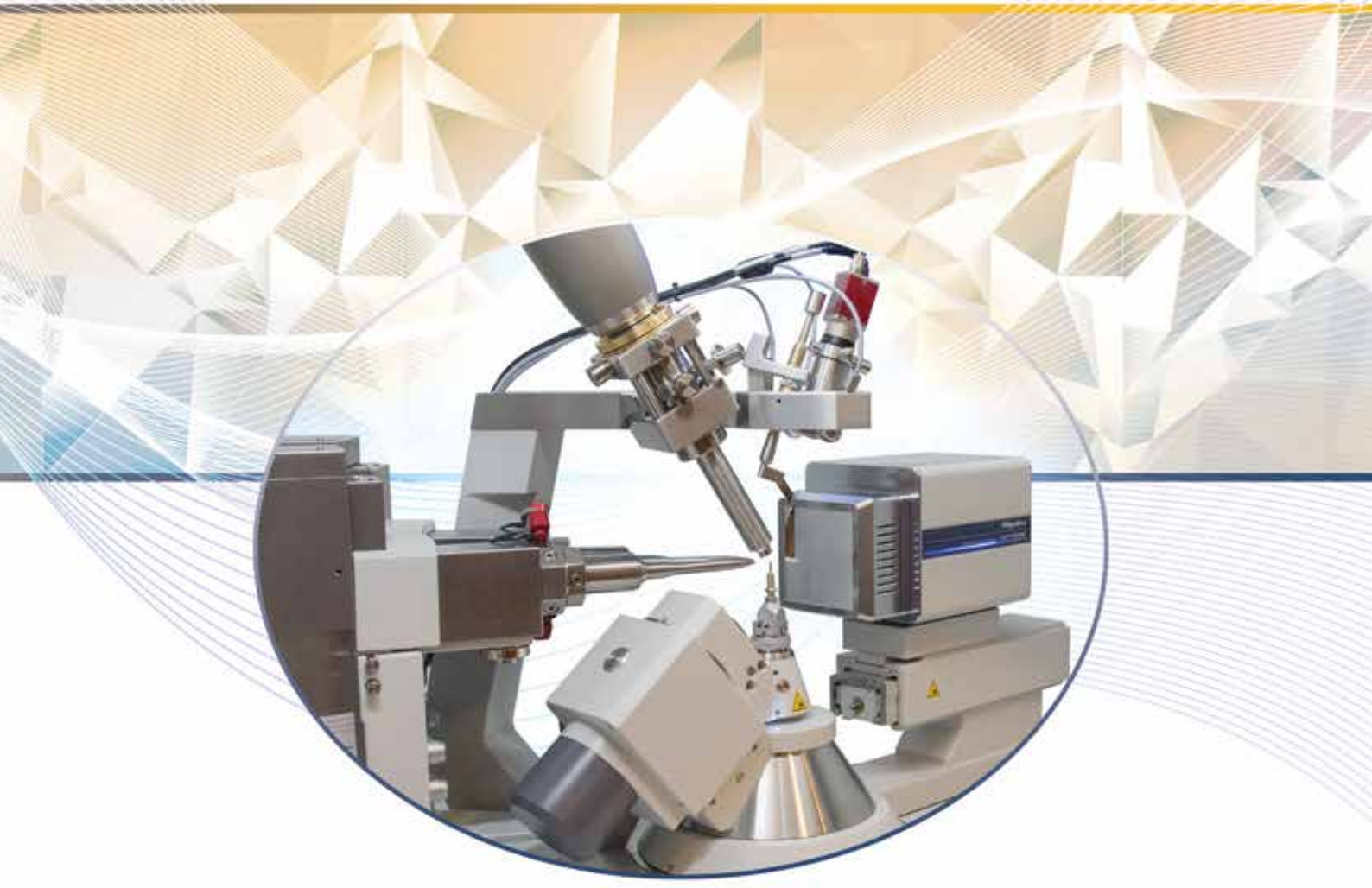
XtaLAB Synergy S

Single crystal X-ray diffractometer

Advanced technologies applied to single crystal diffraction



Rigaku

POWERING NEW PERSPECTIVES

XtaLAB Synergy S – Fast, Precise, Intelligent

CONTINUITY AND INNOVATION

The common goal of any single crystal experiment is to efficiently and accurately measure reciprocal space data. This is true whether you are determining the structure of a novel chemical compound, screening a crystal before a synchrotron trip or measuring highly redundant, high-resolution data for a charge density study or S-SAD phasing. In all cases, the quality of data generated by your diffractometer, as well as the speed and ease by which you can measure the data, is paramount to the success of your research. With your success utmost in our mind, we have produced the XtaLAB Synergy-S, a diffractometer combining leading edge components and user-inspired software tied together through a highly parallelized architecture to produce fast, precise data in an intelligent fashion.

The radiation enclosure for the XtaLAB Synergy-S diffractometer was designed using ergonomic principles to make your experimental experience more rewarding.

KEY FEATURES

- User-inspired CrysAlis^{Pro} software tightly integrated with new goniometer features and highly parallelized for speed and throughput.
- "What is This?" software function for small molecule structure determination in minutes.
- PhotonJet-S, third-generation microfocus X-ray sources with longer tube life, higher-performance optics, improved alignment mechanism and, best of all, higher flux.
- Single or dual source options (Cu, Mo or Ag) with 3-year tube warranty.
- HyPix-6000HE, Hybrid Photon Counting (HPC) detector has extremely low noise and high dynamic range.
- Goniometer includes faster motor speeds, telescoping 2θ arm, electronically controlled brightness of cabinet and crystal lighting, and ±2θ accessibility for more efficient data collection strategies.
- New enclosure conforms to the most stringent of X-ray safety guidelines and offers ample experimental workspace and accessibility.
- True shutterless data collection. The high dynamic range of the detector means that weak and strong reflections can be measured on the same image and there is no need to perform a fast data set to measure strong reflections.

GAP-FREE RECIPROCAL SPACE

There are two types of gaps in reciprocal space, and each type must be accounted for in an ideal instrument. The first gap relates to the completeness of data collection, and is a function of the strategy algorithm that is utilized and the hardware's ability to efficiently execute a strategy. The second gap relates to systematic under-measurement of a specific class of reflections, which can occur, for example, when the noise level of a detector swamps the signal in weak reflections.

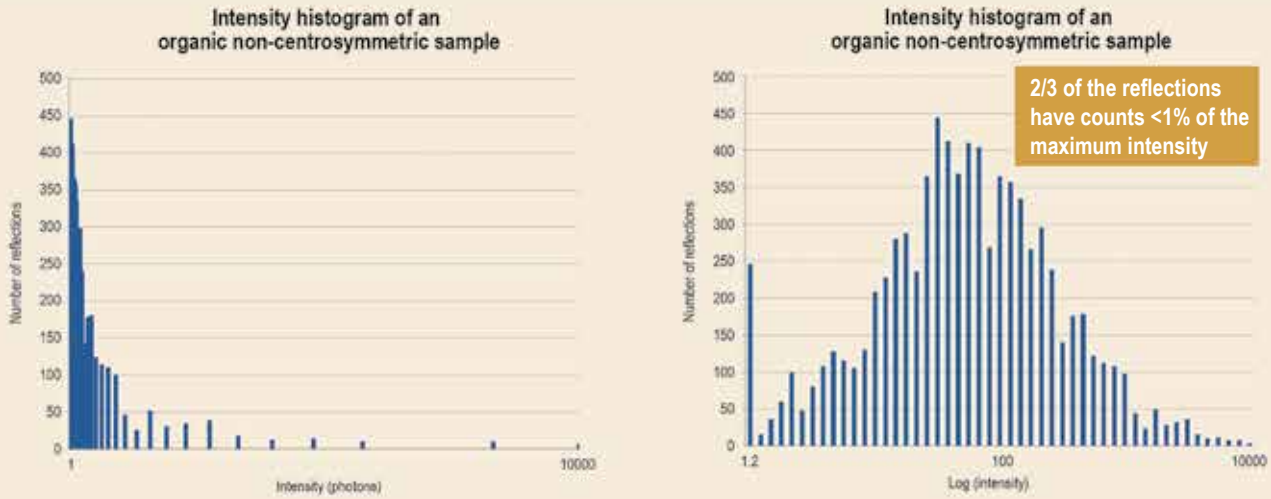
In the past, the process of calculating an efficient strategy was so arduous that users often resorted to a canned set of scans that was known to always produce a complete set of data, albeit in an inefficient and time-consuming manner.

Our approach is different. We think your time is valuable. Our strategy algorithm is quick, highly efficient and easy to use, and thus is a standard part of the workflow. The goniometer plays a key role in efficient data collection; thus we only offer the kappa-geometry goniometer. The kappa design is so much more efficient that it can measure reciprocal space up to 33% faster than with a fixed-chi design. Finally we have optimized slew speeds and even implemented forward and reverse scanning in order to minimize the time between scans.

Gap-free reciprocal space refers not only to measuring a data set to IUCr acceptable completeness, but also to the proper measurement of weak reflections so that they have sufficient information content for use in refinement. A diffractometer that does not allow for accurate measurement of weak reflections introduces a gap in your measurement of reciprocal space. Detectors with a high-noise threshold are the biggest sources of such a gap. We avoid this problem with proper detector selection and proper adjustment of data collection parameters.

Any diffractometer can measure strong reflections well, but the true test of an X-ray detector is the ability to measure weak reflections well. By far the most important factor for accurately measuring weak reflections is the inherent DQE (Detective Quantum Efficiency) of the detector in the area of low count rates. The DQE for low level measurements (<100 photons) can drop off dramatically for certain detector types based on inherent noise limitations of the detector technology. HPC detectors have the same DQE for one photon as for 10,000 photons.

THE IMPORTANCE OF WEAK DATA



Linear (left) and Log (right) plots of the intensity distribution for an organic structure, illustrating that the majority of reflections are weak, with counts less than 1% of maximum intensity.

To understand the importance of weak data in structure analysis, it is informative to look at a typical example. A data set was calculated for an organic non-centrosymmetric structure with an average $I/\sigma = 10$. As shown in the above plots of the intensity distribution as a function of reflection intensity, weak data dominate. The intensity distribution is strongly biased toward low intensities, with 2/3 of the data having intensities lower than 1% of the maximum intensity. Since the majority of reflections are weak, even in a well-diffracting crystal, proper measurement of these weak reflections is crucial to achieve a better refined structure.[†]

[†] Hirshfeld, F.L.; Rabinowich, D. T*reating Weak Reflexions in Least-Squares Calculations.* Acta Crystallogr. 1973, **A29**, 510–513.; Arnberg, L.; Hovmöller, S.; Westman, *S. On the Significance of 'Non-Significant' Reflexions.* Acta Crystallogr. 1979, **A35**, 497–499.

Thus, it is most important to give careful consideration to the choice of detector when configuring a diffractometer, as one should select the detector with characteristics that best suit your experimental needs. Rigaku Oxford Diffraction offers an HPC-based detector because of the extremely low noise characteristics, and high dynamic range allows accurate measurement of weak and strong reflections simultaneously.

HPC detectors are characterized as hybrid pixel array detectors (HPAD) because they are comprised of both a pixelated silicon sensor and silicon electronics, connected at each pixel by a bump bond. In an HPC detector, each pixel is essentially an individual detector. HPC detectors are direct detection devices as opposed to integrating; X-ray photons are directly converted into electric charge in the solid-state sensor, counted and stored immediately. HPC detectors are event driven so noise is not accumulated.

The Importance of Detector Selection

Rigaku's **HyPix-6000HE** detector is based on HPC technology with all the associated benefits of extremely low noise, essentially zero deadtime, and true shutterless data collection.

HyPix-6000HE

The HyPix-6000HE is an 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.

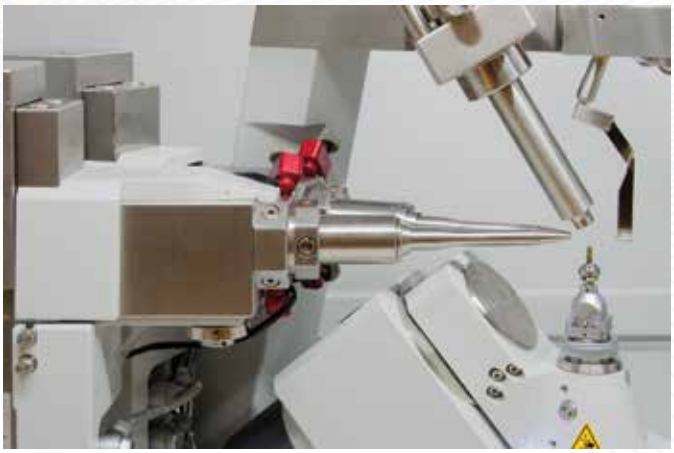
SHARPER PEAKS: Since an HPC does not use a phosphor or have the associated generation of light, the point spread function of an HPC detector is defined by the size of the pixel. This sharpens reflections and improves the ability to resolve large unit cells, or, in normal cells, allows you to move the detector closer to the crystal.

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.

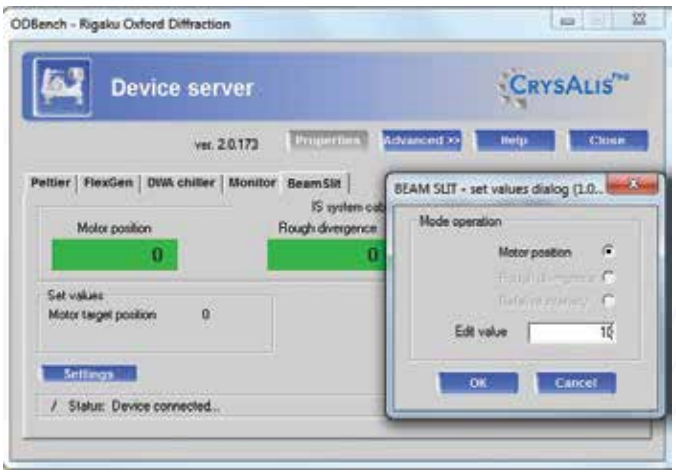
WEAK AND STRONG DATA CAN BE MEASURED TOGETHER: The combination of extremely low noise and high dynamic range means that with an HPC detector you can measure weak and strong reflections reliably on each frame. There is no need to measure two data sets and scale the weak and strong reflections after the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

The Importance of Beam Conditioning



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.

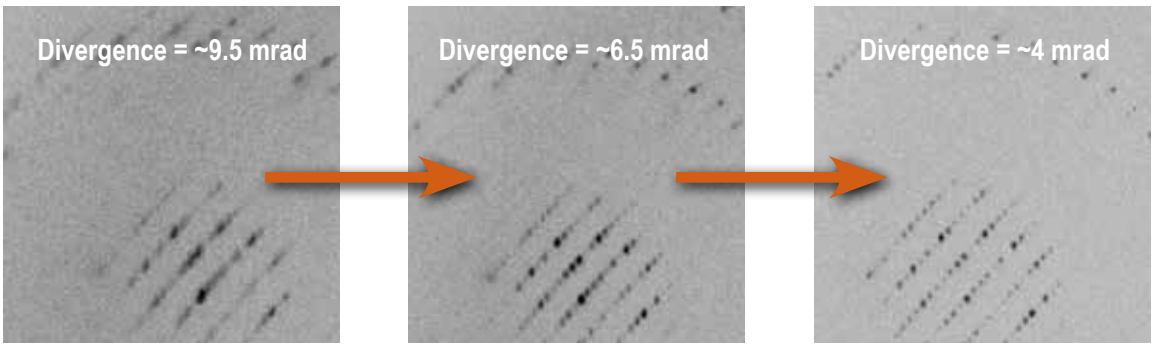
When diffraction events overlap on the detector it becomes difficult or impossible to accurately measure data. This can occur in two particular cases: when one or more unit cell axes are large relative to the wavelength being used and when the diffraction pattern of a twinned sample results in many partially 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 9.2 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.



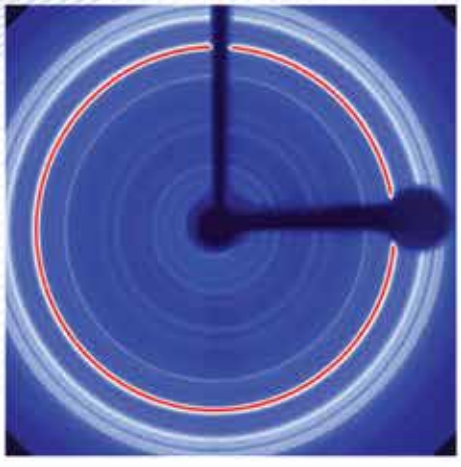
The protein catalase has a 229 Å axis that requires reduction of the divergence angle in order to properly resolve the reflections. These images were obtained at a crystal-to-detector distance of 70 mm.

XtaLAB Synergy S – Designed for Your Success

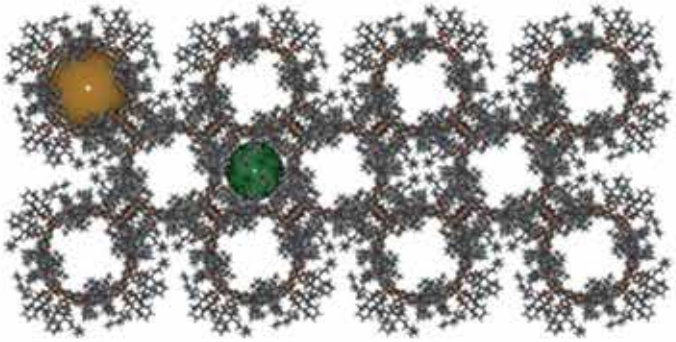
Unique benefits of the XtaLAB Synergy-S

- New PhotonJet-S microfocus sources – third generation microfocus X-ray sources with longer tube life, higher-performance optics, improved alignment mechanism and, best of all, higher flux.
- Single or dual source configurations from a selection of three targets: Cu, Mo, Ag.
- NEW goniometer – with motor speeds that have been **doubled** in order to minimize the time between scans and provide for extremely fast data collection.
- User-inspired cabinet design that features room for your microscope and tools.
- NEW electronically controlled brightness of cabinet and crystal lighting results in optimum video imaging for all types of crystal samples.
- Ultra low-noise, high dynamic range detector.
- Unique telescoping 2θ arm provides total flexibility for your diffraction experiment.
- Enhanced kappa goniometer design with symmetrical 2θ positioning to allow maximum efficiency for data collection strategies.

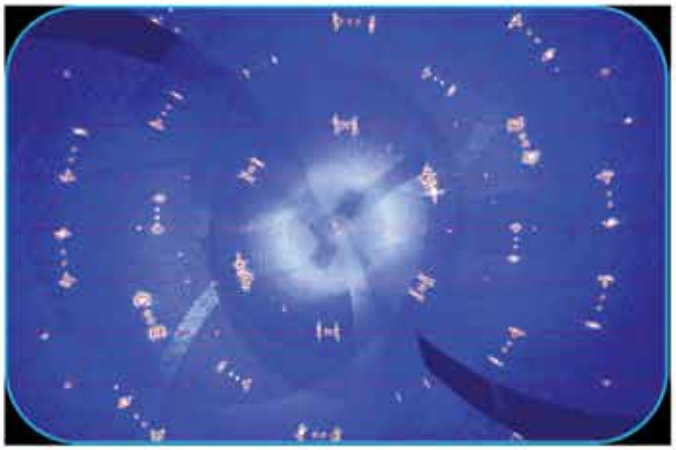
Dual-source configuration for the microfocus X-ray sources.



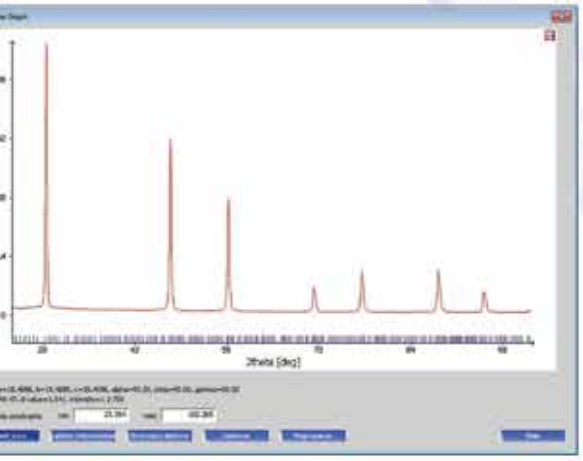
Powder diffraction data can be collected and processed on an XtaL
Identify your bulk material with the easy-to-use tools within CrysAli



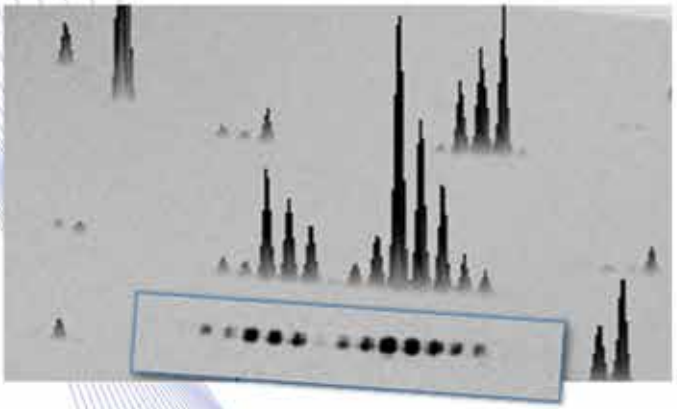
Cage structures are renowned for their weakly diffracting properties due to high solvent content in the pores or channels. The sensitive HyPix-6000HE detector, having high dynamic range, is particularly useful for detecting weak spots alongside the intense ones.



Reconstructed diffraction images can show evidence of super lattices within particular hkl planes. Visualising this phenomenon in two dimensions can make indexing easier. Particularly useful for inorganic samples where atoms have shifted within the lattice.



LAB Synergy-S system.
S[Pro].



Small pixels combined with a single pixel point spread function means you get improved resolution of reflections at the detector, so that you can collect data at shorter sample-to-detector distance and thus to greater resolution at the edge of the detector.

CrysAlis^Pro – the Nerve Center of the XtaLAB S

INTELLIGENCE WHERE IT COUNTS

XtaLAB Synergy-S is controlled by CrysAlis^Pro software, one of the world's most popular data collection and processing packages. CrysAlis^Pro is often referred to as "user-inspired software". Rigaku Oxford Diffraction's software team makes a concerted effort to incorporate features and areas of functionality based on our customers' ideas and feedback.

The design of CrysAlis^Pro features a multi-threaded environment. This means that all hardware and software modules run in parallel to achieve the highest efficiency and speed. This maximizes instrument use by automating mundane tasks, leaving you more time to work out the difficult problems that today's crystallographers face.

Selecting the proper crystal is one of the most important parts of a single crystal experiment. The XtaLAB Synergy-S' parallel architecture allows an incredibly fast initial crystal investigation. For example, once a crystal is mounted you typically know about the diffraction quality in less than ten seconds.

By simply clicking on the CrysAlis^Pro logo on the main screen, the user can select one of the two GUI modes: "SM" for small molecule experiments and "PX" for macromolecular data collection. Each of these modes gives access to customized menus and workflows with default parameters specific for the type of experiments the user wants to carry out.

CrysAlis^Pro SM

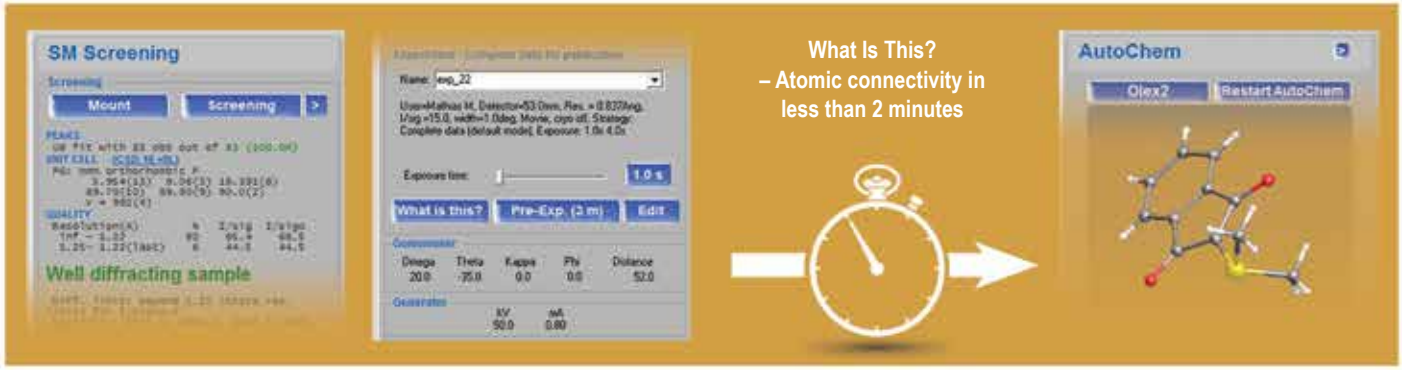
For small molecule samples, CrysAlis^Pro combines automated crystal screening, the fastest, most accurate strategy software available, concurrent data reduction and automatic structure solution with refinement by AutoChem, giving you visual feedback in the shortest time possible.

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 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, taking full advantage of a variety of structure solution and refinement programs with built-in support for multi-core speed enhancements.

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 system, 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.



ynergy-S

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

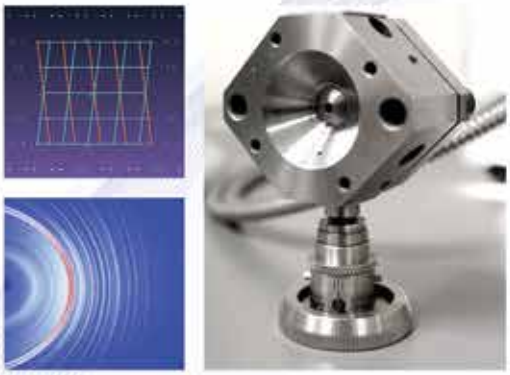
StructureExplorer, based on the AutoChem/Olex2 pipeline, is an integral part of CrysAlis^{Pro} that combines data reduction and finalization with structure modelling and refinement. Key features include:

- 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:

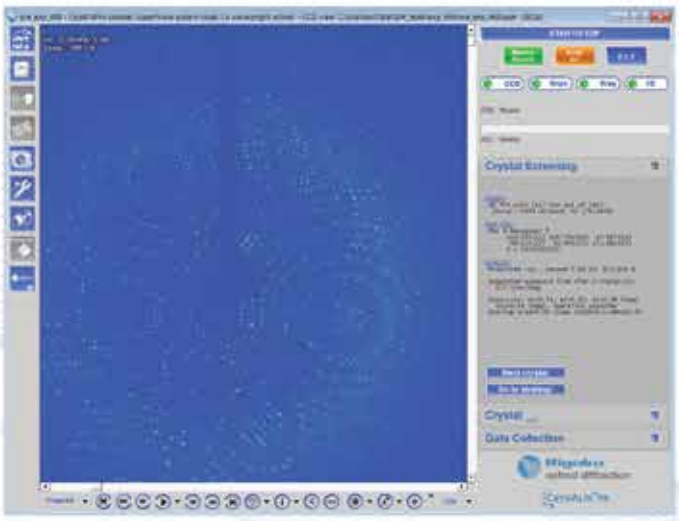
- Powder diffraction experiments, incorporating Gandolfi motion to remove preferred orientation.
- Multi-temperature and multi-wavelength experiments fully controlled by CrysAlis^{Pro}.
- High-pressure data collection with strategy and data reduction optimized for diamond anvil cells.
- Incommensurate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



CrysAlis^{Pro} PX

The XtaLAB Synergy-S 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 and HKL.
- Automatic data scaling and merging using AIMLESS to prepare data for structure determination and refinement by CCP4 and PHENIX programs.



CrysAlis^{Pro} – Graphical User Interface with intuitive workflows. Shown in PX (macromolecular) mode.

The Proof of Any Good Instrument: Great Applicatio

SIGNIFICANTLY IMPROVE DATA QUALITY AND SPEED

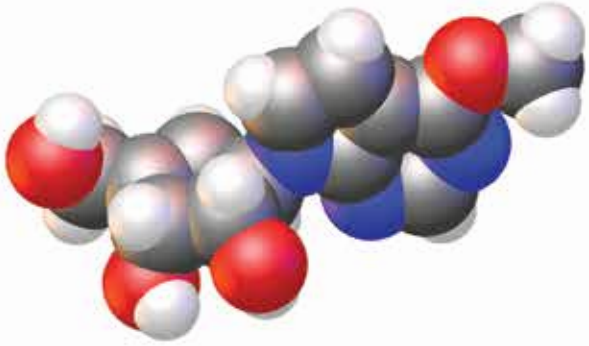
Improve your data quality and data collection speed for small molecule crystals using the XtaLAB Synergy-S. Not only are the sources brighter, but the increased goniometer speed and the ability of the detector to move close to the sample mean that there are great improvements over its popular predecessor, the SuperNova.

NEW SOURCES, HIGHER FLUX

A careful redesign of the entire source, from tube to optics, gives fantastic improvements in intensity. With the same crystal-to-detector distance and the same data collection speed, the XtaLAB Synergy-S provides more than a 50% increase in I/σ compared to the SuperNova. The improvement in I/σ subsequently means that the R_{int} and R_1 of the final structure are considerably lower.

Experiment parameters	XtaLAB Synergy-S AS2	SuperNova AS2
Crystal to detector distance (mm)	52	50
Exposure time (sec./deg)	1	1
Completeness	98.6	97.3
Redundancy	2.1	2.4
I/σ to 0.84 Å	**39**	25
Dose time	6 min. 29 sec.	7 min. 5 sec.
R_{int}	0.018	0.026
R_1 (%)	**2.74**	4.14

Comparison of the Nova source and the XtaLAB Synergy-S microfocus Cu source.



Refined structure of a light atom organic sample.

FASTER GONIOMETER AND CLOSER DETECTOR DISTANCE

Increasing the speed of the goniometer and decreasing the minimum distance of the detector can make huge differences in the total data collection time. Alternatively, this extra time gained could be used to collect more data.

The new goniometer in the XtaLAB Synergy-S moves twice as fast as the SuperNova, and the detector is allowed to approach much closer. These factors, coupled with the advanced strategy calculation, allow you to optimize data collection to suit your requirements as summarized below.

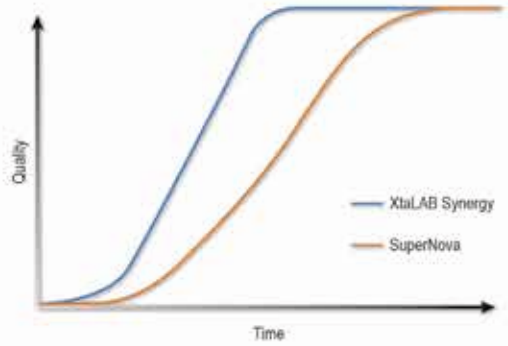


Chart representing the improvements of the XtaLAB Synergy-S over the SuperNova for the same crystal. Higher quality data can be measured in a shorter time.

Experiment parameters	SuperNova AS2	XtaLAB Synergy-S AS2 very fast	XtaLAB Synergy-S AS2 using extra data
Crystal to detector distance (mm)	50	35.5	35.5
Completeness to 0.84 Å	99.2	98.6	99.8
Redundancy	2.7	2.1	2.7
Relative goniometer speed	x1	x2	x2
I/σ to 0.84 Å	26	39	59
Experiment time	12 min. 48 sec.	7 min. 38 sec.	11 min. 17 sec.
R_{int}	0.036	0.021	0.016
R_1 (%)	3.97	3.00	2.54

Experiment details on a light organic chemical sample measured on a SuperNova and the XtaLAB Synergy-S. These results highlight the benefits of the new, faster goniometer, the closer detector distance and increase in source flux of the microfocus source with the Atlas S2 detector.

n Results

FAST SAD PHASING

The true test of any diffraction system is the ability to accurately measure high-quality data that is suitable for structure solution. In particular, it is especially important to have a system with the high accuracy and DQE offered by XtaLAB Synergy-S for measurement of the weak anomalous signal from S atoms in proteins. In this example, we illustrate SAD phasing for a low redundancy lysozyme data set.

Details for integration and scaling	
Space group	$P4_32_12$
Unit cell	77.46 Å, 77.46 Å, 38.01 Å 90°, 90°, 90°
Total # reflections	110,989
# unique reflections	13,699
Completeness (%) (Friedel pairs unmerged)	84.6 (11.5)
Redundancy (Friedel pairs unmerged)	**4.5 (1.1)**
$\langle I/\sigma I \rangle$	34.1 (1.95)
R_{fac} / R_{meas} (%) (Friedel pairs unmerged)	2.5 / 2.8
Chi^2 (last shell) (Friedel pairs unmerged)	1.28 (0.92)

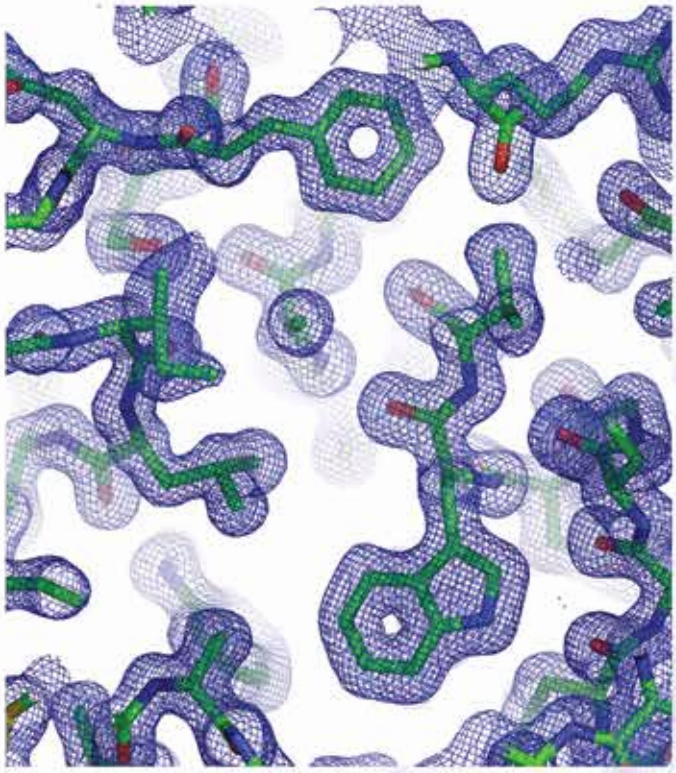
Note: Values in ( ) are for the highest resolution shell.

A data set containing 690 images was collected to 1.6 Å using exposure times of 10 sec. / 0.3° on a PILATUS3 R 200K. Statistics from data processed with XDS, shown above, indicate that the redundancy for this data set is 4.5 overall and 1.1 in the highest resolution shell.

The structure was subsequently solved by S-SAD phasing methods. First, the data were analyzed with SHELXC to check the anomalous signal. Then, SHELXD was used to find the heavy atom (S) sites. Subsequently, the anomalous sites were used in phasing with SHELXE and MLPHARE followed by density modification with DM. The Figure of Merit after density modification was 0.79.

Details for structure solution and refinement	
Resolution for heavy atoms search	1.8 Å
Corr. Coeff. for heavy atoms solution (all data/weak data) # heavy atom sites selected from solution	33.4 / 18.3 10 out of 10
Resolution used for phasing and density modification	1.6 Å
FOM after density modification	0.79
# residues built / # waters added	120 (93%) / 125
R_{fac} / R_{free} after REFMAC refinement	17.5% / 22.5%

Following phasing and density modification, ARP/wARP was used to autobuild 93% of residues. Then, the structure was refined with REFMAC to a final R_{fac} and R_{free} of 17.5% and 22.5%, respectively.



REFMAC σA-weighted 2*m*Fo-DFc electron density map, contoured at 1σ, for lysozyme solved using S-SAD methods.

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JOIN THE BIGGEST USER COMMUNITY OF CRYSTALLOGRAPHERS

www.rigakuxrayforum.com

Here 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.

XtaLAB Synergy S

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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