Crystallography Times

Protein Crystallography Newsletter
Volume 1, No. 10, November 2009

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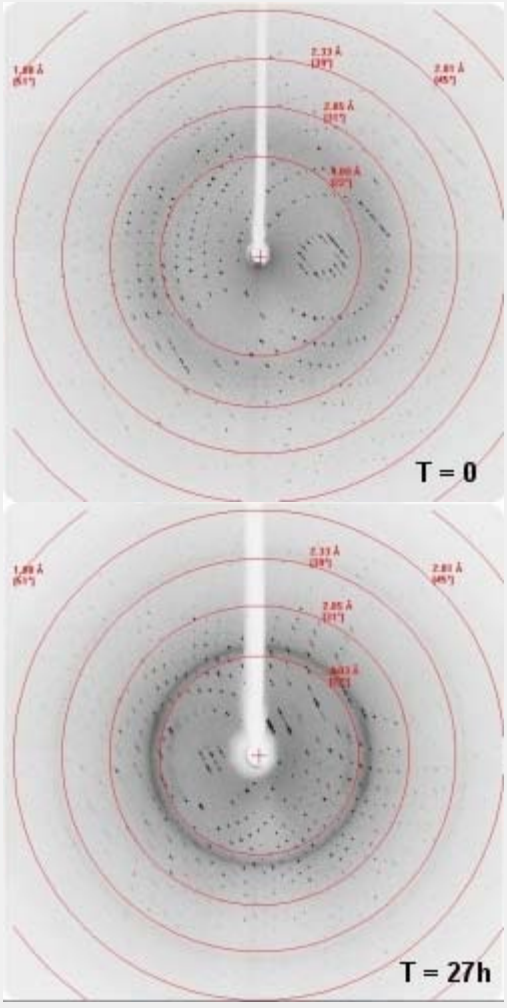


Crystallography in the news

November 19, 2009. On the path to a HIV vaccine, Peter Kwong and colleagues - at the Vaccine Research Center (NIH) - have shown that slight variations in how antibodies interact with their target on the HIV envelope cause conformational changes in the target molecule that render the antibodies ineffective.

November 19, 2009. Berkeley researcher James Berger and his team have shown that the *Escherichia coli* Rho transcription termination factor functions like a rotary engine fueled by the chemical energy in ATP nucleotides; it pulls RNA strands through its interior, an action that enables Rho to walk along RNA chains.

November 18, 2009. Researchers Richard Kuhn, Michael Rossmann and Wen Jiang at Purdue University received a $4 million American Recovery and Reinvestment Act grant - through the National Institutes of Health's National Institute of Allergy and Infectious Diseases - to develop better vaccines and antiviral drugs against flaviviruses and alphaviruses.

November 16, 2009. With the help of a helix-stabilizing strategy, researchers led by Gregory Verdine of Harvard University and James Bradner of Dana-Farber Cancer Institute have developed the first direct inhibitor of the Notch transcription factor complex, which is implicated in a range of cancers.

November 9, 2009. UK based Astex Therapeutics announced that it is to make a first public disclosure of the chemical structure of its potential best-in-class HSP90 inhibitor, AT13387, and will present new preclinical data on the compound.

November 9, 2009. Scientists, headed by José Antonio Márquez from EMBL Grenoble and Pedro Luis Rodriguez from CSICA, discovered that a mechanism for drought resistance in plants involves the structure of the protein PYR1 and how it interacts with the plant hormone abscisic acid (ABA).

No crystal damage with Rigaku UV imaging

UV illumination sources, such as mercury (Hg) illumination or standard LED UV illumination, can cause irrepairable damage to protein crystals - making it nearly impossible to use the original crystal hits for structure solution. However, with Clean Light Technology from Rigaku, original crystal hits may also be used for structure solution, since the illumination does not affect the diffraction quality of the crystals.

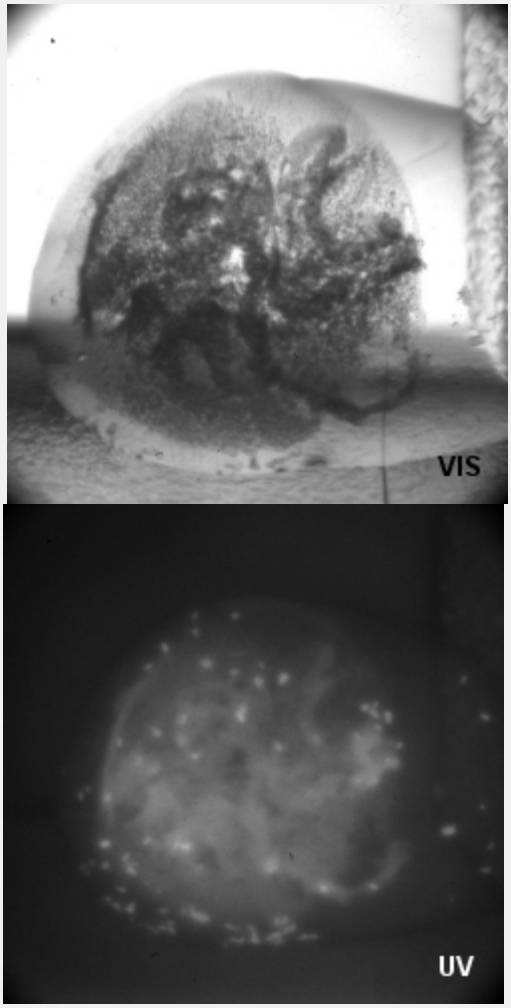
Experiments, using the Clean Light Technology, have shown that original crystals screened with UV can be used for X-ray diffraction data collection, saving valuable time and expense. Clean Light Technology can be focused only onto the well of interest, and additionally "strobed," further minimizing UV exposure time. The resulting average exposure time, over the life of a given experiment, is less than one minute - with average exposure times of 1-2 seconds per imaging session.

Studies have shown that exposure times as high as 50 hours have no effect on the diffraction quality of the crystals, and exposure times of 25 minutes or more have no effect on the electron density maps (see data at left). Rigaku features the award-winning Clean Light Technology in both of our UV imaging systems, the Desktop Minstrel™ UV and the NEW high-throughput Minstrel™ HT UV.

Request more information on Rigaku Clean Light Technology.

	Resolution (Å)	Rmerge (%)	Wilson B_{factor}
Reference	1.85	6.3	21.6
10 m	1.65	5.7	19.8
1 h	1.65	5.6	19.7
4 h	1.85	8.1	21.4
16 h	1.80	7.4	21.4
27 h	1.80	7.4	24.5

Crystal aging as a function of
Clean Light Technology UV exposure.



Demonstration of Rigaku Minstrel UV resolving protein crystals in a heavy precipitate.

Professor Tej P. Singh

Lab spotlight: What is TSSBL?

Tej Singh Structural Biology Lab (TSSBL) is a group of scientists, based in India and led by Professor Tej Singh, who have combined the fields of rational structure based drug design, clinical proteomics and bioinformatics to develop a contemporary lab that focuses on modern drug discovery. Their goal is to design and develop lead molecules that can qualify as the drugs for tomorrow ... drugs that will act in a specific way with minimal side effects and also are way ahead of the existing therapies. Current projects range from drug design against tuberculosis and other bacterial infections to breast cancer and infertility.

Useful links for crystallography

The X-ray Anomalous Scattering site at the University of Washington is intended to serve both as an introductory tutorial to anomalous scattering and as a general tool for designing experiments based on anomalous scattering.

Selected recent crystallographic papers

Techniques and tactics used in determining the structure of the trimeric *ebolavirus* glycoprotein. J.E. Lee, M.L. Fusco, D.M. Abelson, A.J. Hessell, D.R. Burton and E.O. Saphire. *Acta Cryst.* **D65**, Part 11, 1162-1180 (2009).

Structural Basis of Immune Evasion at the Site of CD4 Attachment on HIV-1 gp120. L. Chen, Y.D. Kwon, T. Zhou, X. Wu, S. O'Dell, L. Cavacini, A.J. Hessell, M. Pancera, M. Tang, L. Xu, Z. Yang, M. Zhang, J. Arthos, D.R. Burton, D.S. Dimitrov, G.J. Nabel, M.R. Posner, J. Sodroski, R. Wyatt, J.R. Mascola and P.D. Kwong. *Science* Vol. 326, **5956**, 1123-1127 (2009).

The role of DNA shape in protein-DNA recognition. R. Rohs, S.M. West, A. Sosinsky, P. Liu, R.S. Mann and B. Honig. *Nature* **461**, 1248-1253 (2009).

Structural insight into mammalian sialyltransferases. F.V. Rao, J.R. Rich, B. Rakic, S. Buddai, M.F. Schwartz, K. Johnson, C. Bowe, W.W. Wakarchuk, S. DeFrees, S.G. Withers and N.C.J. Strynadka. *Nature Structural & Molecular Biology* **16**, 1186-1188 (2009).

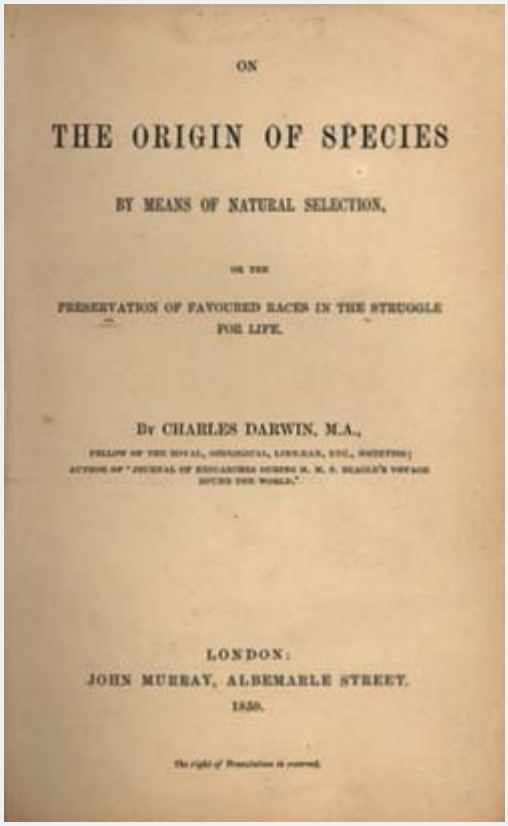
Direct-method SAD phasing of proteins enhanced by the use of intrinsic bimodal phase distributions in the subsequent phase-improvement process. L.J. Wu, T. Zhang, Y.X. Gu, C.D. Zheng and H.F. Fan. *Acta Cryst.* **D65**, Part 11, 1213-1216 (2009).

Book review: *On the Origin of Species by the Means of Natural Selection* by Charles Darwin

This classic was published this month in 1859, yet is not widely read, or at least as widely read as it should be. Paul Swepston and I thought it most appropriate to review Species this month. I actually tried to read this book at about 8 years old and it was clearly too much for me then. It's embarrassing to say I waited four decades to try again.

Darwin's attention to detail and descriptive prose are superb. The theory of evolution is

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


ON

THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

OR THE

PRESERVATION OF FAVOURED RACES IN THE STRUGGLE FOR LIFE.

By CHARLES DARWIN, M.A.,

LONDON:
JOHN MURRAY, ALBEMARLE STREET.
1859.

a classic scientific theory fully capable of discredit by evidence. The good news is that there has been no evidence to refute the principles set forth. In fact, two recent bodies of work show the theory continues to be valid: a recent report on the Framingham Heart study suggests humans are still evolving (Sean G. Byars, Douglas Ewbank, Diddahally R. Govindaraju and Stephen C. Stearns - PNAS). A genomic analysis of 40,000 generations of *E. Coli* (Jeffrey E. Barrick, Dong Su Yu, Sung Ho Yoon, Haeyoung Jeong, Tae Kwang Oh, Dominique Schneider, Richard E. Lenski and Jihyun F. Kim, Nature, 2009) further indicates evolution is an ongoing process. I find it amazing that Darwin was so well able to describe evolution using only observation - bo! th locally with pigeons, dogs and other domestic animals and globally with all the species he encountered on the Beagle.

The Origin of the Species is divided into nine self-described chapters: Introduction; Variation under domestication and under nature; Struggle for existence, natural selection, and divergence; variation and heredity; difficulties for the theory; geologic record; geographic distribution; classification, morphology, embryology, rudimentary organs; and concluding remarks. Each chapter provides a wealth of examples to support Darwin's hypotheses. In addition, each chapter provides its own introduction and conclusion, but I would not skip the middle parts because those are the best parts.

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