# Crystallography Times



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#### **Science Video**

#### Astbury Centre for Structural Molecular Biology



Professor Sheena Radford, winner of the Rigakusponsored Protein Society's 2013 Carl Brändén award, provides an overview of the cutting-edge activities of the Astbury Centre, and how their researchers are integrating molecular biology, physics and engineering to analyse proteins and help design new medicines.

## Watch the Video

#### **International Year of Crystallography**

As everyone is aware by now, 2014 has been declared the International Year of Crystallography by the United Nations. The opening ceremony of IYCr2014 was held at the main UNESCO building in Paris, January 20-21.



Prof. G.R. Desiraju, President of IUCr, at opening ceremony

Rigaku was one of the sponsors of the opening ceremony. The following video was prepared for the event and shown to the audience during the second day.



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# Crystallography in the news

January 2, 2014. Scientists at The Scripps Research Institute (Florida) have revealed an atomic-level view of a genetic defect that causes a form of muscular dystrophy, myotonic dystrophy type 2, and have used this information to design drug candidates with the potential to counter those defects—and reverse the disease.

January 2, 2014. Researchers at the Energy Department's National Renewable Energy Laboratory (NREL) have discovered that an enzyme from a microorganism first found in the Valley of Geysers on the Kamchatka Peninsula in Russia in 1990 can digest cellulose almost twice as fast as the current leading component cellulase enzyme on the market.

January 13, 2014. Combining expertise in biochemistry, immunology and advanced computation, researchers at Duke have determined the structure of a key part of the HIV envelope protein, the gp41 membrane proximal external region (MPER), which previously eluded detailed structural description. "The attractiveness of this region is that...it is relatively conserved," said Leonard Spicer, senior author and a Professor of Biochemistry and Radiology.

January 21, 2014. The United Nations has announced that 2014 is the International Year of Crystallography. An opening ceremony, hosted by the United Nations Educational, Scientific and Cultural Organisation (UNESCO) in Paris on 20 January, was followed by a two-day symposium celebrating the technique.

January 22, 2014. A new study from researchers at the The Scripps Research Institute and the University of North Carolina has discovered the key role that sodium plays in the signaling of opioid receptors in the brain. Researchers used X-ray crystallography to discover that the receptors have a site at which sodium can travel in and out of the receptor, changing the activity in the receptor.

January 24, 2014. Researchers at the Swiss Federal Institute of Technology (ETH) in Zurich have deciphered the structure of part of the ribosome found in mitochondria, the power plants of the cell. The scientists were able to benefit from advancements in the field of electron microscopy and capture images of the mitochondrial ribosome at a level of resolution never achieved before.

January 27, 2014. For protein structure determination, X-ray crystallography typically beats nuclear magnetic resonance (NMR) spectroscopy in terms of accuracy. But a computer program called Rosetta may help NMR catch up. Researchers have used the program to refine the NMR structures of a few dozen proteins and found that, in most cases, the resulting structures were as accurate as those determined by crystallography.

## **Product spotlight: PILATUS 200K HPAD**

PILATUS detectors have revolutionized data collection at protein crystallography beamlines around the world. The characteristics that have made this detector so popular at synchrotrons make it the ideal detector for the home lab environment. In shutterless data collection mode, you can collect more data in a short period of time with no need for rescans due to the extremely high dynamic range.



Rigaku now offers the PILATUS 200K as the standard detector for Rigaku HomeLab systems. PILATUS detectors are true photon counting devices that combine the following features to make them the best commercially available detectors for protein crystallography:

the highest sensitivity
the lowest readout noise
the fastest readout time
the lowest point spread function
fully air-cooled and maintenance free

Ask for more information.

## Lab spotlight: The Iwo Tews Laboratory

Dr. Iwo Tews Lecturer in Structural Biology Principal Investigator (Protein interactions & cell membranes) Centre for Biological Sciences Molecular and Cellular Biosciences Research Group University of Southampton



Dr. Tews' research group's interests are wide ranging, and include vitamin B6 biosynthesis, protein transport across cell membranes, and mycobacterial adenylyl cyclases. For the vitamin B6 biosynthesis work, they are addressing the architecture of the key enzyme complex, PLP synthase, and studying protein-protein interactions, complex formation, activation of the enzymes and the biosynthesis of the vitamin by the enzyme complex. For protein transport, one of their interests is the study of plant chloroplast protein import. Proteins required for photosynthesis are mainly synthesized in the cytosol of plant cells, and thus need to be transported into the organelle. Protein transport is mediated by the Toc-Translocon in the outer chloroplast membrane. The GTPases investigated by the Tews' group are receptors of protein import. Finally, the mycobacterium tuberculosis genome has 15 open reading frames for class III adenylyl cyclases (ACs) and they are investigating ACs that respond to environmental pH and lipid composition.



University of Southampton

Survey of the Month

## Jan 14 eNews

At Crystallography Times, we continue to see a steady growth in publications that utilize biological SAXS as an experimental technique. How do you characterize the use of SAXS in your research activities?

 SAXS has become an important part of our toolkit of characterization techniques in structural biology.

We plan to utilize SAXS in the future but don't currently utilize it.

 We don't plan to utilize SAXS as the information content does not help answer the scientific questions that we are asking.

None of the above.

## **Take the Survey**

#### Last Month's Survey

How do you plan to celebrate IYCr 2014?

Volunteer to teach crystallography to local 16.7% high school students

| Attend the IUCr meeting in Montreal | 66.7% |
|-------------------------------------|-------|
| Party like it's 1999                | 16.7% |



Southampton's Molecular and Cellular Biosciences Research Group seeks to understand the fundamental cellular and molecular mechanisms that underpin basic biological processes, including the structures and interactions of biological molecules, the signals between and within cells, the mechanisms by which cells become specialized and respond to the environment, and understanding how cellular/molecular processes relate to health and disease.

## **Useful link: WIPO Re:Search**

WIPO Re:Search World Intellectual Property Organization: sharing innovation in the fight against neglected tropical diseases.

One of the world's great global health challenges is to overcome the impact of neglected tropical diseases, such as malaria and tuberculosis. These diseases negatively affect the lives of more than one billion people, many of whom live in the world's least developed countries. WIPO Re:Search aims to stimulate more research and development for new and better treatment options for those suffering from these conditions. WIPO Re:Search provides access to intellectual property for pharmaceutical compounds, technologies, and—most importantly—know-how and data available for research and development for tuberculosis, and malaria. By providing a searchable, public database of available intellectual property assets and resources, WIPO Re:Search facilitates new partnerships to support organizations that conduct research into treatment for these diseases, ultimately improving the lives of those most in need.

An important aspect of WIPO Re:Search is the opportunity it creates to transfer knowledge and build capacity at both the institutional and individual, human level. Recognizing the essential human aspect of development, IP Australia, the Australian Government agency that administers intellectual property rights, has generously made available financial resources under a Funds-in-Trust grant to WIPO to enable scientists from developing and Least Developed Countries to take "sabbaticals" at the research facilities of developed country Members of WIPO Re:Search. Placements for these "hosting arrangements" are arranged by BIO Ventures for Global Health, and to date have involved scientists from Cameroon, Egypt, Ghana, Nigeria, and South Africa.

## Selected recent crystallographic papers

**Protein structural ensembles are revealed by redefining X-ray electron density noise**. Therese Lang, P.; Holton, James M.; Fraser, James S.; Alber, Tom. *Proceedings of the National Academy of Sciences of the United States of America*. 1/7/2014, Vol. 111 Issue 1, p237-242. 6p. http://dx.doi.org/10.1073/pnas.1302823110.

**Energetic analysis of the rhodopsin-G-protein complex links the a5 helix to GDP release**. Alexander, Nathan S; Preininger, Anita M; Kaya, Ali I; Stein, Richard A; Hamm, Heidi E; Meiler, Jens. *Nature Structural & Molecular Biology*. Jan2014, Vol. 21 Issue 1, p56-63. 8p. http://dx.doi.org/10.1038/nsmb.2705.

**Membrane protein structure determination** — **The next generation**. Moraes, Isabel; Evans, Gwyndaf; Sanchez-Weatherby, Juan; Newstead, Simon; Stewart, Patrick D. Shaw. *BBA - Biomembranes*. Jan2014, Vol. 1838 Issue 1, p78-87. 10p. http://dx.doi.org/10.1016/j.bbamem.2013.07.010.

**A study of alcohol and temperature effects on aggregation of β-lactoglobulin by viscosity and small-angle X-ray scattering measurements**. Yoshida, Koji; Fukushima, Yurika; Yamaguchi, Toshio. *Journal of Molecular Liquids*. Jan2014, Vol. 189, p1-8. 8p. http://dx.doi.org/10.1016/j.molliq.2013.06.022.

**Dissection of the ATP-Dependent Conformational Change Cycle of a Group II Chaperonin**. Nakagawa, Ayumi; Moriya, Kazuki; Arita, Mayuno; Yamamoto, Yohei; Kitamura, Kyotaro; Ishiguro, Naoki; Kanzaki, Taro; Oka, Toshihiko; Makabe, Koki; Kuwajima, Kunihiro; Yohda, Masafumi. *Journal of Molecular Biology*. Jan2014, Vol. 426 Issue 2, p447-459. 13p. http://dx.doi.org/10.1016/j.jmb.2013.09.034.

**Structure of amyloid aggregates of lysozyme from small-angle X-ray scattering data**. Petrenko, V.; Avdeev, M.; Garamus, V.; Kubovcikova, M.; Gazová, Z.; Šipošová, K.; Bulavin, L.; Almásy, L.; Aksenov, V.; Kopcansky, P. *Physics of the Solid State*. Jan2014, Vol. 56 Issue 1, p129-133. 5p. http://dx.doi.org/10.1134/S1063783414010284.

**Conformation and physical properties of cycloisomaltooligosaccharides in aqueous solution**. Suzuki, Shiho; Yukiyama, Takashi; Ishikawa, Arata; Yuguchi, Yoshiaki; Funane, Kazumi; Kitamura, Shinichi. *Carbohydrate Polymers*. Jan2014, Vol. 99, p432-437. 6p. http://dx.doi.org/10.1016/j.carbpol.2013.07.089.

**Solution conformation of adenovirus virus associated RNA-I and its interaction with PKR**. Dzananovic, Edis; Patel, Trushar R.; Chojnowski, Grzegorz; Boniecki, Michal J.; Deo, Soumya; McEleney, Kevin; Harding, Stephen E.; Bujnicki, Janusz M.; McKenna, Sean A. *Journal of Structural Biology*. Jan2014, Vol. 185 Issue 1, p48-57. 10p. http://dx.doi.org/10.1016/j.jsb.2013.11.007.

**PKA RIa Homodimer Structure Reveals an Intermolecular Interface with Implications for Cooperative cAMP Binding and Carney Complex Disease**. Bruystens, Jessica; Wu, Jian; Fortezzo, Audrey; Kornev, Alexandr; Blumenthal, Donald; Taylor, Susan. *Structure*. Jan2014, Vol. 22 Issue 1, p59-69. 11p. http://dx.doi.org/10.1016/j.str.2013.10.012.

Light-induced Conformational Changes of LOV1 (Light Oxygen Voltage-sensing Domain 1) and LOV2 Relative to the Kinase Domain and Regulation of Kinase Activity in Chlamydomonas Phototropin. Koji Okajima; Yusuke Aihara; Yuki Takayama; Mihoko Nakajima; Sachiko Kashojiya; Takaaki Hikima; Tomotaka Oroguchi; Amane Kobayashi; Yuki Sekiguchi; Masaki Yamamoto; Tomomi Suzuki; Akira Nagatani; Masayoshi Nakasako; Satoru Tokutomi. *Journal of Biological Chemistry*. 1/3/2014, Vol. 289 Issue 1, p413-422. 10p. http://dx.doi.org/10.1074/jbc.M113.515403.

**Characterization of a periplasmic nitrate reductase in complex with its biosynthetic chaperone**. Dow, Jennifer M.; Grahl, Sabine; Ward, Richard; Evans, Rachael; Byron, Olwyn; Norman, David G.; Palmer, Tracy; Sargent, Frank. *FEBS Journal*. Jan2014, Vol. 281 Issue 1, p246-260. 15p. http://dx.doi.org/10.1111/febs.12592.

Structure and Self-Assembly of the Calcium Binding Matrix Protein of Human Metapneumovirus. Leyrat, Cedric; Renner, Max; Harlos, Karl; Huiskonen, Juha; Grimes, Jonathan. *Structure*. Jan2014, Vol. 22 Issue 1, p136-148. 13p. http://dx.doi.org/10.1016/j.str.2013.10.013.

**On the catalytic mechanism and stereospecificity of** *Escherichia coli* **I-threonine aldolase**. Salvo, Martino L.; Remesh, Soumya G.; Vivoli, Mirella; Ghatge, Mohini S.; Paiardini, Alessandro; D'Aguanno, Simona; Safo, Martin K.; Contestabile, Roberto. *FEBS Journal*. Jan2014, Vol. 281 Issue 1, p129-145. 17p. http://dx.doi.org/10.1111/febs.12581.

**Structural Basis of the Autophagy-Related LC3/Atg13 LIR Complex: Recognition and Interaction**. Suzuki, Hironori; Tabata, Keisuke; Morita, Eiji; Kawasaki, Masato; Kato, Ryuichi; Dobson, Renwick C.J.; Yoshimori, Tamotsu; Wakatsuki, Soichi. *Structure*. Jan2014, Vol. 22 Issue 1, p47-58. 12p. http://dx.doi.org/10.1016/j.str.2013.09.023.

**An active beamstop for accurate measurement of high intensity X-ray beams**. Pan, Qiangyan; Wang, Qisheng; Wang, Zhijun; Li, Liang; He, Jianhua. *Nuclear Instruments & Methods in Physics Research Section A*. Jan2014, Vol. 735, p584-586. 3p. http://dx.doi.org/10.1016/j.nima.2013.10.011.

**Dual roles of F123 in protein homodimerization and inhibitor binding to biotin protein ligase from** *Staphylococcus aureus*. Soares da Costa, Tatiana P.; Yap, Min Y.; Perugini, Matthew A.; Wallace, John C.; Abell, Andrew D.; Wilce, Matthew C. J.; Polyak, Steven W.; Booker, Grant W. *Molecular Microbiology*. Jan2014, Vol. 91 Issue 1, p110-120. 11p. http://dx.doi.org/10.1111/mmi.12446.

The *Salmonella enterica* ZinT structure, zinc affinity and interaction with the high-affinity uptake protein ZnuA provide insight into the management of periplasmic zinc. Ilari, Andrea; Alaleona, Flaminia; Tria, Giancarlo; Petrarca, Patrizia; Battistoni, Andrea; Zamparelli, Carlotta; Verzili, Daniela; Falconi, Mattia; Chiancone, Emilia. *BBA - General Subjects*. Jan2014, Vol. 1840 Issue 1, p535-544. 10p. http://dx.doi.org/10.1016/j.bbagen.2013.10.010.

**Polymorphic Protein Crystal Growth: Influence of Hydrationand Ions in Glucose Isomerase**. Gillespie, C. M.; Asthagiri, D.; Lenhoff, A. M. *Crystal Growth & Design*. Jan2014, Vol. 14 Issue 1, p46-57. 12p. http://dx.doi.org/10.1021/cg401063b.

**Equilibrium Sampling Approach to the Interpretation of Electron Density Maps**. Vitalis, Andreas; Caflisch, Amedeo. *Structure*. Jan2014, Vol. 22 Issue 1, p156-167. 12p. http://dx.doi.org/10.1016/j.str.2013.10.014.

*De novo* protein crystal structure determination from X-ray free-electron laser data. Barends, Thomas R. M.; Foucar, Lutz; Botha, Sabine; Doak, R. Bruce; Shoeman, Robert L.; Nass, Karol; Koglin, Jason E.; Williams, Garth J.; Boutet, Sébastien; Messerschmidt, Marc; Schlichting, Ilme. *Nature*. 1/9/2014, Vol. 505 Issue 7482, p244-247. 4p. 2 Diagrams, 2 Graphs. http://dx.doi.org/10.1038/nature12773.

Structural Model for Covalent Adhesion of the *Streptococcus pyogenes* Pilus through a Thioester Bond. Linke-Winnebeck, Christian; Paterson, Neil G.; Young, Paul G.; Middleditch, Martin J.; Greenwood, David R.; Witte, Gregor; Baker, Edward N. *Journal of Biological Chemistry*. 1/3/2014, Vol. 289 Issue 1, p177-189. 13p. http://dx.doi.org/10.1074/jbc.M113.523761.

**A common solution to group 2 influenza virus neutralization**. Friesen, Robert H. E.; Lee, Peter S.; Stoop, Esther J. M.; Hoffman, Ryan M. B.; Ekiert, Damian C.; Bhabha, Gira; Yu, Wenli; Juraszek, Jarek; Koudstaal, Wouter; Jongeneelen, Mandy; Korse, Hans J. W. M.; Ophorst, Carla; Brinkman-van der Linden, Els C. M.; Throsby, Mark; Kwakkenbos, Mark J.; Bakker, Arjen Q.; Beaumont, Tim; Spits, Hergen; Kwaks, Ted; Vogels, Ronald. *Proceedings of the National Academy of Sciences of the United States of America*. 1/7/2014, Vol. 111 Issue 1, p445-450. 6p. http://dx.doi.org/10.1073/pnas.1319058110.



not die 🖉

how bayes' rule cracked the enigma code, hunted down russian submarines & emerged triumphant from two centuries of controversy sharon bertsch mcgrayne

"If you're not thinking like a Sayesian, perhaps you should be." ---John Allen Paulos, *New York Times Book Review* 



Rev. Thomas Bayes

**A Novel 8-nm Protein Cage Formed by** *Vibrio cholerae* **Acylphosphatase**. Nath, Seema; Banerjee, Ramanuj; Sen, Udayaditya. *Journal of Molecular Biology*. Jan2014, Vol. 426 Issue 1, p36-38. 3p. http://dx.doi.org/10.1016/j.jmb.2013.09.014.

Structural aspects of protein synthesis. Janin, Joël. *Crystallography Reviews*. Jan-Mar2014, Vol. 20 Issue 1, p60-61. 2p. http://dx.doi.org/10.1080/0889311X.2013.852543.

#### **Book review:**

*The Theory that Would Not Die: How Bayes' Rule Cracked the Enigma Code, Hunted Down Russian Submarines & Emerged Triumphant from Centuries of Controversy* by Sharon Bertsch McGrayne

Yale University Press, 2011, 336 pages, ISBN: 978-0-300-18822-6.

"It was a matter of applying Bayes' Theorem to estimate the conditional probabilities. Giving due weight to the prior probabilities and ..." No, this is not from a lecture by Gerard Bricogne, but rather from a Robert Ludlum novel, *The Ambler Warning* (2005). I thought this would be a good way to demonstrate how pervasive Bayes' Theorem has become.

McGrayne's book starts off with a short biography of Reverend Thomas Bayes and a simple statement of the theorem that bears his name: prior times likelihood is proportional to the posterior. We learn that Bayes made some errors in convincing others of the validity of the theorem because the prior must often be a guess and scientists did not like the subjective nature of this starting point. The next chapter covers the re-derivation of Bayes' Theorem by Pierre Simon Laplace and how he used it resolve the issue of the stability of the solar system, among many other problems. In the third chapter, readers learn how Bayes' Theorem almost died at the hands of the frequentists yet managed to survive.

Next the author fast-forwards to World War II, in which Alan Turing and his team at Bletchley Park used Bayes' Theorem to decode Enigma. We are next introduced to Arthur Bailey, an insurance actuary, who used the theorem to predict the probability of airplane accidents, and Jerome Cornfield, a researcher at NIH, to show the correlation between smoking and lung cancer in the 1950s.

One of the strengths of Bayes is its ability to predict probabilities when there is no frequency data at all. So, Jimmie Savage used Bayes to help the Air Force come to terms with the very real probability that something bad could happen with all the bombs flying around in B-52s in the 1950s and 60s. To his credit, Curtis LeMay changed Air Force operations in accordance with Bayes. There are many examples of how Bayes has solved difficult problems that frequency-based statistics could not: finding Russian submarines that went missing, finding a lost atomic bomb after a mid-air refueling accident, determining the author of *The Federalist*, helping Google Translate translate and finding the final resting place of Air France 447.

This is one of those books that I probably wouldn't have found without perusing stacks at a bookstore. It is a real gem and reads with the speed of a spy novel. The history and application of Bayes' Theorem is brought out in clear, easy-to-understand language, with detailed footnotes and an extensive bibliography. A humorous piece on religion and Bayes by Michael J. Campbell and some simple, real life examples are provided in the appendices.

What else I am reading or read this month:

*Double Down: Game Change 2012* by Mark Halperin and John Heilemann. A fast read about the circus that has become the American presidential election. It might have been better to wait a year to publish so we have a refresher for 2016.

*The Simpsons and Their Mathematical Secrets* by Simon Singh. I got this for my wife, a mathematician by training, for Christmas but she despises *The Simpsons* so much she won't even open it. An interview with Singh on Science Friday suggests it will a good read.

*The Martian Chronicles* by Ray Bradbury. Great science fiction. Also, great classic science fiction is *Logan's Run* by William Frances Nolan and George Clayton Johnson.

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