

# Crystallography Times

Rigaku

Protein Crystallography Newsletter  
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## Crystallography in the news



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### Speaker's Corner



The Brändén and Hodgkin awards were conferred at the [IX European Symposium of The Protein Society](#) held from May 22-26, 2011 in Stockholm, Sweden.

The Dorothy Crowfoot Hodgkin Award (sponsored by Genentech) was jointly awarded to [Brenda Schulman](#) (St. Jude Children's Research Hospital) and [Wei Yang](#) (NIDDK, NIH). This award is granted in recognition of exceptional contributions in protein science, which profoundly influence our understanding of biology. Dr. Schulman's acceptance talk was entitled "Twists and Turns in Ubiquitin Conjugation Cascades" and was interesting in that it tied into her research at St. Jude.



Dr. [Wei Yang](#)'s talk was entitled "DNA Repair: From Human Disease to Atomic Mechanism" and again was a very interesting talk about how the body locates and fixes DNA problems. Dr. Yang was recognized for her numerous studies that led her to propose a widely accepted model of two metal ion catalysis for a large class of nucleic acid enzymes. In her work, Dr. Yang has used crystallographic and biochemical methods to define molecular mechanisms of DNA repair, replication and recombination.



June 3, 2011. School of Biological Sciences at the University of East Anglia have found that certain species of bacteria could be used for producing clean energy. The researchers recently discovered [proteins in these bacteria that actually carry out the process of transfer of charge](#). The scientists characterized the extra molecular structure of these special purpose proteins with X-ray crystallography.

June 4, 2011. Calcutta could soon have a state-of-the-art research facility - a [third generation high-energy synchrotron](#) - which would be only the fifth of its kind in the world, provided land could be identified for the project within a month from now. To be set up by the Saha Institute of Nuclear Physics (SINP) under the stewardship of the Department of Atomic Energy (DAE), the Rs 6,000 crore project will facilitate futuristic research on material science, crystallography and nano-technology, catapulting India to the big league of scientifically advanced nations.

June 14, 2011. Micromet, Inc. (NASDAQ: MITI) announced the appointment of [Ulrich Grau, Ph.D.](#), as Executive Vice President, Chief Operating Officer. Dr. Grau brings to the company more than 30 years of operations and R&D leadership experience in global biotechnology and pharmaceutical companies, and most recently served as President and CEO of Lux Biosciences, Inc, a clinical stage private ophthalmic company that he co-founded. After receiving his Ph.D. in chemistry and biochemistry from the University of Stuttgart, Dr. Grau spent three years as a post-doctoral fellow at Purdue University in the field of protein crystallography.

June 15, 2011. University of Oregon chemist Professor [Brad J. Nolen](#) was named as one of [22 new Pew Scholars in the Biomedical Sciences](#) by The Pew Charitable Trusts. Nolen, who joined the UO's chemistry department in Fall 2008, studies the molecular basis for regulation of the cytoskeleton, which provides physical support for cells. His lab uses a combination of biochemistry, biophysics, X-ray crystallography and molecular dynamics simulations to investigate the molecular-level regulation processes. Nolen is the second UO winner of this award. Hui Zong, a Professor of Biology and also a member of the Institute of Molecular Biology, was named a Pew Scholar in 2008.

June 16, 2011. A research team led by Professor Brian Bahnson at the University of Delaware and Professor Judith Klinman from the University of California Berkeley reported that enzyme [alcohol dehydrogenase](#) from *Bacillus stearothermophilus* has a Arrhenius pre-factor at 1025, which was eight orders of magnitude larger than previously recorded, thus confirming that more complex factors are contributing to the catalytic reaction than just temperature. The enzyme was characterized across the phase transition temperature threshold at 30°C, revealing trends in the protein's dynamic properties and tunneling based on a non-linear relationship between the rate of the reaction versus temperature at a level never seen before.

June 16, 2011. Structural biologists at Cold Spring Harbor Laboratory (CSHL), led by Associate Professor Hiro Furukawa, have obtained a precise molecular map of the [binding site for an allosteric inhibitor in a subtype of the NMDA \(N-methyl-D-aspartate\) receptor](#), which is commonly expressed in brain cells. The newly discovered binding site - a docking port within the receptor - is important because it is a potential target for drugs that can modulate NMDA receptors, dysfunctions of which have been implicated in depression, schizophrenia, Parkinson's and Alzheimer's diseases as well as stroke-related brain injuries.

June 16, 2011. A symposium at the June 2010 annual meeting of the Research Society on Alcoholism in San Antonio, Texas addressed recent findings concerning the interactions of alcohol with prototype brain proteins thought to underlie alcohol actions in the brain. A [key finding was that combining X-ray crystallography](#), structural modeling, and site-directed mutagenesis may be better suited to studying alcohol's low-affinity interactions than traditional techniques such as radioligand binding or spectroscopy.

June 22, 2011. Researchers at Imperial College London and the University of Surrey, led by Professor Naomi Chayen from the Department of Surgery and Cancer at Imperial College London, have reported a [more effective method for making proteins crystallise](#) using materials called 'molecularly imprinted polymers' (MIPs). MIPs are compounds

The final talk of the session was by Prof. [Michael Rossmann](#), who was hopefully getting good practice for giving a Nobel Prize acceptance speech on the same stage. His talk was entitled "Virus Host Entry," where he discussed three different viruses and showed some of his cool infection videos.



Rigaku Corporation sponsors the Carl Brändén Award that is given each year by the Protein Society. The award is presented to an outstanding protein scientist who has also made a large contribution to education. The winner was [Michael Summers](#), a professor at the University of Maryland Baltimore County as well as an HHMI investigator. He was selected to win this award for his commitment to mentoring of undergraduate students, graduate students and postdoctoral scientists, promotion of ethnic diversity in the biomedical sciences, as well as his groundbreaking accomplishments in advancing understanding of the structural biology of retrovirus structure, assembly and function.



made up of small units that bind together around the outside of a molecule. When the molecule is extracted, it leaves a cavity that retains its shape and has a strong affinity for the target molecule.

June 23, 2011. Roche announced the launch of a [new R&D Institute in France](#) under the lead of the company's Pharma Research and Early Development (pRED) unit. The pRED French R&D Institute will be fully dedicated to collaborative translational research and medicine, with the objective to build in-depth strategic partnerships with leading French academic centers in areas of mutual interest. The pRED French R&D Institute will be managed by a dedicated Roche academic alliances group.

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## Protein crystallization, workflows and data management

Successful use of automation in protein crystallization usually requires standardized workflows that allow for systematic testing of the chemical space. [CrystalTrak™](#) is a software system that is designed around workflows that have been developed in collaboration with some of the most successful protein crystallization facilities worldwide.

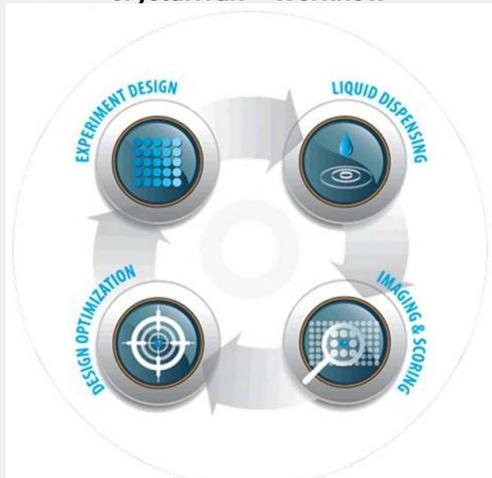
The core idea is a circular workflow of experimental design, liquid dispensing, imaging and scoring followed by optimization. Each step of the workflow allows users to interact with the automation equipment by either setting parameters or reviewing results. Another important concept of CrystalTrak is that at each step information can be captured for further use. For example, if a crystallization hit is found in a plate, it takes only one mouse click to generate a printable report that contains all information related to the hit, such as screen composition, incubation conditions, and details about the protein sample.

If you want to learn more about CrystalTrak, we would like to point you to a recent series of videos, including an [overview](#), [setup of experiments](#), a discussion on [imaging and scoring](#) and demonstration on [fine screen optimization](#).

[Request more information](#) on Rigaku CrystalTrak.

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### CrystalTrak™ Workflow



CrystalTrak is built around the protein crystallization workflow: Experimental design, liquid dispensing, imaging and optimization.

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### Macromolecular Crystallography Class October 26-28, 2011 The Woodlands, Texas

This class is tailored towards the needs of macromolecular crystallographers and their staff. Course format will be a series of short lectures on theory followed by hands-on activities with detectors, X-ray generators, and software. This class will also feature a training session on processing data with HKL.

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### Science Video

X-ray Crystallography at Diamond

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## Lab spotlight: Wang Lab @ Academia Sinica

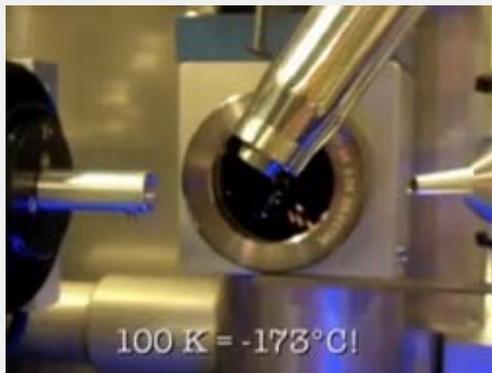
[Andrew H.-J. Wang](#)

Distinguished Research Fellow and Vice President, Academia Sinica; Institute of Biological Chemistry, Academia Sinica  
11 Post Docs, 9 Ph.D. students, 10 lab assistants, 29 alumni.



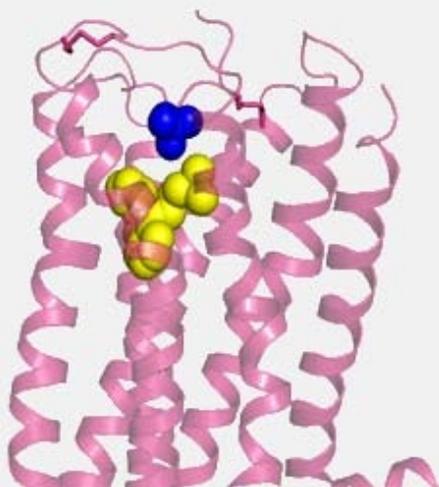
### Structural proteomics, anticancer drugs, X-ray crystallography, NMR and molecular design.

*Structural enzymology:* Several enzymes as potential targets for drug discovery are under investigation. For developing new antibiotics, they focus on prenyltransferases and glyco-related enzymes. For anti-viral and anticancer agents, they analyze proteases (3CL proteases, MMPs), and phosphatases (DuSPs in signal transduction). Studies of potential targets for diabetics and Alzheimer's disease are also in progress. *Protein-anticancer drug-DNA interactions:* Some DNA-binding proteins (like chromosomal proteins and proteins involved in meiosis) and many important anticancer drugs with DNA are of interest. The results can be useful for the design of new anticancer agents. *Search for disease markers:* Proteomic approaches, including 2D-GE and nanoLC, mass spectrometry and bioinformatics, are used to analyze cells and tissues from certain diseases to identify potential marker proteins. They are particularly interested in serum samples. *Proteins from extreme environments:* Microorganisms that live in extreme environments including extreme heat, cold, pH (acidic or alkaline) or radiation resistance have unusual proteins. Some enzymes described above are from those organisms.



[Watch YouTube](#)

### Structure of the Month



The Histamine H1 human membrane protein.  
Source: R&D Press Release - June 28, 2011.

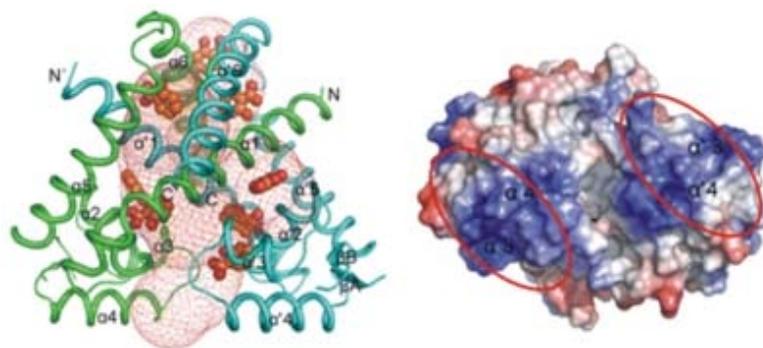
### Funny Science Video

Lab Romance - The Original Gaga Parody



[Watch YouTube](#)

[May Survey Results](#)



### Useful links for crystallography

[Mustang-MR Structural Sieving Server](#) - uses the structural alignment program MUSTANG to structurally align multiple protein structures. The server will also remove residues from the alignment that are below a threshold root mean square deviation (RMSD), producing "sieved" models. These are of practical use in characterizing conformational change (e.g. conserved core residues) and in producing multiple alternative search models for X-ray crystal structure determination using Molecular Replacement.

[Fold & Function Assignment System \(FFAS03\)](#) - provides an interface to the profile-profile alignment and fold recognition algorithm FFAS. A profile-profile alignment utilizes information present in sequences of homologous proteins to amplify the sequence conservation pattern defining the protein family. This method allows detection of remote homologies beyond the reach of other sequence comparison methods. Input into the FFAS03 server is a protein sequence provided by the user. From the sequence, a profile is generated that is then compared to several databases of sequence profiles of proteins and domains from public databases.

### Selected recent crystallographic papers

High-pressure protein crystallography and NMR to explore protein conformations. Collins, Marcus D.; Chae Un Kim; Gruner, Sol M. *Annual Review of Biophysics*, 2011, Vol. 40, p81-98.  
<http://dx.doi.org/10.1146/annurev-biophys-042910-155304>

Interaction of the p53 DNA-binding domain with its N-terminal extension modulates the stability of the p53 tetramer. Natan, Eviatar; Baloglu, Cetin; Pagel, Kevin; Freund, Stefan M.V.; Morgner, Nina; Robinson, Carol V.; Fersht, Alan R.; Joerger, Andreas C. *Journal of Molecular Biology*, Jun2011, Vol. 409 Issue 3, p358-368.  
<http://dx.doi.org/10.1016/j.jmb.2011.03.047>

Radiation damage to DNA in DNA-protein complexes. Spothem-Maurizot, M.; Davidková, M. *Mutation Research: Fundamental & Molecular Mechanisms of Mutagenesis*, Jun2011, Vol. 711 Issue 1/2, p41-48.  
<http://dx.doi.org/10.1016/j.mrfmmm.2011.02.003>

Mining electron density for functionally relevant protein polyserism in crystal structures. Fraser, James; Jackson, Colin. *Cellular & Molecular Life Sciences*, Jun2011, Vol. 68 Issue 11, p1829-1841.  
<http://dx.doi.org/10.1007/s00018-010-0611-4>

Monitoring and validating active site redox states in protein crystals. Antonyuk, Svetlana V.; Hough, Michael A. *BBA - Proteins & Proteomics*, Jun2011, Vol. 1814 Issue 6, p778-784.  
<http://dx.doi.org/10.1016/j.bbapap.2010.12.017>

Raman-assisted crystallography of biomolecules at the synchrotron: Instrumentation, methods and applications. McGeehan, John E.; Bourgeois, Dominique; Royant, Antoine; Carpentier, Philippe. *BBA - Proteins & Proteomics*, Jun2011, Vol. 1814 Issue 6, p750-759.  
<http://dx.doi.org/10.1016/j.bbapap.2010.07.021>

Please rate your agreement with the following:  
 "I enjoy combining a vacation with a scientific conference that is held during a national holiday, especially if it is held in an interesting location."

Strongly Agree	18.8%
Agree	31.3%
Neutral	6.3%
Disagree	25.0%
Strongly Disagree	18.8%

Note the bimodal distribution.

### Survey Question of the Month

When attending a scientific conference, how would you rank the importance of each of the following aspects:

	Very Important	Not Important
Establishing new relationships	<input type="radio"/>	<input type="radio"/>
Renewing old relationships	<input type="radio"/>	<input type="radio"/>
Seeing what new products are available from vendors	<input type="radio"/>	<input type="radio"/>
Learning new science from talks and posters	<input type="radio"/>	<input type="radio"/>
Learning new science from workshops	<input type="radio"/>	<input type="radio"/>
Visiting an interesting city	<input type="radio"/>	<input type="radio"/>

Take Survey  
 or cut-and-paste  
[http://www.surveymonkey.com/s/June\\_eNews](http://www.surveymonkey.com/s/June_eNews)  
 into your browser.

Crystal structure of the maltose transporter in a pretranslocation intermediate state. Oldham, Michael L.; Chen, Jue. *Science*, 6/3/2011, Vol. 332 Issue 6034, p1202-1205. <http://dx.doi.org/10.1126/science.1200767>

The structure of the unliganded extracellular domain of the interleukin-6 signal transducer gp130 in solution. Lorenzen, Inken; Shang, Weifeng; Perbandt, Markus; Petoukhov, Maxim V.; Svergun, Dmitri I.; Waetzig, Georg H.; Rose-John, Stefan; Hilgenfeld, Rolf; Grötzinger, Joachim. *European Journal of Cell Biology*, Jun2011, Vol. 90 Issue 6/7, p515-520. <http://dx.doi.org/10.1016/j.ejcb.2010.09.012>

X-ray crystallography, mass spectrometry and single crystal microspectrophotometry: A multidisciplinary characterization of catechol 1,2 dioxygenase. Micalella, Chiara; Martignon, Sara; Bruno, Stefano; Pioselli, Barbara; Caglio, Raffaella; Valetti, Francesca; Pessione, Enrica; Giunta, Carlo; Rizzi, Menico. *BBA - Proteins & Proteomics*, Jun2011, Vol. 1814 Issue 6, p817-823. <http://dx.doi.org/10.1016/j.bbapap.2010.09.008>

Exploring methionine  $\gamma$ -lyase structure-function relationship via microspectrophotometry and X-ray crystallography. Ronda, Luca; Bazhulina, Natalia P.; Morozova, Elena A.; Revtovich, Svetlana V.; Chekhov, Vladimir O.; Nikulin, Alexei D.; Demidkina, Tatyana V.; Mozzarelli, Andrea. *BBA - Proteins & Proteomics*, Jun2011, Vol. 1814 Issue 6, p834-842. <http://dx.doi.org/10.1016/j.bbapap.2010.06.017>

Extracellular matrix protein in calcified endoskeleton: a potential additive for crystal growth and design. Azizur Rahman, M.; Fujimura, Hiroyuki; Shinjo, Ryuichi; Oomori, Tamotsu. *Journal of Crystal Growth*, Jun2011, Vol. 324 Issue 1, p177-183. <http://dx.doi.org/10.1016/j.jcrysgro.2011.03.021>

Infrared protein crystallography. Sage, J. Timothy; Zhang, Yunbin; McGeehan, John; Ravelli, Raimond B.G.; Weik, Martin; van Thor, Jasper J. *BBA - Proteins & Proteomics*, Jun2011, Vol. 1814 Issue 6, p760-777. <http://dx.doi.org/10.1016/j.bbapap.2011.02.012>

Probing dimerization and structural flexibility of mammalian lipooxygenases by small-angle X-ray scattering. Shang, Weifeng; Ivanov, Igor; Svergun, Dmitri I.; Borbulevych, Oleg Y.; Aleem, Ansari M.; Stehling, Sabine; Jankun, Jerzy; Kühn, Hartmut; Skrzypczak-Jankun, Ewa. *Journal of Molecular Biology*, Jun2011, Vol. 409 Issue 4, p654-668. <http://dx.doi.org/10.1016/j.jmb.2011.04.035>

Structure of the dimeric autoinhibited conformation of DAPK2, a pro-apoptotic protein kinase. Patel, Ashok K.; Yadav, Ravi P.; Majava, Viivi; Kursula, Inari; Kursula, Petri. *Journal of Molecular Biology*, Jun2011, Vol. 409 Issue 3, p369-383. <http://dx.doi.org/10.1016/j.jmb.2011.03.065>

Structural analysis of a novel class of R-M controller proteins: C.Csp2311 from *Citrobacter* sp. RFL231. McGeehan, J.E.; Streeter, S.D.; Thresh, S.-J.; Taylor, J.E.N.; Shevtsov, M.B.; Kneale, G.G. *Journal of Molecular Biology*, Jun2011, Vol. 409 Issue 2, p177-188. <http://dx.doi.org/10.1016/j.jmb.2011.03.033>

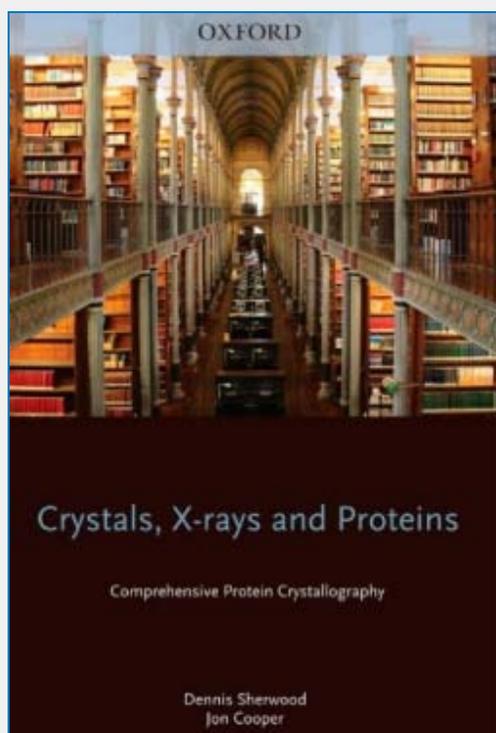
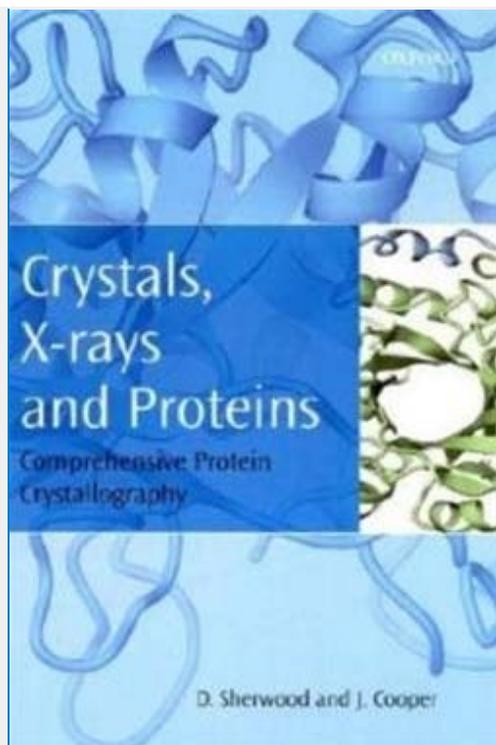
### Book reviews:

*Crystals, X-rays and Proteins - Comprehensive Protein Crystallography*  
 D. Sherwood and J. Cooper, Oxford University Press.  
 ISBN: 978-0-19-955904-6

$$Tf(\text{crystal}) = Tf(\text{motif}) \times [Tf(\text{infinite lattice})] * Tf(\text{shape function}) \quad (1)$$

The Fourier transform of the crystal is equivalent to the FT of the motif (molecule) times the convolution of the FT of the lattice, a series of Dirac delta functions and the FT of the shape function, is all you need to know. Well not really, but if you truly understand this equation then you are a long way to understanding the principles of X-ray diffraction.

The first two-thirds of this book was like a thriller to me. Even though I knew the answer, I wanted to see how the author would address the next topic and I could not put it down. The last third did not have the same grip on me and I kept asking myself what happened - did someone else write Part III? The book is divided into three parts,



but you know that already: Part I is Fundamentals, Part II is Diffraction Theory and Part III is Structure Solution.

Part I and Part II provide an integrated approach to teaching diffraction theory. The author takes the reader through crystal basics and the wave theory of electromagnetic radiation along with the mathematical tools to understand them. In Part II the authors painstakingly develop diffraction theory by analyzing one dimensional lattices then three dimensional lattices. Next the authors explore the concept of lattices with motifs and develop all the details from first principles. The latter includes the derivation of the Laue equations and Bragg's law. I found the step wise description of the Fourier transform and the effect of applying it to various functions and objects something that would help students immensely in understanding the relationship between direct space and reciprocal space.

Part III provides a description of the modern methods for protein crystallography. Much attention is spent on Patterson methods and the phase problem, with the same attention to detail as the first two parts. There is a good description of least squares refinement and the adaptations for constraints and restraints. Maximum likelihood and simulated annealing are also described. However very little about statistics is discussed. This is a very important topic in crystallography and deserves more space. I found Part III lacking in the practical aspects of modern protein crystallography although it is very well referenced.

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