

Protein Crystallography Newsletter

Volume 5, No. 12, December 2013

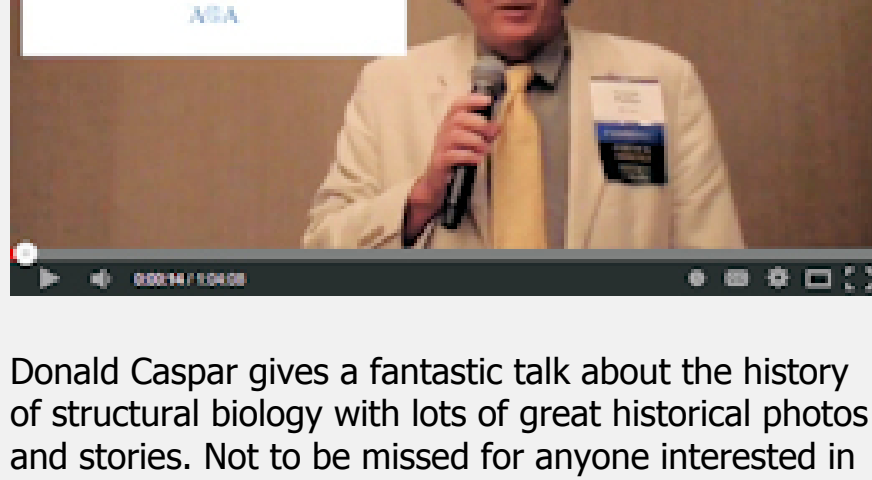
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Science Video

Donald Caspar, Origins of Structural Biology and Trials and Errors in its History: an idiosyncratic view



Donald Caspar gives a fantastic talk about the history of structural biology with lots of great historical photos and stories. Not to be missed for anyone interested in the history of crystallography and the personalities involved. Shown above is George Phillips' introduction to the audience.

Watch the Video

Product in the Spotlight

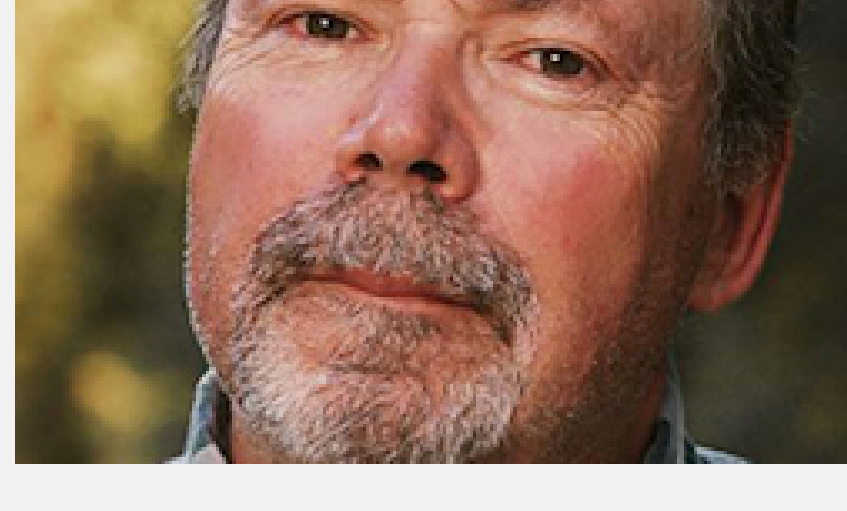


Rigaku Pflipper

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Scientist Spotlight

NIH Names Dr. Philip E. Bourne First Associate Director for Data Science



National Institutes of Health Director Francis S. Collins, M.D., Ph.D., announced the selection of Philip E. Bourne, Ph.D., as the first permanent Associate Director for Data Science (ADDS). Dr. Bourne is expected to join the NIH in early 2014.

"Phil will lead an NIH-wide priority initiative to take better advantage of the exponential growth of biomedical research datasets, which is an area of critical importance to biomedical research. The era of 'Big Data' has arrived, and it is vital that the NIH play a major role in coordinating access to and analysis of many different data types that make up this revolution in biological information," said Collins.

Dr. Bourne comes to the NIH from the University of California San Diego, where he is the Associate Vice Chancellor for Innovation and Industry Alliances of the Office of Research Affairs and a Professor in the Department of Pharmacology and the Skaggs School of Pharmacy and Pharmaceutical Sciences. He also is the Associate Director of the Research Collaboratory for Structural Bioinformatics (RCSB) Protein Data Bank. Dr. Bourne was trained as a physical chemist and obtained his Ph.D. from The Flinders University in South Australia.

Survey of the Month

Dec13 eNews Survey

How do you plan to celebrate IYCr 2014?

- ☐ Volunteer to teach crystallography to local high school students
- ☐ Promote the importance of crystallography to my non-crystallographic colleagues
- ☐ Attend the IUCr meeting in Montreal
- ☐ Create a calendar based on crystallographically significant images and dates
- ☐ Party like it's 1999

Take the Survey

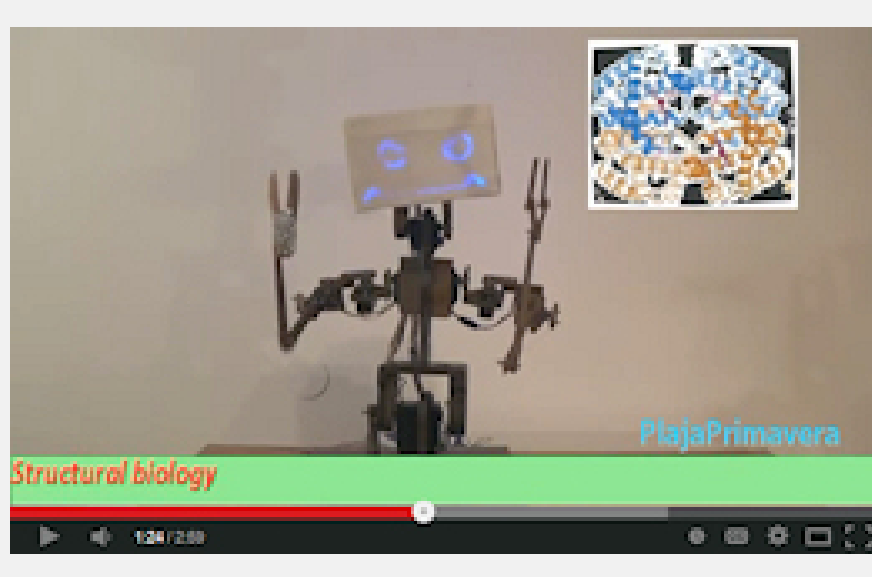
Last Month's Survey

When selecting a Postdoctoral Position, which factor do you feel is most important?

The status of the University	0.0%
The status of the professor	50.0%
The research project	20.0%
How close the nearest beach is	30.0%

Funny or Not Video

What is structural biology?



For all of you aspiring professors - forget about it. As seen in this video, teaching will be done by robots in the future. Time to think about another career path.

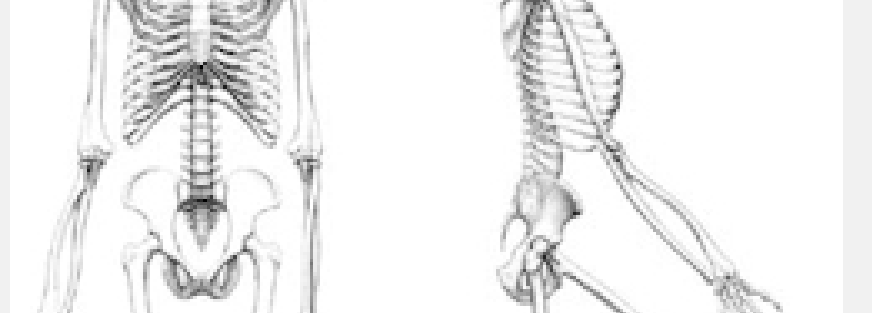
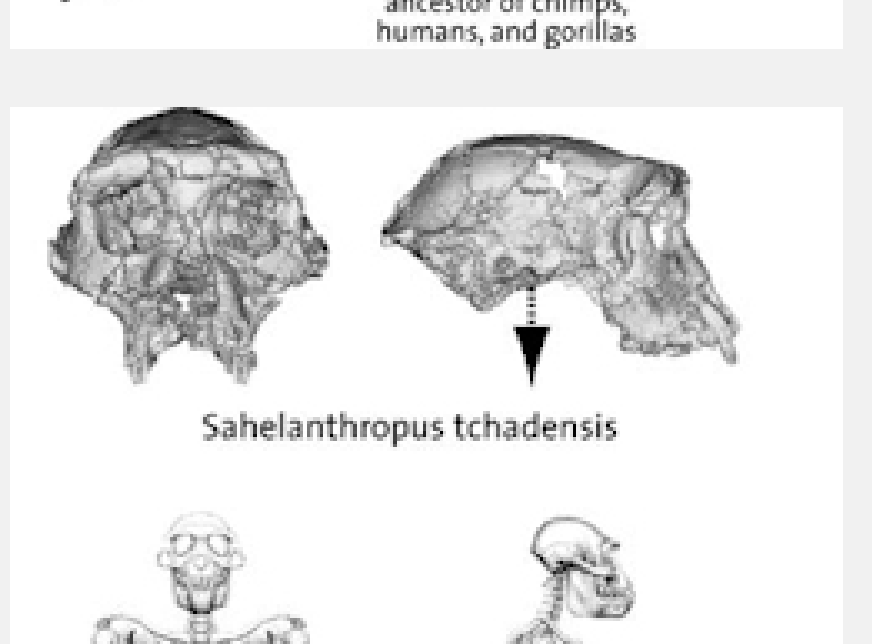
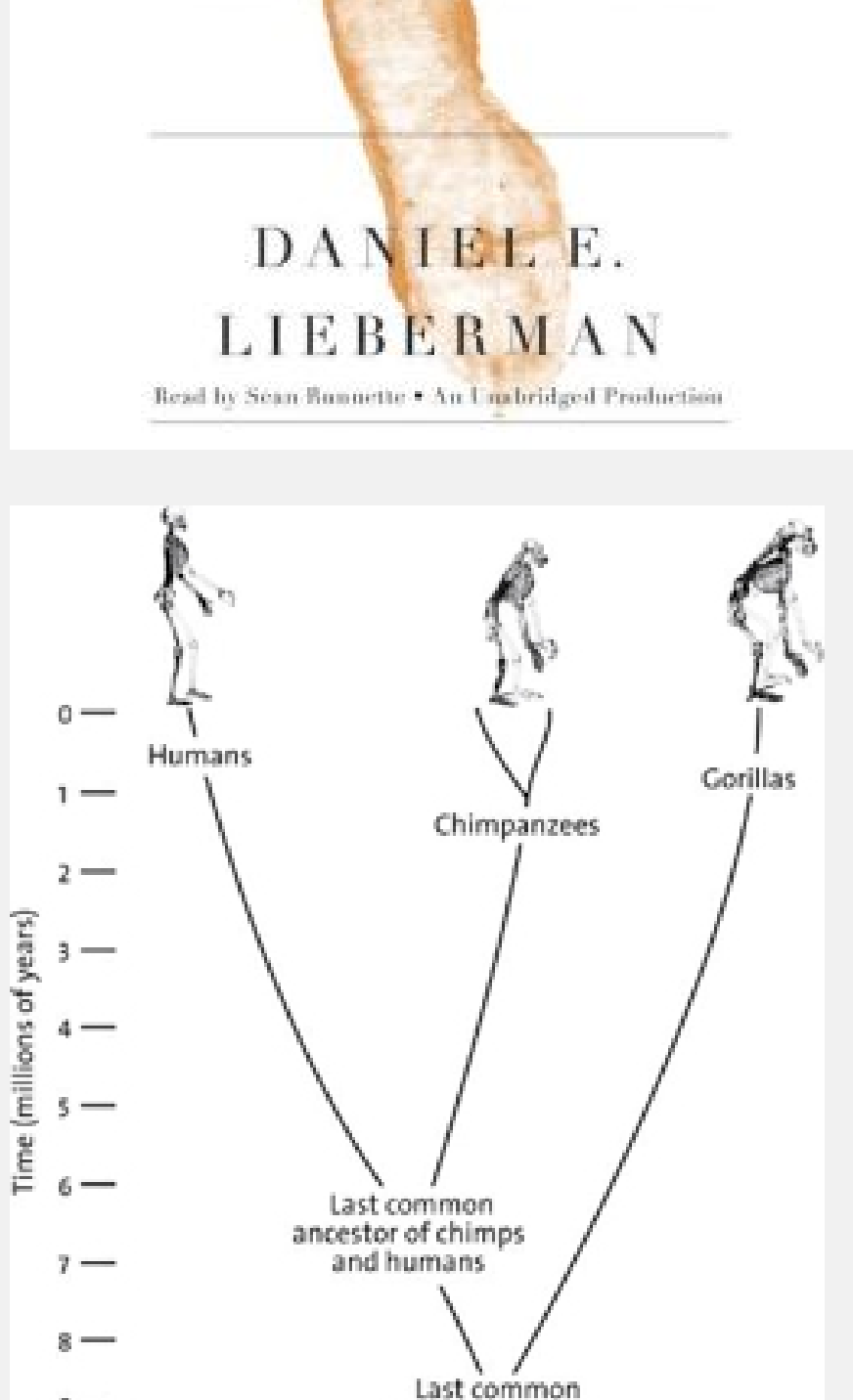
Watch the Video

Book review:

The Story of the Human Body: Evolution, Health and Disease

by Daniel E. Lieberman

pantheon Books, NYC, 2013, ISBN-13: 978-030737941-2



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Crystallography in the news

December 1, 2013. For the first time, researchers at Umea University have succeeded in showing how the DNA polymerase epsilon enzyme builds new genomes. The detailed image produced by these researchers shows how mutations that can contribute to the development of colorectal cancer and cervical cancer lead to changes in the structure of the protein.

December 4, 2013. UC San Francisco scientists have determined, at near-atomic resolution, the structure of a protein that plays a central role in the perception of pain and heat. Led by UCSF postdoctoral fellows Erhu Cao and Maofu Liao, the new research will offer fresh insights to drug designers searching for new and better pain treatments, but it also is a watershed for the field of structural biology.

December 9, 2013. New research finds that the H7N9 avian flu virus is ill adapted for human transmission. At the start of the year there were 132 laboratory confirmed cases, and 37 confirmed deaths, leading to concerns that H7N9 could cause a global pandemic. Using X-ray crystallography, researchers from The Scripps Research Institute examined the proteins that the virus uses to bind to human and avian cells, as well as the human and avian receptors. They found that the virus binds strongly to avian receptors, and only weakly to human variants.

December 12, 2013. Scientists have discovered a second code hiding within DNA. This second code contains information that changes how scientists read the instructions contained in DNA and interpret mutations to make sense of health and disease. A research team led by Dr. John Stamatoyannopoulos at the University of Washington made the discovery.

December 13, 2013. The UK has overtaken the US and now ranks first in one indicator of research quality, according to a new report commissioned by the UK's Department of Business, Innovation and Skills. The report assesses the performance of the UK's research base compared with a number of countries, including China, France, India, Germany, Japan and the US. While the UK represents just 0.9% of the global population, 3.2% of R&D expenditure and 4.1% of researchers, the report found that it accounts for 9.5% of research downloads, 11.6% of citations and 15.9% of the world's most highly-cited articles.

December 16, 2013. SureChem, a collection of over 15 million chemical structures from patents, is to be made freely available through the European Bioinformatics Institute (EBI). A division of Macmillan Science & Education, Digital Science, donated the collection to EMBL-EBI. It is a largely organic chemistry database from patents with a strong bias toward small molecule chemistry used in drug discovery.

December 17, 2013. Researchers from the nanoscience research center CIC nanoGUNE, the Freie Universität Berlin and Neaspec company employ nano-FTIR spectroscopy for label-free chemical and structural imaging of proteins with nanoscale spatial resolution and with sensitivity to single protein complexes of less than one attogram (10⁻¹⁸ gram). nano-FTIR is an optical technique that combines scattering-type scanning near-field optical microscopy (s-SNOM) and Fourier transform infrared (FTIR) spectroscopy.

December 18, 2013. New recommendations for reducing protein crystal damage by X-ray beams have been issued by scientists from two U.S. Department of Energy national laboratories, Argonne and Brookhaven, and the University of Washington, Seattle. The research team examined three different X-ray-based methods for solving protein structures and recommended one called "submicrometer line focusing."

December 18, 2013. St. Jude Children's Research Hospital scientists have identified a protein complex that is essential for jump starting the immune response during the critical first 24 hours of an infection. Researchers showed the protein complex mTORC1 helps to ensure that newly activated T cells have the energy necessary to launch proliferation.

Product spotlight: Pflipper

Mounting and dismounting a sample using tongs is an art for the steady of hand. The Rigaku Pflipper (patent pending) is a tool designed to easily mount or dismount a crystal from a vial while maintaining the crystal at cryogenic temperatures. With the Pflipper you can be assured that your crystal will remain at near liquid nitrogen temperatures during these manipulations.

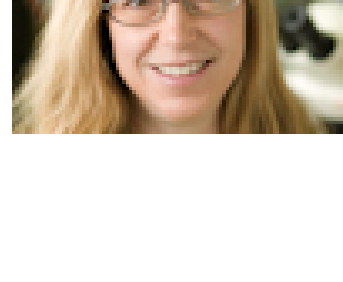
This video demonstrates the mounting and dismounting procedures while showing that the temperature does not rise above -160°C.

The Pflipper works with any low temperature system and any Rigaku multiple-axis goniometer.

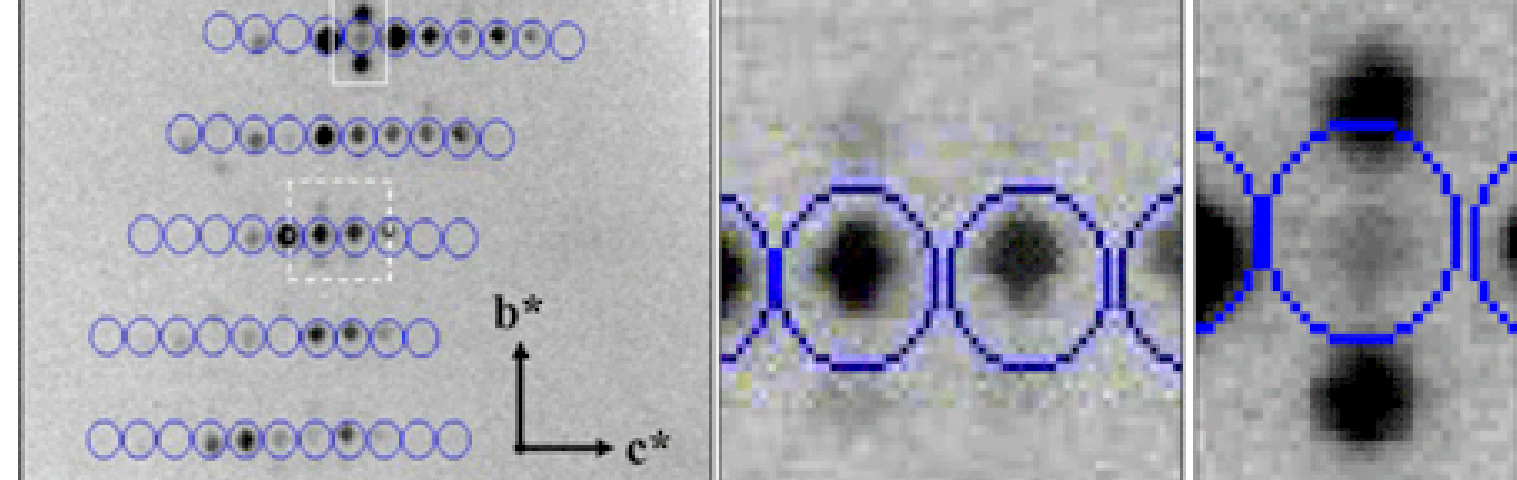
Ask for more information. View a product video.

Scientist spotlight: Gloria Borgstahl

Gloria Borgstahl
Professor, Eppley Institute
Department of Biochemistry and Molecular Biology,
and Department of Pharmaceutical Sciences
University of Nebraska Medical Center



Dr. Borgstahl's group is interested in developing novel X-ray crystallography methods and in studying the macromolecules essential to the maintenance and replication of DNA. Lately they have developed protocols for the processing of incommensurately modulated diffraction data from protein crystals. They have studied these sorts of modulations through computer modeling and have started to create software to refine these structures in (3+1)D superspace.



Modulated Profilin:Actin Diffraction Pattern (main reflections circled)

The Borgstahl laboratory has had a long-standing interest in the proteins involved in DNA metabolism using X-ray crystallography and molecular modeling. In particular they study human replication protein A (RPA) and RAD52. RPA is a single-stranded DNA binding protein that is a key player in DNA metabolism and together with RAD52 they anneal repetitive DNA sequences at double-strand breaks. This annealing reaction is a drug target in BRCA2/PALB2 hereditary cancers. They are studying the structure of RPA and RAD52 and how their annealing activity is regulated by posttranslational modifications and performing screens for small molecule inhibitors.

The missing link: NCBI

The National Center for Biotechnology Information advances science and health by providing access to biomedical and genomic information. It was established in 1988, as a division of the National Library of Medicine (NLM) at the National Institutes of Health (NIH). NLM was chosen for its experience in creating and maintaining biomedical databases, and because as part of NIH, it could establish an intramural research program in computational molecular biology. The collective research components of NIH make up the largest biomedical research facility in the world.

Selected recent crystallographic papers

Small-angle scattering contrast calculator for protein and nucleic acid complexes in solution. Sarachan, Kathryn L.; Curtis, Joseph E.; Krueger, Susan. *Journal of Applied Crystallography*. Dec2013, Vol. 46 Issue 6, p1889-1893. 5p. <http://dx.doi.org/10.1107/S0021889813025727>.

Detergent quantification in membrane protein samples and its application to crystallization experiments. Prince, Chelsy C.; Jia, Zongchao. *Amino Acids*. Dec2013, Vol. 45 Issue 6, p1293-1302. 10p. <http://dx.doi.org/10.1007/s00726-013-1600-3>.

A historical perspective on protein crystallization from 1840 to the present day. Giege, Richard. *FEBS Journal*. Dec2013, Vol. 280 Issue 24, p6456-6497. 42p. <http://dx.doi.org/10.1111/febs.12580>.

A common mechanism underlying amyloid fibrillation and protein crystallization revealed by the effects of ultrasonication. Kitayama, Hiroki; Yoshimura, Yuichi; So, Masatomo; Sakurai, Kazumasa; Yagi, Hisashi; Goto, Yuji. *BBA - Proteins & Proteomics*. Dec2013, Vol. 1834 Issue 12, p2640-2646. 7p. <http://dx.doi.org/10.1016/j.bbapap.2013.09.016>.

Structure of the S100A4/myosin-IIA complex. Ramagopal, Udipi A.; Dulyaninova, Natalya G.; Varney, Kristen M.; Wilder, Paul T.; Nallamsetty, Sridevi; Brenowitz, Michael; Weber, David J.; Almo, Steven C.; Bersnick, Anne R. *BMC Structural Biology*. 2013, Vol. 13 Issue 1, p1-33. 33p. 6 Diagrams, 2 Charts, 4 Graphs. <http://dx.doi.org/10.1186/1472-6807-13-31>.

Recent applications of ATR FTIR spectroscopy and imaging to proteins. Glassford, Stefanie E.; Byrne, Bernadette; Kazarian, Sergei G. *BBA - Proteins & Proteomics*. Dec2013, Vol. 1834 Issue 12, p2849-2858. 10p. <http://dx.doi.org/10.1016/j.bbapap.2013.07.015>.

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Molecular flexibility of *Mycobacterium tuberculosis* ribosome recycling factor and its functional complexes: An exploration involving mutants. Selvaraj, M.; Govindan, A.; Seshadri, A.; Dubey, B.; Varshney, U.; Vijayan, M. *Journal of Biosciences*. Dec2013, Vol. 38 Issue 5, p845-855. 11p. <http://dx.doi.org/10.1007/s12038-013-9381-0>.

Characterization of salt interferences in second-harmonic generation detection of protein crystals. Closser, R. G.; Gualtieri, E. J.; Newman, J. A.; Simpson, G. J. *Journal of Applied Crystallography*. Dec2013, Vol. 46 Issue 6, p1903-1906. 4p. <http://dx.doi.org/10.1107/S0021889813027581>.

Structural aspects of [NiFe]-hydrogenases. Shomura, Yasuhito; Higuchi, Yoshiki. *Reviews in Inorganic Chemistry*. Dec2013, Vol. 33 Issue 4, p173-192. 20p. <http://dx.doi.org/10.1515/revic-2013-0005>.

Crystal structure of the Y-hydroxymuconic semialdehyde dehydrogenase from *Pseudomonas* sp. strain WBC-3, a key enzyme involved in para-Nitrophenol degradation. Jing Su; Cong Zhang; Jun-Jie Zhang; Tiandi Wei; Deyu Zhu; Ning-Yi Zhou; Li chuan Gu. *BMC Structural Biology*. 2013, Vol. 13 Issue 1, p1-20. 20p. 5 Diagrams, 1 Chart, 2 Graphs. <http://dx.doi.org/10.1186/1472-6807-13-30>.

Do-it-yourself histidine-tagged bovine enterokinase: A handy member of the protein engineer's toolbox. Skala, Wolfgang; Goettig, Peter; Brandstetter, Hans. *Journal of Biotechnology*. Dec2013, Vol. 168 Issue 4, p421-425. 5p. <http://dx.doi.org/10.1016/j.jbiotec.2013.10.022>.

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Unintended consequences? Water molecules at biological and crystallographic protein-neel interfaces. Ahmed, Mostafa H.; Habtemariam, Mesay; Safo, Martin K.; Scarsdale, J. Neel; Spyarakis, Francesca; Cozzini, Pietro; Mozzarelli, Andrea; Kellogg, Glen E. *Computational Biology & Chemistry*. Dec2013, Vol. 47, p126-141. 16p. <http://dx.doi.org/10.1016/j.compbiolchem.2013.08.009>.

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Untangling structure-function relationships in the rhomboid family of intramembrane proteases. Brooks, Cory L.; Lemieux, M. Joanne. *BBA - Biomembranes*. Dec2013, Vol. 1828 Issue 12, p2862-2872. 11p. <http://dx.doi.org/10.1016/j.bbamem.2013.05.003>.

Exonic Transcription Factor Binding Directs Codon Choice and Affects Protein Evolution. Stergachis, Andrew B.; Eric Haugen; Anthony Shafer, Wenqing Fu, Benjamin Vernot, Alex Reynolds, Anthony Raubitschek et al. *Science* 342, no. 6164 (2013): 1367-1372. <http://dx.doi.org/10.1126/science.1243490>.

Powder diffraction: what's in a name? Von Dreele, Robert B. *Acta Crystallographica: Section C*. Dec2013, Vol. 69 Issue 12, p1431-1432. 2p. <http://dx.doi.org/10.1107/S0108284113028503>.

Book review:

The Story of the Human Body: Evolution, Health and Disease

by Daniel E. Lieberman
pantheon Books, NYC, 2013, ISBN-13: 978-030737941.2

Daniel E. Lieberman's newest book, *The Story of the Human Body: Evolution, Health, and Disease*, explores the human body and seeks to address the fundamental question: What are human bodies adapted for? After a quick introduction to human adaptation and the processes of natural selection, Lieberman follows the narrative structure suggested by his subtitle, splitting his argument into three parts.

In Part I, titled "Apes and Humans," he looks at the evolutionary history of the human body, tracing the development of bipedalism, dentition, and larger brains in *homo sapiens* and comparing human physiology to that of our ancestors. Then, in Part II, titled "Farming and the Industrial Revolution," he looks at the various good and bad consequences of having what he describes as "Paleolithic bodies in a post-Paleolithic world." The human body is still adapting to the relatively recent development of a farming lifestyle, as opposed to that of hunting and gathering. Even though scientific developments in the past 200 years have given us various vaccines and the ability to combat and nearly eradicate countless diseases that plagued our ancestors, many more have emerged and grown in prevalence due to the revolution in human lifestyles. Technological and industrial developments, though certainly beneficial, have come at a cost to human health. In Part III, "The Present, The Future," Lieberman further explores the negative effects on human health caused by the fallout of the Industrial Revolution, and, as the title suggests, wraps up his argument with some concerns and suggestions for the future to combat these adverse effects of technological evolution on the human body.

What I found delightfully refreshing about Lieberman's work was his rather objective presentation and interpretation of historical and biological evidence. Rather than preach a particularly limited viewpoint from a soapbox regarding his concerns with the modern human diet, he instead approaches these issues from a practical standpoint. Lieberman presents all of these issues through the lens of human evolution, commenting on the conflict not between modern lifestyles and social expectations, but between the former and biological capacities. Obesity in particular has become a hot topic in America, but Lieberman focuses on the biological explanations for its causes from a broad evolutionary perspective. The human body craves fatty foods because the brain requires fat for both growth and function. Since the advent of modern technologies that have amplified the food supply, fatty foods are more readily available than they used to be. The human body has not yet evolved to recognize the higher fat content of the average diet and thus reduce the craving for fatty foods. The industrial and technological revolutions have outpaced the natural progress of human evolution. We have gotten ahead of ourselves, and though there have certainly been tremendous benefits, there have been significant costs as well.

Lieberman's prose flows rather quickly, though there are times where one might think he has gotten too wrapped up in pedantic detail, only to realize a few pages or chapters later that this attention to detail has proved crucial to helping the reader better understand his argument and approach. Thanks to his attention to detail and eloquent presentation of evidence, even someone with no prior experience to evolutionary biology or an extensive understanding of the relevant history can comprehend and enjoy what this book has to offer. An easy, fun read for anyone with an interest in evolutionary biology, or even someone who just needs motivation for a new approach to eating healthily.

Jeanette S. Ferrara
Princeton, Class of 2015