XtaLAB Synergy R

Single crystal X-ray diffractometer

The World's Fastest Diffractometer

Rigaku

POWERING NEW PERSPECTIVES

XtaLAB Synergy R – The World's Fastest Diffractom

The XtaLAB Synergy-R.

INTRODUCTION

A unique combination of cutting edge technologies allows the XtaLAB Synergy-R to claim the title of "World's Fastest Diffractometer". The synergistic effect of a bright X-ray source, a fast goniometer, an extremely low-noise, photon-counting detector, a fast and efficient strategy algorithm, and a highly parallelized control/processing software package leads to an instrument that can perform a single crystal experiment so rapidly that, for normal crystals, XtaLAB Synergy-R can be considered a walkup structure solution machine. For difficult samples, the XtaLAB Synergy-R can greatly reduce data collection time and it has the flexibility to easily help you optimize your experiment.

This tightly integrated instrument has four basic areas of technology. First, the PhotonJet-R X-ray source is based on the widely used MicroMax™-007 HF rotating anode generator with newly designed Osmic confocal optics, a continuously variable slit assembly, and improved alignment capabilities. Second, the efficient kappa goniometer has been sped up to minimize time between frames, as well as allowing ultra-fast scan speeds to take advantage of the bright X-ray source. Third, Rigaku's HyPix-6000HE detector is a direct detection, photon counting detector with extremely low noise and high dynamic range.

Weak and strong reflections can be measured simultaneously on the same frame, thus reducing overall data collection time. Finally, sophisticated software algorithms tie the hardware together to minimize the time it takes to measure and solve single crystal structures.

FAST CRYSTALLOGRAPHY ON A DIFFICULT SAMPLE

WEAKLY DIFFRACTING SAMPLE WITH A LONG UNIT CELL AXIS

To put the XtaLAB Synergy-R to the test, we were kindly donated a sample from the University of Southampton. The sample was challenging in that it had a long axis of nearly 51 Å and was also very weakly diffracting. Data was collected at a temperature of 100 K with the detector distance at 34 mm from the sample. We took advantage of the HyPix-6000HE by running in shutterless mode. This meant that a complete Cu data set was collected to 0.837 Å in 1 hr 17 mins with the total dose time 1 hr 15 mins.

An image of the long axis crystal mounted on a MiTeGen loop.

The data was processed using the automatic algorithms in CrysAlis^{Pro} with a face indexed absorption correction applied.

Sample details	
Crystal dimensions	0.018 mm x 0.030 mm x 0.152 mm
Space group	$P2_1/c$
a, b, c	4.94985 Å, 50.94373 Å, 8.95041 Å
β	99.8624°
V	2223.6 Å^3

EXCELLENT SPOT RESOLUTION

Despite the long unit cell axis and the close detector distance, only 0.61% of spots exhibited any overlap. This very low level of overlap meant that the resulting integration proceeded without the need for reducing the size of the integration mask profile. The figure at the top of the next page is a visual representation of this good spot resolution. When a row of spots is dissected, no overlap is observed.

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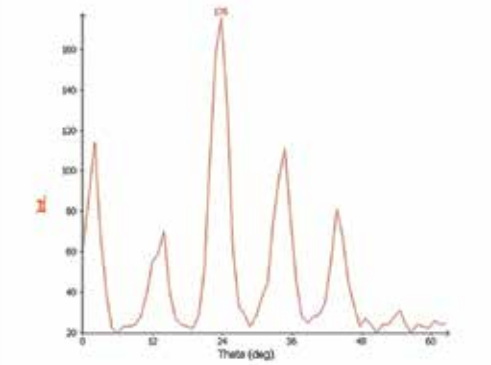
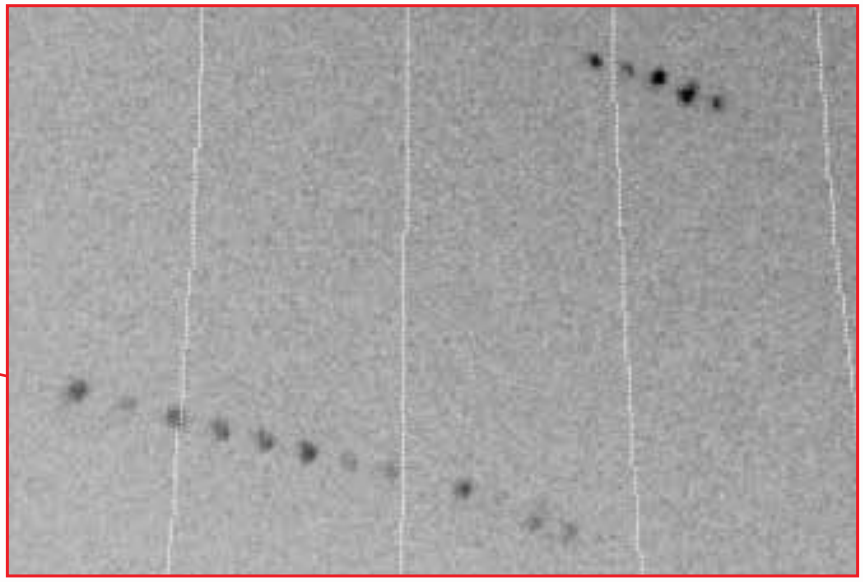
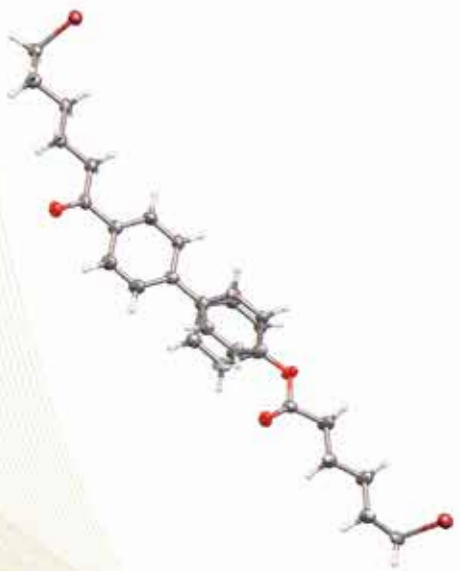




Diffraction images from the HyPix-6000HE detector showing good spot resolution of a long unit cell axis (50.9 Å) sample.

The structure was solved using AutoChem 3.0, and the programs contained within, to give an R-factor of 7.39%. The structure itself displays a static disorder across the terminal pair of carbon atoms of a central six-membered planar ring. This was resolved to a simple 50% distribution over the two positions.

Experiment details	
2θ range for data collection	6.938 to 146.976°
Index ranges	-5 ≤ h ≤ 5, -62 ≤ k ≤ 61, -8 ≤ l ≤ 10
Reflections collected	10825
Independent reflections	4188 [R(int) = 0.0743]
Data / restraints / parameters	4188 / 0 / 299
Goodness-of-fit on F^2	1.122
Final R indexes [I>=2σ (I)]	R_1 = 0.0739, wR_2 = 0.1765
Final R indexes [all data]	R_1 = 0.0937, wR_2 = 0.1844
Largest diff. peak/hole / e $Å^{-3}$	0.90 / -1.10

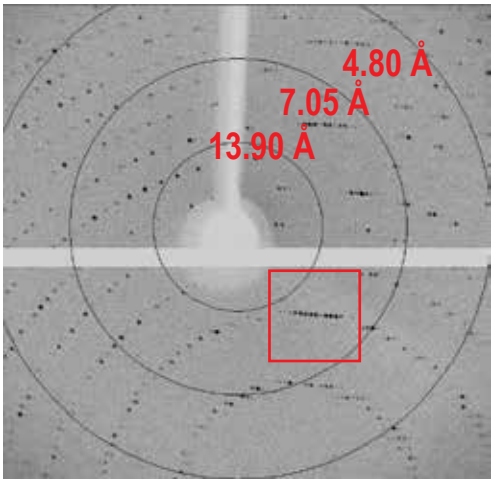


Optimized to accommodate difficult samples

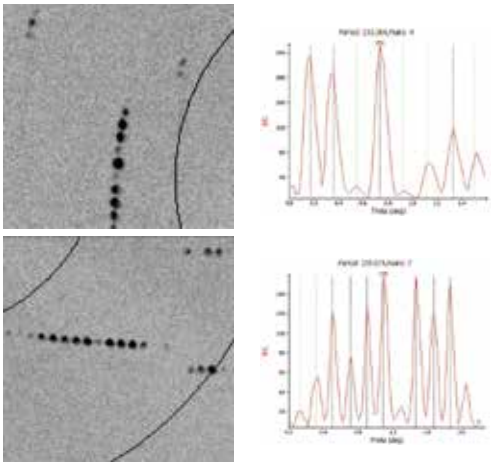
Catalase on the HyPix-6000HE, resolution of 230 Å cell length

Whether you are working on difficult protein samples or difficult small molecule samples, your experiments will be much easier to perform if your hardware is designed for difficult cases. The XtaLAB Synergy-R is equipped with a motor-controlled variable slit system that is particularly useful for resolving reflections from large unit cells.

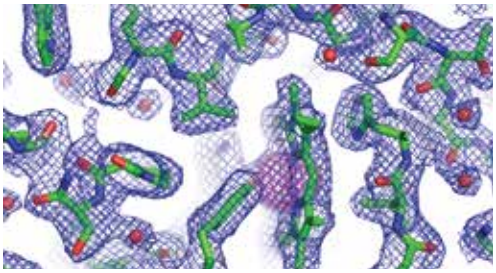
Additionally the HyPix-6000HE detector has a small 100 µm pixel size, combined with a point spread function defined by the pixel size, which means that reflections are more easily resolved at close crystal-to-detector distances.



Detector distance of 120 mm.



Good spot separation at 120 mm.



Representative 2Fo-Fc (blue) and anomalous difference Fourier (magenta) electron density maps for catalase refined to 2.40 Å and contoured at 1.0 rmsd and 4.0 rmsd, respectively.

SCREENING CATALASE USING THE XTALAB SYNERGY-R

Screen images were collected on a crystal of catalase with dimensions of 200 µm x 150 µm x 100 µm, using a HyPix-6000HE detector. Images were collected using CrysAlis^{Pro} and an exposure time of 10 sec. / 0.10º. The figure to the left shows the full diffraction image obtained at a detector distance of 120 mm and with the variable slits in place. The red square indicates the row of reflections used to check for reflection separation at each detector distance.

DATA COLLECTION ON CATALASE USING THE HYPIX-6000HE

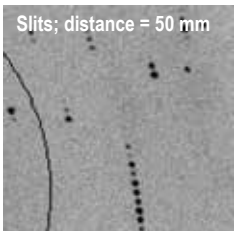
A data set was collected on this crystal with the aim of solving the crystal structure of catalase by molecular replacement. A data collection strategy was calculated by CrysAlis^{Pro} to 2.4 Å and data were collected with CrysAlis^{Pro}.

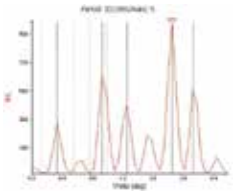
Details for integration and scaling	
Space group	$P2_12_12_1$
Unit cell	85.63 Å, 138.65 Å, 230.27 Å
Resolution	2.40 Å
# observations / unique	568865 / 109667
Redundancy (last shell)	5.8 (1.8)
Completeness (last shell)	89.0% (47.0%)
$\langle I/\sigma I \rangle$ (last shell)	27.6 (1.2)
R_{merge} (last shell)	6.9% (51.9%)

CRYSTAL STRUCTURE OF CATALASE BY MOLECULAR REPLACEMENT

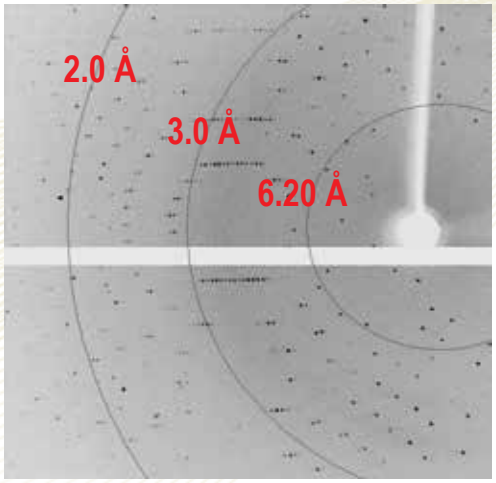
The crystal structure of catalase was solved by molecular replacement in space group $P2_12_12_1$ using HKL-3000R® and using PDB ID '4BLC' as a starting model. The ligands and water molecules were removed from the starting model, but the heme molecules were kept. The R_{fac} and R_{free} values, after molecular replacement, were at 23.8% and 29.2%, respectively. The model was further refined for 10 cycles with Refmac, 1054 water molecules were added with ARP/wARP and 10 more refinement cycles were run. The final R_{fac} and R_{free} were at 18.9% and 27.3%, respectively. All the side chains fitted into their electron density, so no manual adjustment was needed in Coot. The final 2Fo-Fc contoured at 1.0σ is shown to the left. Note how prominent the anomalous difference Fourier peak (contoured at 4.0σ) for Fe in the heme ligand is, and how well it matches the location of the Fe atom.

Gorgeous structure of thaumatin obtained by S-SAD phasing in 2 hr 34 min

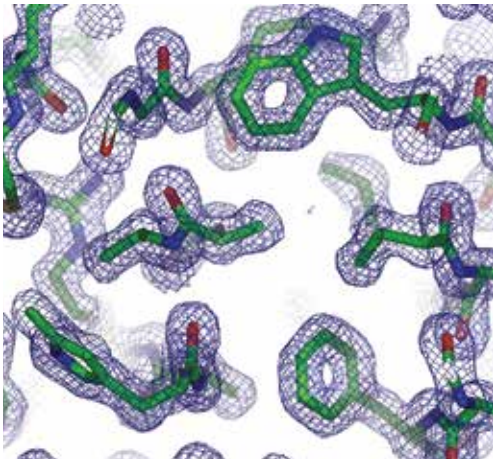




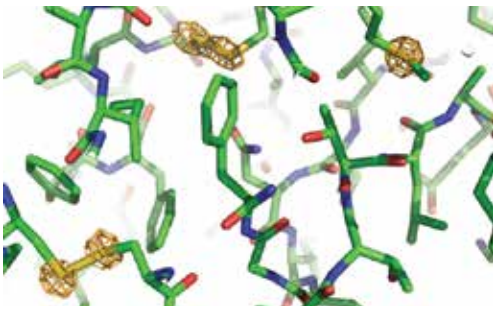
150 Å axis parallel to the rotation axis.



Data collection image.



2Fo-Fc map contoured at 1.5σ.



Anomalous map contoured at 4σ and showing two disulfide bonds and a methionine.

SCREENING THAUMATIN USING THE XTALAB SYNERGY-R

Screen images were collected on a crystal of thaumatin with dimensions of 300 µm x 200 µm x 200 µm, using a HyPix-6000HE detector and the variable beam divergence optic. Images were collected using CrysAlis^{Pro} with the slit at the minimum position and an exposure time of 1-2 sec / 0.25º. At a detector distance of 50 mm, it is easy to see how useful the variable slits are for peak separation.

DATA COLLECTION ON THAUMATIN USING THE HYPIX-6000HE

This thaumatin crystal was used to collect a data set with the aim of solving the crystal structure by the S-SAD phasing method. CrysAlis^{Pro} calculated a strategy for a redundancy of 15 at 1.8 Å. Data from the two best scans in terms of $\langle I/\sigma(I)\rangle$ and R-factors were sufficient to solve the crystal structure and amounted to a data collection time of 2 hours and 34 minutes. With the data processed to 1.7 Å, the overall redundancy was 6.1 with the Bijvoet pairs merged and 3.4 with the Bijvoet pairs separate.

S-SAD PHASING METHOD FOR THAUMATIN

HKL-3000R used SHELXD to find the heavy atom sites, MlPhare and DM for phasing and density modification, ARP/wARP to trace the protein and place the waters and Refmac to refine the model. All 17 sulfur sites were located by SHELXD and the Figure of Merit for subsequent phasing was 78% to 1.8 Å. Using the sequence from PDB ID '1RQW', 99% of the model was built after 6 autobuilding cycles in ARP/wARP, yielding R_{fac} and R_{free} of 18.3% and 21.8%, respectively. A few side chains were then manually adjusted into their electron density, some more water molecules were placed with ARP/wARP and the model was submitted to additional atomic restrained refinements with Refmac. The final R_{fac} and R_{free} were 14.3% and 18.4%, respectively, for a Figure of Merit of 90.3%.

Details for structure solution and refinement	
Resolution for heavy atoms search	2.5 Å
Corr. Coef. for heavy atoms solution (all data / weak data) # heavy atom sites selected from solution	31.0 / 12.7 19
Resolution used for phasing and density modification FOM after density modification	1.8 Å 0.78
# residues built / # waters added	205 (99%) / 202
R_{fac} / R_{free} after 6 autobuilding cycles	18.3% / 21.8%
Final # waters after additional run of ARP/wARP	333
Final R_{fac} / R_{free} after water addition and manual side chain adjustment	14.3% / 18.4%

XtaLAB Synergy R – The World's Fastest Diffractom

KEY SOURCE FEATURES

- **High flux:** PhotonJet-R X-ray source based on the world's most popular microfocus rotating anode X-ray generator: MicroMax-007 HF. Ten times the flux of the current microfocus sealed tube sources.
- **Beam conditioning:** Innovative, continuously variable slit system for easy beam size and divergence selection.
- **Improved performance:** New optics and alignment mechanism for maximum performance and minimal alignment effort.
- **Large user base:** With over 1000 units in use around the world, the MicroMax-007 HF source provides peace of mind for years into the future.
- **Flexible configurations:** Available with Cu, Mo, or Ag or as a dual wavelength model with a double banded, Cu/Mo anode.

KEY GONIOMETER FEATURES

- **Fast:** New, faster motor speeds optimized to take advantage of the high-flux X-ray source.
- **Optimal design:** A kappa geometry design that is so efficient that it can measure reciprocal space up to 33% faster than with a fixed-chi design.
- **Large cell friendly:** New telescoping 2θ arm provides long crystal-to-detector distances necessary for resolving large unit cells.
- **Ergonomic:** Electronically controlled brightness of goniometer illumination and crystal lighting.
- **Designed for efficiency:** Improved ±2θ accessibility for more efficient data collection strategies.

What really matters

Instrument companies love to talk about specifications and Rigaku is no exception. However, we realize that what really matters to our customers is data quality, ease of use, speed, experimental flexibility, ease of maintenance, etc. Specifications only tell part of the story – it is the synergy between all the technologies that provides the real benefit.

Data quality is a function of many things, but two aspects of the XtaLAB Synergy-R have a particularly large impact on data quality: lots of photons hitting the sample and using a detector that is essentially noise free and can measure weak reflections and strong reflections on the same frame. More photons means better I/σ and a low noise detector means that weak reflections are measured better.

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KEY DETECTOR FEATURES

- **Low noise:** The HyPix-6000HE is a photon counting, pixel array detector so there is no noise (e.g. dark current) accumulated during an integration step, and there is no conversion of an analog signal to a digital signal, which would also add noise.
- **Sharper peaks:** The HyPix-6000HE does not use a phosphor or have the associated generation of light - the point spread function of a pixel array detector is defined by the size of the pixel.
- **Better dynamic range:** The HyPix-6000HE has two 16-bit counters, giving it a large dynamic range of 2^{16} with each readout, up to 100 Hz.
- **No rescans:** The combination of extremely low noise and high dynamic range means that with an HPC detector you can measure weak and strong reflections reliably on each frame.
- **Shutterless data collection:** The use of two alternating counters reduces the deadtime due to reading to such a negligible number that shutterless data collection is the default mode.

KEY SOFTWARE FEATURES

- **Large user community:** XtaLAB Synergy-R is controlled by CrysAlis^{Pro} software, one of the world's most popular data collection and processing packages.
- **User inspired:** Rigaku Oxford Diffraction's software team makes a concerted effort to incorporate features and areas of functionality based on our customers' ideas and feedback.
- **Optimized for speed:** Multi-threaded environment. which means that all hardware and software modules run in parallel to achieve the highest efficiency and speed.

s: Key user benefits

Experimental flexibility – For challenging samples, it is always important to have flexibility built into the instrument. XtaLAB Synergy-R offers a number of design features that extend experimental flexibility. A continuously variable computer-controlled slit system makes resolution of large unit cells quite easy. The HyPix-6000HE detector has the ability to suppress fluorescence through energy thresholding.

Speed – When we say that XtaLAB Synergy-R is the world's fastest diffractometer, we are not just referring to the slew speeds. Instead, we mean that XtaLAB Synergy-R can produce structures faster than any other instrument. This is achieved by having a six-fold increase in flux (acceptable counting statistics are achieved quicker), fast slew speeds, fast scan speeds, fast and efficient data collection strategies and a detector that can measure weak and strong reflections at the same time.

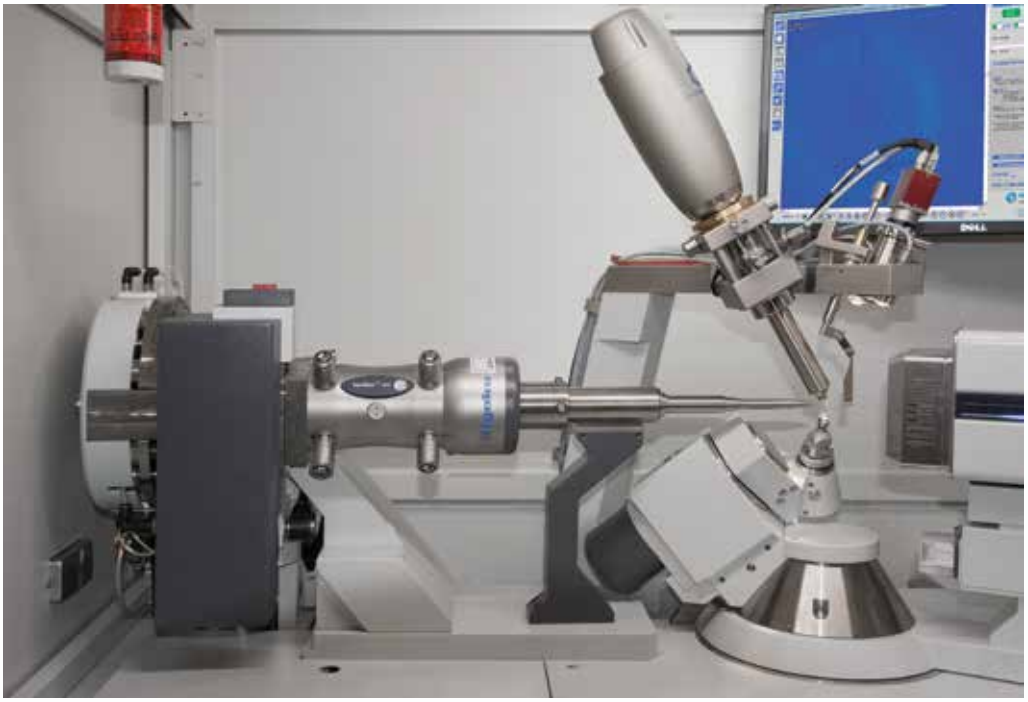
Dual Wavelength Rotating Anode

The Synergy DW diffractometer is so compact that it easily fits in the standard Synergy enclosure.

The Synergy-DW is a truly revolutionary diffractometer. It combines the increased flux that can be obtained from a rotating anode X-ray source with the flexibility of being able to switch between two different wavelengths. Even better, this can all be done with one X-ray source because the rotating anode target is constructed with two different source materials (Cu and Mo) and the optics assembly contains both a Cu and a Mo optic.

The switch between Cu and Mo is accomplished in only five minutes. The anode is automatically translated along the shaft direction to line up the desired anode target material with the cathode assembly. The optics housing is automatically rotated so that the corresponding optic is in alignment with the focal spot on the anode. The mechanism for both movements is so precise that it is not necessary to perform any realignment after switching from one wavelength to the next.

The Synergy-DW is the perfect system for laboratories that work with extremely difficult samples that need the enhanced flux of rotating anode sources, as well as have a large array of samples that can benefit from having Mo and Cu available for structure analysis. The fact that this is accomplished utilizing only one generator means overall maintenance is reduced.



Close up view of the DW anode shifting mechanism and dual wavelength optics assembly.

Innovative Software

CrysAlis Pro SM

For small molecule samples, CrysAlis[Pro] combines automated crystal screening, the fastest, most accurate strategy software available, concurrent data reduction and automatic structure solution with refinement by AutoChem, giving you visual feedback in the shortest time possible.

STRUCTURES IN SECONDS WITH "WHAT IS THIS?"

If the initial diffraction pattern indicates that you can continue, a new feature called WIT, or "What Is This?", collects a rapid data set, indexes the cell, determines if it has been previously published (by searching the Cambridge Structural Database) and simultaneously attempts to solve the structure. For well-diffracting crystals, it is possible to collect data, process it and see the atomic connectivity in one or two minutes. WIT relies on parallelized data collection and data reduction threads, as well as the new AutoChem pipeline.

A quick structure determination serves two purposes. First, it tells you whether this is a molecule or structure of interest, and whether you want to continue or not. Second, and perhaps more important, improved structure information allows the software to do a better job of calculating the strategy for a better, publishable data set.

CrysAlis[Pro] links into Olex2, the world's most popular small molecule structure solution program, via AutoChem, Rigaku Oxford Diffraction's automatic structure solution interface. After the first 25 images of data are collected, AutoChem will try to solve the structure and, as more data are collected, build upon or refine the solution.

After evaluation of these results, the user may want to interact with the experiment to add to the strategy in the middle of the experiment, without disturbing the current data collection.

FULLY INTEGRATED WORKFLOW

StructureExplorer, based on the AutoChem/Olex2 pipeline, is an integral part of CrysAlis[Pro] that combines data reduction and finalization with structure modelling and refinement. Key features include:

- AutoChem and AutoComplete support.
- Simple intuitive viewer.
- One-click twin handling.
- Support of SHELXL2014, SHELXS, SIR, SUPERFLIP, SHELXD, SHELXT and olex2.solve/refine.
- Pre-publication "Checklist" feature with direct links to re-finalization window, for face indexing, and to strategy window, if additional data needs to be collected.

WIDE RANGE OF CRYSTALLOGRAPHIC APPLICATIONS

In addition to standard structure determination from single crystals, a wide range of crystallographic experiments can be performed including:

- Powder diffraction experiments, incorporating Gandolfi motion to remove preferred orientation.
- Multi-temperature and multi-wavelength experiments fully controlled by CrysAlis[Pro].
- High-pressure data collection with strategy and data reduction optimized for diamond anvil cells.
- Incommensurate structures and studies of quasi-crystals.

CrysAlis Pro PX

The XtaLAB Synergy-R is the perfect low-maintenance home lab instrument for collecting high-quality data, as well as screening of crystals for synchrotron experiments. Dedicated protein features include:

- Data collection, processing and scaling in a single package.
- Crystal screening tool for testing crystals in quick succession.
- The fastest, most accurate strategy software available as well as processing and scaling algorithms optimized for macromolecular crystallography.
- Support for importing and processing data from synchrotrons and third-party detectors, including imaging plate, CCD, CMOS and HPC detectors.
- Export of images to MOSFLM, XDS, or HKL.
- Automatic data scaling and merging using AIMLESS to prepare data for structure determination and refinement by CCP4 and PHENIX programs.

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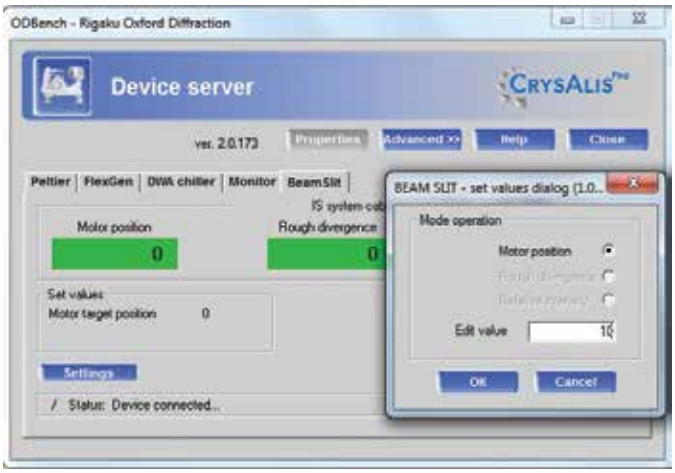
The Synergy slit assembly is integrated into the collimator holder and is controlled by the software package, CryAlis^{Pro}.



Software control of the slit assembly means that optimization of the divergence angle can be quickly carried out without the need to swap hardware or enter the radiation enclosure.

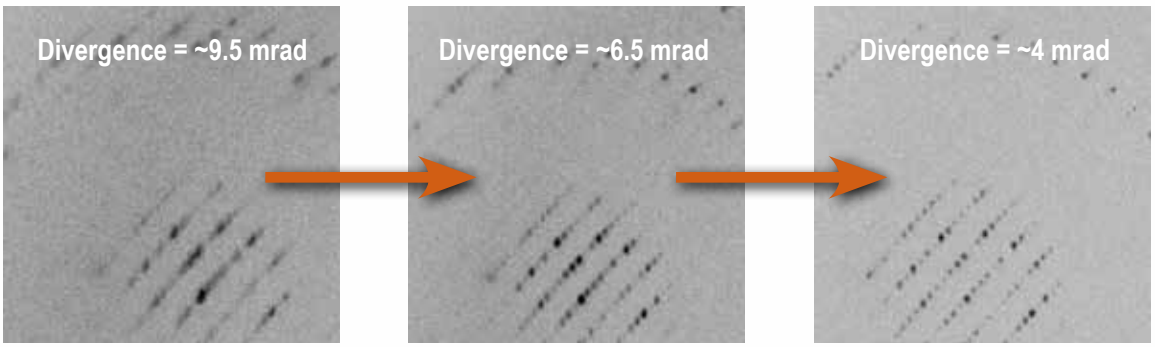
When diffraction events overlap on the detector it becomes difficult or impossible to accurately measure data. This can occur in two particular cases: when one or more unit cell axes are large relative to the wavelength being used and when the diffraction pattern of a twinned sample results in many partially overlapped reflections.

A standard practice for improving resolution between overlapping reflections is to use a longer crystal-to-detector distance. This of course reduces the effective size of the detector in terms of capturing reflections. The proper application of divergence slits will provide more efficient data collection as the detector can remain close to the sample, keeping the effective size of the detector aperture larger. For instance, the diffraction images of the protein catalase shown below have been collected by keeping the detector just 70 mm away from the sample.

Rigaku Oxford Diffraction's variable slit assembly (patent pending) allows the divergence of the beam to be varied continuously between 10 mrad and 1 mrad. The variation of the divergence is operated under computer control through the CryAlis^{Pro} software package.

There are many advantages of a computer controlled variable divergent slit assembly compared to fixed divergence collimators that must be manually swapped. Variable divergence allows the user to minimize divergence reduction for a particular experimental problem while maximizing the flux hitting the sample.

The ability to control the divergence under computer control means that the user can optimize the divergence of a particular sample without entering the enclosure to swap collimators, risking disturbing the sample as well as slowing down the optimization process.



The protein catalase has a 229 Å axis that requires reduction of the divergence angle in order to properly resolve the reflections. These images were obtained at a crystal-to-detector distance of 70 mm.

Rigaku's **HyPix-6000HE** detector is a direct detection, photon counting detector with all the associated benefits of extremely low noise, essentially zero deadtime, and true shutterless data collection.

HyPix-6000HE

The HyPix-6000HE is a Hybrid Photon Counting detector (HPC) detector and some of the benefits of this technology include:

LOWER NOISE: The advantage of a counting detector as opposed to an integrating detector is that there is no noise (e.g. dark current) accumulated during an integration step, and there is no conversion of an analog signal to a digital signal, which also adds noise. With a counting detector, the pulses are immediately digitized as an X-ray event occurs.

SHARPER PEAKS: Since an HPC does not use a phosphor or have the associated generation of light, the point spread function of an HPC detector is defined by the size of the pixel. This sharpens reflections and improves the ability to resolve large unit cells, or, in normal cells, allows you to move the detector closer to the crystal. The small pixel size (100 µm x 100 µm) means smaller peak sizes and easier resolution of nearby reflections.

BETTER DYNAMIC RANGE: The HyPix-6000HE has two 16-bit counters, giving it a large dynamic range of 2^{16} with each readout, up to 100 Hz. With a phosphor-based integrating detector, the gain from the phosphor must be divided into the full-well depth, and the effective dynamic range is much smaller. For phosphor-based detectors, this means that strong reflections must be measured in a separate, fast data collection and later merged with data collected at a slower speed to properly measure the weak data.

WEAK AND STRONG DATA CAN BE MEASURED TOGETHER: The combination of extremely low noise and high dynamic range means that with an HPC detector you can measure weak and strong reflections reliably on each frame. There is no need to measure two data sets and scale the weak and strong reflections after the fact.

TRUE SHUTTERLESS DATA COLLECTION: The use of two alternating counters reduces the deadtime due to reading (the time it takes to switch between the counters) to such a negligible number that shutterless data collection is the default mode. Since weak and strong data can be measured accurately simultaneously, only one data collection is necessary.

XtaLAB Synergy R

Single crystal X-ray diffractometer

www.rigaku.com/products/crystallography

Your Success is Our Focus

The employees of Rigaku Oxford Diffraction are dedicated to providing the best solutions for single crystal analysis, whether it be small molecule or macromolecule related research. Our inspiration comes from helping you solve your difficult experimental problems and our personal satisfaction derives from helping you achieve your research goals.

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info@rigaku.com | www.rigaku.com

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