

Book Reviews

Computer Modelling in Molecular Biology. Edited by J.M. Goodfellow. VCH; Weinheim, New York, 1995. xvi+243 pp. DM 178.00 (hb). ISBN 3-527-30062-7

This book contains eight chapters written by different research groups involved in computer simulation and modelling of protein structures. It thus very conveniently compiles some of the present day knowledge of how different approaches towards descriptions of protein structures can be obtained from a priori information. As this field of research is very active the editor has necessarily had to be selective in what is presented. Although the field could have been more broadly covered in a book like this, the editor has decided to concentrate on classical potential energy based methods, thus essentially leaving out knowledge or rule based methods and quantum mechanical methods. Nevertheless, the book is trying to highlight some of the different areas of the research within this defined field. The classical potential energy methods all require an atomic starting model, a mathematical description of the interaction energy between all pairs of atom types and a definition of the constraints of the system. The basic aim is hereafter to develop methods which can arrive at descriptions of equilibrium configurations of the given molecular system.

Chapter 1 is a general short introduction to the methods used and to some of the types of results which can be calculated using these methods. Chapter 2 describes the enormous task of modelling and predicting protein structures based on sequence information. It demonstrates clearly (in a nice figure) how the outcome of such a task critically depends on the amount of extra information available. For instance, if a sequence differs only slightly from a protein of known structure then reliable modelling can be performed. Predicting a structure only based on sequence information is still a risky business. Chapter 3 contains information on different molecular dynamics simulations on various peptides. Most of these are important agonists or antagonists reacting on biologically important receptors. It is shown that useful results can be obtained provided that some information already exists either on the structure of the receptor or on the structure of the peptide. However, in one case the rather obvious conclusions are drawn that peptides show conformational mobility at Gly residues and conformational rigidity around Pro residues. Chapter 4 contains a wealth of results from molecular dynamics and free energy calculations on the enzyme Barnase and one of its mutants. Here of course the crystal structure is known, which provides a sound basis for judging the validity of the results. Molecular dynamics simulations of Barnase in water result in protein conformations, which are realistic in the sense that they do not deviate too much from the starting model.

Chapter 5 describes the results of molecular dynamics simulations on modelling nucleic acids. These are complicated by the fact that waters are integral parts of the structure and that bulk water has to be treated properly. Calculations on nucleic acids are more than for proteins hampered by the generally poor handling of electrostatics. Modelling of large RNA molecules still needs an uncomfortable amount of interactive graphics modelling producing results prone to subjective judgments, although this indeed can be very useful if sufficient biochemical and functional data are available. Chapter 6 demonstrates how molecular dynamics simulations can be used to enlighten the theory of transport in ion channels. Some insight has thus been obtained into the microscopic states of the permeation process of Na⁺ through the gramicidin A channel. However, it is clear that studying complex biological systems in this way is still beyond the capabilities of modern computational methods. Chapter 7 contains a thorough analysis of modelling and simulations on major histocompatibility complex I and its protein-peptide interactions. This is an ideal system to work with as the crystal structure of MHC-I and of some of its complexes with peptides are known. The question to answer is thus the presumably simple one of modelling a peptide into the groove on the surface of MHC-I. The results show a stable conformation of this peptide and account for the observed variabilities in peptide sequence. Chapter 8 describes a new method for simulations of conformational transitions of large molecules. This has been applied to studies of changes in a sucker pucker angle and of a substrate in the active site of D-xylose isomerase. This method can be used to propose reaction pathways and the possible location of a transition state.

The book as a whole gives interesting views into the achievements of molecular modelling of today. It also demonstrates many of the difficulties and obstacles still lying ahead for this interesting field. It is by now not a trivial matter to model protein structures or to simulate the dynamic behaviour of macromolecules. The presentation is a little uneven as is always the case for a book with many contributors. The somewhat technical and mathematical nature of some of the chapters is very different from the straightforward pedagogical text of chapter 2, where structural homology is exemplified by comparing the letters B and R and pointing out that they have a common core of P. The book unfortunately has very many irritating misprints, where in many places small words like 'of', 'and', 'be', and 'to' have been omitted.

Jens Nyborg

Glial Cell Development. Basic Principles and Clinical Relevance. Edited by K.R. Jessen and W.D. Richardson. BIOS Scientific Publishers; Oxford, 1995. xv+255 pp. \$130.00 (hc). ISBN 1-872748-54-6

'Glial Cell Development' is an excellent new textbook that focuses on a broad range of basic principles of glial cell biology and on the clinical applications of recent developments in the field. The book, consisting of a collection of essays written by glial cell experts, is a pleasant mixture of in-depth reviews and discussions of paradigms that are likely to dominate the field in coming years. In addition, many chapters contain clear illustrations that nicely complement the text. Several chapters deal with issues of the origin of Schwann cells, astrocytes, oligodendrocytes and microglia. The chapter on Schwann cell development is well written and includes a welcome overview of transcription factors that may play roles in fate determination and differentiation. Oligodendrocytes have in many years been studied in

culture paradigms and recent in vivo studies have begun to explore their origin in vivo. The chapter on oligodendrocyte development nicely compiles our current knowledge on oligodendrocyte development obtained from both in vitro and in vivo aspects. In contrast to the biology of myelin-forming glia, the origin of astrocytes is only now beginning to be understood in terms of cell lineage and developmental origin. The chapter on microglia includes a provocative consideration of the origin and function of these specialised scavenger cells. Two chapters in the book deal with myelin-specific genes, their control of expression and the study of the function of these genes in mouse mutants, and a chapter is included that speculates on the evolutionary origin of the myelin sheath. Several chapters in the

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