

Protein-Ligand Interactions: Methods and Applications. Edited by G. U. Nienhaus. Pp. xi + 568. Totowa, New Jersey: Humana Press, 2005. Price (hardback) GBP 87.45, USD 135.00. ISBN 1-58829-372-6.

Since the elucidation of the human genome, and to some extent even before that, the problem of divining the function of a protein given only its amino-acid sequence has been exercising biochemists. With the various post-genomic initiatives to determine the three-dimensional structures of all of the gene products in a given genome, the problem has become ever more pressing – given the *structure* of a protein, how do you find out what it does? One way is to try to identify the physiologically important molecules with which it interacts in the hope that vital functional clues will emerge. Thus, a wide selection of methods that can be applied to give binding information is essential if the wide differences in structure, solubility and function of ligand and protein are to be accommodated. An additional benefit of this methodology is in the search for new drugs. The book *Protein-Ligand Interactions*, one in the *Methods in Molecular Biology* series, sets out a variety of such methods, some well established, others quite new, by which the interactions of proteins with their ligands can be investigated.

The 24 chapters, each written by experts in their technique, cover a wide range of methods from the 'wet' through the biophysical to the computational. While several of the methods will be familiar to most, a few are quite new, or at least their application to biological systems is novel.

book reviews

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The general approach, however, of each chapter is the same: a summary, a general introduction explaining the basic principles of the method and the types of problem that can be tackled, the materials and the instrumentation to be used in some typical experiments, which are then described and the results are shown and discussed. Each chapter ends with notes that amplify points made in the body of the text, and of course, an up-to-date reference list. For the established methods, reference to the seminal early literature is also to be found.

Several of the chapters cover methods appropriate for the time-resolution of the interaction, necessary to examine intermediate states along a reaction pathway. Thus, chapters on X-ray crystallography, IR, Raman and fluorescence techniques deal with binding to haem proteins, GTPases and lysozyme. High-throughput methods are now seen as essential to the pharmaceutical industry if not elsewhere, but only one chapter deals with a fluorescence screening method based around confocal microscopy such that 1536 different binding experiments carried out in 5 µl drops can be monitored in about half an hour. One aim of this method development is to reduce still further the sample volumes and hence total amounts of both protein and ligand required to provide evidence of binding.

It is perhaps to the more unusual methods, however, that many will turn. There is a fascinating chapter on the use of single-molecule fluorescence that detects the conformational fluctuations associated with ligand binding. Equally intriguing is the use of atomic force microscopy to measure directly the interactions of cell surface receptors with immobilised ligands. Several

of the methods also require a fair amount of do-it-yourself equipment assembly as commercial instruments are not available. The details are given in these cases although the setting up of experiments such as the femtosecond time-resolved IR spectrometer is not for the faint-hearted, or indeed the cash-strapped!

Overall, this book contains a variety of extremely useful overviews to the more common methods like ITC, CD, UV and fluorescence spectroscopy, though interestingly there is not a chapter dealing with modern approaches to perhaps the oldest method, equilibrium dialysis. Interestingly, too, in neither of the two crystallography chapters is reference made to the use of careful occupancy refinement for estimating a K_d though this might be considered cumbersome in practice. The book also provides thought-provoking insights into alternative methods that may become more widely used in the future. It is well produced with but a slight dusting of typographical errors throughout, and some of the figures could usefully have been larger or, in the case of protein structures, given in stereo. However, these are minor criticisms of a comprehensive volume that should provide a useful source of information for graduate students and more senior researchers on how to approach a study of protein-ligand interactions.

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