SINGLE-CRYSTAL X-RAY DIFFRACTION

Crystallography Solutions for Drug Discovery and Development

Accurate structures right when you need them

Innovation with Integrity

SC-XRD Driving Drug Discovery and Development

For target validation, drug discovery, and development of solid forms, a detailed atomic understanding of the molecular structure is crucial to streamline the development process, enabling a more efficient and cost-effective pathway to bring new drugs to clinical trials.

Single-crystal X-ray diffraction (SC-XRD) is the most effective technique for unambiguously determining the 3D structure of macromolecules, small molecules, and crystal lattices at atomic resolution. SC-XRD plays a crucial role in various fields, from drug discovery to solid-form development, significantly accelerating research, reducing development times, and providing substantial cost savings.

Target Validation → Hit-to-Lead → Lead Optimization → Solid Form Development → Formulation → Clinical Development → Scale-up

Structural Biologists

- Detailed structures of the target macromolecule from small crystals
- Develop robust crystal forms for structure-based drug design
- Continuously determine structures quickly and reliably
- Reduce time-to-structure

Medicinal Chemists

- Regular, fast structure confirmation to guide decision making
- Accurate structure of APIs with absolute stereochemical assignment

Formulation Scientists

- Understand polymorphism under various conditions
- A complete description of the crystal form of various salts, co-solvates and co-crystals
- Investigate new polymorphs and extend the product life-cycle

In-House SC-XRD: Answers When You Need Them

Bruker's in-house SC-XRD systems provide high-quality structures within hours or even minutes, allowing for quick and accurate answers to important questions.

The D8 QUEST and D8 VENTURE are a family of instruments that can be configured to meet your specific analytical and operational needs. Equipped with high-brilliance microfocus X-ray sources and photon counting detectors, these instruments allow for the analysis of crystal structures that were previously too small for in-house examination.

Our instruments are built for maximum uptime and stability while minimizing ownership costs. Having immediate access to crystal structures allows you to develop more reliable protein crystal systems and conduct more comprehensive analyses of solid forms. This capability also eliminates the time spent waiting for synchrotron beamtime or outsourcing tasks to other laboratories.

Structure-Based Drug Design

Improve crystal quality, reduce project failure rates

Developing robust, well-diffracting crystals of pharmacological targets can be a complex, time-consuming, and costly endeavor. Failing to establish well-diffracting target crystal systems often marks the end of a structure-based drug design (SBDD) project, especially for high-value targets such as epigenetics or GPCRs.

In-house facilities like the D8 VENTURE provide you with the time and flexibility to explore crystallization space more thoroughly, enabling the development of higher quality crystal systems for structure-based drug design. This capability enhances your ability to optimize conditions and achieve better outcomes in your research.

Control your pipeline

Sometimes decisions just cannot wait. Supplementing synchrotron data collection with in-house structure determination eliminates delays associated with waiting for beamtime, providing prompt answers to urgent questions almost immediately. This approach ensures that critical decisions can be made without unnecessary interruptions.

Automated data collection

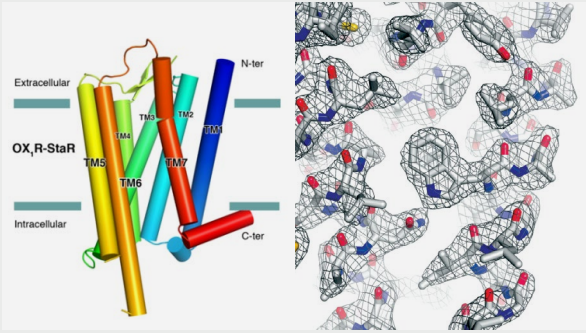
The D8 VENTURE can collect data of synchrotron quality in just hours or even minutes. When operated with SCOUT automated sample handling, it streamlines data collection and processing, allowing the D8 VENTURE to deliver datasets quickly enough to clear backlogs or efficiently fill gaps in beamtime.

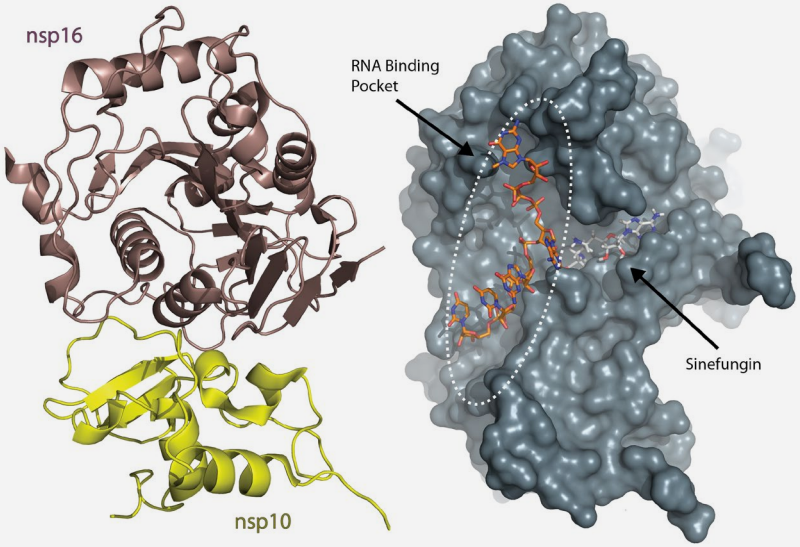
Fast data collection with D8 VENTURE
BRD4 structure solved at 1.7 Å from a complete dataset collected on the D8 VENTURE in 15 minutes.

Synchrotron-Quality Protein Structures

The **D8 VENTURE METALJET** serves as your in-house beamline, delivering a microfocus X-ray beam of intensity comparable to that of third-generation synchrotrons. This capability allows you to solve structures from even the most challenging targets directly in-house.

GPCR drug discovery
Structure of human Orexin-1 receptor showing representative electron density. A complete dataset was collected using the D8 VENTURE METALJET and the structure solved to 2.8 Å (R work/ free 24.4 / 27.2). The resolution and structure R-factors are comparable with other OX1-R structures in the PDB.





SARS-CoV-2 methyltransferase at 2.4 Å
2'-O-RNA methyltransferase (MTase) is a target for antiviral therapy as it is crucial for RNA cap formation, an essential process for viral RNA stability. This MTase function is associated with the nsp16 protein, which requires a cofactor, nsp10, for its proper activity. This crystal structure of the nsp10/ nsp16 complex bound to the inhibitor sinefungin in the active site was solved using the D8 VENTURE METALJET (PDBID 6YZ1, Nat Commun 11, 3717 (2020).

Discovery Chemistry

Visualising your API helps understand the chemistry

Visualizing the 3D atomic structure of a new API provides valuable information about the connectivity and molecular conformation that allows chemists to make the right decisions quickly and helps drive forward development.

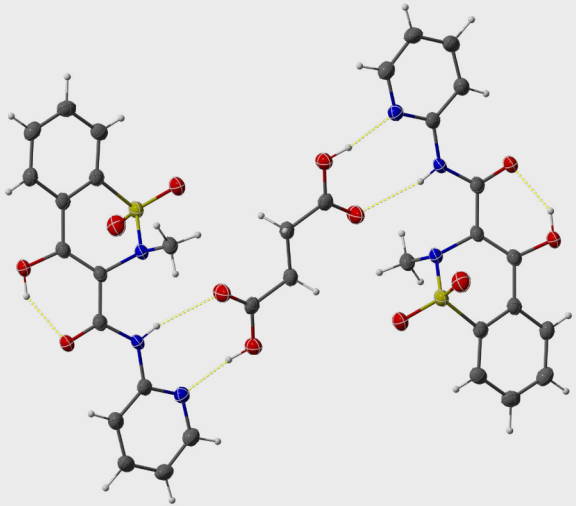
Absolute Structure Determination of Chiral Molecules

SC-XRD is the only experimental method that unambiguously and accurately determines the configuration of molecules containing chiral centers at atomic resolution.

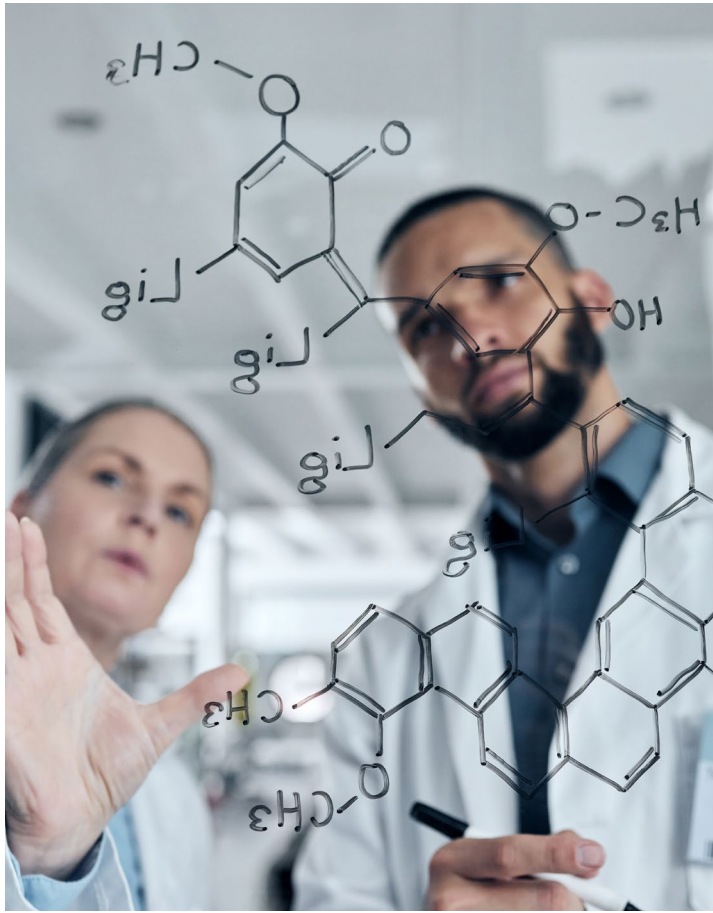
Convenient absolute structure determination is essential to guide synthetic stereochemistry and is essential information for registering new APIs.

Systems that deliver the right answers quickly

The D8 QUEST, with a high-intensity microfocus X-ray source and photon-counting detector, enables atomic resolution structures to be determined from tiny crystals in only minutes. The high-quality data ensures that absolute structure can be determined routinely and easily.



API absolute structure determination
Absolute structure of piroxicam-succinate at atomic resolution. Such structures unambiguously confirm the API chirality and provide details of intermolecular interactions.



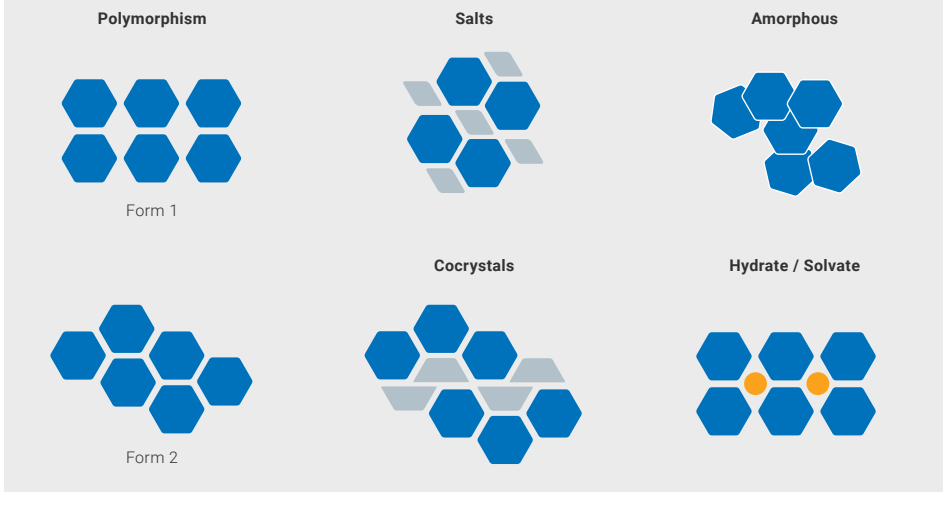
Advanced Solid Form Analysis

SC-XRD provides the most complete structural description of new solid forms. The detailed insight it provides helps in overcoming bottlenecks in solid form optimization and identifies potential risks of polymorphism or inadvertent production of alternative forms.

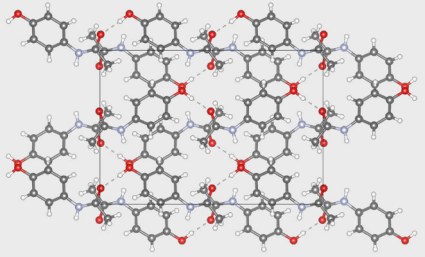
With the development of increasingly complex APIs and new co-crystal forms, being able to directly visualize molecular conformation and intermolecular interactions is increasingly beneficial to guide the development of solid forms with suitable stability, manufacturability, and ADME properties.

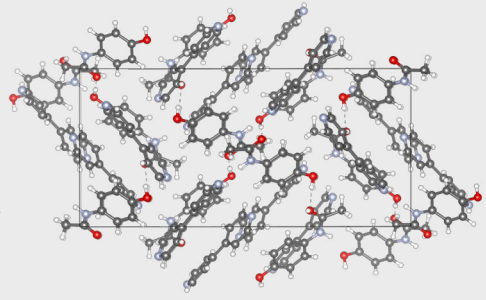
SC-XRD analysis can be performed at non-ambient temperatures and pressures to provide additional valuable information on a solid form's stability during manufacturing and storage.

D8 QUEST and D8 VENTURE systems now enable structure determination directly from tiny crystallites selected directly from the bulk powder preparation, avoiding the need for time-consuming recrystallisation. Furthermore, you can be certain that the atomic structure obtained represents that found in the bulk powder preparation.



Detailed insight into crystal form I
Absolute structure of piroxicam-tatrate at atomic resolution. Such structures unambiguously confirm the API chirality and provide details of intermolecular interactions.





Detailed insight into crystal form II

Benefits of SC-XRD for Solid Form Analysis

- **Simple and reliable:** obtain atomic resolution structures from single crystallites less than ten microns, without the need to recrystallize.
- **Understand the chemical nature of polymorphism:** engineer more stable crystal forms.
- **Micro powder diffraction:** quickly identify phases with micrograms of powder
- **Non-ambient solid form analysis:** investigate the effects of temperature, pressure, and hydration on crystal form.
- **Amorphous and mixed solid forms:** accurately measure total scattering to perform PDF analysis.

D8 Crystallography Solutions

Industry-leading results whatever your requirements

The ideal solution for your laboratory

Structural analysis in the pharmaceutical industry has diverse requirements, and no two laboratories are alike in their needs. Bruker's D8 QUEST and D8 VENTURE solutions for SC-XRD enable you to establish the optimum facility, whatever your goals.

- Combine the X-ray source, detector, and automation to perfectly match your analytical requirements.
- Configure the ultimate instrument to fit your scientific and operational goals.

Stay at the technological forefront

- Bruker SC-XRD systems are designed for upgradability allowing you to take advantage of the latest technologies.
- Bruker provides regular software updates to ensure you have the best data analysis routines and the latest methods for SC-XRD.
- Automate you SC-XRD platform and increase throughput as your need to expand capacity grows.

PHOTON III detectors
State-of-the art photon counting CPADs for the ultimate in speed and data precision.

High-intensity X-ray sources
It all starts with source brightness in a microfocus beam with ultimate stability and uptime.

Precision and speed
Our D8 goniometer is designed for the highest accuracy and precision, superb alignment, and long-term reliability.

Speed, precision, uptime

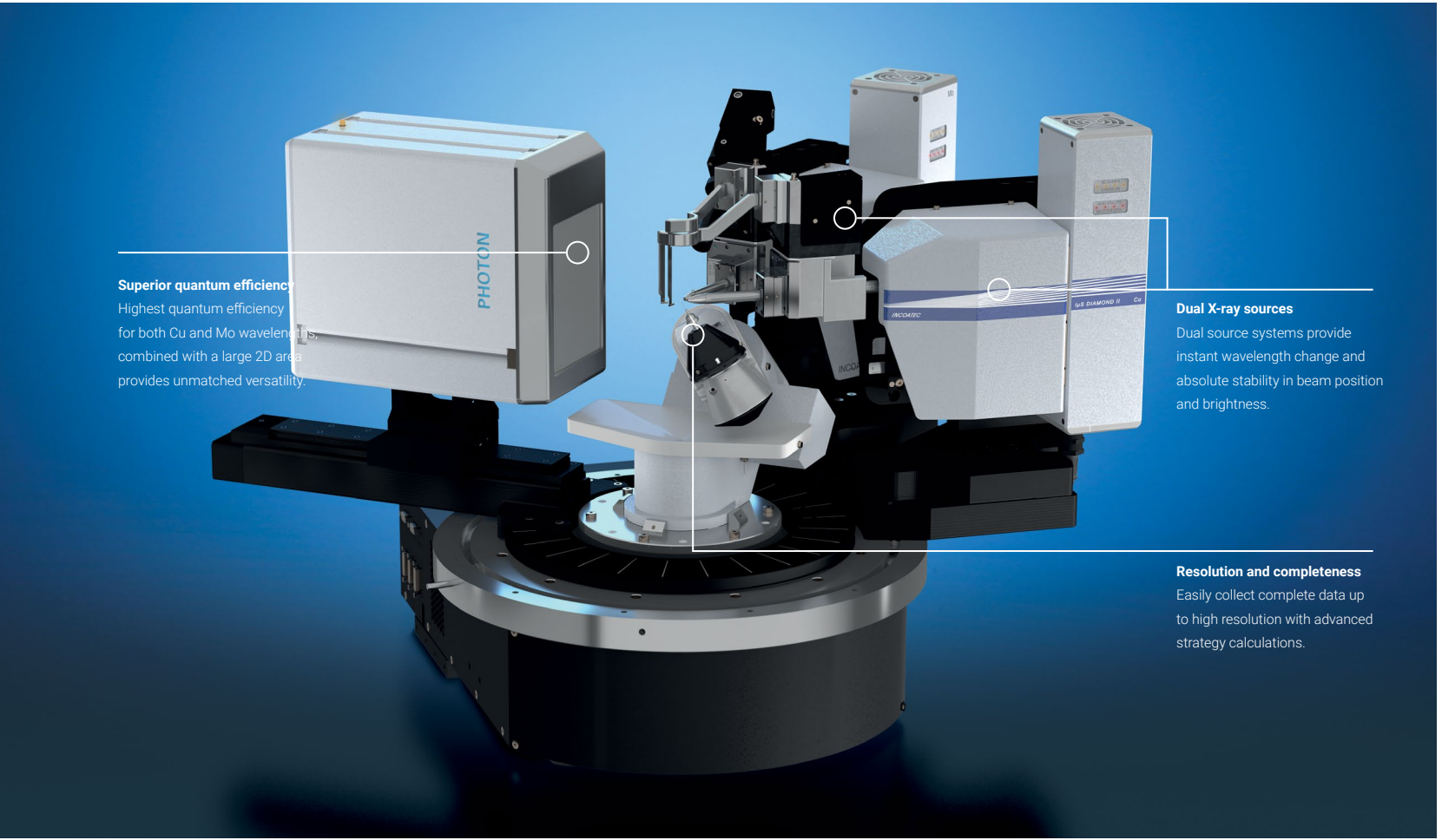
The D8 QUEST and VENTURE are designed with a solid foundation of exceptional performance and unwavering reliability.

Ultra-bright X-ray sources

Bruker's IμS microfocus X-ray sources set the standard for innovation and performance. Offering unmatched brightness and the smallest focused X-ray beam, these sources are perfect for even the smallest, weakly diffracting crystals.
Fully air-cooled and designed without moving parts, our sources ensure maximum reliability and uptime.

PHOTON III detectors

Our state-of-the-art photon-counting CPADs deliver the ultimate in speed and data precision and offer everything expected from a modern detector: noise-free operation, near-ideal quantum efficiency, single-photon sensitivity, and an exceptional dynamic range.
PHOTON III detectors offer the largest active areas, enabling fast and highly efficient data collection.



Dual-wavelength versatility

The D8 VENTURE comfortably supports dual IμS X-ray sources. With access to two X-ray wavelengths, the range of available analyses expands significantly.

High resolution structure determination

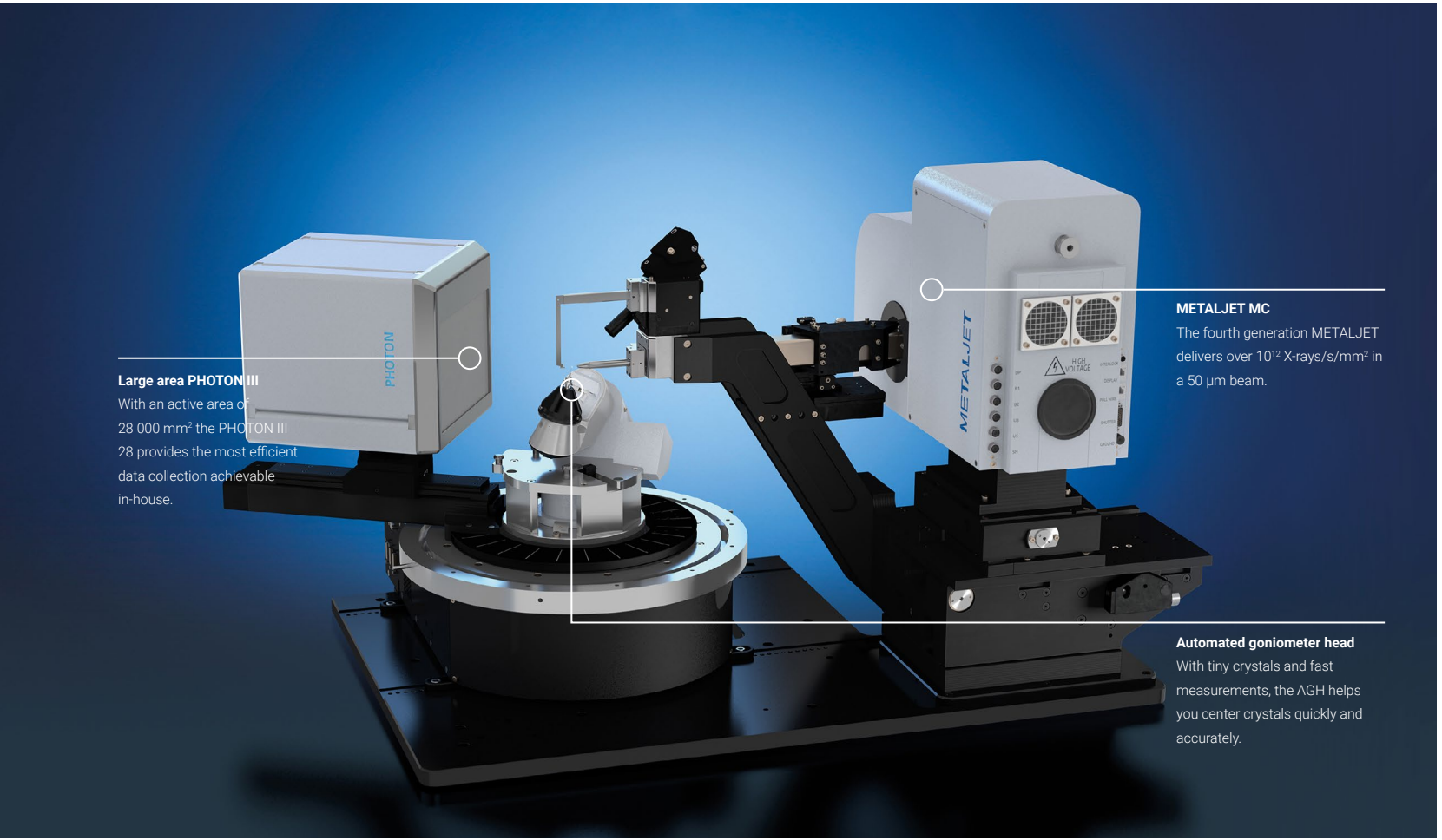
A Mo X-ray source allows for data collection at resolutions up to 0.35 Å, offering valuable insights into intra- and intermolecular bonding properties, including detailed charge density distribution.

Superior data accuracy

Data collection using Mo radiation achieves higher resolution and higher data precision more efficiently than Cu radiation. Measurements using Mo radiation provide the most efficient approach for analyzing the structure of synthetic intermediates and complex solid forms.

Beyond single-crystal XRD

The versatility of a dual-wavelength system broadens the scope of analyses your lab can perform—from phase identification of microgram quantities of powder and high-pressure phase studies to PDF analysis.



Large area PHOTON III
With an active area of 28 000 mm² the PHOTON III 28 provides the most efficient data collection achievable in-house.

METALJET MC
The fourth generation METALJET delivers over 10^{12} X-rays/s/mm² in a 50 µm beam.

Automated goniometer head
With tiny crystals and fast measurements, the AGH helps you center crystals quickly and accurately.

Your In-House Beamline

The D8 VENTURE METALJET delivers performance normally only achieved at 3rd-generation synchrotron beamlines, making it the ultimate in-house solution for the most demanding protein crystallography experiments or a true high-throughput beamline alternative.

Ultra-bright METALJET MC

The fourth-generation METALJET MC is nearly ten times brighter than any other in-house source and focuses the X-rays into the smallest available in-house beam.

Large area PHOTON III detectors

The PHOTON III 28 is the largest detector available for in-house instruments, offering a beamline-like experience. Its large area allows for the collection of high-quality data from protein crystals with extremely large unit cell dimensions.

Automated data collection

For a true beamline experience, the D8 VENTURE can be equipped with the SCOUT sample changer, enabling unattended data collection on up to 48 samples per run.

Powerful and intuitive

Software for data acquisition, processing and structure determination

Bruker SC-XRD systems are provided with comprehensive software suites designed both for protein and small molecule crystallography. Whether you need automated workflows to rapidly reduce your backlog or a complete toolkit for advanced analyses, Bruker software is engineered to help you achieve your objectives.

Ease-of-use

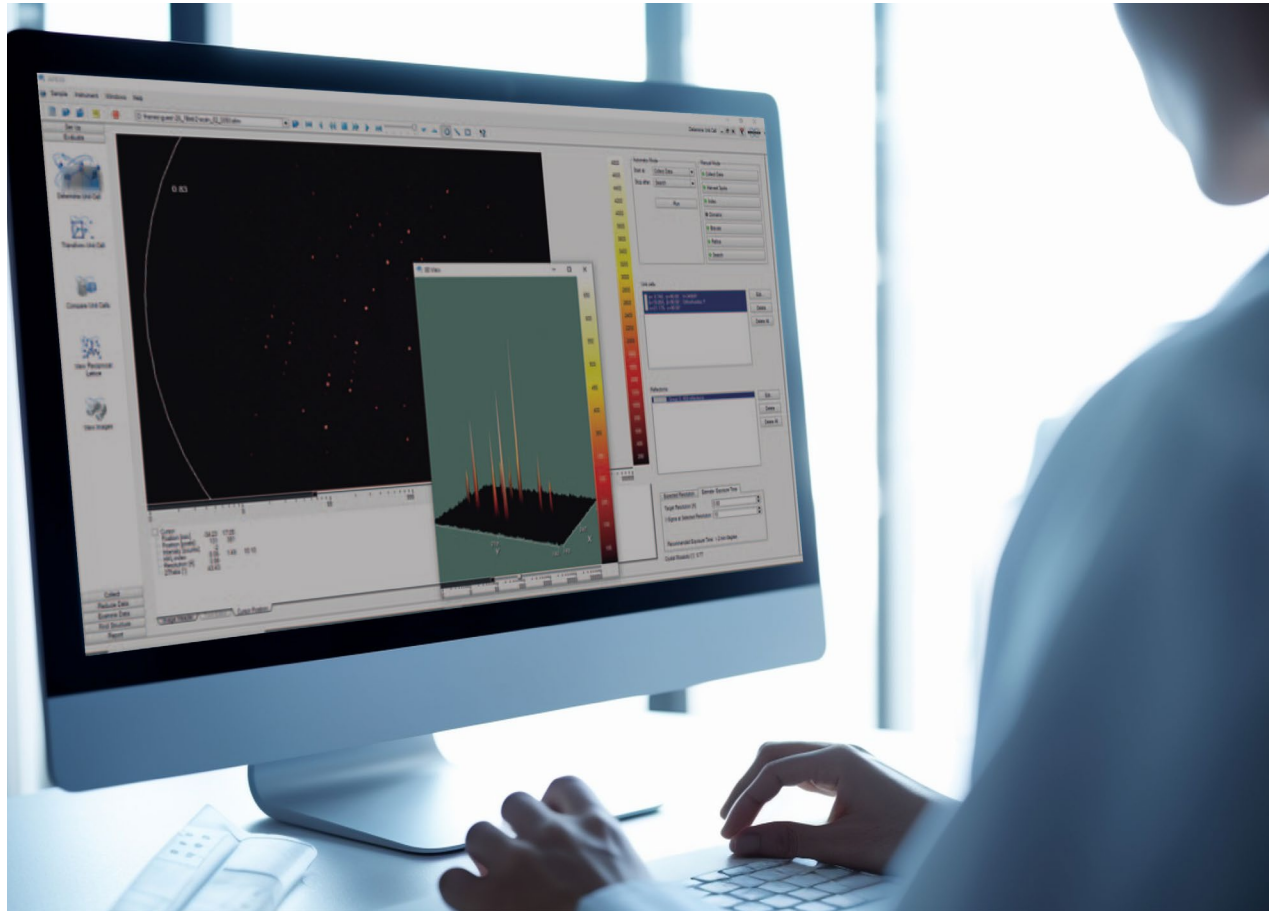
Within a single workspace, you will find all the tools you need for data collection, processing, and structure determination. The intuitive user interface aligns with the experimental workflow, offering clear graphical feedback at every step to help you achieve reliable, high-quality results quickly.

APEX for small molecule crystallography

- Comprehensive tools for conducting advanced analyses on the most challenging samples.
- STRUCTURE NOW – fully automated structure determination to streamline your workflow and help manage a busy schedule.

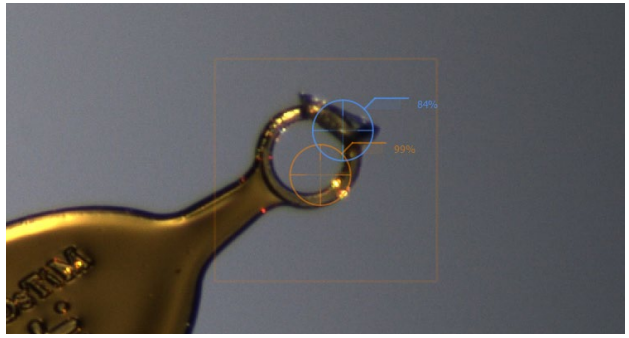
PROTEUM for protein crystallography

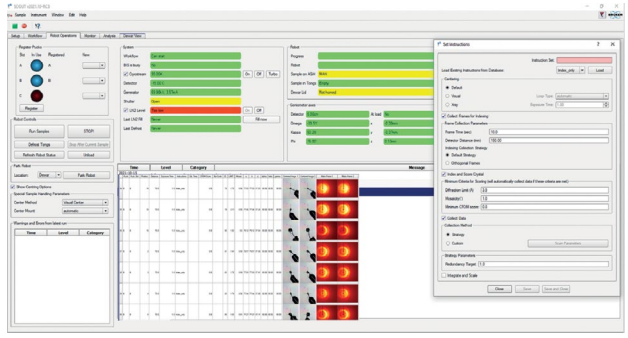
- Indexing and data collection strategies optimized for protein crystallography.
- Process data from synchrotron beamlines.
- Export data to your current structure determination pipeline.



Maximize your productivity

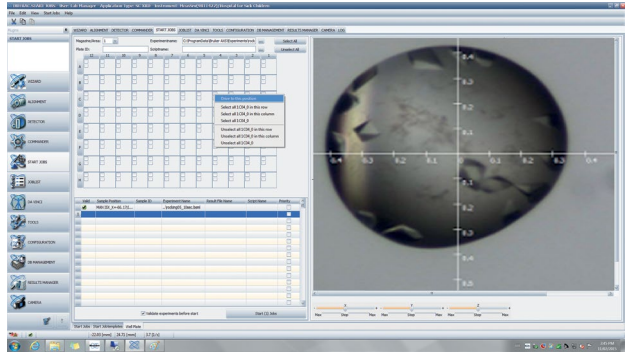
You want to maximize the return on your investment, and the D8 VENTURE is designed to help you do just that. Whether you work in Structural Biology, small molecule crystallography or solid form analysis, gain a deeper understanding by increasing throughput or exploring that extra dimension.





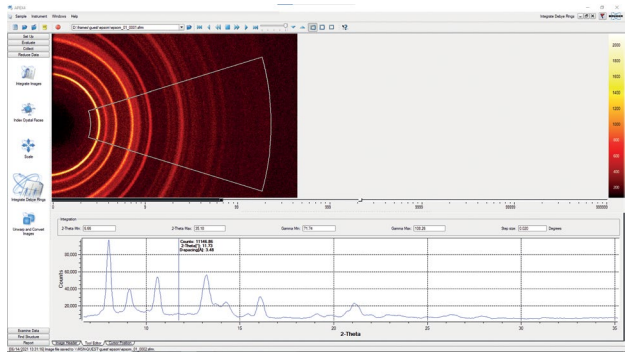
Automated crystal centering

- The Automated Goniometer Head (AGH) uses deep learning to automatically center the crystal when the enclosure doors are closed.
- Accurately centers the smallest crystals.
- Reduces your experiment overhead significantly.



24/7 unattended data collection

- SCOUT automated sample handling maximizes system productivity with fully automated, unattended data collection.
- Collect quality data from up to 48 samples per run.
- Results report output in convenient HTML format compatible with data processing pipelines.



ISX STAGE – in situ plate screening quick and easy

- Rapidly screen crystallization trials directly in 96-well plates to efficiently develop high-quality crystal systems.
- High-throughput phase identification from powders in well plates.

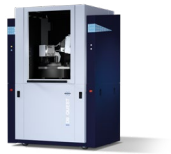
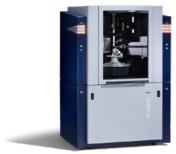
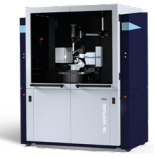
Powder diffraction

- Microfocus beams and large 2D area detector enable you to quickly identify crystalline phases form micrograms of powder.
- A dedicated APEX plug-in processes data from polymers, fibers, and partially-oriented powders and provides export to the full suite of Bruker XRD software.

Systems as individual as your research

Whether you need accurate protein structures, absolute structures of small molecule APIs or detailed insight into solid form structure, Bruker offers the ideal solution for your needs.

Bruker provides the perfect system to meet your analytical throughput, operational requirements or business targets.

	D8 QUEST ECO	D8 QUEST	D8 VENTURE	D8 VENTURE METALJET	D8 VENTURE SCOUT
					
Benefits for Structural Biologists	-	Structure determination of well diffracting systems with moderate throughput. Cost effective tool for optimising crystal conditions	Moderate throughput structure determination. Excellent tool for optimizing crystal conditions	Structure determination form the most challenging projects. Fast data collection time for higher-throughput.	High-throughput structure determination with automated sample handling and data collection. Your in-house beamline.
Benefits for Chemists & solid form scientists	Excellent value for low-throughput structure determination. Automated data collection and processing make structure determination intuitive for the occasional user.	Quality structures quickly in a compact footprint. The perfect balance of performance and convenience.	Fast structure determination from even tiny crystals. Eliminates the need for recrystallisation of solid form preps. Optional Mo source for high-resolution structure determination or high-pressure studies of polymorphism.	Atomic resolution structures in seconds. Ideal for dual-use with structural biologists.	24/7 capabilities provide more measurement time for large user groups.
X-ray source intensity	●○○○○	●●○○○	●●●○○	●●●●●	●●●●●
2nd source option	-	-	✓	-	-
PHOTON III detector sizes (1000 mm^2)	7	7, 14	7, 14, 28	7, 14, 28	7, 14, 28
Automated crystal centring	-	✓	✓	✓	Included
Automated sample changer	-	-	✓	✓	Included
In situ screening	-	-	✓	✓	✓
High-pressure Studies	-	✓	✓	-	-
Typical SM crystal sizes (um)	50 - 500	10 - 300	2 - 300	2 - 200	2 - 200
Typical Protein crystal sizes (um)	-	70 - 300	50 - 300	20 - 200	20 - 200
Investment	●○○○○	●●○○○	●●○○○	●●●●○	●●●●●
Cost of ownership	●○○○○	●○○○○	●○○○○	●●○○○	●●○○○

In-house SC-XRD drive your science and your business

- Accelerate your discovery pipeline and reduce project failures
- Take control - no delays waiting for external data collection
- Leverage synergies with powder diffraction and NMR for more comprehensive results
- Gain deeper scientific insight, improve your outcomes and drive innovation
- Keep your intellectual property secure by managing everything in-house
- Low cost of ownership delivers excellent return on investment
- Improved financials – reduce costs associated with outsourced services
- Expand your service offering and generate additional revenue streams

You focus on the science. We'll focus on you

At Bruker AXS, we consider ourselves not just instrument suppliers, but partners invested in your ongoing success. With Bruker AXS, you benefit from state-of-the-art instruments and an extensive support network, ensuring you are always at your most productive.

Instruments Designed for Maximum Uptime and Productivity

Bruker's instruments are designed for maximum uptime and productivity. They are energy-efficient, with long-life sealed tube X-ray sources running on single-phase power. This not only enhances sustainability but also reduces operating costs. With comprehensive service and support packages, we ensure your instrument is always operational.

Scientific application support

Our Applications Scientists help you achieve your goals by setting up customized analytical methods and consulting on implementation strategies. As your needs evolve, they assist with new measurement methods, user training, and instrument upgrades to keep you ahead of the curve.

LabScape Services and Lifecycle support

Bruker's commitment to unparalleled customer support is embodied in our LabScape concept, which covers everything from initial inquiry to evaluation, installation, and the lifetime of the instrument. LabScape Maintenance Service Agreements, On-Site On-Demand, and Enhance Your Lab programs offer innovative maintenance and service solutions for the modern laboratory.

Bruker AXS – your trusted partner for SC-XRD

Scientists in the pharmaceutical industry worldwide rely on Bruker AXS SC-XRD solutions to successfully drive their drug discovery and development programs. Supported by a network of 22 offices and numerous service centers across six continents, we are dedicated to your success.

The Bruker Advantage

Bruker's third generation, D8 QUEST and D8 VENTURE solutions are the result of continuous development driven by decades of customer feedback. Consequently, D8 systems provide genuine benefit to drug discovery and development by providing better quality answers faster. Designed for maximum uptime and low overhead, Bruker SC-XRD instruments deliver on your investment.

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