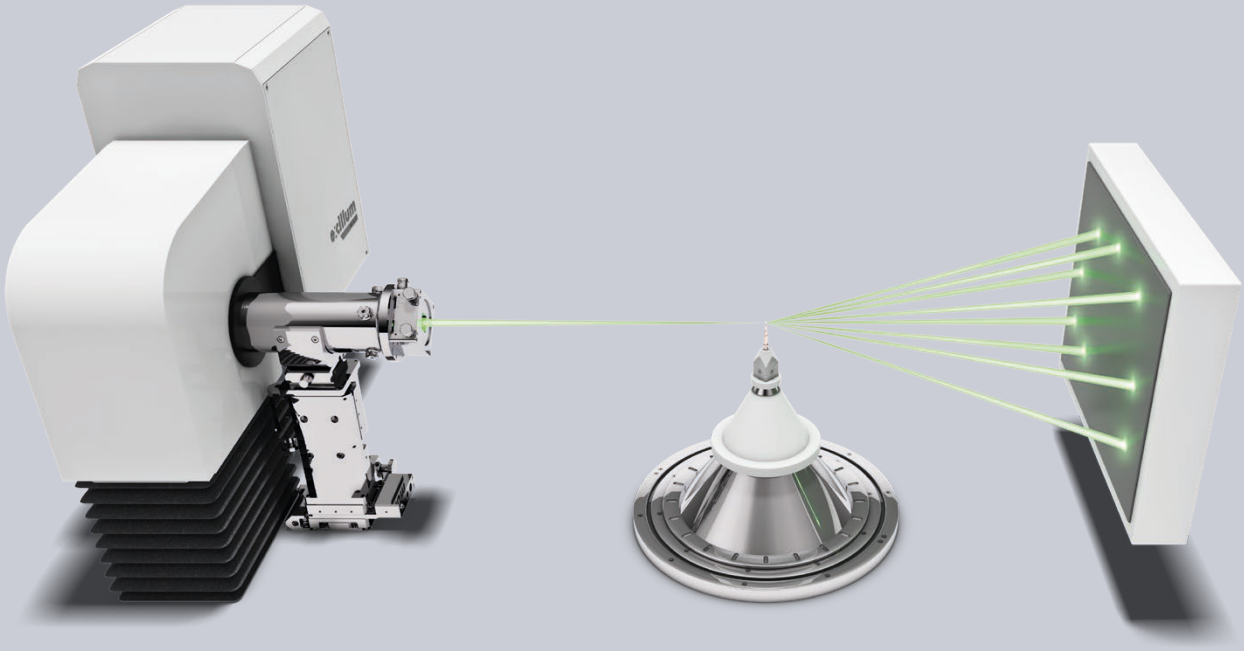
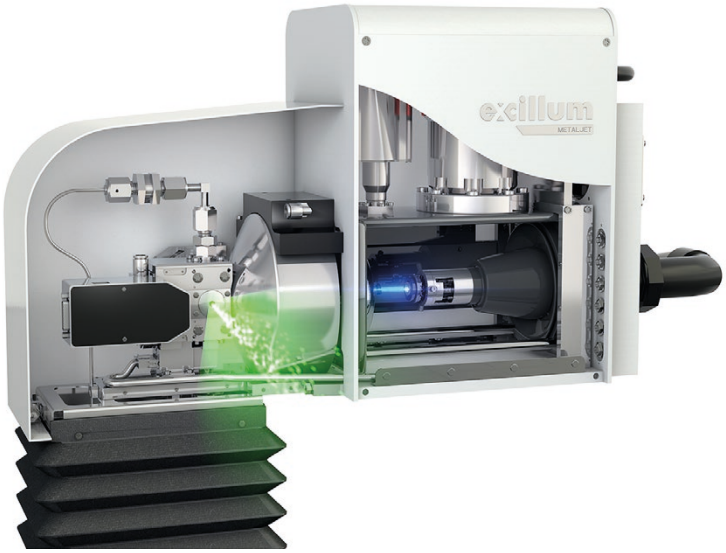
excillum

MetalJet for X-ray analytical applications

SAXS, small molecule and protein crystallography

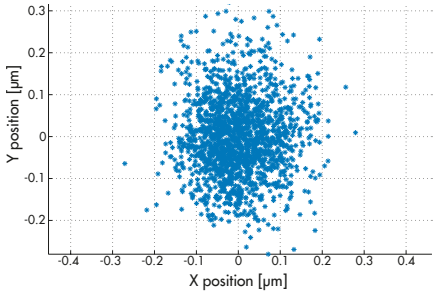




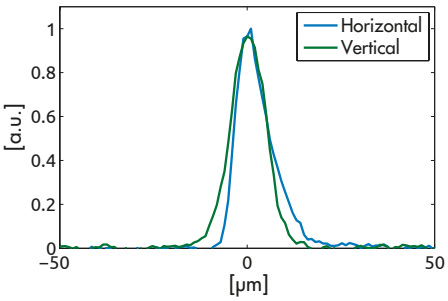
MetalJet D2+

State-of-the-art, high-brilliance X-ray source

The Excillum MetalJet D2+ features our unique metal-jet anode technology and advanced electron optics. Achieving significantly higher brightness and smaller spot sizes than any other available microfocus X-ray source, the MetalJet can create very brilliant and small beams enabling the closest possible performance to synchrotron capabilities in the home lab.



Electron beam spot position over 24 hours



Line profile through electron beam spot maximum

The MetalJet uses a fast flowing liquid jet of metal instead of a rotating anode metal target, thereby removing the limitations of the rotating anode, allowing a greater power loading to be placed on the metal target without risk of destruction. In this way, the MetalJet can generate a higher brilliance, focused beam of X-rays which can be up to a factor of ~10x greater than conventional micro-focus rotating anode X-ray sources.

The Excillum MetalJet D2+ features our unique metal-jet anode technology and advanced electron optics. Achieving significantly higher brightness and smaller spot sizes than any other available microfocus X-ray source,

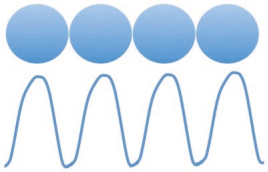
High stability, low divergence for better data

The MetalJet generates a high-stability (<0.1 µm over 24 hours) electron beam spot, which translates to a high stability X-ray beam after the X-ray optic.

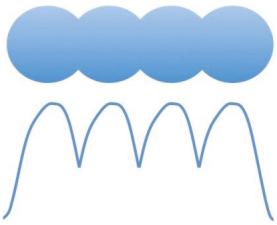
the MetalJet can create very brilliant and small beams enabling the closest possible performance to synchrotron capabilities in the home lab.

The MetalJet uses a fast flowing liquid jet of metal instead of a rotating anode metal target, thereby removing the limitations of the rotating anode, allowing a greater power loading to be placed on the metal target without risk of destruction. In this way, the MetalJet can generate a higher brilliance, focused beam of X-rays which can be up to a factor of ~10x greater than conventional micro-focus rotating anode X-ray sources.

The electron beam spot is tightly focused to typically between 5 and 30 µm in size, resulting in a typical X-ray beam size of 70-100 µm after the X-ray optic; dependent upon the optic.



Lower divergence
- *Better separation*
- *Better defined reflections*
- *Better intensity integration*



Higher divergence
- *Broader reflections*
- *Poorer separation*
- *Poorer defined reflections*
- *Poorer intensity integration*

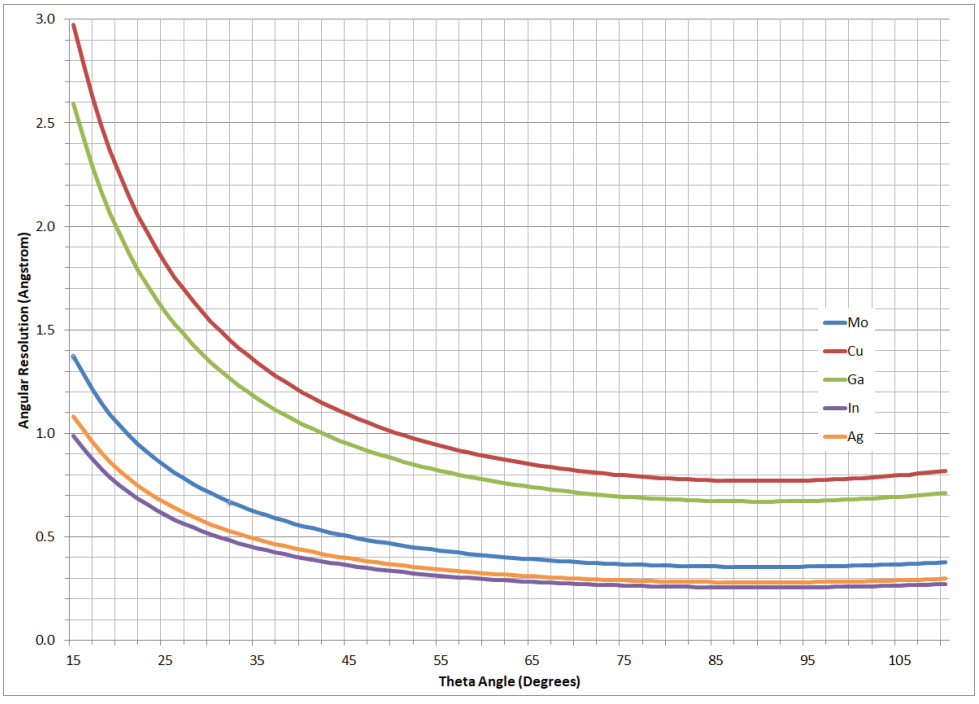
The size, shape and take-off agle of the eletronbeam and thereby the X-ray beam are software controlled and can be adjusted by the user to best fit the sample size and application.

The MetalJet is typically paired with a high quality, low divergence X-ray optic to give the best data quality. When Bragg reflections are closely packed, as in protein crystallography, a low divergence X-ray beam provides better data separation, better positional and better intensity measurements, leading to better overall data quality. In contrast, a higher divergence X-ray beam leads to broader, poorer defined data, which may overlap, merging positional and intensity information leading to inferior overall data quality.

Compact, low maintenance, lower cost of ownership

The MetalJet is extremely compact and is available as a stand-alone X-ray source or upgrade direct from Excillum, or as part of a state-of-the-art X-ray diffraction or SAXS system from one of our equipment manufacturer partners.

The MetalJet never requires costly anode re-polishing or anode replacements, has no moving parts or ferro-magnetic seals. Even the filament has been eliminated by design and replaced with a long life LaB_6 crystal cathode. Together these improvements provide for more up-time, lower maintenance, a lower cost and a greater ease of ownership.



Combining the higher brilliance of the MetalJet and either gallium or indium radiation can provide improved data quality compared to other traditional metal targets due to:

- *Lower air / liquid scatter*
- *Lower absorption and reduced potential radiation damage compared with copper radiation.*
- *Higher accessible resolution*
- *Higher data collection speed and efficiency*

Two wavelength options for up to 0.26 Å resolution

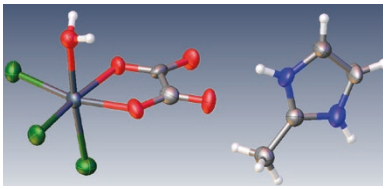
Available with either a gallium (λ =1.34 Å) or an indium (λ = 0.51 Å) rich alloy based target, the MetalJet at 90 degrees in theta, can provide accessible data up to 0.67 Å resolution for gallium and up to 0.26 Å resolution for indium.

Small molecule crystallography

Small molecule crystallography uses X-ray diffraction in the determination and study of the three dimensional structure of a material at the atomic and molecular scale. A single crystal of the sample is required and the resulting X-ray structures provide a to scale 3D visual map of the atom types, their relative arrangement and how they are connected in space. The crystal samples studied are typically, inorganic, organic or organo-metallic compounds, primarily from research in the disciplines of Chemistry, Geology and Physics.

As small molecule X-ray crystallography becomes more automated and routine, there is increasing interest in the study of more difficult and specialist materials in which a high brilliance MetalJet X-ray source is desirable. Use of the MetalJet typically means shorter experiment times, faster structures and higher throughput of samples. Small and weakly diffracting crystals, diffract more strongly, thus providing higher quality data, whilst sensitive crystals can be measured faster with the MetalJet and suffer less degradation accordingly. Twinned crystal data can be more strongly defined using a MetalJet, making it more easily identified and potentially handled. Very weak diffraction effects, inherent to incommensurates, diffuse scattering samples, quasi-crystals and high pressure samples become stronger and may be more readily measured and investigated using the high brilliance X-rays of a MetalJet.

Example small molecule applications

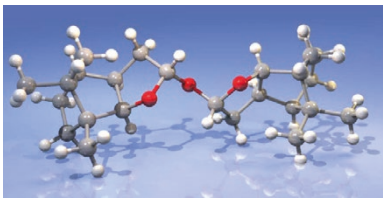


Small crystals

Tin (IV) compounds are interesting as potential catalysts and pharmaceuticals due to their biological activity. As part of a drive to understand these compounds, researchers at the Universities of Montreal, Cheikh Anta Diop and Bourgogne determined the crystal structure of a 50 µm crystal of $[Sn(C_2O_4)Cl_3(H_2O)].(C_4H_7N_2)$ using a MetalJet X-ray source.

- Crystal size: 0.05 x 0.04 x 0.04 mm^3
- R1 = 6.2%

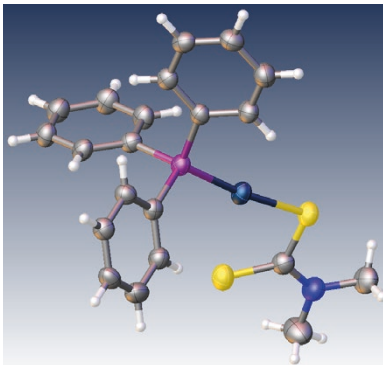
Acta Cryst. 2015. E71, 520–522, M. B. Diop, L. Diop, L. Plasseraud, T. Maris



Absolute structures

Application scientists at Bruker AXS used a MetalJet integrated into a Bruker D8 VENTURE diffractometer to successfully determine the absolute configuration of (2S)-(−)-2,2'-Oxybis(octahydro-7,8,8-trimethyl-4,7-methanobenzofuran), a light atom structure, where the heaviest atoms are three oxygen atoms.

- Flack x = 0.024(39) (Parsons')
- Crystal size: 0.15 x 0.05 x 0.04 mm^3
- Experiment time: 4 hours
- Resolution: 0.75 Å
- Completeness: 96%
- Redundancy: 4
- R1 = 3.18%



Heavy absorbers

A group of researchers from the University of Montreal recently determined the crystal structure of the heavily absorbing compound $[Au(PPh_3)(S_2CNMe_2)]$ using a MetalJet source integrated into a Bruker D8 VENTURE. The compound was part of a study of materials based on d^{10} configured gold (I) compounds which have potential application in the area of luminescent sensors.

- Crystal size: 0.08 x 0.04 x 0.04 mm^3
- R1 = 3.94%
- Absorption coefficient µ (Ga Kα) = 10.57 mm^{-1}

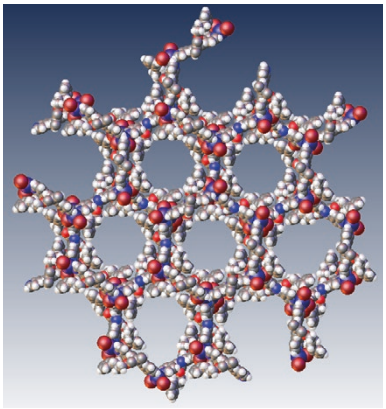
MolBank 2017, 2017(2), M937, N. Bélanger-Desmarais, C. Reber

Extended metal network structures

Researchers at the University of Basel have used a MetalJet mounted on a STOE diffractometer to study the crystal structures of a series of extended three dimensional metal network structures including $[Zn_2Br_4(L)]_n$. This structure exhibited long unit cell edges and a large unit cell volume of 28133.2(9) $Å^3$.

- a = 35.9593(6) Å
- b = 35.9593(6) Å
- c = 25.1227(3) Å
- R1= 8.98%

CrystEngComm, 2017, 19, 2894-2902, Y. M. Klein, A. Prescimone, M. Neuburger, E. C. Constable, C. E. Housecroft



Protein crystallography

Protein crystals are extremely sensitive and poorly defined, due to the large proportion of water within their structures. As a result, protein structures are 'floppy' and the X-ray diffraction data is typically of a much lower resolution quality compared to a small molecule structure. At the same time, the number of atoms present in a protein structure is very high and the data (Bragg reflections) to be collected is very closely packed together.

Protein crystallographers rely on the strongest X-ray sources to combat the issues of air sensitivity, small crystals, low diffraction and densely packed reflections. Traditionally, a high brilliance synchrotron has been used to measure full protein data leading to protein structure determination, whilst home laboratory instruments have been used for protein screening to identify the preferred crystals for measurement at the synchrotron.

High brilliance X-ray sources, such as the MetalJet have made a greater number of protein structures and experiments possible in the home laboratory, thereby accelerating research with ease of access and convenience.

Using the high brilliance MetalJet X-ray source makes weak diffraction data stronger, reducing experiment times and potentially reducing sample degradation. The narrow, focused X-ray beam is ideally suited to measure even the smallest protein crystals, providing compact and well-defined reflections. The higher intensity MetalJet X-rays typically extend the angular resolution limit of the visible protein data collected and provide more precise reflection positions and intensities, leading to higher resolution protein structures.

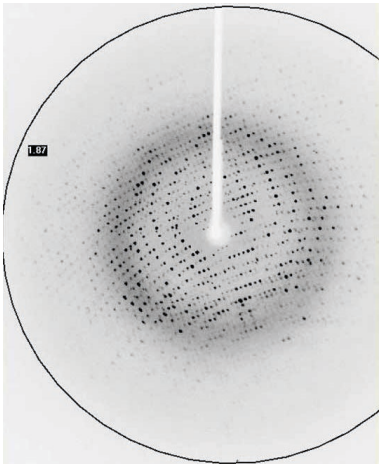
> *"The X-ray source helps a lot, in some cases its use replaces the need for synchrotron. Our main goal with purchasing and using the MetalJet is focused on studying smaller crystals. Working with 30 micron crystals is no longer an obstacle".*
>
> *Dr. Jan Dohnalek, Institute of Biotechnology, Czech Academy of Sciences, BIOCEV*

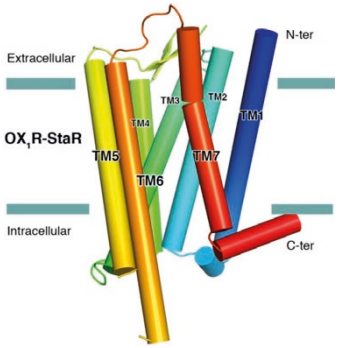
Example protein applications

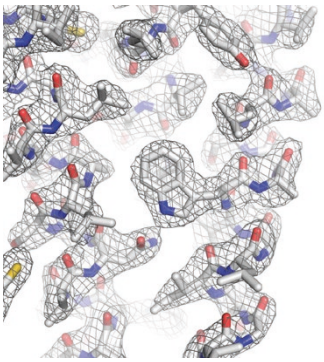
Fast data collection for high throughput screening

As an example of a fast data collection, applications scientists at Bruker AXS recorded data on a crystal of a cyclin-dependent kinase (CDK) using a MetalJet X-ray source mounted on a Bruker D8 VENTURE system. The complete experiment lasted 200 seconds and consisted of 100° of data with the resulting 1.95 Å data allowing for a structure solution by molecular replacement.

- Exposure: 1 second
- Crystal size: 0.1 x 0.08 x 0.05 mm^3
- Completeness: 97.5%
- Multiplicity: 3.68
- R_{merge}: 6.58%
- R_{pim}: 3.58%







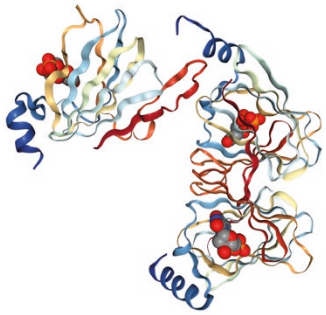
Membrane proteins in-house

The successful data collection and structure solution of membrane proteins is notoriously difficult and is rarely achieved. Even rarer is the successful determination of a membrane protein structure using an in-house X-ray diffractometer system, rather than a high brilliance synchrotron radiation source.

A small crystal of GPCR (Human Orexin receptor Ox1R-StaR®) has been successfully measured at Bruker AXS using an in-house MetalJet X-ray source mounted on a D8 VENTURE diffractometer.

Data were collected in a total experiment time of ~2.5 hours to 2.77 Å resolution and the structure was successfully solved by molecular replacement.

- Scan width: 0.1°
- Exposure time: 6 seconds
- Crystal size: 0.08 x 0.08 x 0.05 mm^3
- Multiplicity: 3.2
- I/sigma: 8.0
- R_{pim}: 7.62%
- R_{work} / R_{Free}: 0.244 / 0.2721

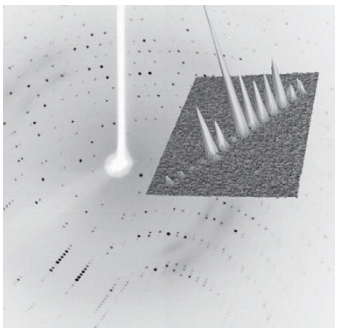


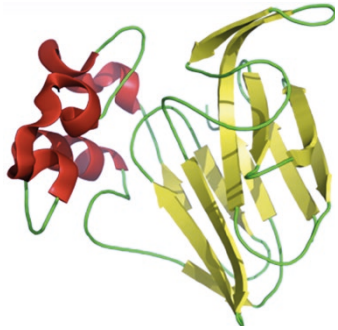
Ligand-enzyme co-crystallisation studies

Researchers at the University of Wisconsin (Department of Biochemistry) and the National Research Council Canada, Human Health Therapeutics, recently solved the structure of WlaRA (TDP-fucose-3,4-ketoisomerase) from Campylobacter jejuni using data collected with a gallium MetalJet D2+ X-ray source.

- Resolution: 2.15 Å
- Completeness: 99.3%
- R_{merge}: 7.1%
- Multiplicity: 7.1

Glycobiology. 2017, 27(4), 358-369, Z. Z. Li, A. S. Riegert, M. F. Goneau, A. M. Cunningham, E. Vinogradov, J. Li, I. C. Schoenhofen, J. B. Thoden, H. M. Holden, M. Gilbert





SAD phasing in-house

Application scientists at Bruker AXS have determined the crystal structure of Thaumatin obtained from Thaumatococcus danielii by sulphur-SAD phasing methods using data collected in-house on a D8 VENTURE diffraction system with a MetalJet X-ray source.

Using one 70 µm crystal, a complete data set was collected to 1.65 Å in <3 hours. The experimental phases were derived from the anomalous signal of the sulphur atoms and these allowed 95% of the protein backbone to be traced.

In-situ X-ray Crystallography

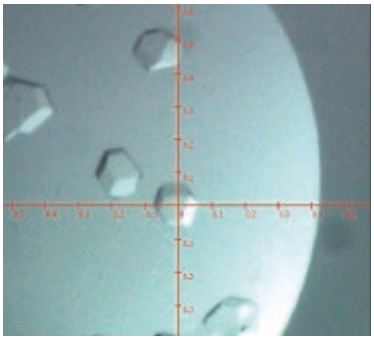
In-situ crystallography is a technique in which protein crystals undergo X-ray diffraction screening and or data collection whilst in a multi-well crystallisation plate and their original growth media/conditions.
Typically, X-rays are directed from one side of the multi-well plate, pass through the plate and crystal and out the opposite side of the plate, where the diffraction data are collected on an X-ray sensitive detector.

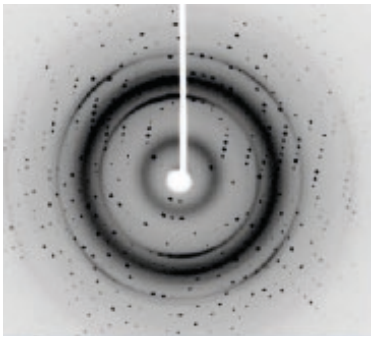
In-situ X-ray diffraction offers the following benefits:

- Automated, rapid screening and identification of large numbers of potential protein crystals without risk of damage to the crystals
- The identification of protein crystals from non-crystalline objects, salt crystals and other impurity crystals
- The identification of the best protein crystals for further X-ray study

Multi-well crystallisation plates are typically of plastic construction and exhibit low X-ray transparency, high X-ray absorption and significant X-ray background scatter, all of which serve to reduce and/or obscure the X-ray diffraction signal to be studied.
The MetalJet is the ideal choice of X-ray source for in-situ X-ray diffraction in the home laboratory due to the following unique combination of technical features:

- The potential to tune the X-ray beam size through the software, means the X-ray beam may be matched to the size of the crystal and precisely focused on to the crystal of interest, rather than a group of crystals. This also means that a much smaller area of plastic plate is illuminated by the X-ray beam leading to reduced background scatter.
- The higher X-ray brilliance of the MetalJet combined with the lower X-ray absorption of gallium radiation; when compared with copper X-ray sources, means that the X-ray signal obtained from in-situ diffraction is greater for the MetalJet.





Images courtesy of Bruker AXS.

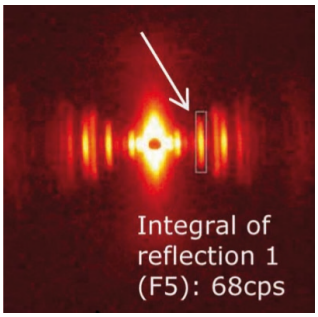
Small Angle X-ray Scattering (SAXS)

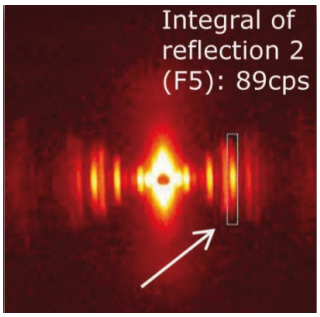
Small Angle X-ray Scattering is used to study the structure of materials in the 1 nm to ~200 nm range. The materials typically studied include polymers, metals, colloids, liquid crystals and biological samples e.g. proteins. The information determined relates to the particle size, shape, distribution and orientation, porosity, surface features and internal structure. A SAXS sample requires very little preparation and results are representative of the bulk material. The scattered signal is typically recorded at diffraction angles of <6° and the sample is positioned at a long distance from the detector. The measured scattered signals are accordingly extremely weak.
For this reason, SAXS measurements benefit from the use of a high brilliance X-ray source such as the MetalJet, which makes weak scattering effects, stronger, more visible and more readily studied.

Example SAXS applications

Fibres

Application scientists at Bruker AXS have used a NANOSTAR instrument equipped with a MetalJet (200W at 70kV) to record a series of SAXS scattering plots of a very thin fibre from a rat tail tendon. Providing intensity gains of more than 50x compared to state-of-the-art sealed microfocus tubes.

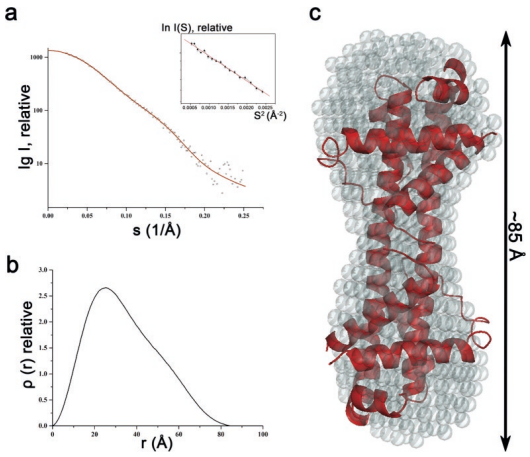




Biological (BioSAXS)

Researchers at Nanyang Technical University, A*STAR, University of Louisville, Rosalind Franklin University of Medicine and Science and Kyung Hee University have used a MetalJet equipped SAXS instrument to study the Bcl-xL protein, a key regulator in mitochondrial calcium ion transport. The protein was treated with a mild detergent and studied during the formation of a dimer resulting from three-dimensional domain swapping (3DDS) of helices α6-α8 between two monomers.

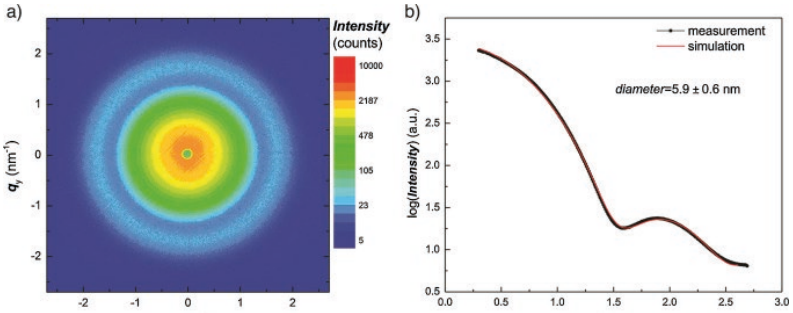
Sci. Rep. 5, 10609 (2015), S. Rajan, M. Choi, Q. T. Nguyen, H. Ye, W. Liu, H. T. Toh, C. B. Kang, N. Kamariah, C. Li, H. Huang, C. White, K. Baek, G. Grüber, H. S. Yoon.



Metals and colloids

Researchers at the Slovak Academy of Science and STU Centre for Nano-diagnostics performed in-situ tests on a strain gauge, based on a monolayer of colloidal gold nanoparticles deposited on a flexible Mylar foil. The tests were monitored by SAXS where the high brightness of the MetalJet allowed a very fast data collection, with 10 seconds temporal resolution.

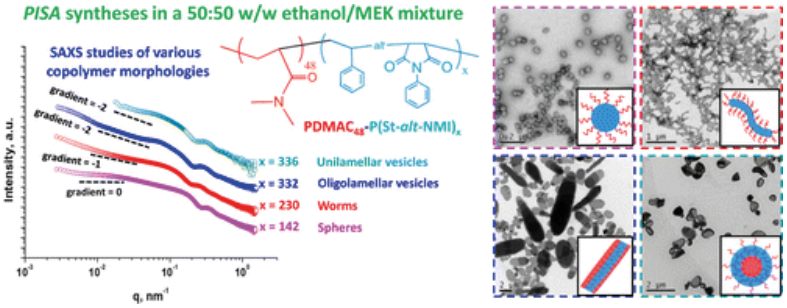
Sensors and Actuators A: Physical, 2016, 241, 87-95, K. Vegso, M. Jergel, P. Siffalovic, M. Kotlar, Y. Halahovetsa, M. Hodasa, M. Pellettaa, E. Majkovaa



Polymers

The investigation of polymers is one of the main areas of focus of the Soft Matter Analytical Laboratory (SMALL) at the University of Sheffield. Following a £2 million infrastructure investment in 2016 and the purchase of a new SAXS system with a gallium MetalJet X-ray source, their first new resulting publication was a co-polymerisation study of Styrene with N-Phenylmaleimide.

Macromolecules, 2016, 49 (18), 6731–6742, P. Yang, O. O. Mykhaylyk, E. R. Jones, S. P. Armes.



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