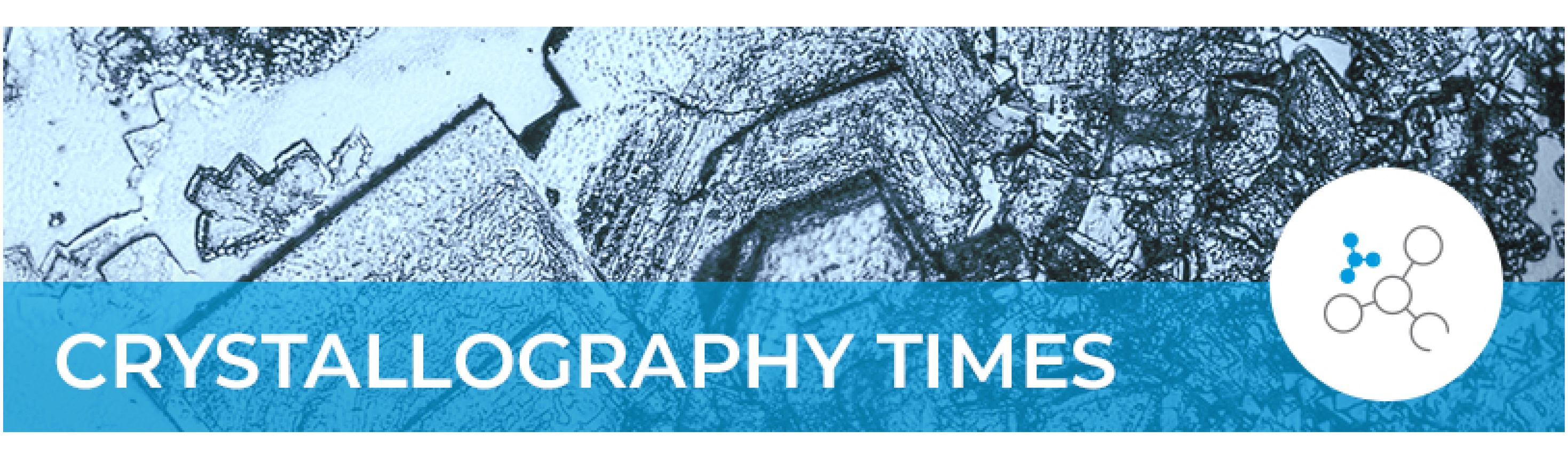


Volume 13, No. 2, February 2021

WELCOME

Good day everyone. The severe weather in the central U.S., and particularly Texas, has caused many people in these areas to go without electricity for hours and even days. If you are one of those people, we hope the impact is minimal and that, by the time you read this, things will be close to normal.

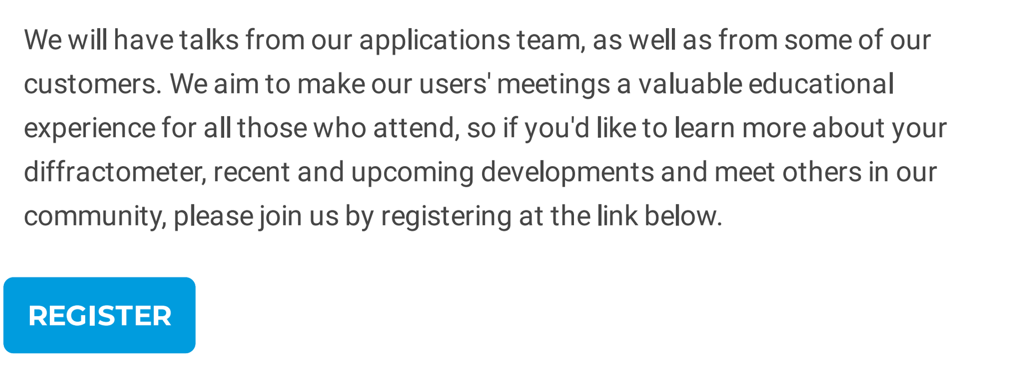
In this month's *Crystallography Times* we're announcing a Virtual Users' Meeting on April 7–8, 2021. We hope you can join us for a fun and enlightening couple of days. We also highlight our most popular diffractometer for protein crystallography, the XtaLAB Synergy-R, and Bernhard Spingler's laboratory at the University of Zurich.

Our monthly features include papers of crystallographic interest, a couple of videos on the amazing perovskites, links pointing to novel methods of small molecule crystallization, a review on a book about skepticism in a data-driven world and our monthly survey.

Stay safe,

Joe

UPCOMING EVENT



We would like to invite you to join us for our Single Crystal Online Users' Meeting, to be held on April 7–8, 2021. The meeting will be held online via Zoom and will take place at 14:00–17:00 GMT on both days to allow our users from across Europe and the Americas to attend. We intend to hold an additional meeting at a time more suitable for the Asia-Pacific region shortly afterward, so watch for another announcement soon.

We will have talks from our applications team, as well as from some of our customers. We aim to make our users' meetings a valuable educational experience for all those who attend, so if you'd like to learn more about your diffractometer, recent and upcoming developments and meet others in our community, please join us by registering at the link below.

REGISTER

CRYSTALLOGRAPHY IN THE NEWS

January 7, 2021: Researchers in Australia and the U.S. report the synthesis and characterization of the first compound with a Be-N double bond.

January 18, 2021: Researchers in the U.S. report the first structures of a cobalamin-dependent radical SAM methylase, TsrM from *Kitasatospora setae*, with and without substrate.

January 22, 2021: Scientists in China have developed a chiral iridium catalyst that preserves Z configuration in allylic substitution reactions.

January 22, 2021: Researchers in Germany have generated electron-induced characteristic X-ray and bremsstrahlung radiation from a waveguide cavity.

January 27, 2021: Researchers in France, Israel and the U.K. have determined high-resolution crystal structures of the ground (light-adapted) and dark-adapted states of Archaerhodopsin-3.

January 27, 2021: Scientists in the U.K. and U.S. report that diamond maintains its structure at 2 terapascals (5X the pressure at the earth's core).

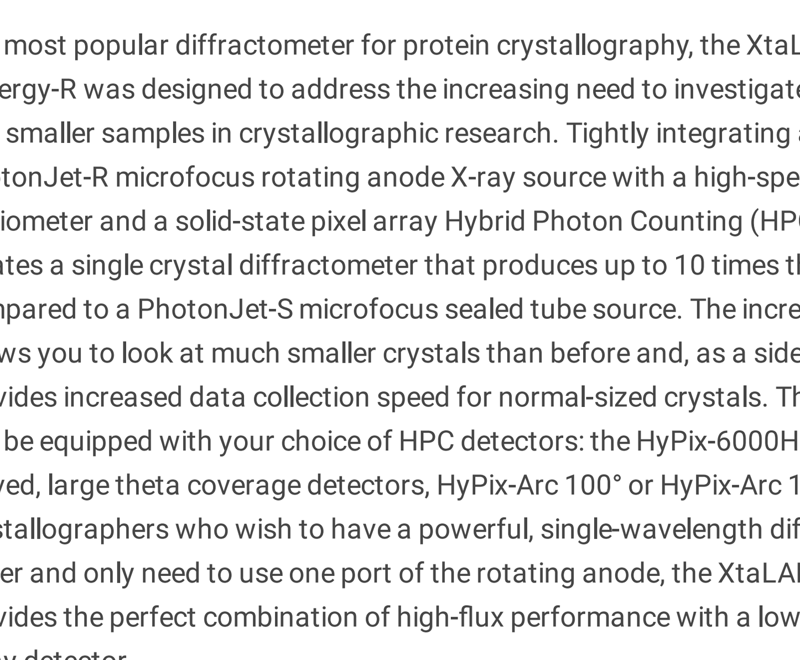
February 5, 2021: Researchers in India and the U.S. report the crystal structure of a messenger RNA complexed with polyadenylate at a resolution of 2.89 Å that reveals multiple modes of interaction between the RNAs.

February 11, 2021: Scientists and astronauts are entering phase II of the Real-time Protein Crystal Growth study (RTPCG-2) aboard the International Space Station.

February 12, 2021: Scientists from Germany, Sweden and the U.S. report four nanobodies that bind to the SARS-CoV-2 spike protein and prevent infection of cells by targeting two distinct epitopes on the spike protein.

PRODUCT IN THE SPOTLIGHT

XtaLAB Synergy-R

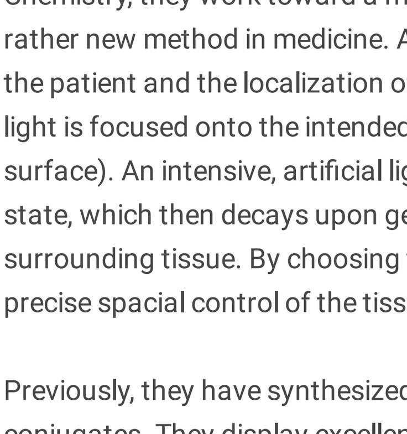


Our most popular diffractometer for protein crystallography, the XtaLAB Synergy-R was designed to address the increasing need to investigate smaller and smaller samples in crystallographic research. Tightly integrating a PhotonJet-R microfocus rotating anode X-ray source with a high-speed kappa goniometer and a solid-state pixel array Hybrid Photon Counting (HPC) detector creates a single crystal diffractometer that produces up to 10 times the flux compared to a PhotonJet-S microfocus sealed tube source. The increase in flux allows you to look at much smaller crystals than before and, as a side benefit, it provides increased data collection speed for normal-sized crystals. The system can be equipped with your choice of HPC detectors: the HyPix-6000HE or the curved, large theta coverage detectors, HyPix-Arc 100° or HyPix-Arc 150°. For crystallographers who wish to have a powerful, single-wavelength diffractometer and only need to use one port of the rotating anode, the XtaLAB Synergy-R provides the perfect combination of high-flux performance with a low-noise HPC X-ray detector.

Enhance your ability to resolve large unit cells and lattices when you select the optional motorized variable beam slit in order to alter divergence to adapt the source to your sample's requirements. The XtaLAB Synergy-R provides the highest level of user safety with multiply redundant electromechanical safety circuits built into the ergonomically designed radiation enclosure.

RESEARCHER IN THE SPOTLIGHT

Prof. Dr. Bernhard Spingler
Chemistry Department
University of Zurich



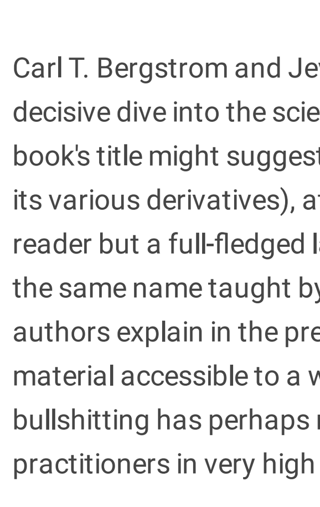
Bioinorganic Chemistry and Crystallography in the Spingler Group

The Spingler group is working in two research areas: Bioinorganic Chemistry and Method Development of Single Crystal Growth. In the field of Bioinorganic Chemistry, they work toward a more efficient Photodynamic Therapy (PDT), a rather new method in medicine. After administration of a photosensitizer (PS) to the patient and the localization of the photosensitizer in the tissue of interest, light is focused onto the intended area of treatment (normally close to a surface). An intensive, artificial light source transforms the PS into its excited state, which then decays upon generation of radical oxygen species that kill the surrounding tissue. By choosing the area that is irradiated with the laser light, precise spacial control of the tissue to be destroyed can be achieved.

Previously, they have synthesized novel nanometer-sized porphyrin-platinum conjugates. They display excellent light toxicity when irradiated with visible light, but essentially no dark toxicity against various human cancer cell lines. The platinum complexes are characterized by a high singlet oxygen quantum yield, an excellent light-to-dark toxicity ratio (>5000) and IC50 values upon irradiation with visible light down to 19 nM. They are now working on systems that absorb more in the red visible wavelength range.

Part of the group currently studies innovative ways of improving the crystallization of small molecules, which can also be used for the salt screening of active pharmaceutical ingredients (API).

BOOK REVIEW



Calling Bullshit: The Art of Skepticism in a Data-Driven World
By Carl T. Bergstrom and Jevin D. West
ISBN: 9780525509189

Carl T. Bergstrom and Jevin D. West's recent co-authored work is a delightful and decisive dive into the science of skepticism—and the art of bullshitting. As the book's title might suggest, it is chock-full of mild profanity (namely "bullshit" and its various derivatives), at times more than simply garnering a chuckle from the reader but a full-fledged laugh. The book gets its title from a collegiate course of the same name taught by the authors at the University of Washington. As the authors explain in the preface, the book serves as a means of making the course material accessible to a wider audience, particularly in a time when the art of bullshitting has perhaps reached an all-time high, even landing some of its best practitioners in very high offices.

Perhaps the most critical initial takeaway the authors offer is the idea that the art of bullshit and the science of skepticism are not new concepts—indeed, they date back to the days of Plato and his early philosopher compatriots. The ability to challenge information presented to you and not take it as fact without careful thought and analyses is not a natural one, but a learned one. Bergstrom and West set out to show their readers how, offering a myriad of illustrative examples from a diverse series of disciplines.

The first chapter, "Bullshit Everywhere," re-affirms what its title suggests it will. Every discipline, every field, every career path, every outlet for information you could possibly imagine, has the capacity to be full of bullshit and bullshitters. One example the authors offer—which is quite frequently cited in works explicating the critical importance of reproducibility and skepticism in scientific inquiry—is the infamous 1998 study published in *The Lancet* by Andrew Wakefield, a British physician.The study suggested that inflammatory bowel diseases and autism in children were related to patterns of early childhood vaccination, namely the MMR vaccine. However, Wakefield's co-authors retracted their participation in the study in 2004, and *The Lancet* fully retracted the study in 2010. In 2011, Wakefield lost his license to practice medicine in the UK. But the damage of his bullshit had been done. Twenty-two years later, we live in a world full of "anti-vaxxers" who refuse to vaccinate their children, leading to outbreaks of diseases long thought to be eradicated.

In the subsequent eight chapters, Bergstrom and West offer numerous examples of bullshitters and bullshitting. They discuss the importance of "Medium, Message, and Misinformation" in Chapter 2; "The Nature of Bullshit" in Chapter 3; "Causality," or rather, the critical concept that correlation does not equal causation, in Chapter 4; "Numbers and Nonsense" in Chapter 5; "Selection Bias" in Chapter 6; "Data Visualization" in Chapter 7; "Calling Bullshit on Big Data" in Chapter 8; and "The Susceptibility of Science" in Chapter 9.

The final two chapters, titled "Spotting Bullshit" and "Refuting Bullshit" respectively, are undoubtedly the crux of the book's most critical offering, as they instruct the reader on both how to spot bullshit and how to refute it. As books go, this one is very straightforward—no bullshit—with regards to what you're getting and where you're getting it chapter-wise. In "Spotting Bullshit," the authors provide a list of critical questions for their audience to ask when faced with any new piece of information, such as "What is the source?" and "Does it seem too good to be true?" They even offer a subset of questions to ask specifically when vetting information purveyed via the Internet—whether from social media or a "reputable" news outlet. In "Refuting Bullshit," they offer critical advice for calling others on their bullshit in a constructive way, regardless of the context, reminding their readers that one does not call out bullshit to make themselves feel better or smarter than the bullshitter, but to educate them, and to show the bullshitter there is another way.

Bergstrom and West's writing style is fluid and cohesive—there is never really a sense of who is writing which section, unless the respective author specifically identifies themselves. This leads to a smooth and entertaining read, with a consistently challenging and irreverent tone. It is a biting but gripping summer read—perfect for a making a long flight pass quickly.

Jeanette S. Ferrara, MFA

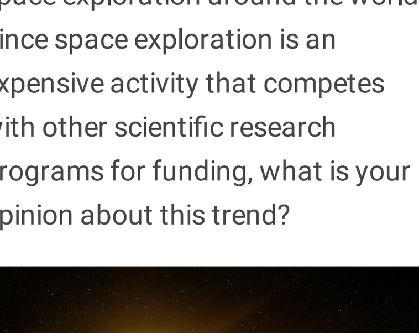
RIGAKU TOPIQ WEBINARS

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.

RIGAKU REAGENTS

Wizard Classic:

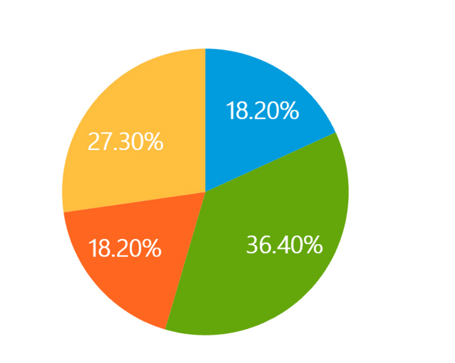
Rigaku Reagents' Wizard Classic screens were designed to increase the probability of producing crystals during the coarse screening crystallization trials of biological macromolecules. Wizard Classic screens offer a large range of crystallants, buffers, and salts, covering a broad range of crystallization space, at pH levels from pH 4.5 to pH 10.5. They are proven to be a highly effective starting point for screening, with non-repeating formulations. Each of these screens is offered in either a 96 deep well block plate format or in 10 ml tubes.



SHOP HERE

SURVEY OF THE MONTH

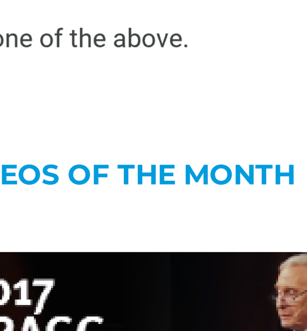
There has been a recent increase in space exploration around the world. Since space exploration is an expensive activity that competes with other scientific research programs for funding, what is your opinion about this trend?



TAKE THE SURVEY

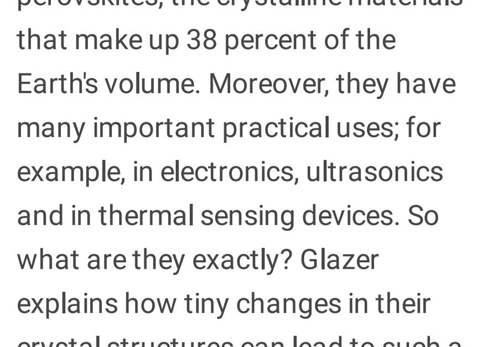
LAST ISSUE'S SURVEY RESULTS

Which of the following statements best describes your COVID-19 life?



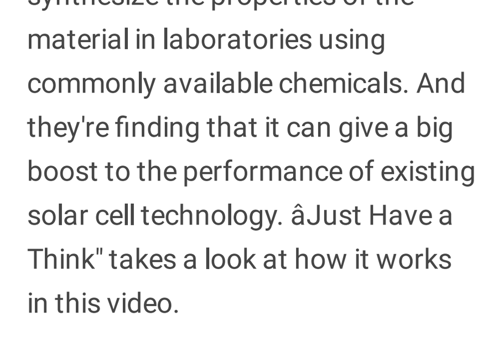
- My cooking skills have improved.
- My drinking skills have improved.
- I've watched everything available on every streaming service.
- I've become better friends with my significant other.
- I've become better friends with my dog.
- None of the above.

VIDEOS OF THE MONTH



The Wondrous World of Perovskites with Mike Glazer

In the 2017 Bragg Lecture at the Royal Institute, Mike Glazer unearths the vital world of perovskites, the crystalline materials that make up 38 percent of the Earth's volume. Moreover, they have many important practical uses; for example, in electronics, ultrasonics and in thermal sensing devices. So what are they exactly? Glazer explains how tiny changes in their crystal structures can lead to such a vast array of different properties and why they are so important in our daily lives. This Discourse is supported by the Bragg Lecture Fund and was filmed on March 31, 2017. Mike Glazer is an Emeritus Professor of the Oxford University Department of Physics.



Perovskite Solar Cells: Game Changer?

Just Have a Think: Perovskite mineral was discovered over 150 years ago, but it's only recently that scientists have been able to synthesize the properties of the material in laboratories using commonly available chemicals. And they're finding that it can give a big boost to the performance of existing solar cell technology. âJust Have a Think" takes a look at how it works in this video.

USEFUL LINKS

Some Thoughts About the Single Crystal Growth of Small Molecules

This highlight critically compares various techniques to grow single crystals when only a few milligrams of the compound of interest are available. The authors describe vapor diffusion, evaporation, cooling, and layering techniques, as well as crystallization in gels. A table of successfully applied solvent/antisolvent combinations for initial screening is given. Additionally, a comprehensive table of 107 solvents with their boiling points, densities and dielectric constants helps to optimize the crystal growth.

Spingler, Bernhard; Schnidrig, Stephan; Todorova, Tonya; Wild, Ferdinand (2012). *Some thoughts about the single crystal growth of small molecules.* CrystEngComm, 14(3):751-757.

A High-throughput Screening Method for the Nano-crystallization of Organic Cations

The generation of solid salts of organic molecules is important to the chemical and pharmaceutical industry. Commonly used salt screening methods consume a lot of resources. The authors employed a combination of ion exchange screening and vapor diffusion for crystallization. This technique is semi-automatic and requires just nanoliters of the solution of the analyte to be crystallized. This high-throughput screening yielded single crystals of sufficient size and quality for single-crystal X-ray structure determination using an in-house X-ray diffractometer. The broad scope of the method has been shown by challenging it with seven very different organic cations whose aqueous solubilities vary by a factor of almost 1000. At least one crystal structure for six out of seven tested cations was determined; four out of the successful six had never been crystallized before. The method is extremely attractive for high-throughput salt screening, especially for active pharmaceutical ingredients (APIs), as about 40 percent of all APIs are cationic salts. Additionally, this is a new and very promising procedure for the crystallization of salts of organic cations.

Nievergelt, Philipp P; Babor, Martin; Äejka, Jan; Spingler, Bernhard (2018). *A high-throughput screening method for the nano-crystallization of salts of organic cations.* Chemical Science, 9(15):3716-3722.

JOIN US ON LINKEDIN

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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