Absolute Configuration Determination for Light Atom Structures using Low Power Microfocus X-ray Sources

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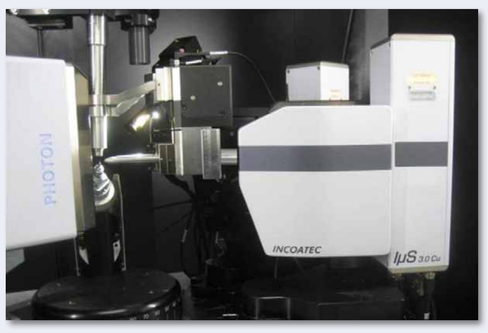
10 years IμS Celebrate the power

The determination of the absolute configuration for light atom structures is central to research in pharmaceuticals and natural products synthesis [1,2,3]. In the absence of elements heavier than silicon, it is often problematic to make a significant assignment of the absolute configuration. Besides the introduction of new methods to evaluate the Bijvoet differences [4,5] and improvements in refinement software [6], the assignment of the absolute structure for light atom compounds has become easier with the advent of high-intensity microfocus sources [7,8,9], as the increased flux density improves the anomalous signal by improving the counting statistics.

Incoatec Microfocus Source IμS

Since its introduction in 2006, the Incoatec Microfocus Source IμS has become the gold standard for low power low maintanance home-lab X-ray sources. The IμS combines a low power microfocus X-ray sealed tube with dedicated Montel multilayer mirrors and delivers intensities beyond those of traditional rotating anode sources. With more than 800 sources sold world-wide, the IμS is the market-leading microfocus source for X-ray diffraction applications, such as single crystal diffraction on small molecule and protein crystals as well as small angle scattering.

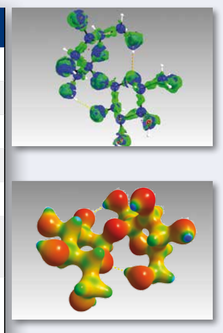
- Low power microfocus sealed tube
- Air-cooled
- Operated typically at 50 W
- Power load ~ 5 kW/mm²
- Montel multilayer mirrors
- Available for Cu-Kα, Mo-Kα, Ag-Kα
- Typical intensities ~ 3 x 10^{10} phts/s/mm² (Cu-Kα), ~ 3 x 10^{9} phts/s/mm² (Mo-Kα)
- Single port source



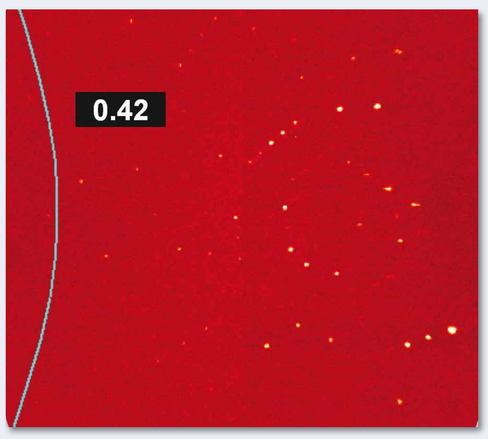
The latest generation of the IμS, the air-cooled IμS 3.0 source, contains the new Incoatec X-ray Tube *IXT* and is the first and only microfocus X-ray source that is designed for X-ray diffraction. Numerous small improvements in the design of the source, such as optimized take-off angles, and a new mounting concept (Quick-lock principle) for true downstream alignment with swappable optics make the IμS 3.0 the most user-friendly, yet most powerful microfocus X-ray source ever.

Sample1: Larger Crystal of Sucrose using Mo Radiation
a = 7.7189(2) Å, b = 8.6628(2) Å, c = 10.8085(3) Å, ß = 102.999(1)°, T = 100 K, Z = 2, P2$_1$, $C_{12}H_{22}O_{11}$

Source	Mo-IμS$^{High\ Brilliance}$
Total time [d]	3
Exposure time [s/°]	6 - 100
Resolution [Å]	0.41 (0.51 - 0.41)
Multiplicity	7.7 (5.1)
<I/σ>	47.2 (18.3)
*R*1, *wR*2 [%] (IAM) *R*1, *wR*2 [%] (Multipole)	2.47, 6.63 1.48, 2.28
Flack *x(u)* (IAM) Flack *x(u)* (Multipole) Parsons *Q*	0.00(15) 0.02(5) 0.03(4)



Sucrose: <|ΔF²$_{ano}$|>/<F²> = 0.06% (Mo), 0.30% (Cu)

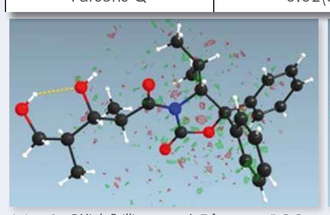


Typical diffraction pattern of the sucrose crystal, recorded with Mo-IμS HB (right), electron density and residual electron density (after IAM refinement,left, above) and electrostatic potential (left, below) of sucrose.

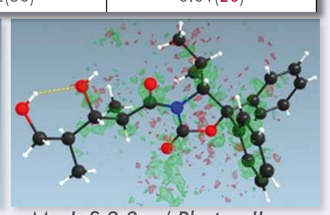
Sample 2: Diphenyloxazolidin-2-one derivate
a = 8.4167(17) Å, b = 13.761(3) Å, c = 19.304(4) Å, T = 100 K, Z = 4, P2$_1$2$_1$2$_1$, $C_{25}H_{31}NO_5$

Data comparison on a medium well diffracting crystal of a typical pharmaceutical small molecule compound (0.12 x 0.10 x 0.09 mm³), using Mo radiation.

Source	Mo-IμS$^{High\ Brilliance}$	Mo-IμS 3.0
Detector	Photon 100	Photon II
Exposure time [s/0.3°]	35; 15 h	35; 15 h
Max. Resolution [Å]	0.64	< 0.56
Resolution [Å]	0.80 (0.90 - 0.80)	0.80 (0.90 - 0.80)
Multiplicity	12.7 (9.1)	11.7 (9.3)
<I/σ>	41.6 (9.7)	55.2 (18.8)
*R*1 (all), *wR*2 (all) [%]	7.17, 14.77	8.11, 18.43
d(C-C) [Å]	1.387(4)	1.390(3)
Flack *x(u)*	0(1)	0(1)
Parsons *Q*	0.02(30)	0.01(20)



Mo-IμS$^{High\ Brilliance}$ w/ Photon100

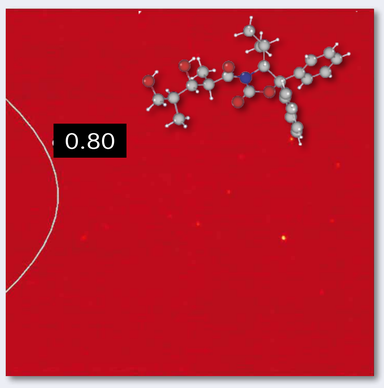


Mo-IμS 3.0 w/ Photon II

Data comparison on a medium well diffracting crystal of a typical pharmaceutical small molecule compound, using Cu radiation.

Source	Cu-IμS$^{High\ Brilliance}$	Cu-IμS 3.0
Detector	Photon 100	Photon 100
Exposure time [s/°]	4 - 12; 5 h	4 - 12; 5 h
Resolution [Å]	0.78 (0.88 - 0.78)	0.78 (0.88 - 0.78)
Multiplicity	10.8 (7.5)	10.7 (7.5)
<I/σ>	27.7 (11.7)	32.2 (14.8)
*R*1, *wR*2 [%]	3.88, 9.88	3.61, 9.20
d(C-C) [Å]	1.386(4)	1.389(3)
Flack x(u)	0.00(24)	0.04(22)
Parsons Q	0.07(9)	0.05(7)

Sample 2: <|ΔF²$_{ano}$|>/<F²> = 0.05% (Mo), 0.26% (Cu)

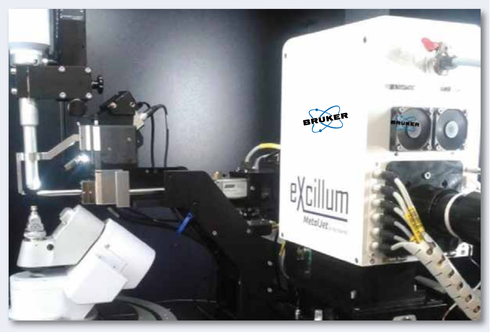


Molecular structure and typical diffraction pattern of sample 2 recorded with a Cu-IμS 3.0.

METALJET X-ray Source

The brilliance of conventional X-ray sources using a solid metal target is limited by the maximum power load that can be applied without melting the anode material. The METALJET X-ray source technology has overcome this limitation, as it uses molten alloys containing Gallium and Indium as high-speed liquid metal-jet targets instead of fast spinning solid metal targets. Therefore, power loads of more than 100 kW/mm² in a spot size of 20 μm or smaller can be applied, which are an order of magnitude larger than those of modern microfocus rotating anodes.

- High-speed liquid metal-jet target
- Air-cooled
- Operated typically at 200 W
- Power load > 100 kW/mm²
- Synchrotron-class Montel multilayer mirrors
- Available for Ga-Kα (1.34 Å), In-Kα (0.51 Å)
- Typical intensities ~ 4 x 10^{11} phts/s/mm² (Ga-Kα), ~ 5 x 10^{9} phts/s/mm² (In-Kα)
- Dual port source

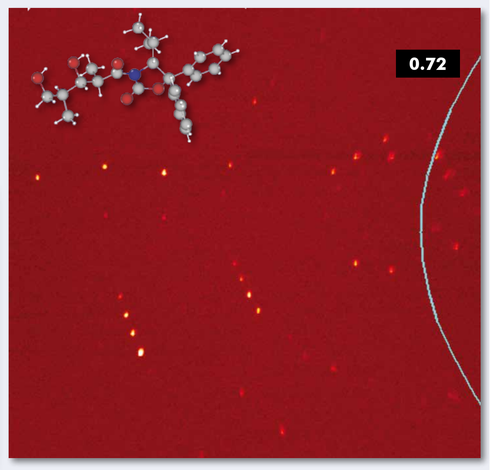


The HELIOS MX mirrors for Ga-Kα (9.3 keV) and In-Kα (24.2 keV) are synchrotron-class optics tailor-made for the METALJET source for single crystal diffraction applications, optimzed to preserve the extreme brightness of the source. They deliver a small and intense X-ray beam that is much brighter than what is currently achieved with microfocus rotating anode sources. As the energy of the Ga-Kα line is close to the Cu-Kα line, the METALJET using a Gallium rich alloy as target is the source of choice for ultimate performance in the home lab for applications such as protein and pharmaceutical crystallography, as well as small angle scattering.
By using an Indium rich target, the yield from the In-Kα line, which is close to the Ag-Kα line, can be maximized, giving highest performance for structure determination on absorbing materials and for high-pressure experiments using DAC's. The very short wavelength minimizes the absorption and leads to a compression of the q-space. Compared to Ag-Kα, about 50% more unique data are accessible.

Sample 2: Diphenyloxazolidin-2-one derivate, 0.12 x 0.10 x 0.09 mm³
a = 8.4167(17) Å, b = 13.761(3) Å, c = 19.304(4) Å, T = 100 K, Z = 4, P2$_1$2$_1$2$_1$, $C_{25}H_{31}NO_5$

Source	Ga METALJET	Cu μ-RAG
Exposure time	2 - 4 s/°, 2 h	2 - 4 s/°, 4 h
Resolution [Å]	0.71 (0.81 - 0.71)	0.78 (0.88 - 0.78)
Multiplicity	13.7 (3.7)	25.8 (7.1)
<I/σ>	42.5 (19.3)	60.5 (14.4)
*R*1, *wR*2 [%]	4.25, 11.33	4.53, 12.21
Flack *x(u)*	0.07(22)	0.00(20)
Parsons *Q*	0.03(4)	0.07(4)

Sample 2: <|ΔF²$_{ano}$|>/<F²> = 0.19% (Ga), 0.26% (Cu)

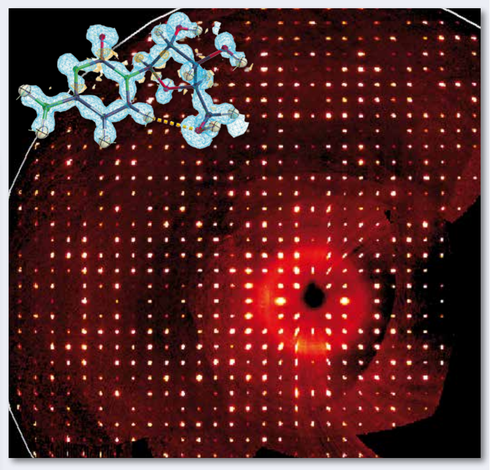


Typical diffraction pattern of the Diphenyloxazolidin-2-one derivate, recorded with the METALJET.

Sample 3: Larger Crystal of Cytidine
a = 5.0742(2) Å, b = 13.9292(6) Å, c = 4.7144(6) Å, T = 100 K, Z = 4, P2$_1$2$_1$2$_1$, $C_9H_{13}N_3O_5$

Source	Ga METALJET	Cu μ-RAG
Exposure time	1 s/°, 1 h	1 s/°, 1 h
Resolution [Å]	0.71 (0.81 - 0.71)	0.81 (0.90 - 0.81)
Unique data	2981 (925)	2000 (499)
Multiplicity	6.97 (4.67)	7.86 (3.44)
<I/σ>	62.88 (49.12)	78.23 (43.02)
*R*1, *wR*2 [%]	2.73, 7.15	2.21, 5.86
Flack *x(u)* (IAM) Flack *x(u)* (INVARIOM)	0.00(17) 0.01(3)	0.00(18) n.a.
Parsons Q	-0.01(3)	-0.02(3)

Cytidine (<|ΔF²$_{ano}$|>/<F²> = 0.20% (Ga), 0.27% (Cu))

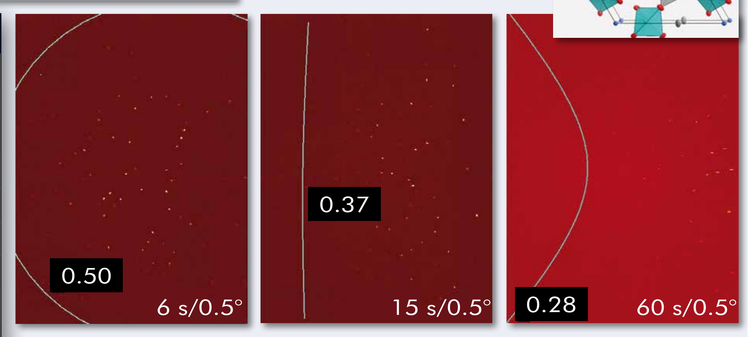


Calculated precession pattern of the 0kl layer, recorded with the METALJET, and deformation density of Cytidine.

Sample 4: Crystal of a Highly Absorbing Langasite-type (Lanthanum Gallium Silicate) Compound: Z = 1, P321

Source	In METALJET
Total time [d]	2.7
Exposure time [s/0.5°]	6 / 15 / 60
Resolution [Å]	0.28 (0.38 - 0.28)
Multiplicity	37.1 (26.7)
<I/σ>	38.2 (21.6)
R_{int} (%)	7.93 (16.77)
*R*1, *wR*2 (%)	2.78, 7.44
Flack *x(u)*	0.057(7)
Parsons *Q*	0.058(2)

Sample 4: <|ΔF²$_{ano}$|>/<F²> ~ 4% (In)



Data statistics and typical diffraction patterns of a small Langasite crystal at low, medium and high resolution, collected with a D8 VENTURE 2nd Gen. and the METALJET source using an In rich alloy.

Literatur
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