Volume 15, No. 11, November 2023

INTRODUCTION

This month, I am going to focus on a piece of good news. Two weeks ago, Boby et al. published a paper in *Science* with authors from over 100 institutions in the COVID Moonshot Consortium. This heroic open science effort produced a potent potential inhibitor for SARS-CoV-2 Mpro. I hope collaborations like this will be a model for addressing future pandemics or other big science problems in the future.

Our Researcher in the Spotlight is Dr. Lauren Hatcher from the University of Cardiff, who has provided a description of the Technique of the Month, photocrystallography, and will be giving a TOPIQ webinar on the subject at the end of January.

You might notice I have added a set of dates for the Rigaku School for Practical Crystallography for January. The format will be similar to previous schools. However, the lectures will be prerecorded so we can start working toward an on-demand school with all the features of the live school save live Q&A. In January, we will have Rigaku scientists on hand for the Q&A session and will develop an FAQ based on these questions. We will have an exam and certificates of attendance and achievement for the January school as well as the forthcoming on-demand version. We look forward to seeing you in January.

The Product in the Spotlight is the XtaLAB Synergy-R diffractometer, which is the diffractometer Lauren Hatcher uses for her research. Lee Daniels provides tips on using CCDC's CellCheckCSD. I found a really cool video of the month and some interesting crystallographic papers. Finally, Jeanette reviews *American Prometheus: The Triumph and Tragedy of J. Robert Oppenheimer*. I read the book but have not yet seen the movie, so no spoilers!

Be safe,
Joe Ferrara

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 and electron diffraction, X-ray fluorescence and X-ray imaging. You can watch recordings of our past sessions here.

UPCOMING WEBINAR:
TOPIQ | Pump-multiprobe Photocrystallography on the XtaLAB Synergy-R system
Wednesday, January 31, 2024 at 09:00 CST

Presenter: Dr. Lauren Hatcher, Cardiff University
In this Webinar we will describe a new setup, developed in collaboration between Cardiff University and Rigaku, that enables the collection of pump-probe Photocrystallography data down to a time-resolution of 10 ms, producing full, 3D structures at regular time-points to create 3D molecular movies.
Register now>

UPCOMING EVENTS:
Rayons X et Matière 2023, Bordeaux, France, November 21-24, 2023.

CCP4 Study Weekend 2024, Decision making in MX - how to be a productive structural biologist, EMCC, Nottingham, UK & Virtual, January 3-5, 2024.

Rigaku School for Practical Crystallography, January 15-19 and 22-26, 2024.

We now have a full-scale war in the Middle East, earthquakes In Afghanistan an ongoing war in Ukraine, and humanitarian crises elsewhere. With some much suffering, perhaps it is a good time to donate to larger relief organizations like the International Red Cross and Red Crescent Movement, so they can distribute relief as needed.

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To keep up to date on the latest news and events from Rigaku Oxford Diffraction, follow our Twitter feed.

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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.

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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.

JOIN HERE

TOPIQ | Pump-multiprobe Photocrystallography on the XtaLAB Synergy-R system

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Read more about TOPIQ | Pump-multiprobe Photocrystallography on the XtaLAB Synergy-R system >

Wednesday, January 31, 2024 at 09:00 CST
Time Zone Converter

Presenter
Dr. Lauren Hatcher, Cardiff University

REGISTER NOW

RESEARCHER IN THE SPOTLIGHT

Dr. Lauren Hatcher

Lauren began her career in Prof. Paul Raithby's group at the University of Bath, where she obtained a PhD in Chemistry studying Molecular Photocrystallography in 2014. Following postdoctoral positions in the study of metastable materials (EP/K004956/1, EPSRC) and in continuous manufacturing and advanced crystallization as part of the CMAC consortium (EP/P006965/1, EPSRC), Lauren moved to Cardiff University in 2020. She currently holds a Royal Society University Research Fellowship, using dynamic X-ray diffraction methods to study photoactive crystals for solar energy applications. Lauren has continued to develop photocrystallography as a technique, both at Cardiff and in collaboration with National Facilities, including Diamond Light Source. At Cardiff, she has recently acquired a bespoke XtaLAB Synergy-R from Rigaku Oxford Diffraction to facilitate pump-probe diffraction experiments in the home X-ray lab.

TECHNIQUE IN THE SPOTLIGHT: PHOTOCRYSTALLOGRAPHY

Photocrystallography involves the determination of the complete, three-dimensional structure of a light-sensitive material, while its switchable components are in a photoactive metastable or transient excited state.[1, 2] Photocrystallography experiments typically involve the use of bespoke set-ups to irradiate the single crystal in-situ on the diffractometer, allowing concomitant photoactivation without impeding the data collection. Photoactivation is typically achieved with lasers, although LED illumination set-ups have become increasingly popular.[3, 4]

The lifetime of the photoexcited state to be studied dictates the type of photocrystallography experiment that is conducted. For irreversible processes or long-lived metastable species that can be cryo-trapped, the so-called "steady-state" photocrystallographic method is used in which defined periods of irradiation are alternated with a standard single-crystal X-ray data collection. However, short-lived excited states require the use of time-resolved methodologies, such as stroboscopic pump-probe measurements that require the synchronization of short light and X-ray pulses.[5] Due to the complexity of such experiments and their inherent flux limitation, time-resolved photocrystallography studies have typically been conducted at National Facilities. With the advent of fast-readout detectors, pump-probe synchronization can now be achieved by electronic gating of the detector response. This, and the increasing availability of bright, low-cost and compact LED and laser diode set-ups, is now enabling researchers to move time-resolved photocrystallography experiments into the home X-ray lab.[6]

1. P. Coppens, *Angewandte Chemie International Edition*, 2009, **48**, 4280-4281.
2. P. Raithby, *IUCrJ*, 2015, **2**, 5-6.
3. L. E. Hatcher, M. R. Warren, J. M. Skelton, A. R. Pallipurath, L. K. Saunders, D. R. Allan, P. Hathaway, G. Crevatin, D. Omar, B. H. Williams, B. A. Coulson, C. C. Wilson and P. R. Raithby, *Communications Chemistry*, 2022, **5**, 102.
4. R. Kaminski, K. N. Jarzembska, S. E. Kutyla and M. Kaminski, *Journal of Applied Crystallography*, 2016, **49**, 1383-1387.
5. J. M. Cole, *Acta Crystallographica Section A*, 2008, **64**, 259-271.
6. N. Casaretto, D. Schaniel, P. Alle, E. Wenger, P. Parois, B. Fournier, E.-E. Bendeif, C. Palin and S. Pillet, *Acta Crystallographica Section B*, 2017, **73**, 696-707.

PRODUCT IN THE SPOTLIGHT

XtaLAB Synergy-R

HIGH-FLUX ROTATING ANODE X-RAY DIFFRACTOMETER

Benefits

- Faster, accurate data collection due to high-speed kappa goniometer, high-flux rotating anode X-ray source, fast, low-noise X-ray detector, and highly optimized instrument control software.
- Improve your ability to investigate small samples due to the increased flux from the rotating anode X-ray source as well as the extreme low noise of the HyPix X-ray detectors. Noise free images mean you can count longer for weakly diffracting crystals without a loss in data quality arising from detector noise.
- Highest level of user safety with multiply redundant electromechanical safety circuits built into the ergonomically designed radiation enclosure.
- Minimize your downtime by utilizing built-in online diagnostics and troubleshooting to diagnose and fix almost all problems without a site visit.
- Automatically solve structures and determine what your sample is in a few seconds before committing to a full dataset by using the "What is this?" feature.
- Increased data collection speed due to the increased flux of the X-ray source.
- Enhance your ability to resolve large unit cells, twins or incommensurate lattices when you select the optional motorized variable beam slit in order to alter divergence to adapt the source to your sample's requirements.

XtaLAB Synergy-R
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 as 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 hybrid photon counting 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, well-integrated 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.

PhotonJet-R
The PhotonJet-R comes from the same pedigree as the MicroMax™-007 HF, of which there are well over 1000 units in use around the world. The PhotonJet-R X-ray source applies the lessons learned over the development and lifetime of the MicroMax-007 rotating anode to produce a new generation, high-performance rotating anode source. With the source mounted directly onto the goniometer, the XtaLAB Synergy-R provides a stable and robust solution that ensures consistently high performance. Confocal optics, designed by Rigaku Innovative Technologies, offer a high-brilliance X-ray beam and the optional continuously variable slit assembly gives the user the ability to adjust high brilliance versus low divergence depending on the needs of the sample being studied.

Proven Reliability
The PhotonJet-R source was designed with reliability in mind. Clever Rigaku engineering makes filament changes easy, like swapping a printer cartridge, with no need to realign the source each time. Scheduled maintenance involves one annual visit from a Rigaku engineer, as with all XtaLAB Synergy diffractometers, and typically takes 1-2 days. With the anode exchange program, you get the benefit of rotating anode power with the convenience of sealed tubes.

Beam Conditioning
Where overlapping peaks are a concern, e.g. large unit cells, twins or incommensurate lattices, high beam divergence is undesirable. On the PhotonJet-R source, a software-controlled, motorized variable beam slit is available as an option to alter divergence to adapt the source to your sample's requirements. For those samples where intensity matters most, the slit can be fully opened giving the highest flux. For those where peak sharpness and overlap are factors, the beam can be limited to a divergence anywhere between 1 to 10 mrad.

HyPix Detectors
Rigaku's own HyPix family of HPC detectors use solid state pixel array technology to enable direct X-ray photon detection and counting. Direct X-ray photon detection means that X-ray photons are counted instantaneously as they arrive at the detector. There is no conversion to visible light by a scintillator so the energy of the photon can be assessed at moment of detection. This leads to essentially noise-free images. The HyPix detectors feature a 100 Hz frame rate, which allows for data fine slicing even at the fastest goniometer speeds. The HyPix detectors incorporate dual counters, enabling several modes of operation. Rapid alternating counter electronics (RACE) technology enables the 100 Hz zero dead time mode and ensures that no pixel is blind for more than a few nanoseconds during exposure to X-rays. The high dynamic range mode combines the counters to offer a massive 31-bit counter depth. Dual thresholding offers differential modes and selective signal suppression.

CrysAlis^{Pro}
The XtaLAB Synergy-R comes complete with CrysAlis^{Pro}, our user-inspired data collection and data processing software for single crystal analysis. Designed around an easy-to-use graphical user interface, CrysAlisPro can be operated under fully automatic, semi-automatic or manual control. CrysAlis^{Pro} combines automated crystal screening, the fastest and most accurate strategy software available, concurrent data reduction and automatic small molecule structure solution. CrysAlis^{Pro} can operate either in a protein or small molecule dedicated workflow. Popular third-party protein data processing packages can easily process diffraction data if desired. Visual feedback is provided for each step with clear, color-coded guidance so that both novices and experts can collect high-quality data in the shortest time possible.

AutoChem
AutoChem is the ultimate productivity tool for small molecule chemists, offering fast, fully automatic structure solution and refinement during data collection. Developed in collaboration with OlexSys Ltd (Durham University, UK), AutoChem works in conjunction with Olex² where more advanced structure solution and refinement functionality exists. AutoChem is seamlessly integrated within CrysAlis^{Pro} and forms an integral part of our 'What is this?' feature. The 'What is this?' feature gives you structures quickly and ensures you are not wasting time collecting full datasets on known samples or starting materials. WIT is an alternative pre-experiment option which is used to plan your full data collection.

TIP OF THE MONTH

CellCheckCSD

What is it?
CellCheckCSD is a free tool from the Cambridge Crystallographic Data Centre that very quickly checks your unit cell against the Cambridge Structural Database (CSD). With CellCheckCSD installed, CrysAlis^{Pro} displays how many times unit cells similar to your result appear in the database.

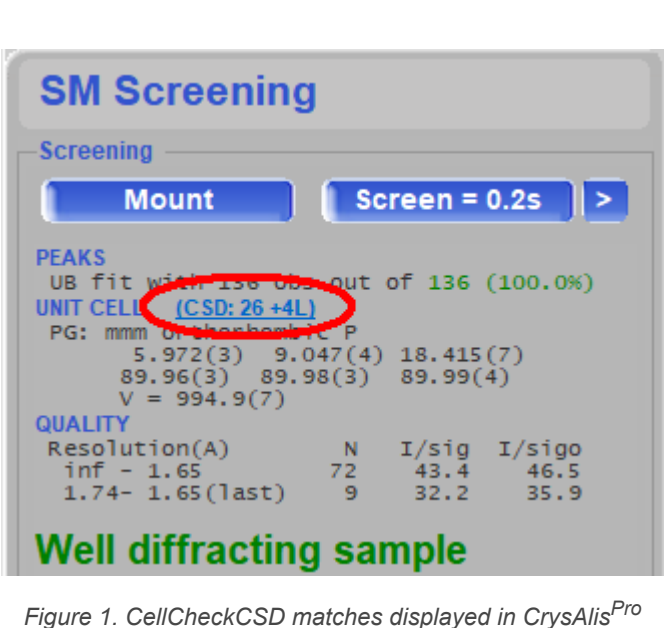


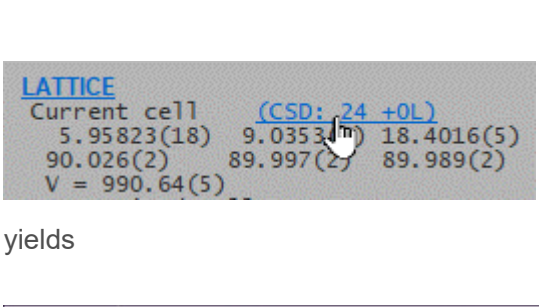
Figure 1. CellCheckCSD matches displayed in CrysAlis^{Pro}

Why should I use it?
While CellCheckCSD may find matches that have no chemical relationship to your crystal (the search is only on cell dimensions), you'll sometimes find that the crystal you mounted is known, or that you've chosen a crystal of your starting material. You may get a very quick list of structures of your compound collected under different conditions to which to compare. And CrysAlis^{Pro} keeps a local database of structures you've already collected; CellCheckCSD informs about those also.

How do I use it?
To get started, download the installer from CCDC (You will need a CCDC account. If you don't have one, you'll be prompted to create one.)
Link to CCDC CellCheckCSD >

The free download includes every current entry in the CSD, but only the cell dimensions, formula, space group, and the CSD refcode. The most recent version was released October 4, 2023 and contains 1,278,846 entries.

CrysAlis^{Pro} will recognize CellCheckCSD and display the results automatically. Click on **CSD:<n>** at any time to see the results; i.e., this



yields

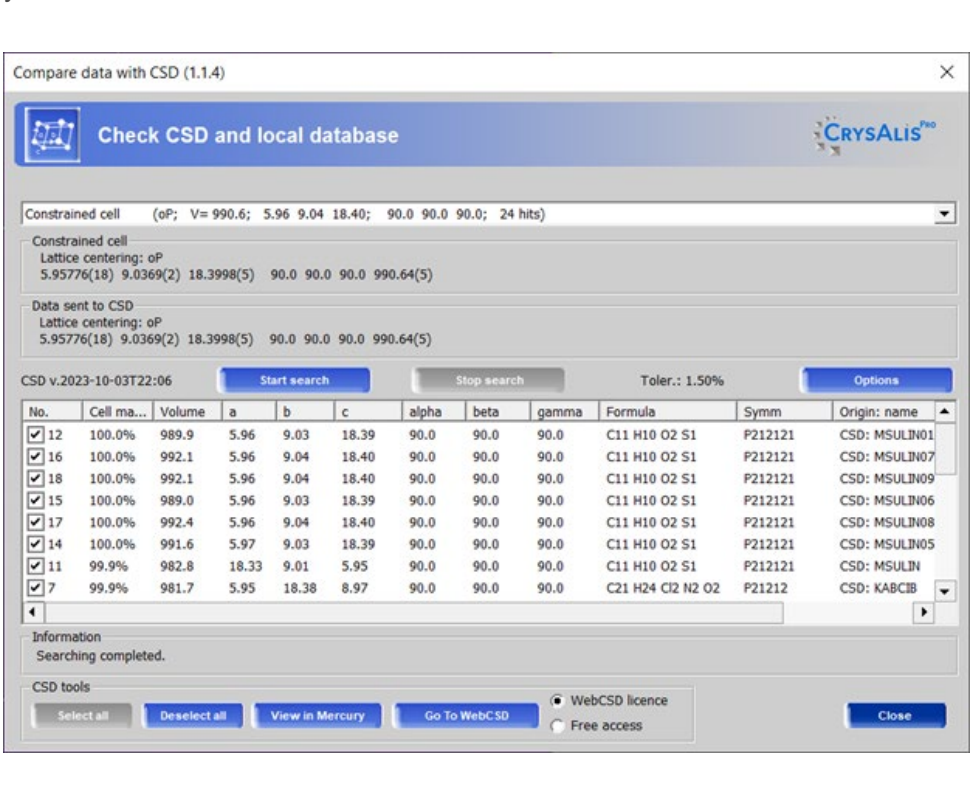


Figure 3. CSD and Local Database

If you have the full CSD installed, view the results by pressing the **View in Mercury** or the **Go To WebCSD** button. Without a license, you may still use the **Go To WebCSD** button to view the structures on the CCDC Access Structures web page. Use the boxes on the left to choose which structures are loaded.

Mercury will load all the hits chosen:

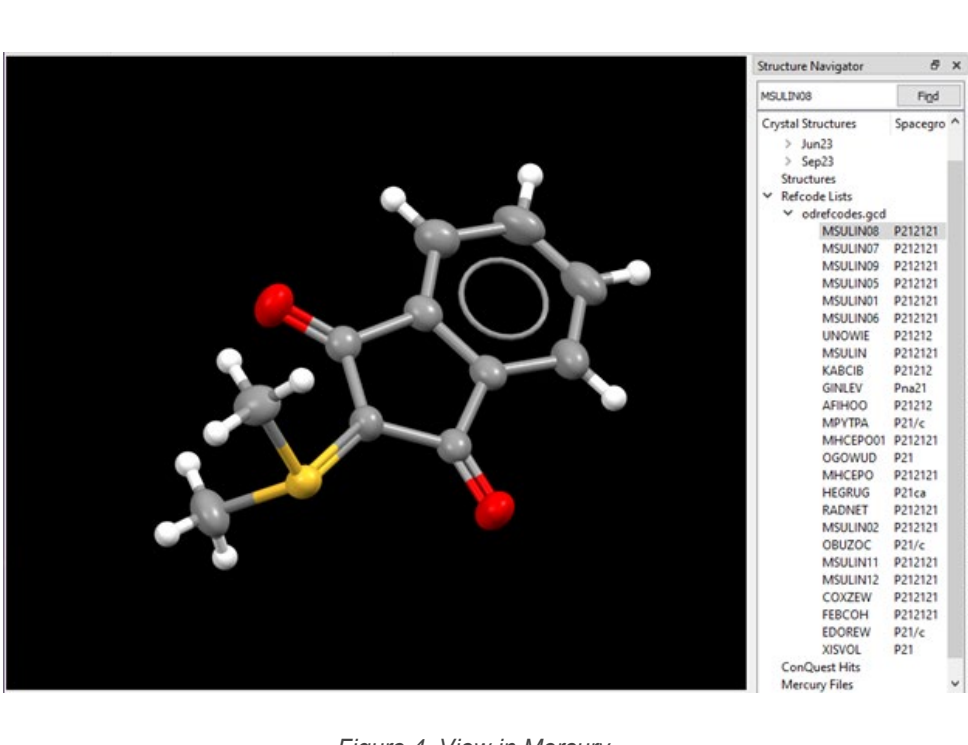


Figure 4. View in Mercury.

Alternatively, WebCSD will provide the information:

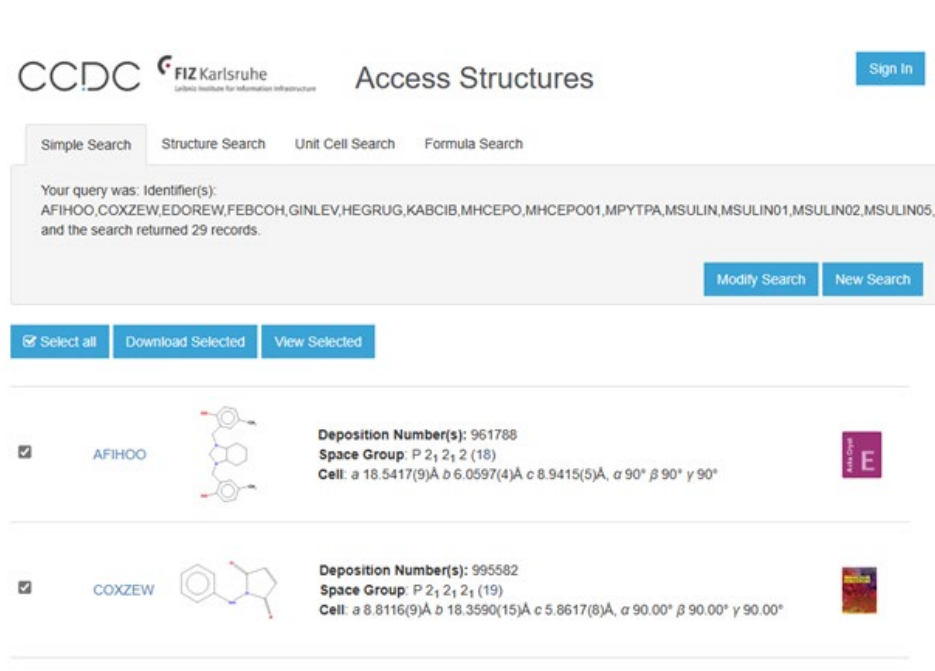


Figure 5. View in WebCSD.

Note that WebCSD sorts the results alphabetically by refcode rather than by the cell match percentage.

The **Options** button allows you to adjust the search settings and also enables the local database search. With local search enabled, your existing data sets are included in the search, a very helpful option if you have frequent in-house compounds that are not included in the CSD.

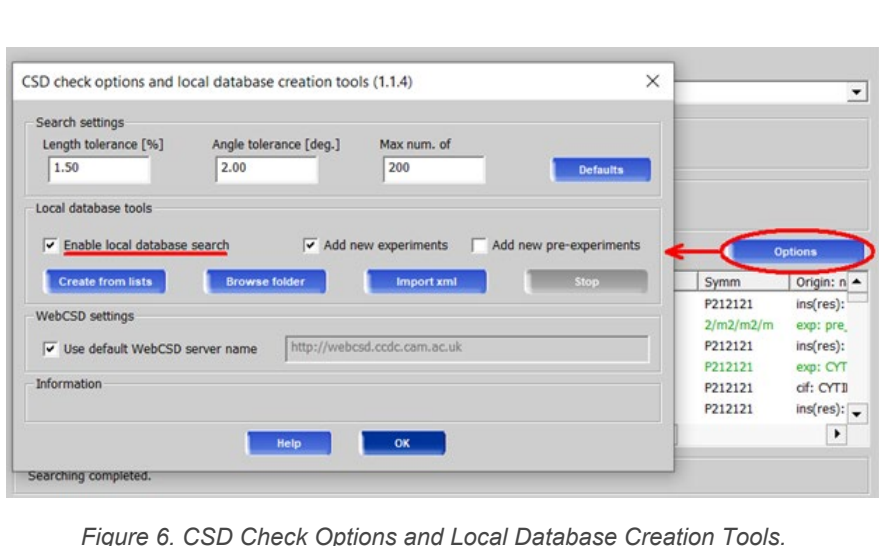
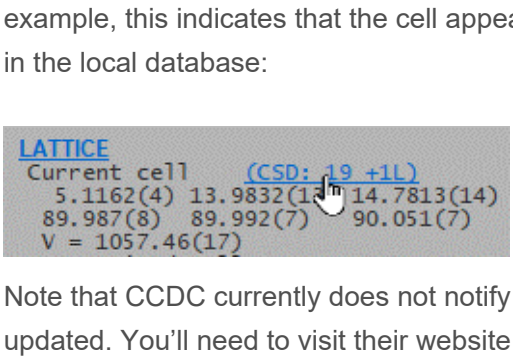


Figure 6. CSD Check Options and Local Database Creation Tools.

Results from the local database appear as a separate number. For example, this indicates that the cell appears 19 times in the CSD and once in the local database:



Note that CCDC currently does not notify users when CellCheckCSD is updated. You'll need to visit their website to check for updates.

Thanks to our friends at CCDC for working with us many years ago to develop CellCheckCSD.

CRYSTALLOGRAPHY IN THE NEWS

Researchers from the Scripps Research Institute have developed palladium catalysts with hydrogen-bonding ligands that allow the arylation of distal sp^3 carbons in free alcohols.

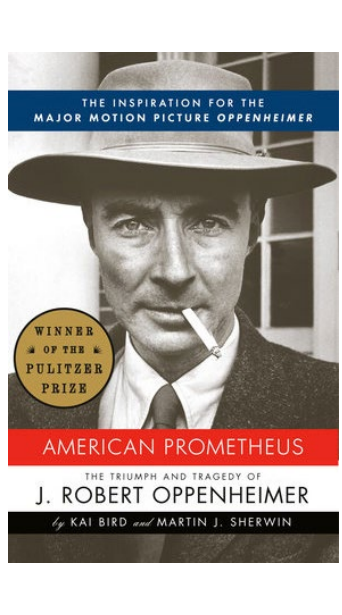
Scientists from Germany, Italy and the US have synthesized and characterized reactive high-spin iron(IV)-oxo sites through dioxygen activation in a MOF.

Researchers from over 100 institutions collaborated openly in the COVID Moonshot Consortium to find a promising inhibitor for SARS-CoV-2 Mpro.

Scientists from Chile, China and Germany have synthesized and characterized an all-metal fullerene: $K@Au_{12}Sb_{20}]^{5-}$.

Researchers from the Sweden and the US have solved the single crystal structures of a number of macrocyclic pharmaceuticals from the powders using MicroED.

BOOK REVIEW



Review: *American Prometheus: The Triumph and Tragedy of J. Robert Oppenheimer*
By Kai Bird and Martin J. Sherwin
ISBN 9780735726262

Kai Bird and Martin J. Sherwin's *American Prometheus: The Triumph and Tragedy of J. Robert Oppenheimer* is a doorstopper. The Pulitzer Prize-winning biography of one of America's most recognizable scientists clocks in at over 700 pages–about a hundred of which are footnotes and indices. Published in 2005, *American Prometheus* has recently skyrocketed back into the zeitgeist and the top of *The New York Times'* Bestseller List because it inspired director Christopher Nolan's summer blockbuster biopic *Oppenheimer*.
Having seen the film before reading the book, the film probably would have been easier to follow and made more sense having read the book first. Even though *Oppenheimer* has an over 3-hour runtime, Nolan left out plenty of contextualizing commentary and historical details that *American Prometheus* does not.
Bird and Sherwin break Oppenheimer's life story into five parts. The first details his childhood, education at Harvard College and his doctoral pursuits in Europe, as well as the beginnings of his career at the University of California, Berkeley. The second begins with his introduction to Jean Tatlock, the Communist Party member whose relationship with Oppenheimer would continue even after his marriage to Katherine Puening and was the subject of significant investigation by the United States government regarding his ability to receive and maintain security clearance. This second part mostly follows his burgeoning career at Berkeley and his establishment as a premier American physicist.
The third part details Oppenheimer's role in the Manhattan Project and the development of the atomic bomb, ending with the successful Trinity test. The fourth part details the dropping of the bombs on Hiroshima and Nagasaki, effectively ending the war. Bird and Sherwin also follow Oppenheimer's career after the war, describing the lingering guilt he expressed over the hundreds of thousands of civilians who died following the bombing. Oppenheimer vehemently opposed the development of a hydrogen bomb that would be more powerful and devastating than the uranium-core atomic bomb his team engineered at Los Alamos. He also became the director of the Institute for Advanced Study in Princeton, New Jersey, developing a relationship with fellow physicist Albert Einstein, amongst others. Part Five details Oppenheimer's security hearing and how the subsequent loss of his security clearance impacted his career and personal life, up to his early death at the age of 62 from cancer.
Overall, Bird and Sherwin do their very best to paint neither a positive nor negative portrait of Oppenheimer and those in his orbit, but to paint an honest one. The sheer volume of interviews with people who knew or interacted with Oppenheimer, whether the feedback was positive, negative, or neutral, is a testament to Bird and Sherwin's dedication to providing the reader with as many perspectives on the man's actions and personality as possible. One of the most intriguing aspects of *American Prometheus* is the inclusion of FBI wiretap transcripts. For much of Oppenheimer's career, he was being monitored, and it's interesting to see exactly what he was saying that caused the United States government so much concern. *American Prometheus* won the Pulitzer Prize for a reason, and it's an excellent read, regardless of whether you choose to watch the film it inspired.

Review by Jeanette S. Ferrara, MFA