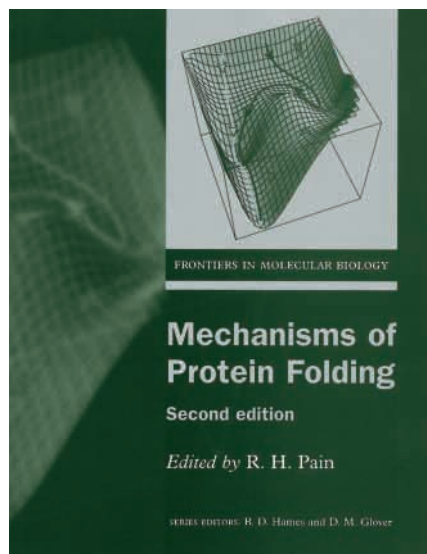


Protein oregami



Mechanisms of Protein Folding

edited by Roger H. Pain

Oxford University Press (2000) 433 pages. ISBN 0-19-963788-1
£35

Even after many years of research by numerous groups, our understanding of protein folding is still not at the stage where the structure of a protein can be predicted from its amino acid sequence alone, even though the experiments of Anfinsen in the 60s demonstrated this should be possible in principle. This second edition of *Mechanisms of Protein Folding*, like the first, is focused on the experimental study of protein folding. Although only seven years have passed since the first edition, there has been a remarkable expansion in our knowledge of *in vitro* and *in vivo* protein folding during this period. There have been the impressive crystal structures of GroEL and other chaperones, and major enhancements in experimental techniques to study protein folding, in particular to look at the very early stages of folding.

The first seven chapters of the book cover the current theoretical models of protein folding, its kinetics and the current experimental methods used to study folding. These are reviews by leading experts in the fields. The first chapter, by Dobson, covers the 'new' and 'old' views of protein folding, and Chapter 6

looks at the molten globule. These views, which at times can appear contradictory, are merging together and to some extent may be rather like the discussions in quantum theory of whether an entity is a particle or a wave, in which the answer is both! For proteins, the folding behaviour of different folds and the experimental setup may emphasise one of these views more than the others. The other chapters focus on specific experimental techniques and show how experiments have pushed back the boundaries of time so that very early events (sub-millisecond) of protein folding can now be studied.

Two further chapters cover proline isomerisation and disulphide bond formation, the other two major factors controlling the rate of monomeric globular protein folding. Up to this point, the book has essentially concentrated on the folding and stability of monomeric globular proteins, mainly *in vitro*. The chapters have also contained quite detailed information. Of more interest to the general reader are two chapters that cover recent work on the assembly of multi-subunit structures and the actions of chaperones. It is in the multi-subunit structures chapter that there is a section that discusses membrane protein folding, whose importance I would have thought merited a chapter of its own - although this may reflect the relative paucity of experimental work in this area compared with globular proteins. The chapter on chaperones provides a good overview of the various chaperone families and their functions, and looks at the differences between Archaea and eukaryotes.

Three chapters are devoted to case studies of the folding of three proteins: apomyoglobin, collagen and haemagglutinin. The apomyoglobin case covers a standard globular protein, whereas the other two are more unusual and interesting. The collagen case looks at the 'folding' of a non-globular protein, the collagen triple-helix, including the aggregation into fibrils. The haemagglutinin case covers the folding of a large, membrane-attached protein *in vivo*, in which the protein chain is not completely synthesised before protein folding starts to occur. These last five chapters remind us that there is a lot

more to protein structure and the generation of biological function than monomeric globular protein folding, and are much more useful for non-experts in protein folding.

The final chapter covers diseases associated with protein misfolding, including various mutations that cause specific conformational changes leading to disease - for example, sickle-cell haemoglobin and, of course, the prion diseases, in which aggregates of misfolded proteins cause the damage.

This book is a valuable snapshot of the state of experimental studies of protein folding at this time. It provides an excellent example of a book at the frontiers of molecular biology, the title of the series. For this reason it does require some background knowledge of protein folding, both theoretical and experimental - it is not for the uninitiated. As a scientist simulating protein folding *in silico*, I found it a very useful collation of the experimental data available and a reminder of issues that tend to be ignored.

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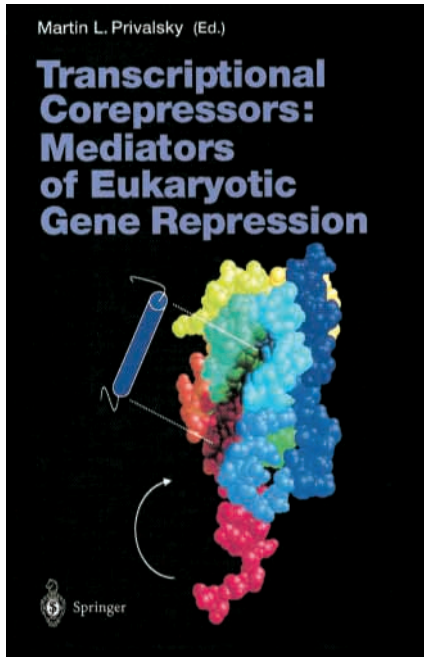
The great repression

Transcriptional Corepressors: Mediators of Eukaryotic Gene Repression

edited by Martin L. Privalsky

Springer-Verlag (2001) 190 pages. ISBN 3-540-67611-2
£79/\$119

Not so long ago it was thought that eukaryotic transcription was regulated entirely by activation of genes that were otherwise inert. This view has since been squelched by the burgeoning field of transcriptional repression. Transcriptional corepressors, binding to transcription factors and actively preventing transcription, are clearly important for tight control of gene expression. Martin Privalsky has



brought together an outstanding group of investigators to produce a succinct yet thorough survey of this field. This collection of reviews is well organized, and describes recently discovered corepressor complexes and the mechanisms they might use to exert their repressive effects. The first chapter orients the reader to the organization of chromatin structure and how it may be altered by chromatin-remodeling activities, including the covalent modification of histones. The lucid discussion of these issues is now poignant, as well as informative, given

the recent untimely death of one of the authors, Dr Alan Wolffe, a leader in this field. The second chapter, by Kuzmichev and Reinberg, focuses on multiprotein complexes containing histone deacetylases (HDACs) as critical regulators of the repressed state. Chromatin structure and HDAC complexes are appropriately featured throughout the book. Thus, the first two chapters nicely set the stage for subsequent chapters focused on corepressors in model organisms, corepressors used by specific transcription factors, and the role of corepressors in leukemia.

The chapter by Roth links classical repressors to Sin3, Tup1p and Hir corepressors in yeast. Mannervik's chapter highlights the roles of Groucho, CtBP and HDACs in *Drosophila* development. Two chapters are dedicated to nuclear hormone receptors and their corepressors N-CoR and SMRT. A review by Ordentlich, Downes, and Evans describes the ability of nuclear receptors to recruit HDACs through interaction with corepressor proteins. This precedes Privalsky's in-depth analysis of the regulation of nuclear receptor corepressor function. These chapters successfully provide continuity without redundancy. Harbour and Dean provide a very concise review of the repression characteristics of the retinoblastoma protein cell cycle transcription factor, and Wotton and Massague extensively review the role of

Smad corepressors in TGF β family signaling. In the final chapter, Guidez and Zalent explore the role of corepression in the pathogenesis of human leukemias, explaining in molecular terms how fusions of such factors as PML and PLZF with retinoic acid receptor α lead to aberrant recruitment of corepressors and dysregulation of normal cell growth and differentiation.

While the focus of this book is clearly on corepressor-complex-mediated recruitment of chromatin-modifying activities to transcription factors of choice, this is balanced in many chapters by substantial attention to alternate means of repression, such as interruption of basal factor recruitment. Overall, this book is a brief, well-written and understandable introduction to the world of transcriptional corepressors. It is a valuable reference for those in the field and is worth reading cover-to-cover by those interested in an overview of this emerging area.

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