do they demand (for example) such a tightly focused, stable, rapidly tunable, monochromatic X-ray beam? Are experiments on virus crystals really brilliance-driven?' Given the diversity of interests and backgrounds of the intended readers, it is a particular strength of the author that he presents much complex material in a straightforward and generally comprehensible style. Although some topics, such as the fundamentals of crystallography, are dealt with only briefly, they are amply described in other texts, and the comprehensive reference list provides enough pointers to the research literature to satisfy the most enthusiastic reader. The numerous line drawings are of high quality, but the halftone prints seem to have suffered severely in the production process, and they are of more limited value.

Besides describing the present state of play, Helliwell offers many pointers to the next innings, so much so that a researcher looking for novel topics to pursue in the next grant application will find several here. As an example, a chapter is devoted to diffuse X-ray scattering from macromolecular crystals, where the high information content of the diffraction pattern is immediately apparent, but where the means of extracting that information in structural terms remain to be fully developed. Another chapter deals with ongoing developments in Laue diffraction, both static and time-resolved, and there are speculations on, *inter alia*, the use of ultra-short X-ray wavelengths, novel X-ray detectors, and the use of Bijvoet ratios rather than differences.

Today, conducting experiments at a synchrotron rather than in the home laboratory is always more complicated, subject to extreme time pressures and often more stressful. It is an enterprise to be undertaken only when the scientific benefits are marked. However, with the arrival of powerful and accurate multiple-wavelength anomalous dispersion (MAD) phasing techniques, where the experimental measurements are most readily made with synchrotron radiation, it seems likely that quite soon the majority of macromolecular crystallographers - not just those studying virus structure, or microcrystals, or exotic time-resolved problems - will choose to use synchrotron sources. This book will be their one essential reference.

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Time-resolved macromolecular crystallography. Edited by D. W. J. CRUICKSHANK, J. R. HELLIWELL and L. N. JOHNSON. Pp. v + 174. Oxford University Press, 1992. Price £35.00. ISBN 0-19-855781-7.

This book is a compendium of contributions presented at a discussion meeting on Laue diffraction held by the Royal Society in January 1992. All but one of them were first published in the *Philos. Trans. R. Soc. London Ser. A* (1992). **340**, 167-334. In publishing these papers separately, the editors have made available to the macromolecular crystallographic community a volume that describes the current state of the art of the Laue technique, its advantages and disadvantages, its current successful applications and its future expectations. The book gives a good overview of the problems associated with this difficult but rewarding diffraction technique, which many believe offers the key to unlock the puzzle of structure-function relationships in macromolecules.

The opening paper, by D. W. J. Cruickshank, (6 pp.) presents an interesting historical perspective to the technique. It includes extracts from letters from both Ralph Wyckoff and Linus Pauling, clearly showing that many of the problems that we face today in collecting and analyzing Laue diffraction data had already been encountered by the pioneers of the field over 70 years ago. The second paper, 'Time-resolved crystallography: principles, problems and practice', (16 pp.) by K. Moffat, Y. Chen, K. Ng, D. McRee & E. D. Getzoff, presents an overview of a modern Laue diffraction experiment. After stating the assumptions upon which proposals for time-resolved crystallography are based, the authors discuss its five major components: the X-ray source and optics, reaction initiation, reaction monitoring, X-ray data acquisition, and data reduction and analysis; using results drawn from their work on the photoactive yellow protein and a natural product, briarane B. Chapter 3, 'Time course of chemical and structural events in protein crystals measured by microspectrophotometry', (18 pp.) by G. L. Rossi, A. Mozzarelli, A. Peracchi & C. Rivetti, summarizes the use of polarized absorption spectroscopy to characterize activity in the crystalline state, with results from five protein systems. Simultaneous use of microspectrophotometry and X-ray diffraction during a time-resolved experiment will enable the crystallographer to better characterize the system of interest . In Chapter 4, H. D. Bartunik, L. J. Bartunik & H. Viehmann in 'Time-resolved X-ray diffraction studies of enzymes under cryoconditions', (12 pp.) describe the use of scanning Laue diffraction and cryocrystallography to study enzyme mechanisms. They summarize the uses and advantages of these techniques and present, for the first time, direct evidence of a covalent O—C bond between a serine protease and a productive substrate, demonstrating that cryocrystallography can yield detailed structural information on substrate intermediates. In Chapter 5, 'Synchrotron X-ray crystallography techniques: time-resolved aspects of data collection', (12 pp.) J. R. Helliwell compares the time scales for the rotation, Weissenberg and Laue data-collection methods at synchrotron sources, with particular attention to the wavelength-dependent factors in Laue diffraction. Two detector systems are presented: the three-dimensional toast rack, which maximises the number of processable spots on a Laue film by reducing the number of spatially overlapped reflections, and a charged coupled device (CCD) for monitoring changes in integrated spot intensities as a function of time, so as to check radiation damage in a protein crystal. Next, J. E. T. Corrie, Y. Katayama, G. P. Reid, M. Anson & D. R. Trentham, in 'The development and application of photosensitive caged compounds to aid time-resolved structure determination of macromolecules', (12 pp.) discuss practical and theoretical considerations when using various caged compounds for synchronous reaction initiation in the crystal.

'Time-resolved diffraction studies on glycogen phosphorylase b', (18 pp.) by E. M. H. Duke, A. Hadfield, S. Walters,

S. Wakatsuki, R. K. Bryan & L. N. Johnson, is the first of a series of articles reporting results on specific enzyme systems. The authors discuss in some detail how the loss of low-resolution data from Laue data sets, caused by the harmonic overlap problem, affects difference Fourier maps of a small substrate (1 deoxy-1-amido-α-D-glucose) bound at the catalytic site of glycogen phosphorylase b. Their results show that deconvolution of the harmonically overlapped reflections improves map quality and hence interpretation. In the following paper, 'On the scope and limitations of the Laue method in kinetic crystallographic studies with macromolecules', (8 pp.) I. Anderson, I. J. Clifton, S. L. Edwards, V. Fülöp, A. T. Hadfield, J. Hajdu, P. Nordlund, P. Phizackerley, M. Soltis & S. Wakatsuki provide a summary of Laue diffraction results prior to the meeting and discuss the limitations that mosaic crystals, the loss of low-resolution data and data processing have on the technique. The authors suggest that the Weissenberg method of data collection could be a suitable alternative method for rapid data collection, removing some of the inherent limitations of the Laue method.

The next two papers present results using photoactivation as a means of triggering the enzymatic reaction. The first, 'Time-resolved crystallography on H-ras p21', (10 pp.) by A. Sheidig, E. F. Pai, I. Schlichting, J. Corrie, G. P. Reid, A. Wittinghofer & R. S. Goody, describes the first successful use of a caged compound and Laue diffraction to monitor the enzymatic reaction. The article summarizes the progress that has been made towards understanding the conformational changes occuring in the protein product p21 of the H-ras proto-oncogene during and as a result of hydrolysis of GTP at its active site. In 'Can Laue catch Maxwell?: observation of short-lived species by Laue X-ray crystallography', (12 pp.) D. Ringe, B. L. Stoddard, J. Bruhnke, P. Koenings & N. Porter advocate that, instead of caging the substrate, one should cage the protein. They illustrate this approach with results from a photoreversible covalent inhibitor for γ-chymotrypsin. In the following paper, 'Laue diffraction as a tool in dynamic studies: hydrolysis of a transiently stable intermediate in catalysis by trypsin', (16 pp.) P. T. Singer, R. P. Carty, L. E. Berman, I. Schlichting, A. Stock, A. Smalås, Z. Cai, W. F. Mangel, K. W. Jones & R. M. Sweet describe trapping a transiently stable intermediate of another serine-protease - trypsin - and study the deacylation by triggering the reaction using a pH jump. Their results suggest that a water molecule gradually moves closer to the carbonyl C atom of the scissile ester bond as time proceeds. These observed differences in the water structure as a function of pH should help to rationalize the differences in stability of the ester bond.

In an extension of earlier monochromatic studies, A. Liljas, M. Carlsson, K. Håkansson, M. Lindahl, L. A. Svensson & A. Wehnert in 'Laue and monochromatic crystallography on carbonic anhydrase', (10 pp.) show that the Laue method can distinguish between subtle differences in the binding of small anions to carbonic anhydrase, and therefore should be capable of revealing the small changes that accompany enzymatic reactions. A review of more conventional monochromatic methods for studying enzymatic reactions, with results drawn from three enzyme systems, is presented in 'Conventional X-ray diffraction approaches to the study of enzyme mechanism: serine proteinases, aminoacyl-tRNA synthetases and xylose isomerase', (12 pp.) by D. M. Blow, P. Brick, C. A. Collyer, J. D. Goldberg & O. Smart. In the concluding paper entitled 'Art is long and time is fleeting: the current problems and future prospects for time-resolved enzyme crystallography', (12 pp.) G. A. Petsko offers his comments on the challenges and problems facing potential Laue crystallographers in the future. He provides a good summary of most of the problems discussed in greater length in other articles, together with some possible solutions.

This volume will be of great help to a macromolecular crystallographer with an enzyme system of potential interest for time-resolved studies. The pioneering work of the authors will enable the crystallographer unfamiliar with the field to learn about the pitfalls and problems of the technique. The book should serve as a good reference source for much of the ground-breaking theoretical work that made the Royal Society meeting possible. It is, however, repetitious at times, especially with regards to the problems associated with the technique. This is, in part, as a result of its nature - a collection of research papers from many different laboratories - and unanimity as to what those problems are. However, solutions to the problems are as plentiful as the papers in the book, and suggest that this technique has an exciting future.

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