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# Book reviews

**Structure-based Drug Design**
Pandi Veerapandian (Ed.)
Marcel Dekker, New York, 1997, 656 pp.
ISBN: 0-8247-9869-4, $175.00.

Structure-based drug design has come of age, the tools have been proven and examples of clinically useful compounds underline its importance. Indeed, most major pharmaceutical companies now have in-house protein crystallography. The individual elements of this multidisciplinary subject are to be found in many original papers and reviews, but the publisher Marcel Dekker first brought some of these elements together with two companion books in 1989 and 1992 on 'Computer-aided drug design' of proteins and then 'Nucleic acid targeted drug design'. These included sections on the tools of the trade and some promising applications. The current volume edited by Pandi Veerapandian is timely, and updates the previous volumes by focusing on the key successes of structure-based drug design, together with newer examples relevant to a diverse spectrum of health care issues. Cancer, heart disease and antivirals (including a special section on AIDS) form the major divisions.

The three dimensional structures of lysozyme, ribonuclease, chymotrypsin, carboxypeptidase and haemoglobin deduced in the 1960s have been widely used as models to describe the structure and function of enzymes, ligand binding and cooperativity. The design of ACE inhibitors based on the carboxypeptidase structure fired the imagination of many interested in the application of this approach. Now the human genome project coupled with modern gene expression technology allows exciting new targets to be quickly obtained in milligram amounts for biochemical and structural analysis. This together with the advent over the last decade of high power X-ray sources, better detectors, and fast computers with remarkable graphics has resulted in the ability for many new structures to be solved each year, and in this case the relevant drug target proteins for man.

The 656 page volume contains 22 well written and illustrated chapters from authors in both industry and academia. Most deal with one particular enzyme and the design of its inhibitors and these range from HIV proteinase, reverse transcriptase and integrase, through matrix metalloproteinases, thrombin, factor Xa and renin. Other chapters include applications to the bradykinin receptor, sodium channel, interferon, interleukin-1, and rhinovirus. The final three chapters focus on the integration of the computational and combinatorial chemistry approaches with the structure-based approach, and the design of peptidomimetic and nonpeptide compounds for peptide binding targets. The book describes several inhibitors which have reached the market for which the structure-based approach has had a significant role, and a few such as the HIV proteinase inhibitor DMP323 which have reached clinical trials and were designed entirely by this approach. The book is therefore recommended as a comprehensive applications reference with in-depth analysis and as a marker showing that structure-based drug design has now truly come of age.

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