

# Evolving Methods for Macromolecular Crystallography

## The Structural Path to the Understanding of the Mechanism of Action of CBRN Agents

Edited by

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## PREFACE

This volume comprises papers presented at the 2005 edition of the “Crystallography of Molecular Biology” courses that have been held since 1976 at the Ettore Majorana Centre for Scientific Culture in Erice, Italy. This series of courses is renowned for bringing leaders in the field of macromolecular crystallography together with highly motivated students, in a beautiful and intimate location that encourages people to interact. The warm and informal atmosphere at these Erice conferences, especially these on crystallography, has helped to foster long-term scientific interactions and new international friendships that have often lasted for the lifetime of the scientists. The course was financed by NATO as an Advanced Study Institute and by the European Commission as a EuroSummerSchool.

The papers span the breadth of material presented in the course, which emphasized the practical aspects of modern macromolecular crystallography and its applications. One must start with crystals: Bergfors showed how to improve initial crystals through seeding, while Byrne discussed the difficult problem of crystallizing membrane proteins. The collection of optimal diffraction data requires both careful preparation of cryo-cooled crystals (Garman) and proper processing of the diffraction images (Leslie). To obtain images of electron density, one needs estimates of the phases of the diffracted spots. Sheldrick presented the background to the single-wavelength anomalous diffraction (SAD) method, which has been gaining popularity, and McCoy discussed the basis of modern maximum likelihood methods for treating information in experimental phasing. When a related structure is known, the phases can be obtained by molecular replacement, which can use stochastic search methods (Glykos) or tree search methods based on maximum likelihood (Read). There is also the promise that *ab initio* phasing methods will contribute at least at low resolution (Lunin). Initial phases can be improved dramatically by density modification (Turk). Increasingly, all these methods can be automated (Adams), an important step to increasing the throughput of structural genomics efforts (Baker). At times, structural genomics provides structures without a known function, but Thornton showed that structure alone can shed light on function. Careful analysis of structures can provide an explanation for disease processes at the atomic level (Jaskolski). The climax of this volume, as of the course, is the demonstration by Sayre that diffraction can be used to image single particles as large as cells.

Most of the real organizational work for the course was done by Paola Spadon and Lodovico Riva di Sanseverino, who, between them, found most of the funding, corresponded with applicants and selected participants,

made the logistical arrangements, and reminded us patiently when we needed to do something. Lodovico brought a wealth of experience to bear, having been a mainstay of the Erice meetings since their inception. John Irwin played an essential role, organizing all the information technology (IT) facilities needed to conduct tutorials and demonstrations in a computer (CPU)-intensive field like macromolecular crystallography.

Paola, Lodovico, and John were joined as Fellows of the Loyal Order of Orange Scarves by a set of enthusiastic volunteers: Vito Calderone, Laura Cendron, Sonia Covaceuszach, Federica Morandi, Elena Papinutto, Nicola Pasquato, Fabiana Renzi, and Donatella Tondi. Together they dealt with any of the day-to-day emergencies that arise in running a course like this.

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