countered. Many researchers are even convinced that the expression and purification of membrane proteins in a functional state and in sufficient quantity is the major bottleneck in the structural biology of membrane proteins.

In this book, approaches toward overcoming this barrier for membrane proteins are described from a structural genomics point of view. In general, structural genomics is an approach in which a large number of targets are produced in parallel by means of high-throughput technologies and subjected to structural studies. Dealing with structural genomics of membrane proteins in particular requires joint efforts in many areas of modern life sciences, which are covered by this book. Therefore, the reader is provided with detailed information about the overexpression of membrane proteins in bacterial, yeast, insect, and eukaryotic systems. Next, solubilization, purification, and crystallization strategies are described. However, the book is not restricted to X-ray crystallography. Rather, it provides a general overview of structural approaches suitable for membrane proteins, including electron microscopy of two-dimensional crystals, atomic force microscopy, and NMR.

It is quite frequently observed that overexpressed proteins do not adopt their native fold. Rather, these proteins are "deposited" within the cell in the form of inclusion bodies, which in principle can be refolded into their native three-dimensional structure. Much effort has been undertaken in the past to refold soluble proteins, but the refolding of membrane proteins is a rather new strategy toward the overproduction of a given protein of interest; *Structural Genomics on Membrane Proteins* also covers this promising strategy. Of course, structural genomics of membrane proteins requires parallelization and high-throughput technology. To satisfy this demand in the field of membrane proteins, chapters have also been included that cover production strategies, miniaturization, and an overview of structural genomic networks specialized in membrane proteins. These provide the reader with an opportunity to view the fascinating world of membrane proteins through the eyes of a structural genomics researcher. Notably, three chapters are devoted to current approaches in bioinformatics, molecular modeling of membrane proteins, and drug-discovery techniques for G-protein-coupled receptors. It is important to remember that it is not always necessary to remove membrane proteins from their natural environment, the biological membrane. Recent advances in fluorescence labeling of membrane proteins in living cells provide a new avenue to study the interactions of membrane proteins with other molecules within the cell and their spatial and temporal distribution and organization within the membrane.

Research on membrane proteins is an exciting field, and editor K. H. Lundstrom has organized material that covers the many aspects of this particular research area. This book provides insight into the various disciplines, approaches, problems, and solutions in membrane protein research. Clearly, it is a challenge to cover all aspects of this research area, but the editor and authors have achieved a balance between detail and importance without losing the main focus. Many leading experts have provided an excellent overview that is helpful for students and researchers who wish to familiarize themselves with this field. Also worth mentioning are the excellent table of contents and keyword index, which are very helpful in finding a given topic and its corresponding details. This book is also recommended for experts in membrane protein research or structural genomics because it not only provides an excellent overview, it also offers a detailed and balanced view on the daily challenges in working with these fascinating proteins, especially from a structural genomics perspective.

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Structural Genomics and High Throughput Structural Biology

Edited by *Michael Sundström*, *Martin Norin*, and *Aled Edwards*.

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Modern drug discovery suffers from low efficiency and high cost. One potential way to address these questions is through genomics research. Structural genomics has increasingly provided new means for enhancing structure-based drug design approaches. Also, the stricter demands on drug safety have presented a strong case for improved design of drugs with fewer side effects. Here, structure-based drug discovery might also play a significant role. In this sense, the new opportunities for drug development provided by structural genomics and high-throughput structural biology have recently received much attention. It is therefore with great pleasure that I welcome this new book by Sundström, Norin, and Edwards.

The editors have assembled an interesting mixture of authors representing important scientists in the field of structural biology from both academia and industry. The composition of the chapters is also successful and gives the reader a nice overview of structural genomics. Strong emphasis has been dedicated to the crystallization process and methods. The modeling aspects have also been described in detail with a special chapter dealing with the validation of structural information. I found most of the chapters very informative and highly adequate for getting a picture of the methodology, also for scientists not directly involved in crystallography and comparative modeling. The layout of the book is good. However, the size of the figures is generally too small and many of the structures suffer substantially from the black and white presentation.

The overview on structural genomics describes the field well and introduces the key players, such as the major structural genomics centers. The lessons learnt from the pilot phase of structural genomics are also interestingly presented. The following two chapters deal with protein purification and crystallization.

The section on protein expression is rather thin and focuses almost only on *E. coli*-based expression, explaining the limitations related to codon usage, post-translational modifications, and protein co-expression. Unfortunately, no alternatives to prokaryotic expression systems are presented. The protein purification is described minimally, and the book would have benefited from an approach similar to that taken in the chapter on crystallization methods. Automation and miniaturization issues are well presented in relation to the crystallization methods. Further detailed descriptions of crystallography procedures follow in the chapter on high-throughput crystallography. I found the chapters describing the relationship between structural information and function particularly interesting (chapters 6 and 9). The book clearly addresses the difficulties encountered for novel protein structures for which functional activity is unknown and how to approach these issues in applied drug discovery. The chapters dealing with modeling issues (comparative modeling and ab initio modeling) fits well into the book theme and provide plenty of useful insight. Moreover, the two chapters dealing with validation of structural information and problems in computational structural genomics present serious efforts to discuss the errors in existing models and the difficulties encountered in computational interpretation of data from structural genomics initiatives. Finally, the last chapter tries to summarize the current status of applied structural genomics. This is a good approach, which also includes a brief summary of the key players, both public and private entities, in structural genomics today. Rather disappointingly, however, and further discussed below, very little attention is paid to membrane proteins. It is especially unfortunate that several networks focusing uniquely on membrane proteins are not mentioned at all. For instance, the EU-funded E-MeP network, established in 2004, overexpresses 100 prokaryotic and 200 eukaryotic membrane proteins. The privately funded MePNet consortium (established in 2001) has focused uniquely on 100 G-protein-coupled receptors (GPCRs) and has managed to produce more than 30 GPCRs at structural-biology-compatible levels in bacterial, yeast, and mammalian cells.

Unfortunately, the book suffers to some extent from some outdated information. This is clearly a dilemma of all printed material, as we are today spoiled with the immediacy of internet-based information. In quite a few chapters, the authors refer to the current situation in 2004. However, the book was printed in 2006, which makes the data look old. Certainly, author deadlines are much earlier than the publication date of the book, but it should have been the responsibility of the editors to update the information or request it from the authors.

Another shortcoming is the near total neglect of structural genomics on membrane proteins. Clearly, structural characterization is far more difficult for membrane proteins, and success in this area has been very modest, as the authors correctly point out. However, 50–60% of the current drug targets are based on GPCRs, and 70% of existing medicines are based on membrane protein targets (including ion channels and transporters). For this reason, it would have been adequate to pay more attention to this important group of proteins. Moreover, there is no reference to another book published by CRC Press in 2006 dedicated to membrane proteins, entitled *Structural Genomics on Membrane Proteins* (edited by Lundstrom). If not the authors, at least the publisher should have been aware of this other book. Also quite disturbingly, there is hardly any information available in the book on protein expression. The authors repeatedly (especially in chapters 2 and 12) give the impression that *E. coli*-based recombinant protein expression is the only applicable system. Occasionally, suggestions are given that cell-free protein production might be useful in the future. There is no mention of yeast or animal cell expression. Despite that, there are several eukaryotic membrane protein structures obtained from protein expression in *Pichia pastoris* published in 2005 (Jidenko et al., *Proc. Natl. Acad. Sci USA* **2005**, *102*, 11 687–11 691; Long et al., *Science* **2005**, *309*, 897–903; Long et al., *Science* **2005**, *309*, 903–908). Moreover, numerous reviews between 2001–2004 have highlighted high-level expression of correctly folded and functionally active membrane proteins from Baculovirus-infected insect cells (Sarramegna et al., *Cell Mol. Life Sci.* **2003**, *60*, 1529–1546) and Semliki Forest virus-infected mammalian cells (Lundstrom, *Biochim. Biophys. Acta* **2003**, *1610*, 90–96; Lundstrom, *Comb. Chem. High Throughput Screen*. **2004**, *7*, 431–439), which are therefore available for structural biology applications. To further underscore the advance in structure determination of membrane proteins, although it occurred after the publication of the book reviewed herein, the 3D X-ray crystal structure was solved for the β2 adrenergic receptor expressed from Baculovirus vectors in insect cells (Rasmussen et al., *Nature* **2007**, *450*, 383–387; Cherezov et al., *Science* **2007**, *318*, 1258–1265).

In summary, *Structural Genomics and High Throughput Structural Biology* is a most welcomed addition to the scientific book market. I am convinced that structural biologists will find the information in the book very useful. Moreover, the compact format of data should also find readers from the scientific community in general and perhaps also serve as a textbook for specified higher education programs.

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