

Crystallography Times

Rigaku

Protein Crystallography Newsletter
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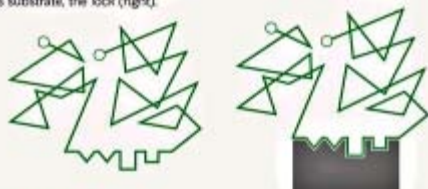
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ORDERS OF DISORDER

A central tenet in molecular biology states that the function of a protein depends on its fully folded three-dimensional structure. In the new view, protein segments can function when transiently or durably disordered.

LOCK AND KEY

In the conventional view, an enzyme folds up immediately into a unique and stable 3D shape, the key (left). Its shape perfectly matches and allows it to bind its substrate, the lock (right).



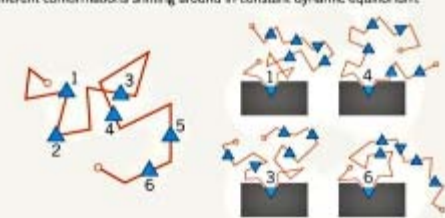
FOLD AS YOU BIND

A disordered part of the gene-regulatory protein CREB (left) uses the lock to mould itself into the shape of the key when the two meet (right), rather than folding beforehand.



SHAPE SHIFTING

The signaling protein Sic1 remains disordered in its bound state, and each of six phosphate groups occupies the binding site in turn. The protein is a mix of different conformations shifting around in constant dynamic equilibrium.



[Structural biology: Breaking the Protein Rules](#)

Crystallography in the news



March 9, 2011. In a recent news article entitled *Structural Biology: Breaking the Protein Rules*, the [dogma that dictates that proteins need a structure](#) to function is discussed relative to function within disordered proteins.

March 12, 2011. Scientists from The Scripps Research Institute have determined a new structure from a medically important superfamily of proteins, called G protein-coupled receptors (GPCRs), that recognize and respond to a wide array of signals, including odors, hormones, neurotransmitters, and light. Fei Xu, a graduate student in the Ray Stevens lab and the first author of the paper, reported the [structure of the human A2A adenosine receptor](#), a member of the GPCR family sometimes referred to as the caffeine receptor, bound to a full agonist.

March 15, 2011. U.K. Science Minister David Willetts met scientists, engineers and industrial partners at [Diamond Light Source](#), the UK's national synchrotron facility, and formally inaugurated Diamond's Phase III development. In October 2010, the U.K. government confirmed further funding for Phase III expansion, creating an additional 10 advanced beamlines between 2011 and 2017, which will bring the total to 32.

March 21, 2011. Organizers of European Lab Automation (ELA) 2011 announced that [Advances in Protein Crystallography](#) will be among the sessions of the upcoming conference & exhibition. The inaugural event will take place from 30 June to 1 July in Hamburg, Germany.

March 22, 2011. As understanding genes, roles in disease requires understanding how proteins fold, a series of recent papers - published by researchers at MIT's Computer Science and Artificial Intelligence Laboratory - have demonstrated a promising [new fast technique for modeling such protein folding](#).

March 23, 2011. Proteros Biostructures GmbH announced that it has entered into a [strategic collaboration](#) with Nimbus Discovery, LLC to deliver X-ray protein crystal structures for multiple targets. Under the agreement, Proteros will provide structures from a catalogue of ready-to-use proteins for rapid X-ray structure analysis of protein-ligand complexes.

March 23, 2011. New information that could help in the fight against asthma has been obtained by an international collaboration of scientists utilizing the Advanced Photon Source at Argonne National Laboratory. The research on a particular human transmembrane protein - by investigators from the Stanford Univ. School of Medicine, Trinity College Dublin, the Univ. of Limerick, Friedrich Alexander Univ., D. E. Shaw Research, the Univ. of Michigan Medical School, and the Univ. of Wisconsin-Madison - set out to understand how one of the G protein-coupled receptors (GPCR), the [β2-adrenergic receptor](#), works at a molecular level. An unusual approach to protein crystallization was also reported.

March 23, 2011. A team of biologists at the Salk Institute for Biological Studies has recently deciphered a molecular code that regulates availability of a brain channel that modulates neuronal excitability, a discovery that might aid efforts to treat drug addiction and mental disorders. Paul Slesinger, Ph.D., Associate Professor in the Clayton Foundation Laboratories for Peptide Biology, and colleagues detail how a [regulatory factor called SNX27 distinguishes a brain channel protein called GIRK](#) (short for G-protein-coupled inwardly rectifying potassium channels) from structurally similar proteins and then targets it for destruction.

March 28, 2011. Mitegen LLC, a provider of consumables for X-ray diffraction, announced the release of a [new crystal mounting tool](#) for researchers performing X-ray diffraction experiments. The innovation is said to

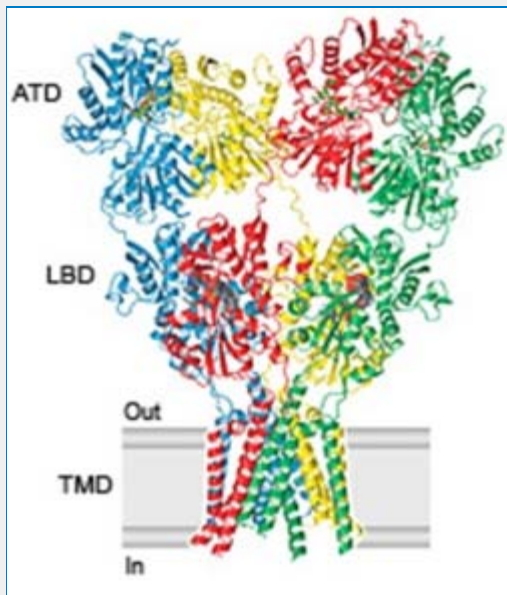
October 26-28, 2011
The Woodlands, Texas

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. Class will also feature a training session on processing data with HKL.

Rigaku MicroMax™ -003



Rigaku MicroMax-003 sealed tube microfocus X-ray source integrated with a R-Axis IV++ IP detector.



The [Gouaux laboratory](#) studies the molecular principles underpinning the structure and function of chemical synapses.

Funny Science Link
"In Da Lab" - Lab Safety Parody

provide the greatest rigidity while maintaining the lowest background.

Product spotlight: MicroMax™-003

Upgrade your old RU-style rotating anode to a MicroMax-003 sealed tube microfocus X-ray source. The MicroMax-003 X-ray generator provides the best combination of fluence and low maintenance of any sealed tube source today. The tightly coupled microfocus generator and confocal optics are designed from the ground up to provide researchers with the most reliable X-ray source possible. The combination of ease of maintenance and the high intensity beam make this the ideal source for current owners of old RU style rotating anode generators. With its 90 μm beam size the X-rays produced by this source are ideal for the small and weakly diffracting crystals seen in today's structural biology laboratories. Additionally, the 3-year tube warranty means you will not have to worry about the upkeep involved with your current RU generator.

[Request more information](#) on the Rigaku MicroMax-003.

Lab spotlight: Gouaux Lab @ HHMI

Eric Gouaux, Ph.D. is a senior scientist at the Oregon Health & Science University, Vollum Institute and Investigator at the Howard Hughes Medical Institute. The Vollum Institute is dedicated to basic research focusing on gene regulation, structural biology, cell signaling, molecular neuroscience and synaptic modulation with implications for human diseases ranging from autism and other neurodevelopmental disorders to Parkinson's disease, multiple sclerosis, psychiatric diseases and mechanisms of drug addiction.



Members of the [Gouaux laboratory](#) (16 members including postdocs, graduate students, and senior research associates) study the molecular principles underpinning the structure and function of chemical synapses. These specialized junctions are the primary sites of communication between neurons and are fundamental to the development and function of the peripheral and central nervous systems. Disruption of signal transduction at chemical synapses is implicated in a broad range of diseases, disorders and injuries and thus their studies not only provide fundamental insights into a crucial element of the nervous system but they also can be exploited for the development of new therapeutic agents.

Useful links for crystallography

[SSedit - Single \(Short\) Sequence Editor](#) is a MacOS X application, written by Dr. [Peter Stockwell](#), University of Otago, for viewing and editing single sequences. Input and output files in FASTA, NRBF, Staden and other formats are supported, with the capability to recognise some by the file extension name. SSedit will display nucleic acid sequences in double stranded form, can reverse and complement the sequence and can translate to peptide sequences using various genetic codes including user-created ones. Sequences of arbitrarily large length can be processed, limited by available memory on the computer. Search functions are provided and printer listings and screen displays can be extensively controlled. External sequences can be inserted in whole, or in part, into the main sequence at the active position. SSedit v6.08 works with MacOS 10.5 (Leopard) or later and is distributed as a universal application. Documentation is included.



[Watch on YouTube](#)

February Survey Results

Predict the next structural biologist to win a Nobel Prize?

1st Place: Michael Rossmann
2nd Place: Eric Gouaux

Survey Question of the Month

With all the uncertainty of research funding in many parts of the world, it is natural to fantasize about what job you might take if you left science. Choose your "dream job" below (select one):

☐ Brain surgeon

☐ Truck/lorry driver

☐ Chef

☐ Waiter/waitress

☐ Politician

☐ Lawyer/attorney

☐ Professional Sudoku player

☐ Other (please specify)

[Take Survey](#)
or cut-and-paste

http://www.surveymonkey.com/s/dream_job
into your browser.

Selected recent crystallographic papers

RosettaEPR: An integrated tool for protein structure determination from sparse EPR data. Hirst, Stephanie J.; Alexander, Nathan; Mchaourab, Hassane S.; Meiler, Jens. *Journal of Structural Biology*, Mar2011, Vol. 173 Issue 3, p506-514. DOI: <http://dx.doi.org/10.1016/j.jsb.2010.10.013>

Transport according to GARP: receiving retrograde cargo at the trans-Golgi network. Bonifacino, Juan S.; Hierro, Aitor. *Trends in Cell Biology*, Mar2011, Vol. 21 Issue 3, p159-167. DOI: <http://dx.doi.org/10.1016/j.tcb.2010.11.003>

NMR analysis demonstrates immunoglobulin G N-glycans are accessible and dynamic. Barb, Adam W.; Prestegard, James H. *Nature Chemical Biology*, Mar2011, Vol. 7 Issue 3, p147-153. DOI: <http://dx.doi.org/10.1038/nchembio.511>

Model of the Trimeric Fiber and Its Interactions with the Pentameric Penton Base of Human Adenovirus by Cryo-electron Microscopy. Liu, Hongrong; Wu, Lily; Zhou, Z. Hong. *Journal of Molecular Biology*, Mar2011, Vol. 406 Issue 5, p764-774. DOI: <http://dx.doi.org/10.1016/j.jmb.2010.11.043>

Heterosubunit Composition and Crystal Structures of a Novel Bacterial M16B Metallopeptidase. Maruyama, Yukie; Chuma, Asako; Mikami, Bunzo; Hashimoto, Wataru; Murata, Kousaku. *Journal of Molecular Biology*, Mar2011, Vol. 407 Issue 1, p180-192. DOI: <http://dx.doi.org/10.1016/j.jmb.2011.01.038>

Interaction of copper(II) with the non-steroidal anti-inflammatory drugs naproxen and diclofenac: Synthesis, structure, DNA- and albumin-binding. Dimiza, Filitsa; Perdihi, Franc; Tangoulis, Vassilis; Turel, Iztok; Kessissoglou, Dimitris P.; Psomas, George. *Journal of Inorganic Biochemistry*, Mar2011, Vol. 105 Issue 3, p476-489. DOI: <http://dx.doi.org/10.1016/j.jinorgbio.2010.08.013>

Protein crystallization at oil/water interfaces. Silver, Barry R.; Fülöp, Vilmos; Unwin, Patrick R. *New Journal of Chemistry*, Mar2011, Vol. 35 Issue 3, p602-606. DOI: <http://dx.doi.org/10.1039/C0NJ00822B>

Laser-induced nucleation in protein crystallization: Local increase in protein concentration induced by femtosecond laser irradiation. Iefuji, Natsuko; Murai, Ryota; Maruyama, Mihoko; Takahashi, Yoshinori; Sugiyama, Shigeru; Adachi, Hiroaki; Matsumura, Hiroyoshi; Murakami, Satoshi; Inoue, Tsuyoshi; Mori, Yusuke; Koga, Yuichi; Takano, Kazufumi; Kanaya, Shigenori. *Journal of Crystal Growth*, Mar2011, Vol. 318 Issue 1, p741-744. DOI: <http://dx.doi.org/10.1016/j.jcrysgro.2010.10.068>

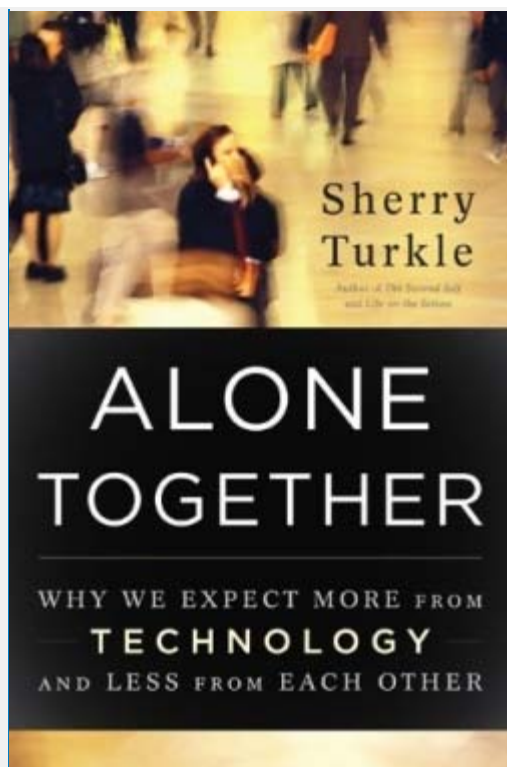
Metals in proteins: cluster analysis studies. Tamames, Juan A. C.; Ramos, Maria João. *Journal of Molecular Modeling*, Mar2011, Vol. 17 Issue 3, p429-442. DOI: <http://dx.doi.org/10.1007/s00894-010-0733-5>

Crystal Structure of *Escherichia coli* BamB, a Lipoprotein Component of the β -Barrel Assembly Machinery Complex. Kim, Kelly H.; Paetzel, Mark. *Journal of Molecular Biology*, Mar2011, Vol. 406 Issue 5, p667-678. DOI: <http://dx.doi.org/10.1016/j.jmb.2010.12.020>

The Crystal Structure of BamB Suggests Interactions with BamA and Its Role within the BAM Complex. Noinaj, Nicholas; Fairman, James W.; Buchanan, Susan K.. *Journal of Molecular Biology*, Mar2011, Vol. 407 Issue 2, p248-260. DOI: <http://dx.doi.org/10.1016/j.jmb.2011.01.042>

Structure/function of human killer cell immunoglobulin-like receptors: lessons from polymorphisms, evolution, crystal structures and mutations. Campbell, Kerry S.; Purdy, Amanda K. *Immunology*, Mar2011, Vol. 132 Issue 3, p315-325. DOI: <http://dx.doi.org/10.1111/j.1365-2567.2010.03398.x>

Crystal structure of a potassium ion transporter, TrkH. Yu Cao; Xiangshu Jin; Hua Huang; Derebe, Mehabaw Getahun; Levin, Elena J.; Kabaleeswaran, Venkataraman; Pan, Yaping; Punta, Marco; Love, James; Jun Weng; Quick, Matthias; Sheng Ye; Kloss, Brian; Bruni, Renato; Martinez-Hackert, Erik; Hendrickson, Wayne A.; Rost, Burkhard; Javitch, Jonathan A.; Rajashankar,



Sherry Turkle

Kanagalaghatta R.; Youxing Jiang. *Nature*, 3/17/2011, Vol. 471 Issue 7338, p336-340. DOI: <http://dx.doi.org/10.1038/nature09731>

Structural characterization of CYP165D3, a cytochrome P450 involved in phenolic coupling in teicoplanin biosynthesis. Cryle, Max J.; Staaden, Jessica; Schlichting, Ilme. *Archives of Biochemistry & Biophysics*, Mar2011, Vol. 507 Issue 1, p163-173. DOI: <http://dx.doi.org/10.1016/j.abb.2010.10.017>

The beginning of a beautiful friendship: Cross-linking/mass spectrometry and modelling of proteins and multi-protein complexes. Rappsilber, Juri. *Journal of Structural Biology*, Mar2011, Vol. 173 Issue 3, p530-540. DOI: <http://dx.doi.org/10.1016/j.jsb.2010.10.014>

Structure based design of heat shock protein 90 inhibitors acting as anticancer agents. Doddareddy, Munikumar Reddy; Thorat, Dhanaji Achyutrao; Seo, Seon Hee; Hong, Tae-Joon; Cho, Yong Seo; Hahn, Ji-Sook; Pae, Ae Nim. *Bioorganic & Medicinal Chemistry*, Mar2011, Vol. 19 Issue 5, p1714-1720. DOI: <http://dx.doi.org/10.1016/j.bmc.2011.01.023>

Book review:

Alone Together:

Why We Expect More From Technology and Less From Each Other

Sherry Turkle, Basic Books 2011

ISBN: 978-0465010219

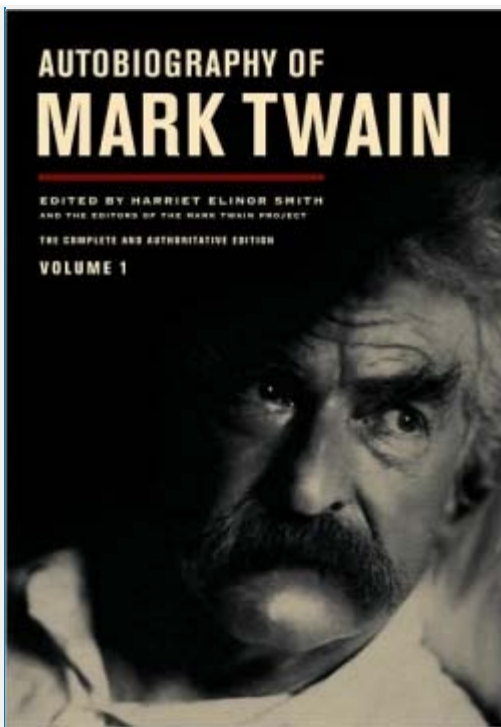
A good friend recommended this book and, about halfway through reading it, I heard an interview with the author on *Science Friday*. The interview is worth a listen and the book, at least the second half, is worth reading.

The author uses a number of case studies and personal interviews with subjects of all ages to substantiate her points. Her book is divided into two parts, with a conclusion that synthesizes the discussion in each.

The first part discusses the interaction of humans with computers and robots. Turkle first looks at how people, mostly children and the elderly, interacted with fad items like Tamagotchis and Furbies. She then draws some conclusions about how these individuals might interact with robot caretakers replacing parents too busy to look after a child in the former case, and adults too busy to care for their infirm parents in the latter. She suggests that, at least for the very young and very old, the substitution of a robot for a human, emotionally, is possible since neither group knows better.

In the second part, the author reviews our interactions with others through the technology of networks: the internet, cell phones, texting, MySpace, Twitter, Facebook. We treat these methods as distinctly different from direct, interactive communication. Turkle suggests that we may be more open or less careful. As an example, we have forgotten how to pick up the phone and engage in real time conversation. She captures well our sense of loneliness when we can't access email or SMS. Is our failure to disconnect ruining our lives? Our children's?

She asks if we have lost our sense of privacy. What does the future hold? At what point do we become so antisocial that we no longer care to see other humans? Is that the point at which a computer program or a robot is sufficient companionship for us? This is what ties the first and second parts of the book together. At what point does it no longer matter with whom we communicate, and a computer becomes sufficient to satisfy our need to be social?



Autobiography of Mark Twain, Vol. 1

Mark Twain, University of California Press 2010
ISBN: 978-0520267190

My mother gave me a copy of this for my birthday last year. I let it sit on the nightstand before cracking it open because I had heard some less than stellar reviews and, frankly, it was heavy and I was afraid it would hurt the dog if I fell asleep and it tumbled off the bed. I wish I had ignored the bad reviews.

The introduction, by editors from the Mark Twain Project, describes Clemens' strict rules for the publication of this book: nothing for 100 years after his death, a second edition 25 years after the first edition, and a third and final edition another 25 years later, each disclosing a little more. The reason for this is that Clemens wanted to be honest but not offend anyone nearly or recently deceased.

It turns out that, although this is a long book, it is by no means tedious. Clemens' philosophy on autobiography is to write about what you want when you want. Herein lies a problem: if you expect the autobiography to follow chronological order then you will be disappointed. However, if you treat this book as a series of short biographical sketches and essays (after the introduction) you will be treated to the gift of Clemens' prose and a time capsule of American politics, religion, business, home life and war. What I found most fascinating is that little has changed in the past 100-plus years. For example, I found the story of Clemens' threat to sue the phone company for breach of contract for failure to install a line humorous yet contemporary.

I enjoyed reading this and look forward to Volumes 2 and 3.

Joseph D. Ferrara, Ph.D.



Mark Twain

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