Xenocs
Reflecting Future Technology
Newsletter
Vol. 6 — December 2006

Editorial : Quality X-rays

Xenocs is proud to announce that we received ISO 9001:2000 certification in October of 2006. The certification is linked to our core values at Xenocs, the first one being Customer Satisfaction. The ISO certification is another way of saying that we listen to our customers and always strive to deliver customer satisfaction through quality products and service.

Quality is what we strive for when innovating and bringing new solutions to our customers, helping them to improve equipment performance and to rapidly achieve an optimal return on investment.

Quality is what we deliver with the GeniX platform that delivers x-ray beam performance several times that achievable with standard sealed tubes, while consuming a mere 50 W. And while achieving performance levels equivalent to that of traditional rotating anodes, the GeniX system is far superior in terms of cost of ownership, reliability, and stability.

Peter Høghøj,
President and CEO

The GeniX system is now available in several configurations optimised for a range of applications. As you will see inside the newsletter, customer feedback is enthusiastic.

So look to Xenocs for high quality x-rays.

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Beams and brilliance

When striving to optimise an x-ray analytical measurement it is worth stepping back to look at your equipment. As shown in Fig. 1, the "heart" or "application engine" of an x-ray analytical instrument has several key components. Detectors have seen very important progress over the past decades, in particular position sensitive detectors that are available with resolution, dynamic range, and efficiency adequate for most applications. With the detection side being increasingly refined, one turns to the beam delivery side of the instrument to find ways of improving instrument performance. Typically, instrument and measurement performance includes parameters such as small sample and mapping capabilities, resolution, and throughput. As shown in Fig. 2, these parameters translate into key x-ray beam properties when taking into account the requirements of a given application.

The beam properties can be described as photon distribution in real-space, angular space, in energy, and in time. These properties are in turn linked to key beam delivery components, in particular the x-ray source, the optics, and the beam-path. The beam intensity per solid angle and per unit area in the relevant part of the spectrum is normally termed brilliance and is meas-

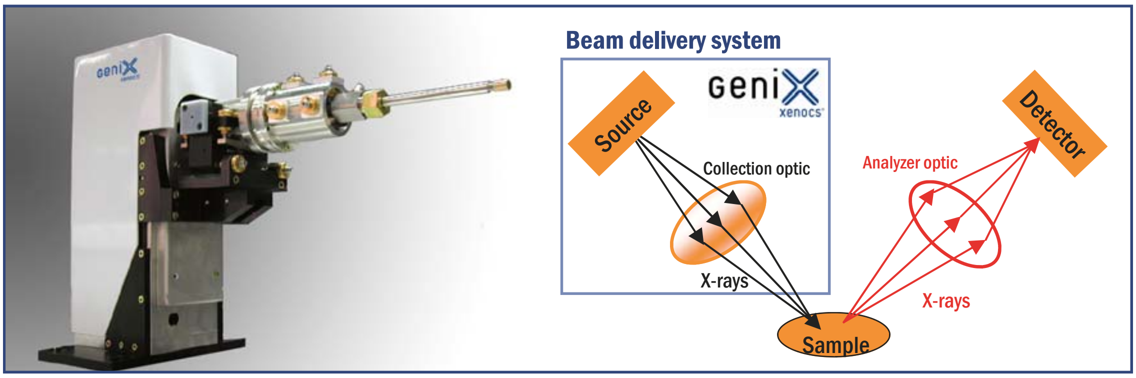

Fig. 1: Key components of an X-ray analytical equipment

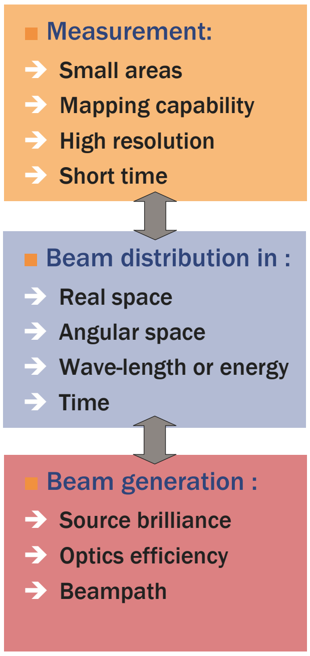

Fig. 2 : The path from measurement to beam generation

ured in photons/mrad²/mm²/s/bandwidth.

Brilliance, of course, starts with the source. At best, the optics and beam path preserve the brilliance of the source while transforming the phase space distribution of the beam into a useful (optimum) distribution. Over the last decade x-ray optics capable of efficient phase-space transformations have become available. This is opening a new paradigm in x-ray beam delivery because we can now create high brilliance x-ray beams by collecting large solid angles of radiation from small x-ray sources as an alternative to the brute-force method of using ever larger and more power-consuming sources to generate more intensity. As an analogy, you might think of the headlights of your car where the parabolic reflector and lenses (the optic) directs the light where you need it. Just using a larger and higher power light bulb without the reflector would not be very efficient.

Single reflection aspheric multilayer coated optics are highly efficient in collecting radiation from small sources and creating beams suited for a range of applications. While synchrotron sources are highly successful scientific instruments, electron bombardment x-ray sources are the rule for research laboratory, industrial and medical use. The main performance limitation for electron bombardment sources is the heat load on the anode. Since the electron to x-ray conversion efficiency is quite low, most of the electron beam energy is deposited in the surface layer of the anode. For large electron beam footprints most of the heat is evacuated in the depth of the anode, but for footprints comparable to the surface layer thickness the periphery of the electron beam gives a significant contribution to heat transport. This effect makes it possible to achieve much higher anode power densities and brilliance for micro-focus x-ray sources.

As seen in Fig. 3, modern micro-focus tubes achieve power densities of several times that of standard sealed tubes. In fact, the power density and brilliance is close to that of traditional rotating anodes. The GeniX system combines a micro-focus tube with Xenocs' single reflection aspheric multilayer coated optics. Customers have tested the system in a number of applications and the first preliminary results are presented in the following articles. As expected, the high brilliance translates into better results in less time for a number of applications. And all this using just 50 W...

X-ray source	X-ray source size (mm)	Power (W)	e-beam (mm²)	Power density (W/mm²)
Sealed tube	1.2 x 0.4	2200	12 x 0.4	460
Microfocus tube	0.050	50	0.3 x 0.05	3330
Rotating anode	0.300	5000	3 x 0.3	5500
Micro-focus rotating anode	0.070	800	0.7 x 0.07	16000

Fig. 3: X-ray source brilliance is linked to the electron beam and anode properties. If the anode material, take-off angle, and the electron energy are fixed, then x-ray source brilliance will essentially depend on the power density of the electron beam. The micro-focus tube configuration for Copper radiation corresponds to an x-ray brilliance of about 10^{10} ph/s/mm²/mrad²/0.25% bandwidth.

High-throughput Sulphur-SAD phasing of Elastase using a STOE-IPDS2T diffractometer equipped with a XENOCS GeniX Cu *Kα* microbeam system

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
Courtesy of Marc Schiltz. Laboratoire de Cristallographie. École Polytechnique Fédérale de Lausanne (*EPFL*). Switzerland.

Solving protein crystal structures by single-wavelength anomalous diffraction (SAD) from sulphur atoms has become a widely advocated technique in recent years[1]. This method has several appealing features: (1) Since it uses the anomalous scattering properties from sulphur atoms that are naturally present in protein molecules, the haphazard step of preparing heavy-atom derivatives is removed; (2) Data can be collected away from the absorption edge, using laboratory equipment operating either with Cr *Kα* [2] or Cu *Kα* [3] radiation. On the other hand, given that the anomalous scattering strength from sulphur atoms is rather weak at these wavelength (f''=0.557 at Cu *Kα*), the data have to be collected with a very high degree of accuracy, completeness and redundancy[4]. Such measurements are therefore ideal to test the capabilities and performances of a laboratory diffractometer setup.

The *STOE* image-plate system *IPDS2T*, equipped with a *GeniX* microbeam system manufactured by *XENOCS* (Fig. 4) was used to collect a highly redundant data set from crystals of porcine pancreatic Elastase, a 26 kDa protein of 240 amino acids (1826

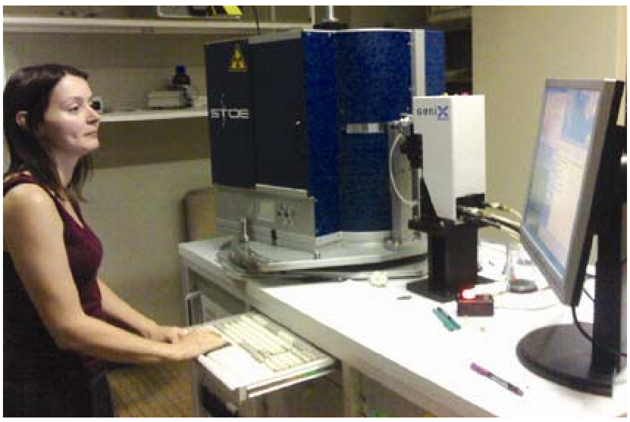

Fig. 4: The combined *GeniX-IPDS2T* setup installed at *EPFL*-Lausanne.

non-hydrogen atoms) containing 10 sulphur atoms (8 Cys + 2 Met). The crystals belong to space group P2(1)2(1)2(1) with cell parameters 51.31 58.02 75.41 Å.

The *GeniX* microbeam system was operated at 50 kV, 1 mA. The circular image plate (scanned surface: 170 mm radius) was positioned at a distance of 150 mm from the sample with zero 2-theta offset, thus allowing data to be collected at a maximum resolution of 1.89 Å. A highly redundant data set, consisting of two 0–180° omega-scans recorded at two different phi angles (0° and 90°) was collected . The data comprise a total of 360 frames, each corresponding to a 1° omega rotation and an exposure of 300 seconds. Fig. 5 displays an example of a data frame. The frames were indexed and integrated with the *MOSFLM*[5] program. Data reduction (scaling and merging) was carried out with the program *SCALA*[6] from the *CCP4*[7] package. Details of data reduction statistics are given in Table 1.

The reduced data were then fed into the *autoSHARP*[8] software package, using the program defaults for all non-compulsory input parameters. Detection and refinement of sulphur atoms, SAD phasing and phase improvement by density modification, chain tracing, model building and refinement of the structure were carried out in a completely automatic fashion, without further user intervention. The final model consists of 237 residues (out of 240), refined to R=15.5% and R-free=21.2%.

As can be seen from Table 1, the data quality is indeed very high. Though the anomalous differences are small, the *SHELXD* heavy atom detection method, as implemented in *autoSHARP*, readily located 8 out of the 10 sulphur atoms. The two additional sulphurs were located by the automatic procedure for analysing residual maps. The SAD phases are of very good quality as is evidenced in Fig. 6, where the experimental electron density map computed from SAD phases and after density modification, but prior to any model building, is displayed. The structural model of elastase, as retrieved from the PDB data-bank, is superimposed to this map. As can be seen, the agreement is very good.

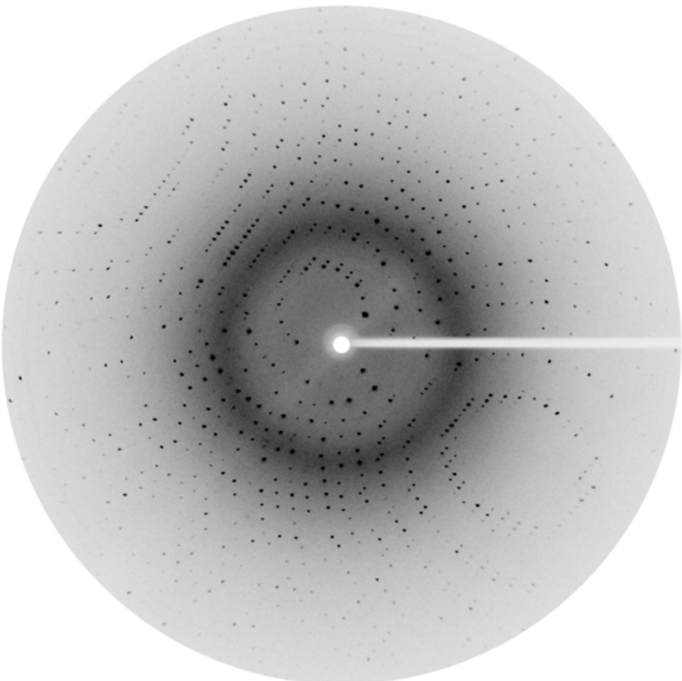

Fig. 5: Diffraction frame recorded on an elastase crystal. Scan width: 1° (omega), exposure time: 300 sec. Crystal-detector distance: 150 mm. Resolution at edge (170 mm from the centre): 1.89 Å.

	Overall	Inner Shell	Outer Shell
Low resolution limit / Å	27.09	27.09	1.98
High resolution limit / Å	1.87	5.93	1.87
Rmerge	0.047	0.025	0.141
Rmeas (within I+/I–)	0.050	0.027	0.152
Rmeas (all I+/I–)	0.050	0.029	0.151
Rpim (within I+/I–)	0.018	0.010	0.057
Rpim (all I+/I–)	0.013	0.008	0.041
Fractional partial bias	-0.003	-0.008	0.003
Nb. of observations	257953	8637	29515
Nb. of unique reflections	18621	687	2246
Mean I/sd(I)	44.2	73.9	18.6
Completeness (%)	97.4	99.1	82.1
Multiplicity	13.9	12.6	13.1
Anomalous completeness (%)	97.1	99.8	81.0
Anomalous multiplicity	7.3	7.5	6.8

Table 1: Data reduction statistics

As a conclusion, the quality of the data produced by the combined *GeniX*-*IPDS2T* setup installed at *EPFL*-Lausanne is capable of solving a 26 kDa protein structure in a quasi-automatic fashion by sulphur-SAD.

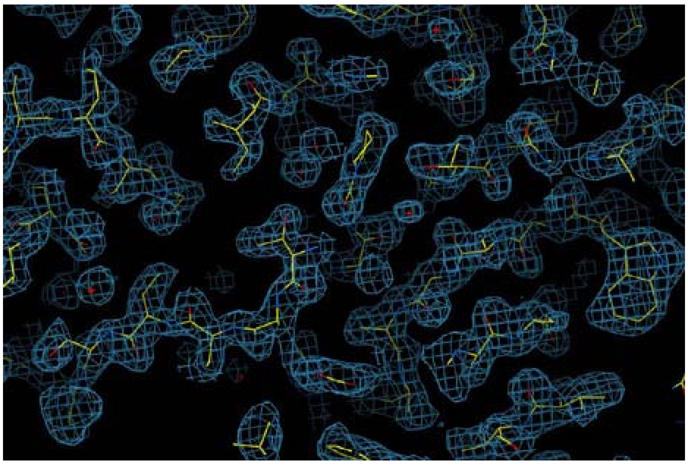

Fig. 6: Experimental electron density map computed from Sulphur-SAD phases and after density modification, but prior to any model building. The structural model of Elastase, as retrieved from the PDB databank, is superimposed to this map. As can be seen, the agreement is very good.

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GeniX Mo Small Spot

The demand for tightly focused Mo X-ray beams has increased over recent years due to the usefulness of this radiation for applications such as microdiffraction, high pressure crystallography, and small molecule diffraction. Currently, sealed tubes coupled with graphite monochromators are the standard for Mo diffraction applications. However, despite delivering high integrated flux, graphite monochromators cannot deliver high flux density on a small spot (i.e. less than 200 microns) with good spatial resolution.

To address this shortcoming Xenocs introduces the GeniX Mo Small Spot, an extension of the industry proven GeniX product platform, for diffraction applications requiring Mo radiation (geological samples, small molecules…).

The GeniX Mo Small Spot, combining a single reflection multilayer optic and a 50 W microfocus sealed tube, delivers $2x10^6$ photons/sec of Mo Kα radiation on a $100x100\ \mu m^2$ focal spot (FWHM). The focusing power of the optic eliminates the need for pinholes, making the GeniX an excellent choice for work that precludes placing any beam-conditioning elements between the optic and the focal plane. For specific applications, the system can easily be adapted to achieve smaller spot sizes. Furthermore, the smart power management extends the source lifetime, lowering the cost of ownership and increasing the up-time, while the intuitive user interface of the control unit provides functionality for both standalone and integrated use.

With its unprecedented stability and reliability, the GeniX Mo Small Spot provides a significant performance increase over traditional sealed tubes, making it an excellent upgrade choice for these sources. It also proves a reliable, cost-effective, and low-maintenance alternative to expensive rotating anodes sources.

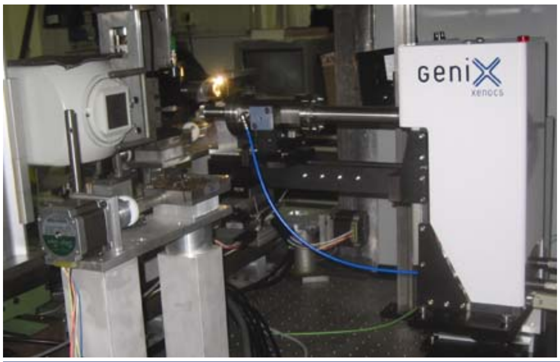

Fig. 7 : GeniX Mo Small Spot on a high pressure set up

Xenocs receives ISO 9001 certification

We are proud to announce the recent ISO 9001:2000 accreditation of Xenocs by Bureau Veritas Certification. This certification is another indication of the commitment to quality that Xenocs upholds in the development, manufacturing, and commercialization of X-ray components, X-ray sources, and X-ray beam delivery systems.

ISO 9001 is recognized worldwide as the comprehensive international standard that defines quality. It provides independent annual auditing to ensure both compliance and continuous improvement initiatives in all aspects of the organization.

The ISO 9001:2000 certification indicates that the policies, practices and procedures of Xenocs ensure consistent quality in the services and products we provide our customers. With this certification, our customers can be confident that Xenocs and all its employees are dedicated to maintaining the highest efficiency and responsiveness in achieving our ultimate goal – complete customer satisfaction.

Our ISO 9001:2000 certification not only anticipates our customers' demands, but also demonstrates our commitment to providing our customers with products and services of the highest possible quality.

ISO 9001 BUREAU VERITAS Certification

Forthcoming Conferences 2007 :

Date	Event	Place
January 22-24	36th National Seminar on Crystallography	Chennai (Madras), India
January 24-25	Advances in Protein Crystallography	South San Francisco, USA
February 19-22	PPXRD6 - The 6th Pharmaceutical Powder X-ray Diffraction Symposium	Barcelona, Spain
March 05-09	Joint annual Meeting of the German Society for Crystallography (DGK) and the German Society for Crystal Growth (DGKK)	Bremen, Germany
March 11-14	WCPCW - The West Coast Protein Crystallography Workshop	Pacific Grove, USA

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