Crystallography Times

Protein Crystallography Newsletter
Volume 1, No. 9, October 2009

In this issue:

Continuing Education Webinar
Taking the edge off: The softer side of in-house SAD phasing
Presenter: Joseph D. Ferrara, Ph.D.
November 19th at 10:00 AM EST
(15:00 GMT)

Crystallography in the news

October 24, 2009. Structural studies undertaken by a team, under the leadership of Dr. Dierk Niessing of the Helmholtz Zentrum München and the Gene Center at Ludwig-Maximilians-Universität (LMU) in Munich, have now determined the three-dimensional structure of Pur-alpha and gained insights into the molecular function of the protein behind fragile X tremor/ataxia syndrome (FXTAS).

October 21, 2009. Rice University scientists, led by Prof. Jane Tao, have won a $1.5 million, 4 year grant from the National Institutes of Health (NIH) to scrutinize the influenza A virus for clues that could lead to more effective antiviral drugs. Investigations will focus on the form and function of the nucleoprotein (NP), one of fewer than a dozen proteins encoded by the flu virus.

October 7, 2009. This year's Nobel Prize in Chemistry was awarded to Venkatraman Ramakrishnan, Thomas A. Steitz and Ada E. Yonath for using X-ray crystallography to elucidate the molecular structure and function of the ribosome.

October 2, 2009. Scientists from the Lawrence Berkeley National Laboratory and the Scripps Research Institute, led by John Tainer and Paul Russell respectively, have uncovered the role played by the least-understood part of a first-responder molecule - a protein complex called Mre11-Rad50-Nbs1 (or MRN for short) - that rushes in to bind and repair breaks in DNA strands, a process that helps people avoid cancer.

October 1, 2009. Research groups at the European Molecular Biology Laboratory (EMBL), the Institut de Biologie Structurale (IBS) and the Institut Albert Bonniot - respectively led by Christoph Müller, Carlo Petosa and Saadi Khochbin - have discovered a new way to read the histone code. Their work shows how a protein found only in developing sperm cells, Brdt, directs tight re-packaging of sperm DNA.

Screen more crystals with less effort

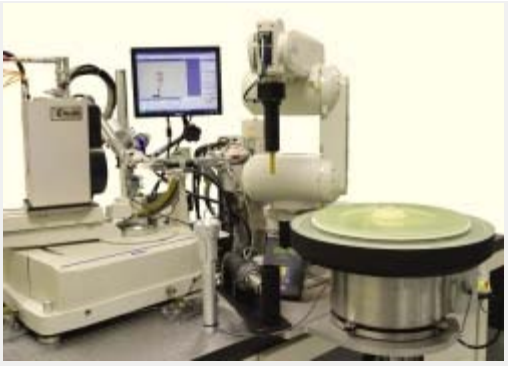
As structural biology projects have become more challenging, it has also become more difficult (in many cases) to get good diffracting crystals. Often it is necessary to screen many crystals to find one that diffracts well or in order to determine the best cryo protection conditions.

The Rigaku ACTOR™ sample changing robot is designed to automate the tedious process of mounting and screening crystals. Automated sample mounting also provides the added benefit of a reproducible mount and recovery process that minimizes the potential for crystal damage and ice formation that sometimes occurs with hand mounts.

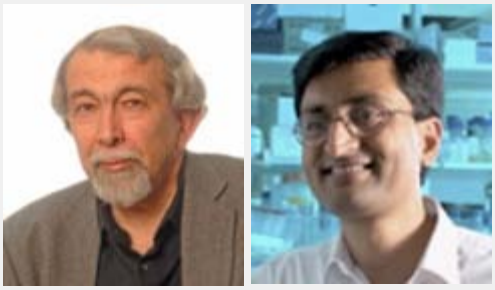
ACTOR is a complete system that has been continuously developed over the past eight years to provide the most comprehensive and complete commercial solution for automated sample mounting and screening. Accurate automatic sample centering, optimized sample handling and storage, and a software control package with integrated screening, ranking and data collection functions makes ACTOR the ideal sample mounting robot for the home X-ray lab or synchrotron beamline.

Request a copy of the ACTOR brochure or view a video of ACTOR.

Lab spotlight: What is CMTP?



ACTOR sample changing robot
(with a Saturn 944+ CCD detector in lower image).



CMTP is jointly directed by Prof. Tom Blundell (left) and Prof. Ashok Venkitaraman (right).

CCP4
STUDY WEEKEND 2010
Nottingham, UK

CCP4 Study Weekend (6th - 8th January 2010)
"From Crystal to Structure with CCP4"

Survey Question

What percentage of structures do you solve at home?

- < 25%
- 25-50%
- 50-75%
- >75%

The Cambridge Molecular Therapeutics Programme (CMTP) is an interdisciplinary initiative at the University of Cambridge, jointly directed by Professors Ashok Venkitaraman and Tom Blundell, that seeks to address the limited repertoire of molecular targets accessible to conventional methods for lead discovery and the high attrition rate during early clinical development in therapeutic areas such as oncology. The CMTP harnesses a unique and interdisciplinary spectrum of leading academic expertise in Cambridge for the discovery and development of drugs against cancer and infectious diseases.

Useful links for crystallography

MACiE, which stands for Mechanism, Annotation and Classification in Enzymes, is a collaborative project between the Mitchell Group at the Unilever Centre for Molecular Informatics part of the University of Cambridge and the Thornton Group at the European Bioinformatics Institute. MACiE currently contains 223 fully annotated enzyme reaction mechanisms, which comprise 218 EC numbers (161 EC sub-subclasses) and 310 distinct CATH codes.

Science Podcast interview with Venki Ramakrishnan discussing two papers (*vide infra*) regarding the structure of ribosomes - Schmeing et al. and Gao et al. (16 October 2009).

Selected recent crystallographic papers

The Structure of the Ribosome with Elongation Factor G Trapped in the Posttranslocational State. Y. Gao, M. Selmer, C.M. Dunham, A. Weixlbaumer, A.C. Kelley and V. Ramakrishnan. *Science*, DOI: 10.1126/science.1179709 (published online: October 15, 2009).

The Crystal Structure of the Ribosome Bound to EF-Tu and Aminoacyl-tRNA. T.M. Schmeing, R.M. Voorhees, A.C. Kelley, Y. Gao, F.V. Murphy, J.R. Weir and V. Ramakrishnan. *Science*, DOI: 10.1126/science.1179700 (published online: October 15, 2009).

Template strand scrunching during DNA gap repair synthesis by human polymerase. M. Garcia-Diaz, K. Bebenek, A.A. Larrea, J.M. Havener, L. Perera, J.M. Krahn, L.C. Pedersen, D.A. Ramsden and T.A. Kunkel. *Nature Structural & Molecular Biology* **16**, 967-972 (2009).

An epistatic ratchet constrains the direction of glucocorticoid receptor evolution. J.T. Bridgham, E.A. Ortlund and J.W. Thornton. *Nature* **461**, 515-519 (2009).

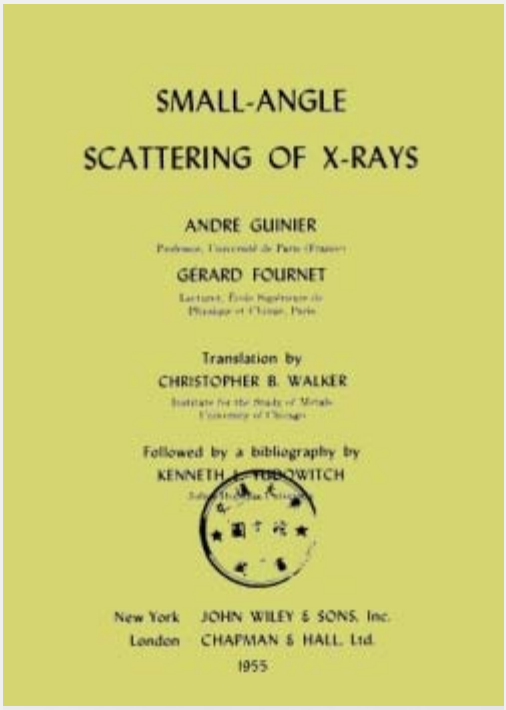
Book review:

Small-Angle Scattering of X-rays

by André Guinier and Gérard Fournet;
translated by Christopher B. Walker

Published in 1955, this book is long out of print and quite difficult to find. Fortunately, Dr. Angela Criswell located a copy for this retrospective review. Given that SAXS is such a "hot topic" these days, it was remarkable to find that this old tome is still a relevant and useful reference for researchers today.

Click on image or here to take the one question survey.



André Guinier
© *IUCr:Creative Commons attribution.*

To frame the perspective of the authors, it is notable that they opined (in chapter 6) that "These remarks explain why the study of proteins [dilute solutions] offers one of the best applications on this method. As a matter of fact, a large number of investigations have already been carried out on proteins, as is shown in the bibliography at the end of the text. We believe that it is in this field that small-angle scattering can give the most valuable and important results from a general point of view."

We are coming up on the 50th anniversary of the publication of Structure of Hæmoglobin: A Three-Dimensional Fourier Synthesis at 5.5 Å. Resolution, Obtained by X-Ray Analysis. [Nature 185, 416-422 (1960)] by Perutz, Rossmann, Cullis, Muirhead, Will and North. Guinier and Fournet did not foresee the explosion in protein structure that would start five years later. Yet, it is quite interesting that, 55 years after the publication, structural biologists have come back to SAXS as a tool for understanding the solution structure of proteins - that stage before crystallography takes over.

Chapter 1 provides a very basic introduction to the scattering process, while Chapter 2 explains the theory in detail. Readers should be forewarned: Chapter 2 provides an in depth overview of the mathematical background behind the calculation of the radius of gyration, pair distribution function and even the second virial coefficient. Chapter 3 provides a detailed discussion of the three pinhole SAXS camera. The only detectors available then were Geiger counters and film so the reader must keep in mind that there has been 55 years of instrument development in the interim. Nevertheless, the discussion is useful in understanding modern SAXS cameras. Chapter 4 introduces readers to the interpretation of results. Chapter 5 compares the SAXS method with other then state-of-the-art techniques to validate the results from Chapter 4. Chapter 6 goes through a number of applications, with the first part of the chapter devoted to the study of proteins in dilute solutions. Finally, an extensive bibliography is provided, that is obviously only current to 1955.

There are more modern textbooks and reviews on this subject, and the tools for collecting data and generating results have changed in the intervening 55 years, but anyone who is seriously interested in learning about SAXS would benefit from reading this classic text.

Joseph D. Ferrara, Ph.D.

Rigaku Americas
e-mail: info@Rigaku.com
Tel: (281) 362-2300

Rigaku Europe
e-mail: info@Rigaku.com
Tel: +[44] 1732 763 367

Rigaku Corporation
e-mail: rinttyo@rigaku.co.jp
Tel: +[81] 3-3479-0618

Rigaku China
e-mail: info@rigaku.com.cn
Tel: +[86] 010-82800840