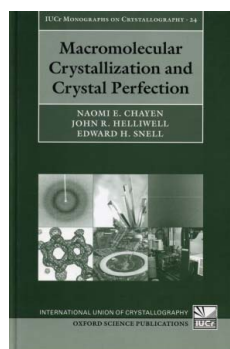


book reviews

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Macromolecular Crystallization and Crystal Perfection. By Naomi E. Chayen, John R. Helliwell and Edward H. Snell. Pp. xi + 221. Oxford University Press, 2010. International Union of Crystallography Book Series, Monographs in Crystallography 24. Price (hardback) £65. ISBN: 978-0-19-921325-2.

This book is highly recommended to anyone interested in the determination of macromolecular structures by diffraction methods. It presents an overview of what one needs to think about in the initial stages of macromolecular crystal structure determinations, that is, when one is trying to grow crystals. The authors describe the methods that can be used for doing this and the problems that might be encountered. Most significantly they suggest ways to deal with any difficulties that are found along the way. When each aspect of appropriate crystallographic methods is discussed, a useful list of references (43 pages long) is provided for those who would gain from a more detailed study. The small glossary, however, is in need of expansion to assist student readers and could have benefitted from definitions of many concepts introduced in the book. Since crystallization is a rapidly moving branch of macromolecular structure determination, one would assume that it will be necessary for updated new editions of this book to appear in the near future as instrumentation and information on the subject progress.

If you want to crystallize a biological macromolecule for which only a small quantity is available what should you do? The authors describe the types of screening setups presently used to establish conditions, such as temperature, concentration of solubilizing and precipitating agents and pH, that work best in producing crystals of the particular macromolecule being studied. They show that the search for the best crystallization method becomes less random for the investigator if information on the phase diagram of the substance being crystallized can be mapped; the use of such a diagram (shown in Figures 2.1 and 4.1) is highly recommended for all crystallization trials. For best results one aims to go from a highly supersaturated 'precipitation zone' to a more moderately supersaturated 'nucleation zone' where crystallization is initiated when molecular aggregates form. However, one should not stay too long in this zone but proceed to the low supersaturation 'metastable zone' before too many small crystals start to grow. Then, hopefully, a few large, well

ordered single crystals may be obtained. Photographs reproduced in the book illustrate the results obtained as crystallization proceeds in several of various possible pathways through the phase diagram. This screening can be efficiently aided by high-throughput crystallization robotics.

The experimental setups used to grow crystals include batch crystallization, vapor diffusion, liquid/liquid diffusion (including microfluidic chips) and dialysis. The assistance, for example, of streak seeding with animal hairs and of dynamic light scattering are also described. At this stage crystals suitable for X-ray or neutron diffraction may have been obtained. The reader is reminded, however, that not all good-looking crystals will provide data for a satisfactory structure determination.

But what does one do when no crystals are obtained? Several possibilities, such as adding small relevant molecules, covalently modifying the protein, mutating the macromolecule by replacing polar amino acids to smaller side chains such as alanine, selecting the same material from a different biological source or enzymatically breaking up the macromolecule and studying only the biologically active portion, are possible tactics to try. Further options include growing crystals in a gel, or the use of microgravity which eliminates density-driven turbulence (an expensive option). If the crystal quality is poor and defies improvement the authors suggest that the experimenter should aim to improve the instrumentation, that is, the beamline and detector. Some ways of doing this are presented in a very useful chapter.

Then the authors proceed, assuming that crystals have been obtained, to discuss the diffraction pattern obtained and what it tells us about the extent to which the crystal structure is well ordered. It is important, of course, that the best possible measurement of the diffraction pattern should be made. The higher the resolution, with a greater the number of diffraction data, the better the crystal structure that is obtained. If the crystal were perfect the X-ray or neutron diffraction pattern would show only rays diffracted at Bragg angles. However, there is often additional information in the background of the diffraction pattern where Bragg reflections are not expected to occur. This leads in the book to discussions of twinning, radiation damage, and short- and long-range disorder, all of which can reduce the signal-to-noise ratio of the diffraction data that the X-ray or neutron crystallographer was hoping for. Short-range disorder is characterized by thermal diffuse scattering (atomic vibrations), static disorder scattering (differences in atomic positions from unit cell to unit cell) and solvent disorder. Long-range disorder involves mosaicity (misalignments of domains). This can be probed by reflection profiling and topography (determining how much of the

crystal contributed to the Bragg reflection). Twinning is described in a separate chapter that lists clues that would alert the crystallographer to its existence. It is a common problem and there are several types of twins. Sometimes all that is needed to eliminate twinning is a change in the crystallization conditions (such as the use of chemical additives), use of a small incident beam that may only interact with one of the twins, or attempts to cut the specimen crystal and separate the twins. Maintaining the diffractibility of crystals and the pros and cons of cryocooling to prevent radiation damage are discussed, and humidity control during crystallization is also recommended. To my surprise powder diffraction studies of macromolecules are also described in an interesting chapter. There is no discussion of the methods used to solve the phase problem and obtain an electron-density map; they are left for other authors to present.

Finally, I was delighted to see a discussion of the future of macromolecular structure determination, including taking into account results from other physical methods. Obviously sources of radiation for use in diffraction and the instrumentation to measure diffraction data will improve in the future, and this led the authors to thoughts about other methods, such as lensless X-ray diffraction microscopy of noncrystalline structures (such as yeast cells) and the possibility of the use of an X-ray laser. Again I recommend this excellent text to all who want to grow macromolecular crystals.

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