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Book Reviews

Biological Membranes: Structure, Biogenesis and Dynamics; Edited by J.A.F. Op den Kamp, Springer Verlag; Berlin, Heidelberg, New York, 1994; x + 356 pages. DM 228.00. ISBN 3-540-57731-9.

This volume derives from a NATO Advanced Study Institute course held in June 1993, covering lipid dynamics, protein–lipid interactions, membrane protein structure and folding, the translocation of proteins through and their insertion into membranes, and intracellular protein traffic. There are 34 contributions in all, divided about equally amongst these topics; they vary considerably in length and format, some being overviews and others experimental reports.

'Lipid dynamics' includes a wide-ranging review of the roles of phospholipids in cellular functions (Dowhan), and shorter papers on intracellular lipid traffic and the functions of phospholipid exchange proteins. 'Protein–lipid interactions' contains a survey of the use of NMR and ESR spectroscopy in this area (Watts), followed by papers on the interaction of lipids with particular proteins, and of the role of lipid composition in protein sorting in epithelial cells. 'Protein structure' includes a brief exposition of NMR techniques as applied to membrane protein structure, and contributions on pathways of (soluble) protein folding, protein turnover, and the structures of porins and some pore-forming polypeptides. The section on protein insertion and translocation covers the familiar ground of signal peptide structure (Gierasch), topology rules (von Heijne) and bacterial protein secretion (Wickner and Leonard), as well as more specialized contributions on related topics, including the translocation and mode of action of some bacterial toxins and viral proteins. 'Intracellular traffic' is otherwise given rather short shrift, with coverage of post-translational modification in the endoplasmic reticulum. Golgi disassembly and reassembly and organelle inheritance in budding yeast, but surprisingly little on the topical areas of targetting and retention of organellar proteins, or on vesicular traffic.

In many ways this volume epitomizes the strengths and weaknesses of symposium proceedings. It is not really able to convey the multidisciplinary interaction that was clearly the object of the conference, and the participants' discussion is not included. What remains is a collection of rather formal, and sometimes apparently unrelated, contributions. Much of the work is already reported elsewhere, often in lengthier and more detailed form, and none of the papers is likely to be the definitive description of the work. An expert reader is unlikely to find anything of great novelty in his own area; on the other hand a browser may very well learn a lot, and at the very least will be provided with (fairly) up-to-date references on some specialized topics. Although one of the topics is exhaustively treated, there are illuminating contributions on all of them, and those teaching courses in membrane biochemistry at a fairly advanced level will certainly find this book a source of much useful material.

David K. Apps

The Protein Folding Problem and Tertiary Structure Prediction; Edited by K.M. Merz Jr. and Scott M. Le Grand, Birkhäuser; Boston, 1994; x + 581 pages. $99.00. ISBN 3-7643-3693-5.

Proteins, during their 'life cycle', serve multiple functions: before fulfilling their biological roles as catalysts or receptors etc., they have to fold to form their unique three-dimensional structure; finally they have to be accessible to degradation, serving as a nutrient or allowing regeneration. Next to transcription and translation, protein folding is the most important reaction in the living cell. In the overall transfer of information from the DNA to the protein level, 50 years of in vitro studies have shown that protein self-organization is an autonomous and spontaneous process which does not require either additional information or the input of energy. Due to the one-to-one relationship of an individual amino acid sequence and its specific solvent structure, one would predict that there must be a 'code of protein folding' in terms of an algorithm allowing the prediction of the three-dimensional structure from a given primary structure. In spite of the continuous efforts of physical biochemists for more than 30 years, this 'second half of the genetic code of protein translation' still awaits elucidation. The growing importance of the problem is evident, thinking of the Human Genome Project, protein design, 'synzymes', site-directed mutagenesis, etc. Correspondingly, there has been an increase in activity in the field which is reflected both by an explosion of semi-empirical and theoretical approaches and an increasing number of monographs and Conference Proceedings. It started 15 years ago with the 1st International Conference in Regensburg; in 1982 C. Ghélis and J. Yon's book 'Protein Folding' appeared, and since 1984 regular AAA Meetings have been devoted to the topic. In 1989, G.D. Fasman edited a volume of 798 pages, 'Prediction of Protein Structure and the Principles of Protein Conformation'; finally, in 1992, T.E. Creighton followed with a comprehensive collection of excellent articles covering both experimental and theoretical approaches to the protein folding problem.

The present book differs from the previous publications in three important points: (i) coming fresh from the press, it illustrates the enormous increase in the power of computers, supporting Shneior Lifson's optimistic prospect "that further creative imagination, penetrating wisdom and hard word work will finally lead to a solution of the problem"; (ii) it is focused on more specialized topics, mainly theoretical approaches, from simulated annealing and molecular dynamics to side chain packing and neural networks; (iii) most of the authors differ from those who contributed to earlier volumes, to the effect that the careful reader does not find many of the common references quoted in previous monographs. Since there is no name index, this kind of search is not trivial; names such as R.L. Baldwin, J.-R. Garel, M.E. Goldberg, P.S. Kim and F.X. Schmid occur only once or twice, others are missing altogether. One obvious reason is that the editors define 'the protein folding problem' in terms of "tertiary structure prediction". As a consequence, the topics treated, e.g. in the AAAS Selected Symposium 89 (edited by D.B. Wetlaufer) are ignored. The same holds for the 'kinetics' and 'pathways' of folding; protein 'stability' is only discussed in connection with the role of interior side chain packing (J.H. Hurley).

Instead of the traditional topics, the discussion refers to the following problems: A. Roitberg, R. Elber, S.R. Wilson and W. Cui apply simulated annealing algorithms to a number of model systems. T.N. Hart and R.J. Read discuss the docking of flexible ligands to proteins using a Monte Carlo approach. Next come S.M. Le Grand and K.M. Merz with a review of current developments in the application of the genetic algorithm, and R.E. Bruccoleri with applications of his CONGEN program. Distance geometry and molecular dynamics are covered by W.R. Taylor, A. Aszódi, A. Caflisch and M. Karplus. G.M. Crippen and V.N. Maiorov describe a contact potential function that

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can identify the native fold of a protein within a large pool of conformers; a similar reduction of the complexity of the problem, this time referring to side chain packing, is accomplished by J. Desmet, M. de Maeyer and I. Laster's 'dead-end elimination' method. Two extremes are discussed by R. Unger and M. Sippl: the first focuses on short structural motifs and how they may be used to predict the tertiary structure, while M. Sippl, S. Weitckus and H. Flöckner apply their 'knowledge-based mean field' method to a 'polyprotein' containing all known 3D structures in one single chain. Finally, N.T. Ngo, J. Marks and M. Karplus give a detailed account of the computational complexity of the protein structure prediction problem and its relation to the Levinthal paradox. The chapters review the areas of current research up to 1993. Thus, the reader gets an excellent introduction into the complex field with all the background required to follow up recent progress. Most of the articles are written for the specialist or the established scientist in the field of theoretical molecular biology. For the beginner, chapters in T.E. Creighton's book 'Protein Folding' might be a good starting point in order to get the necessary background.

Rainer Jaenicke

Molecular Biology of Diabetes I. Autoimmunity and Genetics; Insulin Synthesis and Secretion; Edited by B. Draznin and D. LeRoith, The Humana Press; Totowa, NJ, 1994; xv + 404 pages. $89.50. ISBN 0-89603-286-8.

Part one of 'Molecular Biology of Diabetes' carries the subtitle 'Autoimmunity and Genetics; Insulin Synthesis and Secretion'. The ambitious purpose of this volume is to bring the latest knowledge of diabetes-related research in a comprehensive manner to students, teachers, and researchers. In the preface the editors state that the chapters are written by most of the world's experts in the field. The discouraging excerpt from this is – as an European – that more than 90% of the world's expertise resides within the USA.

This volume is divided into to the two subparts: 'Molecular Mechanisms of Autoimmunity and Genetics of Diabetes' (90 pages) and 'Molecular and Cellular Aspects of Insulin Synthesis and Secretion' (307 pages). This page number allocation may be the natural bias of the editors but unfortunately also reflects the quality of the chapters. Of the four chapters dealing with autoimmunity and genetics, two are technically orientated, i.e. one chapter discusses the value of transgenic mice in the study of the nature of IDDM, and the other deals with pancreatic islet transplantation. The islet transplantation chapter deals with the xenotransplantation situation, but not human islet transplantation. These chapters are nice overviews but have little conceptual contribution to make to the field. The two other chapters of this first section deal with the pathogenesis of IDDM and target molecules in the autoimmune processes. There is a good overview of the possible role(s) of T cells in the pathogenesis, but the authors do not pay much attention to other existing hypotheses of the pathogenesis. The genetics is dealt with in 2–3 pages scattered over the four chapters. This seems not enough to justify the title of this volume.

The part on 'Molecular and Cellular Aspects of Insulin Synthesis and Secretion', in contrast, has many excellent review chapters. The chapters on the insulin gene structure and regulation, glucose-regulated insulin secretion (which includes a section on the potential therapeutic implication of engineered, insulin-secreting cell lines), and the chapters on the role of GTP in insulin regulation, on ion channels and gap junctions deserve special attention. However, a common feature of part two is the limited space used for a focused discussion of the 'molecular biology of diabetes'.

Why the editors have not left out the first four chapters and change the title to, e.g. 'Molecular Biology of the Beta cell' is not clear to me. The overall impression would then have appeared more comprehensive. Thus, for the first part of this volume, I do not think the purpose of the editors is fulfilled, whereas the second part includes several excellent reviews. Finally, I find it annoying that cross-references are to wrong chapters or even to a chapter which does not exist, and that figures are numbered wrongly.

Flemming Pociot

Fluorescent Probes in Cellular and Molecular Biology; Edited by Jan Slavik, CRC Press; Boca Raton, FL, 1994. 295 pages. ISBN 0-8493-6892-8.

There are many advantages in using fluorescence techniques to measure and locate things inside cells, the most obvious being that most new probes can be used in living cells. A disadvantage has been that a fair knowledge of physics and chemistry is needed to interpret and understand the fluorescence signals that the probes provide. A book that provides this sort of knowledge has been lacking. The deficit is amply made up for by Slavik's guide. His preface shows that he has set out to provide "easily understandable introductory reading for biologists and medical people who wish to start working with fluorescent probes". I thoroughly concur with him that "the book gives a comprehensive overview of the main application fields, allowing the reader to get a basic orientation and feeling for what fluorescent probes can do". The good intentions of an author's preface often founder on difficulties of scope and presentation, but in this book we have a guide that, if anything, surpasses the promises of its preface. I have never read so comprehensive or lucid an introduction to the optical principles and techniques of fluorescence measurement. He never loses sight of his reader, always presenting the physics and chemistry in a way best suited to "biologists and medical people".

The basic principles and properties of fluorescent probes are dealt with in an introductory chapter. Their interactions with cells, how to get them, where they go and what they sense once inside, form the basis of chapter two. Having got us interested, he turns to the theory of fluorescence in chapter three. I think it is telling and characteristic of his approach that he first deals with the biology before turning to the physical and chemical theory. The fourth, and by far the longest chapter, is on instrumentation: spectrofluorimeters, photomultipliers, light sources, polarization measurements, optics, resolution and image acquisition and storage are all discussed clearly and with careful (but not fussy) attention to the important physical principles that underlie the working of these sorts of instruments; important because lack of understanding can lead to bad mistakes of interpretation when it comes to presenting one's results. The last five chapters give a detailed treatment of different classes of probe: those that sense solvent polarity, membrane fluidity, membrane potential, intracellular ions and, finally, those probes that can be used to tag proteins and measure molecular dimensions using resonance energy transfer or to tag specific cellular organelles.

Armed with this book, any biologist or medical person can reach with confidence the Molecular Probes Inc. catalogue and plan a fluorescence approach to answering questions in cell biology and medicine. The book is even well written and at times witty. "Fluorescence techniques have a bright future" says the first subheading on page 1. Though you may greet this with an amused but sceptical smile, if you read to the end, you will be convinced.

Michael Whitaker