

Of Primary Importance and Hidden Complexity

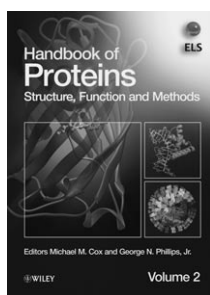
Handbook of Proteins: Structure, Function and Methods

Edited by Michael M. Cox and George N. Phillips, Jr.

Wiley-VCH, Weinheim 2007, 1378 pp. (2 vols), hardcover € 469.00.—ISBN 978-0-470-06098-8

Proteins are one of the key components of life. Their importance is already implicated in their names, derived from the Greek "prota", which means "of primary importance". All functions of living organisms are related to proteins. They exert a vast number of different functions in the cell, ranging from catalysis to signalling and ligand recognition or transport to structural proteins. Consequently, many labs around the world focus on proteins, their structures, their functions, their interactions, proteins in isolation, within the cellular context or their role in the shaping of organs or organisms.

To keep up with the ever-growing knowledge about proteins can sometimes be a daunting task. The *Handbook of Proteins: Structure, Function and Methods*, a two-volume set, addresses exactly this dilemma. By providing the reader with a comprehensive overview but also with detailed insights into proteins structure, function and interaction, as well as the respective techniques, it allows novices and professionals alike to dwell on virtually all the different facets of protein-related issues. The articles, which are written by specialists from the respective fields, are derived from Wiley's *Encyclopedia of Life Sciences* (ELS), a comprehensive collection of over 4200 peer-



reviewed articles covering all aspects of life sciences. Articles are divided into two groups according to their complexity: introductory articles focus on the basic concepts and have been written primarily for undergraduates or nonspecialists. Advanced articles provide a deeper understanding of a particular topic. All articles are summarized by a short abstract and a table of contents.

Volume 1 focuses on protein structure, synthesis and degradation as well as on enzymes, enzyme activity, and enzyme cofactors. Volume 2 covers protein interaction with ligands, DNA, or other proteins as well as on techniques for protein production, isolation, and purification, techniques for protein characterization, and techniques for interaction studies.

The section entitled "Protein Structure" comprises 37 papers about general principals of factors influencing protein structures, structure classification, structural motifs, protein stability, structure prediction and databases. The "Protein Synthesis" section focuses on chaperons and protein folding, codon usage, protein synthesis inhibitors and postsynthetic modification. "Protein Degradation" covers aspects such as amino acid degradation, proteolysis and degradation by lysosomes, proteasomes and the ubiquitin pathway. Enzymes, being one prominent class of proteins, are covered by three sections. The first section, entitled "Enzymes" covers general aspects of enzyme kinetics, activity and specificity. The second section "Enzyme Activity" focuses on different mechanisms of catalysis, regulation and inhibition. The third section "Enzyme Cofactors" gives a nice overview of the most important cofactors such as haem, coenzyme A, NAD⁺, NADP⁺.

Volume 2 starts with "Protein-Ligand Interaction" with general aspects of interaction, shape complementarity and cooperativity. The next two sections "Protein-Nucleic Acid Interactions" and

"Protein-Protein Interactions" focus on more structural aspects of recognition as well as on protein interaction networks. The more theoretical part concludes with a section about "Membrane Proteins" with examples of ATPases and ion channels as well as their function in endocytosis and protein translocation. The second part of volume 2 is devoted to techniques. "Production, Isolation and Purification" gives an overview of protein production methods and expression hosts but also includes solid-phase peptide synthesis. Additionally, techniques for protein isolation and purification are given with a comprehensive selection of methods for electrophoresis and chromatography. The following section "Techniques: Characterization" contains a comprehensive selection of biochemical and biophysical methods for almost all aspects of protein characterization. While each topic cannot be covered in detail owing to the complexity of many biophysical methods, this extensive selection of techniques gives an excellent overview, and thus, provides an excellent guide for choosing the most suitable methods. The book ends with the section "Techniques: Interactions", which includes prediction, computational or experimental analysis of protein-protein, protein-ligand and protein-DNA interactions, as well as array-based proteomics.

Each of the papers, which start with a short abstract and a brief introduction, is subdivided into several shorter paragraphs, which are also listed in the table of contents next to the title. This well-arranged format combined with the clear layout and full-colour figures makes it very easy to extract the main points from each article. Cross-referencing between articles and the very detailed subject index facilitate a more detailed study of a topic of interest. In summary, the *Handbook of Proteins: Structure, Function and Methods* presents a comprehensive guide to modern protein sci-

ence and at the same time provides an enjoyable read to extend or refresh one's knowledge. It combines theoretical aspects with modern techniques and will be invaluable to all researchers in the vast area of protein science, from students to senior investigators.

Katja Arndt

University of Freiburg (Germany)

DOI: 10.1002/cbic.200800399

Methods in Molecular Biology, Volume 426: Structural Proteomics, High-Throughput Methods

Edited by Bostjan Kobe, Mitchell Guss and Thomas Huber.

Humana Press, Totowa 2008, XXVI + 601 pp., hardcover \$ 99.00.—ISBN 978-1-58829-809-6

It is said that we live in the *postgenomic* era. That phrase has a particular finality to it that possibly understates how much we still have to learn about what makes us, and other species, tick. Perhaps, more sensibly, we could be said to reside in the *perigenomic* era, a time when the sequencing of DNA genomes is advancing apace, probably accelerating away almost beyond the capability of geneticists and bioinformaticians to keep up. So what then? How will we make sense of all this one-dimensional information and better understand and exploit biology? The truth is that a major chunk of the real *postgenomic* era is going to be the science of understanding the genome-encoded data in three dimensions, and probably—if you count how these biological structures change in time—four dimensions. In principle, the methodologies required to approach this challenge have long been established and are practiced widely around the globe. Nevertheless, arguably (and I stress *arguably*, as there are some who would say that investment in the field has been misplaced), in order to properly exploit the ever-growing genomic information in any reasonable timeframe, the practice of structural and functional analysis of biological macromolecules

needs to be speeded up. Hence the fashion over the past 5–10 years for funding agencies to plough significant resources into the field of structural proteomics—the attempt to determine and catalogue protein structure (and thereby maybe function) in ever higher throughput. It is beyond doubt that, at least in part because of this investment, more and more protein structures are being solved at an ever faster rate. Whether these efforts are proving fundamentally useful to the wider biological community, it is perhaps too early to say. What is clear, however, is that this influx of resources has heralded a step-change in scope, utility and often throughput of methods and technologies that facilitate the practice of protein expression, purification, and structural analysis.

This book compiles an impressive array of contributions from a variety of contributors—some in large structural genomics consortia, others in traditional, single PI-led laboratories—that document a very significant fraction of these methods, usually in a format that is accessible to any jobbing structural biologist, or those other molecular biologists with an inkling to press their molecular targets into crystal screens or NMR tubes. Gratifyingly for this reviewer, who frankly has made his career more by sitting in front of an NMR spectrometer than actually producing samples to put in the instrument, many of the contributions include candid hints and notes about how the procedures can go wrong, as well as how to do them right, and I have come away from this commission glad to have been exposed to many of the exhortations to good practice that the contributors urge on the reader. Before I got stuck into the book, I was concerned that it would contain many chapters where different large consortia listed and perhaps boasted about their structure determination throughput, either to justify their funding or to defend the charge that the funds could have produced similar, or indeed more high-profile, results if distributed via the normal channels (and also to bang on about getting past the “low-hanging fruit”). In fact I found very little of this, and instead very much came away with the impression that, in order to meet the

aforementioned *postgenomic* challenges, we will need to work smarter (and no doubt harder too) by adopting the emerging technologies contained within. Certainly it will be the case that, in the study of protein structure and function, each protein will (by its nature) have its own physicochemical properties, and present an individual window of tractability for detailed analysis. These are the characteristics which the diverse physical and biochemical methods described in this book attempt to address.

In sum, this is a book it is useful to have to hand, not so much for how to solve crystal structures or perform standard NMR analyses (which are topics widely described elsewhere), but rather a volume that prompts new thinking about how to approach structural biology with a view to maximizing the likelihood of a positive outcome. The compendium covers both “standard” high-throughput approaches to bioinformatics domain boundary predictions, protein expression and purification, and preliminary structural analysis and more specialized “frontier” areas such as micro-coil NMR, protein crystallisation in heterogeneous and restricted geometry phases, and combined cross-linking/mass spectrometry analysis of protein complexes. There is less about the challenges posed by post-translational modifications, and the combinatorial complexities implied by obligate heterodimers and larger macromolecular assemblies. Nevertheless, for me, reading this book helpfully addresses, in a largely state-of-the-art manner, possibly the ugly secret of the overall pursuit of protein atomic coordinates in three dimensions, namely that a very large fraction of the time the experiments do not succeed or at least the protein target will not cooperate. In the absence of a robust answer to the Protein Folding Problem, the presence of which would paradoxically eliminate the need to tackle the task we started out with, we probably have little other choice than to heed the lessons that this book helps to disseminate.

Paul C. Driscoll

MRC National Institute for Medical Research (UK)