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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book discuss aspects of glial cell-axonal interactions during development and repair. The discussion of the potential use of cultured glial cells to repair demyelinated lesions and to support the regeneration of traumatic CNS injuries is an interesting inclusion in the book, which, if possible, will revolutionise modern medicine. Invertebrates have for a long time represented a fruitful paradigm for the identification of regulatory genes that play roles in mammalian development and the final chapter in the book gives an interesting overview of glial cell development in the insect nervous system.

In conclusion, 'Glial Cell Development' gives an excellent overview of a broad range of topics in modern glial cell research and the book is valuable for researchers working in the field as well as for newcomers, students and others with interest in neurobiology.

Niels Aagaard

YAC Protocols. Methods in Molecular Biology, vol. 54. Edited by D. Markie. The Humana Press; Totowa, 1995. x+378 pp. $69.50 (pb). ISBN 0-896-03313-9

Laboratory or methods manuals are almost always useful publications: often they are the result of didactic efforts of their authors, enacted to finding a way to focus and verify their own protocols, otherwise frequently ill-defined. Of course they are (or are meant to be) of great help to colleagues in the field who desire to enrich their experimental tools with a novel technique. They could also represent, if and when the methodological details are accompanied by appropriate overviews, an advantageous observatory to newcomers to the field.

In order to meet all these plausible goals, a book of this sort requires inter alia a panel of authors and/or an editor who both share the awareness of the above scopes and possess the competence to present concisely the underlying theory and precisely the various protocols in question.

'YAC Protocols', volume 54 of the successful series 'Methods in Molecular Biology', gets close to responding fully to the aforementioned criteria. It is timely, since it appears almost 10 years after the publication in Science of the epochal YAC paper by Burke, Carle and Olson; 10 years in which the yeast artificial chromosomes (YAC) have contributed remarkably to the advancement of the various genome projects. Yet, it has been reliably stated that the YACs may have made their time at least as megacloning vectors, and are likely to yield the way to other cloning systems, possibly of prokaryotic origin, such as the PAC (phage P1-based artificial chromosomes) and the BAC (factor F-based artificial chromosomes), the main reason being the substantially unresolved problem of 'co-cloning' and this is an issue deserving some reflection.

Co-cloning is also known as 'chimerism'. It consists in the undesired apposition within the same YAC of fragments derived from unlinked regions of the genome under study: it is an inconvenience which could seriously mislead mapping and sequencing efforts. Admitted from the very beginning of the YAC technique, co-cloning has been unfortunately minimised by the original YAC apostles, who claimed it could be kept well below 10%; even if later acknowledged to be more conspicuous, it was deemed as marginally important, easy to be spotted and eventually eliminated in subsequent years (also through the use of recombinant deficient hosts). Yet, at the conclusion of the first 5 year phase (mapping) of the Human Genome Project, reliable commentators have issued a rather severe sentence of the future of the YACs, and this is so just because of the chimerism, now recognised to affect 50–60% of most of the generally available YAC libraries.

In front of all this, it is frankly a bit disappointing to see that a book on YAC protocols devotes only a few pages to the detection of chimerism (Chapter 11 deals with this problem and is one of the shortest), and neglects any discussion on the two distinguishable causes of co-cloning (co-ligation of different restriction fragments in vitro, and recombination between different constructs taken up in vivo by the same host cell), as well as on the possible remedies (dephosphorylation of the genomic fragments rather than of the chromosomal arms, or at least a ratio of dephosphorylated vector to phosphorylated insert higher than ten, as recommended in Chapter 1; and finally the use of a transformation ratio DNA/spheroplasted cells lower than here suggested, which turns out to be close to, if not higher than, ten, as well as the adoption of recombination defective strains as hosts, as already mentioned). This is an omission which seems to amount to considering co-cloning as unavoidable, a sort of 'original sin', which probably is not deserved.

On the positive side, it should be noticed that the various chapters are loaded with useful tips and information; if one wanders through the notes one has the chance of stumbling happily into real treasure chests of illuminating and curious details, of the nature one, in less competitive years and fields, used to learn by chatting with friendly colleagues in front of a beer during breaks at a meeting.

Thus, the chapters on the transfer of YAC into novel hosts, be they different yeast strains or mammalian cells, represent very instructive reading for those who intend to use the yeast artificial chromosomes as vector to dissect other more or less complex genomes, or for those who strive to exploit the YAC as intermediates of more ambitious constructs, such as the MAC (Mammalian Artificial Chromosome), probably likely to be used for manipulative rather than for analytical purposes. Not only for them, somehow broader surveys of the chromosome features, such as telomeres, and in particular centromeres and DNA replication origins (admittedly much simpler in yeast than in higher eukaryotes), would have contributed to a better and broader overview of the field of artificial chromosomes as the last addition to the synthetic approach to the study of life.

Vittorio Sgaramella

Guidebook to the Small GTPases. Edited by M. Zerial and L.A. Huber. A Sambrook and Tooze publication at Oxford University Press; Oxford, 1995. xix+476 pp. £29.50 (pb). ISBN 0-19-859944-7

This book puts together information on the small GTPases, a family of proteins where our knowledge has exploded in recent years. With the discovery of the regulatory role of the Ras protein, governed by its binding alternatively to GTP and GDP, and the discovery of a large number of homologous proteins with similar characteristics, a fruitful field of research has developed, leading to improved understanding of the regulatory proteins of several biological processes. The common biochemistry of these proteins, and the lack of homology of several proteins regulating or being regulated by similar structures are fascinating challenges for the interested molecular biologist, and much of the focus in the field today is on unraveling the mechanisms by which the small GTPases affect the activities of other proteins.

These characteristics makes it possible to use information from one biological system to the other – provided you get access to it. This is one aspect of the uses of this book.

In this guidebook, information on the GTPases themselves, the proteins that activate and inactivate them as well as their effectors (or presumed effectors) is given. They are organized in logical sections, where a common format has been attempted for each entry: After a brief summary, information on nucleotide sequence (gene), amino acid sequence (protein), posttranslational modifications, localization, interacting components (activators, inactivators, substrates) and functional studies (and references) is presented. Each protein is presented with one to two pages, with tabular material, drawings as well as the occasional picture presenting primary data. Needless to say, not all proteins have all information, and ironically, the mamma-