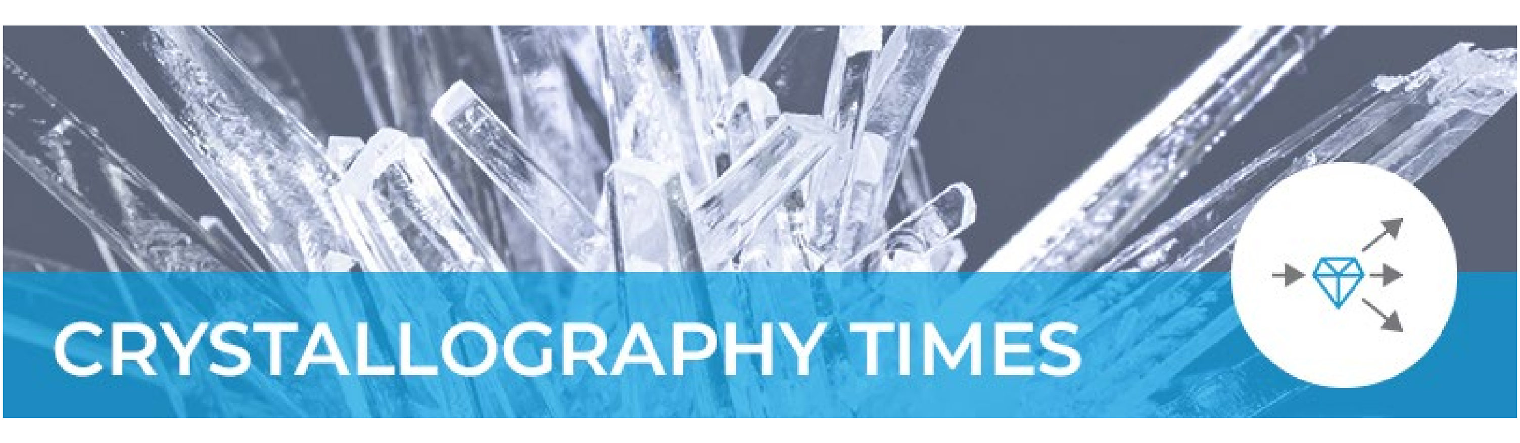


Volume 13, No. 11, November 2021

WELCOME

This month we are returning to our traditional format with a Product in the Spotlight and a User Laboratory in the Spotlight, Crystallography in the News, interesting links and a book review.

Last month we held our first 3DED/MicroED workshop and it was a resounding success, with almost three hundred people participating. Speakers included Christos Malliakas (Northwestern University), Brandon Mercado (Yale University), Enrico Mugnaioli (University of Siena), Lukas Palatinus (Institute of Physics of the Czech Academy of Sciences), and Hongyi Xu (Stockholm University), as well as our own Sho Ito, Fraser White and Akihito Yamano. Despite a power failure in the UK on the second day, the workshop went well. You can watch the lectures from the Workshop area at the Rigaku X-ray Forum. To round out the workshop, this month's product in the spotlight is the XtaLAB Synergy-ED.

The laboratory in the spotlight is that of Christer Aakeröy from Kansas State University, a recent addition to the Rigaku family of users. The interesting links include an open access paper on high-pressure electron diffraction and a website documenting the life of Linus Pauling. Our videos of month consist of two interviews with Lisa Keefe on the involvement of IMCA-CAT in the discovery of Pfizer's anti-COVID drug candidate. Finally, Jeanette reviews the newly released *Plagues Upon the Earth: Disease and the Course of Human History.*

Take care,

Joe

PRODUCT IN THE SPOTLIGHT

XtaLAB Synergy-ED
The World's First Fully Integrated Electron Diffractometer

The XtaLAB Synergy-ED is a new and fully integrated electron diffractometer, creating a seamless workflow from data collection to structure determination of three-dimensional molecular structures. The XtaLAB Synergy-ED is the result of an innovative collaboration to synergistically combine our core technologies: Rigaku's high-speed, high-sensitivity photon-counting detector (HyPix-ED) and state-of-the-art instrument control and single crystal analysis software platform (CrysAlis^{Pro} for ED), and JEOL's long-term expertise and market leadership in designing and producing transmission electron microscopes. The key feature of this product is that it provides researchers an integrated platform enabling easy access to electron crystallography. The XtaLAB Synergy-ED is a system any X-ray crystallographer will find intuitive to operate without having to become an expert in electron microscopy.

LEARN MORE

LAB IN THE SPOTLIGHT

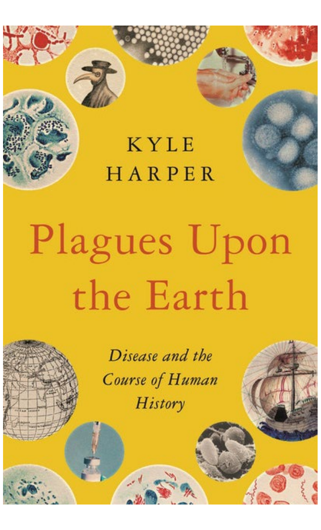
Christer Aakeröy, D.Phil., M.Sc. FRSC
University Distinguished Professor
Kansas State University

The Aakeröy group synthesizes new organic molecules as well as coordination complexes using both conventional and mechanochemical synthetic protocols and subsequently they employ non-covalent interactions (such as hydrogen- and halogen bonds) to assemble molecular building blocks into supramolecular architectures with precise dimensions, topologies, and motifs.

Control over the assembly of molecules into extended networks is rapidly becoming an important target in both materials chemistry and biotechnology and through systematic structural studies they then correlate a wide variety of physical properties of the bulk materials with specific features of the individual building blocks. By translating molecular function into predictable intermolecular recognition, they can create versatile pathways for improving processing, performance and shelf-life of a wide range of specialty chemicals such as pharmaceuticals, agrochemicals, dyes, non-linear optical and energetic materials.

Aakeröy Group Spring 2020

BOOK REVIEW



Plagues Upon the Earth: Disease and the Course of Human History
By Kyle Harper
ISBN: 9780691192123

Kyle Harper's *Plagues Upon the Earth: Disease and the Course of Human History* is longer than your average read these days, clocking in at 509 pages, not including the nearly 200 pages of appendices and indexes. But it's not as long as you might expect, given the title and the subject matter—in fact, it might almost seem rather short. Despite the book's length and density—both literal and figurative—*Plagues Upon the Earth* is a solid read for anyone looking to take a dive into the history of humanity and its diseases.

Harper assumes a rather daunting task as he sets out to document and describe the dual histories of humanity and the infectious diseases to which humans are susceptible. It is a tricky duality to balance between "microorganisms" and "macrohistory," but Harper does an excellent job, never veering too deeply into the historical context or the microbiological sciences. He interweaves the two narratives quite seamlessly, making it evident that, as impactful as plagues have been on human history, the course of human history has in many ways dictated or influenced the nature and effectiveness of its plagues.

Plagues of the Earth begins with a brief introduction in which Harper dictates his strategy for leading the reader through the intertwined histories of humanity and its diseases. He provides critical contextual information, such as the meaning of the "paradox of progress," which he revisits repeatedly throughout the book. He also provides a historical roadmap for the history of globalization in the context of the evolution of infectious diseases, breaking it into six separate periods: prehistoric globalization, Iron Age globalization, peak Old-World globalization, the Columbian Exchange, fossil-energy transport, and the age of jet plane travel.

Harper uses this roadmap of periods of human globalization, and subsequent microbial globalization, to break *Plagues of the Earth* into four parts based on the predominant change in human culture that happened in the given historical period it covers. Each part has three sizable chapters presenting information in predominantly chronological order—like any engaging historical writer, Harper injects critical context where needed without bogging down the narrative.

Part I, "Fire," starts at the very beginning, both in terms of human history and in terms of any reader's general understanding of human diseases. Harper answers some fundamental questions like "What is a parasite?" and "What is a pathogen?" Before digging too deeply into the different diseases that have plagued humanity, and some that continue to, Harper lays as firm a foundation as he can, explaining that the pathogens that negatively impact humans fall into five evolutionary groups, or taxa: viruses, bacteria, protozoa, helminths (worms), and fungi. From the start, Harper reaffirms his motivations, informing the reader that due to their limited impact on the course of human history, and by corollary the limited impact of human history on the spread of fungal diseases, fungi will largely be left by the wayside—except, as Harper notes, in their capacity to infect plants, which has had dire consequences for human agriculture (think: Irish potato famine). If you are only here for the fungi, skip to Chapter 11.

Part II, "Farms," describes the impact of the shift from a hunter-gatherer society to a predominantly agricultural one in conjunction with its impact on increasing potential vectors for the spread of human diseases. One disease readers might recognize from more recent history, tuberculosis, also known as consumption, makes an appearance. This respiratory bacterial infection has been plaguing humans for thousands of years—and still does today, with over 10 million people contracting it annually and 1.5 million succumbing to it.

Part III, "Frontiers," covers the periods of global expansion and colonization of the last 600 or so years. In it, Harper carefully teases apart the highly contested "virgin-soil" hypothesis, a theory popularized by Jared Diamond's *Guns, Germs, and Steel.* The idea of European immunological superiority triumphing over indigenous populations is, as Harper makes quite clear, critically and evidently fraught in describing the demographic disaster that defined the era of exploration.

Part IV, "Fossils," brings us into the modern age, with the advent of fossil fuel usage spurring the Industrial Revolution and all the technological advancements that have followed. As always, the paradox of progress has been a separate plague on humanity—the idea that advancements that bring our society and culture forward ultimately weaken its defenses against pathogens that literally spread overnight. Four hundred years ago, the fastest anyone could cross land was by horse. Disease spread was limited by the speed with which its human and animal vectors could traverse great distances. Now, global jet plane networks enable the spread of pathogens from continent to continent in a matter of hours.

You might be sick and tired of reading about human-borne diseases in this time of ongoing global pandemic and I wouldn't blame you for thinking *Plagues Upon the Earth* is worth passing on. Unlike most books of its kind published in the last year or so that capitalize on the renewed popular fascination with pathogens spurred by the current coronavirus pandemic, *Plagues Upon the Earth* doesn't end with some trite conclusion designed to make you feel better about a world that seems to be falling apart at the seams. But given its narrative context, *Plagues Upon the Earth* is almost, even if just the teensiest bit, comforting. Pandemics like COVID-19 are nothing new in the greater context of human history.

Harper makes clear that, for as long as there have been humans, there have been bacterial, viral, and parasitic diseases that prey on evolutionary vulnerabilities in our species. Some of our earliest pre-human ancestors had parasitic worms (and some of us still do); the "so-called Middle Ages," as Harper puts it, had Black Death (bubonic plague); some of our grandparents and great-grandparents and great-great grandparents had the H1N1 influenza A virus; and we have severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Although every pandemic is new and terrifying in its own way, the similarities across the ages can be oddly comforting—or of course, completely disconcerting.

Jeanette S. Ferrara, MFA

RIGAKU TOPIQ WEBINARS

Rigaku has developed a series of 20–30 minute webinars that cover a broad range of topics in the fields of X-ray diffraction, X-ray fluorescence and X-ray imaging. You can register here and also watch recordings if you cannot attend live sessions.

CRYSTALLOGRAPHY IN THE NEWS

September 7, 2021: Scientists from the ASU and UCLA have determined the structure of the human adenosine receptor from a single nanocrystal in LCP using MicroED.

September 19, 2021: Scientists in Germany and the UK have used ionic liquids to melt the unmeltable ZIF-8 MOF.

October 12, 2021: Scientists at Nagoya University have synthesized and characterized cyclo [c.c.c.c.c.c.e.e.e.e.e.e] dodecakis benzene, infinitene, a figure-eight shaped molecule.

October 13, 2021: Researchers in Japan have prepared an elastic metal–organic crystal with a densely catenated backbone.

November 2, 2021: Scientists at Pfizer have developed an orally bioavailable SARS-CoV2-3CL protease inhibitor that is already in a Phase I trial.

November 11, 2021: Not crystallography *per se* but nevertheless interesting: scientists from Italy, the U.K. and the U.S. have used RoseTTAFold and AlphaFold to generate accurate models of core eukaryotic protein complexes within the *Saccharomyces cerevisiae* proteome.

VIDEOS OF THE MONTH

Lisa Keefe and her team at IMCA-CAT were involved the determination of the structure of Pfizer's anti-COVID drug, PF-07321332, a SARS-CoV2-3CL protease inhibitor. Here are links to Lisa's interviews with local TV networks in Chicago:
FOX32 >
NBC5 >

USEFUL LINKS

A simple pressure-assisted method for MicroED specimen preparation

Jingjing Zhao, Hongyi Xu, Hugo Lebrette, Marta Carroni, Helena Taberman, Martin Högbom & Xiaodong Zou

Abstract
Micro-crystal electron diffraction (MicroED) has shown great potential for structure determination of macromolecular crystals too small for X-ray diffraction. However, specimen preparation remains a major bottleneck. Here, we report a simple method for preparing MicroED specimens, named Preassis, in which excess liquid is removed through an EM grid with the assistance of pressure. We show the ice thicknesses can be controlled by tuning the pressure in combination with EM grids with appropriate carbon hole sizes. Importantly, Preassis can handle a wide range of protein crystals grown in various buffer conditions including those with high viscosity, as well as samples with low crystal concentrations. Preassis is a simple and universal method for MicroED specimen preparation and will significantly broaden the applications of MicroED.
Read open access paper >

Linus Pauling: The Nature of the Chemical Bond, A Documentary History

Utilizing over 2,500 manuscript pages, nearly 100 photographs, and more than four hours of audio and video, this website tells the story of a cornerstone achievement of twentieth century science. In 1926 Linus Pauling, then a promising young doctoral candidate, set sail for Europe to study quantum mechanics with an eye toward applying this new physics to problems in structural chemistry. Pauling's ensuing program of research would result in a remarkable series of landmark publications that revolutionized the scientific world's conception of how atoms join together to form molecules. In 1939, Pauling's ideas were bundled into a book that was uniformly recognized as an instant classic. In 1954, twenty-eight years after his first fateful trip, Pauling would return to Europe to receive the Nobel Prize in Chemistry, awarded for "research into the nature of the chemical bond and its application to the elucidation of complex substances." Pauling won a Nobel Prize in 1954 for his earlier insights into the nature of the chemical bond. The state department was forced to give him a passport this time so that he could accept the honor.

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Our LinkedIn group shares information and fosters discussion about X-ray crystallography and SAXS topics. Connect with other research groups and receive updates on how they use these techniques in their own laboratories. You can also catch up on the latest newsletter or *Rigaku Journal* issue. We also hope that you will share information about your own research and laboratory groups.

JOIN HERE

RIGAKU X-RAY FORUM

At rigakuxrayforum.com you can find discussions about software, general crystallography issues and more. It's also the place to download the latest version of Rigaku Oxford Diffraction's CrysAlis^{Pro} software for single crystal data processing.

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