessary for the modeler to write computer programs and software can be obtained from commercial software companies and academic laboratories. Molecular modeling can now be performed in any laboratory or classroom.

Computational techniques, represented by molecular modeling, play a valuable role in the drug design process. This role makes computational techniques important parts of a successful and profitable drug design process. Most importantly, drug design projects may fail without the efforts of experts in computational modeling. Drug design is such a difficult problem that every relevant technique is often utilized to its best advantage. Computational modeling techniques have a long history of providing useful insights, new suggestions for molecular structures to synthesize, and cost-effective (virtual) experimental analysis prior to synthesis.

These techniques and some useful concepts in medicinal chemistry field are discussed in the book "Computational drug design – a guide for computational and medicinal chemists", by David C. Young. In the short introduction the author discusses the difficulties in the process of drug design, the effective costs involved and the valuable role that computational techniques play in that process. "There is no one best computational drug design technique, many techniques are used at various stages of the drug design project", says Young.

The book is divided into three parts. (1) The drug design process, (2) Computational tools and techniques and, (3) Related topics.

The first part, "The drug design process", is divided in seven chapters, where the author describes the properties that make a molecule a good drug, target identification, target characterization, the drug design process for a known protein target, the drug design process for an unknown target, drug design for other targets and compound library design.

In these first chapters it is defined useful medicinal chemistry concepts like hits and leads, depicted some biochemical and cell-based assays, and explained about animal testing and human clinical trials. Concepts like activity, bioavailability, toxicity, drug side effects and drug interactions are also described. An useful topic about "Metrics for drug-likeness" deserves to be emphasized, since drug-likeness is an important concept often discussed in the medicinal chemistry classes. The author also cites several recent studies related to this area, important as supplementary texts for the classes.

In the second part, "Computational tools and techniques", it is discussed homology model building, molecular mechanics, protein folding, docking, pharmacophore models, QSAR, 3D-QSAR, quantum mechanics in drug design, de novo techniques, cheminformatics and ADMET.

Some molecular modeling methodologies such as homology modeling, docking and QSAR are very useful in the drug design process and deserves our attention, especially when used in medicinal chemistry classes. In this context, I missed the synonym of homology modeling, named "comparative modeling", that the author did not cite in the text.

The chapter on QSAR is summarized, but contains the essential informations for a good understanding of the methodology and discusses the main descriptors used in the quantitative analysis. I missed the names of the 3D-QSAR programs that the author did not mention, like CoMFA, CoMSIA and Catalyst.

I highlight the docking chapter, where the author wrote with clarity. It was an easy-reading and very informative text, citing advantages and disadvantages of the methodology.

The chapter on ADMET added new information to those already reviewed in the first part, with expanding concepts.

In the third part, "Related topics", it is discussed bioinformatics, simulations at the cellular and organ level, synthesis route prediction, proteomics, prodrug approaches and future developments in drug design. Proteomics is one of the newest fields discussed in the textbook. The author highlighted the importance of this field and the human genome project.

Computational drug design provides a description of computational techniques and the roles that play in the drug design process. This book covers a wide range of computational drug design techniques in an easily understood, nonmathematical format. The emphasis is on understanding how each method works, how accurate it is, when to use it, and when not to use it.

Researchers will find this text to be an excellent overview of the entire drug design process. Professors of medicinal chemistry and related disciplines will use the texts as complements for the students.

Monique Araújo de Brito
Email: moniquebrito@id.uff.br
Department of Pharmacy, Fluminense Federal University, Niterói Brazil.