

PROTEIN CRYSTALLIZATION

Second Edition

edited by

TERESE M. BERGFORS

Preface to the Second Edition

Obtaining crystals is currently the bottleneck despite the amazing progress in the field of structural determination by X-ray crystallography. The aim of this book is to help you procure crystals of good quality. It is intended for active practitioners, the foot soldiers at the lab bench.

The earliest incarnation of this book was a photocopied manuscript based on students' questions. I began to compile materials and protocols by way of answering them. The fact that this book is now in its second edition, completely revised and updated, is an evidence of the rapid development and importance of crystallization.

The accumulated knowledge on practical aspects of protein crystallization is scattered in many different sources or in the form of local lab lore. The value of a book on crystallization is that it gathers the material and organizes it in one place. The authors of the chapters are leading experts in their techniques and areas and many of them are also active as teachers. My goal as editor has been to provide an overall unity and cohesion to the 17 chapters. The chapter styles vary—some are written as reviews and others are informal and practical. There are frequent cross-references between chapters to help the reader find additional information on a topic. Some overlap of material has been permitted intentionally for the benefit of the readers who will be dipping into the book, rather than reading it from cover to cover.

If you already have the first edition of *Protein Crystallization*, why should you buy this second edition? You will find that almost all of the material is new. The first edition was published in 1999, when high-throughput consortia were in their infancy. In the few years since then, high-throughput methods have contributed to the miniaturization and automation of crystallization experiments as well as a vast pool of data on crystallization screening. New strategies, based on these data, are taken up in two separate chapters by Newman and Rupp. Automation is becoming affordable even for small laboratories and its importance will grow. Other chapters new for this edition cover guidelines for choosing automation for crystallization. These have been written by Luft, DeTitta, and Rupp, based on their expertise from high-throughput laboratories.

Also new for this edition are chapters on mass spectrometry (Gao and Zhang), microcalorimetry (Yeh), counterdiffusion (García-Ruiz), heavy-atom derivatization (Dauter and Dauter), selenomethionine proteins (Larsson) and engineering proteins to make them more amenable to crystallization (Qiu and Janson). Zeelen has contributed again from his library of crystallization pictures so that this section now contains four pages of color plates. Interpretation of the phenomena in the crystallization drop is an area in which beginners (and automated visual recognition systems) have great difficulty. To my mind it is the ability to recognize promising leads and knowing what to do with them that constitutes the proverbial green thumb in crystallization. Study the photographs and compare your drops with them—the time will be well invested.

McPherson opens the book once again with some basic advice. Seeding is reviewed by Mac Sweeney and D'Arcy and an extensive seeding exercise is included. The chapter on crystallization methods is in much greater depth and includes excellent illustrations and phase-diagram explanations by Luft. For the chapter on dynamic light scattering, Nobbmann explains the theoretical principles and I cover the practical issues. Chayen, Garman, and I have updated and expanded the chapters we wrote for the first edition. Membrane proteins are not treated as a separate chapter in this edition although they are covered within chapters as appropriate. This is because there are now several books specifically on the crystallization of membrane proteins, for example, So Iwata's *Methods and Results in Crystallization of Membrane Proteins*, also published by International University Line.

The laboratory exercises are grouped together for this edition in a separate section to facilitate their use in courses. Many new ones have been added. The exercises have been tested in the "Practical Protein Crystallization" course that I have been running since 1994 at Uppsala University, as well as courses elsewhere. Your feedback on these, or any aspect of the book, is greatly welcomed—please send any questions or suggestions to me, terese.bergfors@icm.uu.se.

Acknowledgements

The authors generously took their time to contribute to this book. I am indebted to them for their efforts. It has been a privilege to work with them and I have learned many things from the numerous discussions we shared this past year.

I thank my colleagues who read the chapters and exercises and gave me valuable input. Some of my test readers deserve special mention: Anna Jansson, Bror Strandberg, Lars Liljas, Wojciech Krajewski, Gerard Kleywegt (all from Uppsala University), Jonas Vasur (Swedish Agricultural University), Joe Ng (University of Alabama in Huntsville), and Inés Muñoz (CNIO, Madrid). Matti Nikkola (Karolinska Institutet, Stockholm) and Christina Skans extricated me from some murky linguistic cul-de-sacs with their impressive knowledge of English. Mark Harris (Uppsala University) gave me invaluable help with the figures and his patience in explaining PhotoShop to me over and over verges on the saintly. Professor Alwyn Jones (Uppsala University) generously allowed me to devote myself to the book without interruption. Dr. Igor Tsigelny (International University Line) is editor of the series in which this book is a part. I am grateful to him for the opportunity to turn my photocopied papers into a book that has now reached its second edition. I thank Stefan Odestedt for sorting out the mysteries of Microsoft Excel for me and his moral support in general. Finally, I extend my deepest appreciation to my daughter, Carmen, for her forbearance yet once again during my preoccupation with this book.

Uppsala, Sweden, March 2009

Terese Bergfors