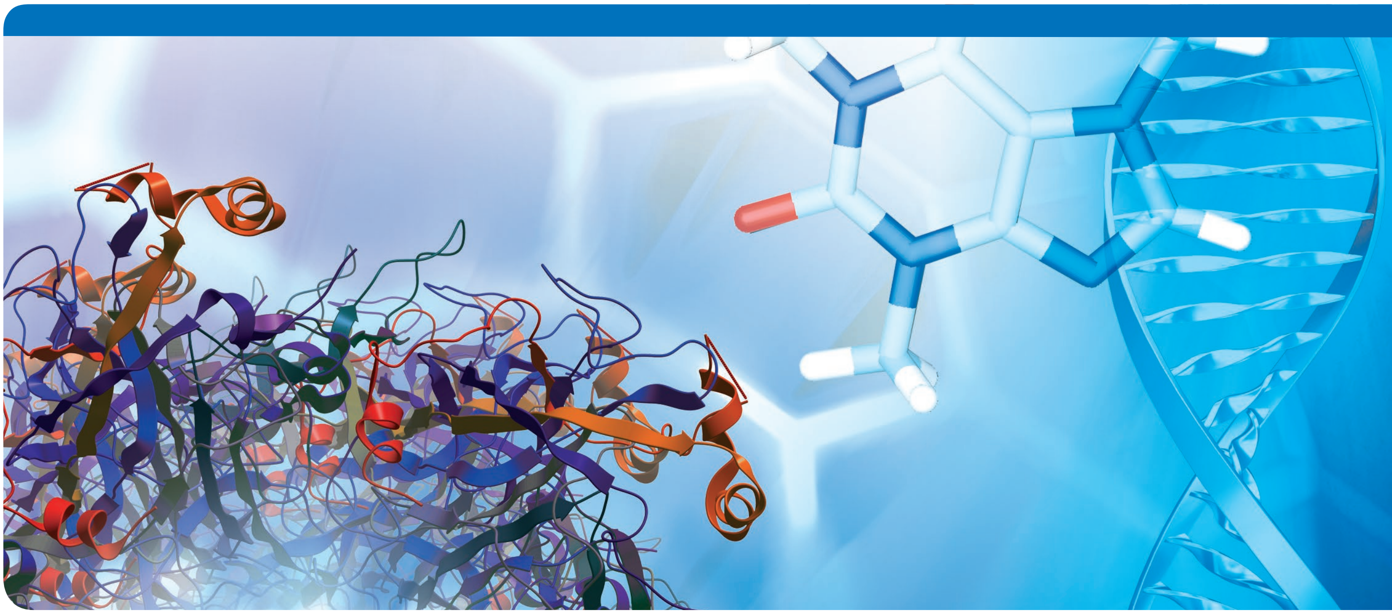


Technical Note SC-XRD 4

Characteristics and Relative Performance of Laboratory X-ray Sources for Macromolecular Crystallography

Introduction

Today's modern laboratory X-ray sources apply the very same principle that was used to produce X-rays when they where discovered the first time: energetic electrons impact a metal target, creating bremsstrahlung and characteristic X-rays. However, while the method used to generate X-rays has not changed, source technology has advanced significantly. Both modern microfocus sealed tubes and microfocus rotating anodes have increased greatly in brightness over the last several years. In combination with recent improvements in multilayer X-ray optics, laboratory sources can now rival the intensity of second-generation synchrotron beam lines.

This rapid development in technology has given the user more options than ever before—but it can also lead to confusion about how the various sources perform compared to one another. This Technical Note discusses the characteristics and relative performance of the principal X-ray sources now available for the home laboratory: microfocus sealed tubes, microfocus rotating anode generators, and liquid-metal sources.

Overview of source technology

Microfocus sealed-tube sources are now available with intensities up to 10 times that of a "classic" rotating anode (5-6 kW, 300 micron focus, BLUE-type optics, see Table 1). Microfocus sealed-tube sources have the advantage of lower capital and operating costs compared to rotating anodes. Microfocus tubes also require significantly less power than rotating anode systems (typically <100 W) and thus require only standard, single-phase power. The IμS 3.0 microfocus source offered by Bruker does not require 3-phase power nor water cooling, which means simpler installation and no special room preparation.

Modern microfocus rotating anode generators achieve significantly higher intensity: up to about 45 times higher than a classic rotating anode generator (or more than 3 times higher than a microfocus sealed tube). They do require more routine maintenance than a microfocus tube (such as periodic filament changes and anode refurbishment), though the maintenance requirements are significantly lower than older-style conventional rotating anodes due to the lower total power loading and improvements in anode and vacuum seal technology. These sources are suitable for screening and data collection for samples as small as 20-25 microns (depending on diffraction quality).

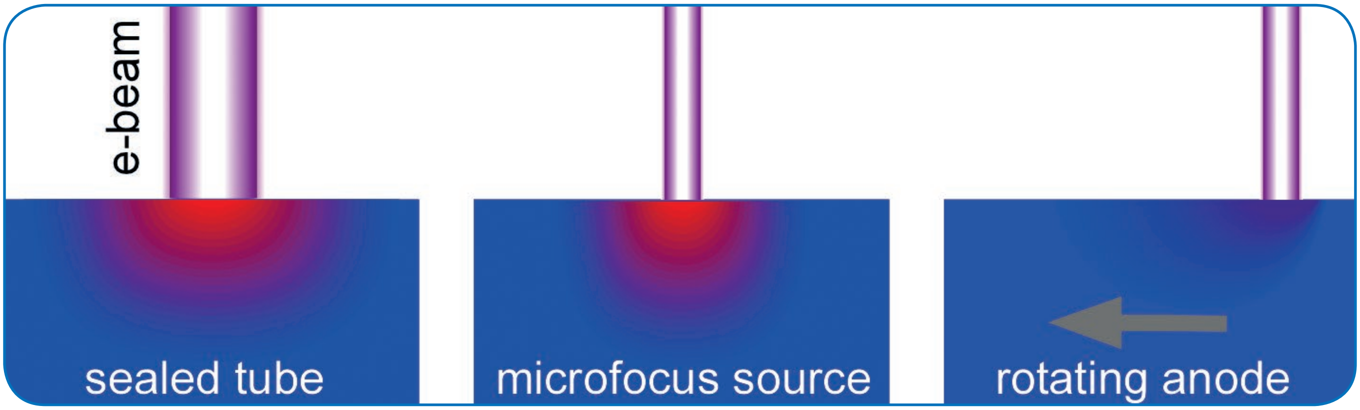


Figure 1: Temperature distributions in target cross-sections underneath the electron beam. Power density is the same for each source (cold regions shown in blue, hot regions shown in red).

Finally, liquid-metal-jet sources boast the highest brilliance and intensities available in the home lab—more than 120 times higher than a classic rotating anode. These sources are suitable for the most demanding home lab applications such as screening, *de novo* structure solution, and high-resolution data collection for micron-sized crystals. Maintenance requirements are similar to those of rotating anodes. They operate at only 200 W primary power and thus do not require 3-phase power or external water cooling.

Characterization of X-ray sources

X-ray sources are characterized by their *brightness, intensity* and *flux*. Though these values are sometimes confused, it should be understood that they are in fact distinct quantities:

Brightness is defined as the number of characteristic photons emitted per unit area, per unit time and per unit solid angle. Bright sources can thus provide an X-ray beam that is intense with a small angular spread—ideal for crystallography. It is important to note here that *brightness is a property of the source that cannot be improved by optics.* That is, optics can increase intensity (see below) but they cannot increase brightness (in fact, real optics decrease the beam's brightness due to non-ideal reflectivity). Simply put, brightness is the "quality" of the emitted X-rays. All other things being equal, the brightest source will deliver the most intensity at the sample and produce the best data.

Table 1: Relative brightness, maintenance requirements, costs, installation requirements, and applications of home lab X-ray sources.

	Relative Intensity	Maintenance Requirements	Relative Cost	Installation Requirements	Typical Applications
"Classic" Rotating Anode	1[1]	High	1	3-phase power, water cooling	
Microfocus Sealed Tubes	4-12	None[2]	0.5	None	Sample screening, data collection on crystals which exhibit medium to strong diffraction
Microfocus Rotating Anode	20-45[1]	Medium[3]	2-4	3-phase power, water cooling	Sample screening, data collection on most sample types
Liquid-Metal Source	>120	Medium[4]	5	None	All crystals including weak diffractors and micron-size samples

[1] Typical intensity decreases by 30% after only a few 100 hours of operation, due to anode roughening.

[2] Typically, the tube must be replaced every 3 years.

[3] Typically, the filament must be replaced 2-3 times per year, and the anode refurbished annually.

[4] Typically, the nozzle and cathode must be replaced 3-4 times per year, and the exit window protection replaced annually.

Several factors determine the brightness of an X-ray source. Examples are the energy distribution and spatial profile of the electron beam which impacts the target anode and the angle at which the emerging X-rays are taken from the target. The most important factor, however, is the electron power density: bright sources have a concentrated electron beam at the target. Only a small fraction of the electron energy is converted into X-rays, so most of the incident energy is dissipated into the target as heat. The power density and thus the brightness are limited by the target material's melting temperature and by the efficiency with which heat is removed from the area where the electrons impact the target.

Laboratory source development has therefore concentrated on techniques for removing the heat as efficiently as possible. Figure 1 shows the simulated temperature distribution in the targets of different source types. The electron beams differ in size, but not in power density. Conventional sealed tubes have long and wide electron beams, so that a large area of the target is heated. Heat generated in the middle of this spot can mainly flow in just one direction: toward the cooled interior of the target (Figure 1). Heat flow parallel to the surface is minimal, thus limiting the cooling efficiency. It is for this reason that conventional sealed tubes achieve the lowest power density and thus the lowest brightness of any laboratory X-ray source.

Microfocus sealed tubes have small electron beams and heat only a small area of the target. Heat can then also flow sideways, improving the thermal cooling efficiency. This allows this type of tube to achieve significantly higher power loading and thus higher brightness.

In rotating anode generators, the target is moved relative to the electron beam. Cold parts of the target are moved into the electron beam, continuously providing an extremely large effective cooling efficiency. The modern microfocus rotating anode takes advantage of both these effects to achieve the highest available brightness in a home source.

IμS 3.0 microfocus sealed tube source.

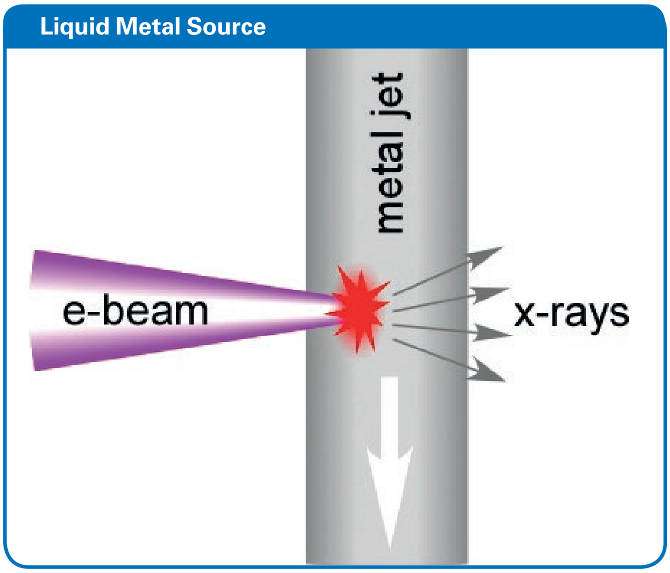


Figure 2: The operating principle of a liquid-metal anode source.

As noted above, both sealed-tube and rotating anode microfocus sources are limited by the anode's melting point. It is possible to achieve higher power loading by using a liquid-metal anode.

Bruker is the first to offer a liquid-metal-jet source for macromolecular crystallography. This source uses a jet of liquid Gallium as the anode. Ga is suitable because of its low melting point (near room temperature), its low vapor pressure, and also because its Kα energy (9 keV) is similar to that of Cu Kα (8.1 keV). Like a rotating anode, the METALJET can be operated with either one or two active ports.

The METALJET anode achieves the highest performance of any laboratory-based X-ray source: more than 120 times the intensity of a classic rotating anode.

Another great advantage of the METALJET is that its brilliance is constant over time. In a rotating anode, the specified intensity is only achieved for a few hundred hours of operation, because the electron beam gradually causes degradation of the anode surface. After one year of operation, the intensity of a rotating anode typically declines by 30-50%. However, unlike a rotating anode, the METALJET's electron beam always sees a fresh, clean anode surface.

Intensity is the number of X-rays per unit area per unit time at the sample position. Intensity is given by the brightness of the source times the convergence angle of the optics squared (this is the well-known Liouville's theorem). Simply put, intensity characterizes the combination of the tube and the optics. To first order, the diffracted signal is equal to approximately the intensity times the crystal size. Therefore, intensity is often the most useful way to compare source performance.

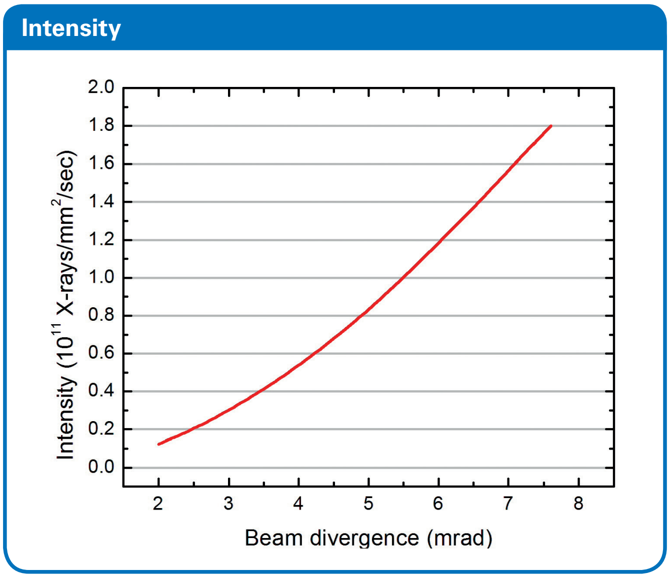


Figure 3: Intensity at the sample versus beam divergence (for the TXS microfocus rotating anode generator with HELIOS MX optics). Note that the maximum intensity is achieved at the highest divergence. For crystals with long unit cells, a smaller divergence must be used (see below) and thus the intensity is therefore decreased.

Intensity and brightness are related by the well-known Liouville's theorem

$$I = BR\alpha^2 \qquad (1)$$

Where I is the intensity (in X-rays/mm^2-sec), B is the brightness of the tube, R is the reflectivity of the optics, and α is the divergence angle of the optics (also often called the "convergence angle"—the two terms are equivalent since the beam *converges* from the optic to the focus and then *diverges* after the focus with the same angular spread).

By considering Liouville's theorem, it can be understood that optics work by trading beam divergence for intensity. That is, the more divergent the focused beam from the optics, the higher will be the diffracted signal from the sample. This is why, over the past several years, optics designers have concentrated on designing ever-larger mirrors that can achieve higher divergence.

The practical implication of this is that optics with increasing divergence angles will increase the diffracted signal (which is obviously a good thing) while also increasing the size of the diffracted spots (which is typically not such a good thing). Thus, while some divergence of the beam is desirable, too much cannot be tolerated.

So, what is the optimal beam convergence? Theory and tests show that convergence angles on the order of 5-8 mrad produce the best data for most samples. This is discussed in more detail below.

Flux is the total number of X-rays emitted by the source. This is typically not as useful a measure for comparison because it does not give a direct indication of how many X-rays will actually illuminate the sample (and thus it is not as directly related to the diffracted signal as is intensity).

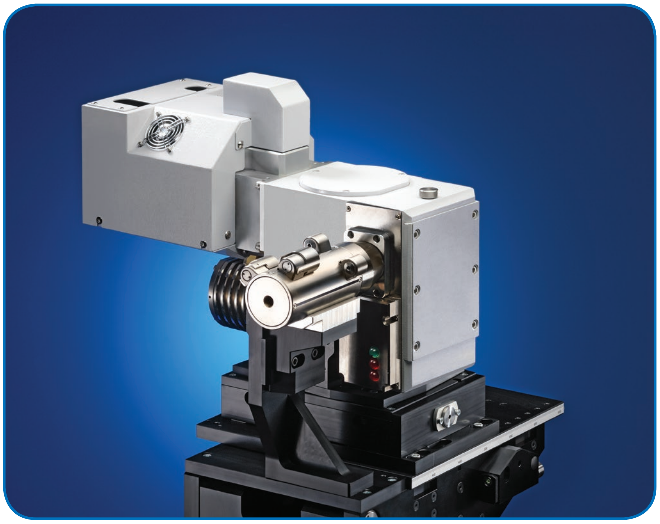
Microfocus source performance: is it only about the power?

So, given that the intensity is the single most important characteristic of a source, it may be surprising that many sources do not specify the intensity at all but rather specify only the primary power. For example, one may see a microfocus source specified as "50 W". What does this mean? Are all 50 W sources the same? Is 50 W better than 30 W?

The truth is that the primary power can be misleading as an indicator of performance. As above, we know from Liouville's theorem that the *intensity at the sample is proportional to the power density, not the total power*. So, for example, a 30 W tube with a 20 micron focus is fully 1000 times more brilliant than a 3000 W tube with a 1 mm focus!

Another important aspect of the source's performance is the design and quality of the optics. In particular, for microfocus performance, low figure errors (essentially low "waviness") are crucial to the final intensity. For example, for a 20 micron anode focus, Bruker low-figure-error mirrors with 2 mrad arcsecond figure errors are up to 3 times more efficient than equivalent conventional mirrors with 10 arcsecond errors. This is especially crucial for METALJET applications.

So, with all these complicated variables, how should one compare sources? The best way is to *consider the intensity at the sample at the same divergence*. This takes into account all the important parameters that determine the source performance, including brilliance and optics performance. This is why



TXS microfocus rotating anode source.

Bruker specifies the intensity for each and every source configuration and guarantees that the user will achieve this same intensity in real-world applications.

IμS 3.0: the importance of advanced tube design

From our partners at Incoatec, Bruker has long enjoyed the best quality X-ray optics. Incoatec optics feature the highest reflectivities, the lowest figure errors, and the largest collection solid angle available anywhere.

In addition, our third-generation microfocus source, the IμS 3.0, benefits from having the only microfocus tube on the market specifically designed and optimized for X-ray diffraction applications. The tubes used in other microfocus sources were designed for Non-Destructive Testing (NDT), and thus these tubes are not optimized for X-ray diffraction. In particular, NDT tubes typically have lower brilliance due to non-optimal anode geometry.

The third-generation Bruker microfocus tubes employed in the IμS 3.0 are designed and manufactured by Incoatec specifically for X-ray diffraction. With a completely-optimized anode geometry, they achieve—by far—the highest brilliance, contributing to an intensity more than two times higher for Cu radiation than other microfocus tubes. Not to mention legendary tube lifetimes and reliability...

Air cooling versus water cooling: which is better?

As noted above, the relatively low power of the IμS 3.0 microfocus source allows it to be air cooled. This provides the user with a number of benefits including ease of installation, lower operating costs, and lower noise.

METALJET liquid-metal source.

Of course, it is more challenging to design an air-cooled tube; the tube must incorporate sophisticated feedback mechanisms to maintain constant temperature in the face of variations in the external air temperature. The IμS is currently the only source to have mastered this technology: a tube with a highly stable output and very long tube lifetime, superior to the best water-cooled designs.

The stability of the IμS with respect to changes in air temperature is demonstrated in Figure 4, which shows the measured intensity diffracted from a 100 micron crystal (vitamin C) over 5.5 hours. The ambient temperature was varied by approximately 3° Celsius per hour during the measurement yet the measured diffraction varies by less than 0.19% (rms).

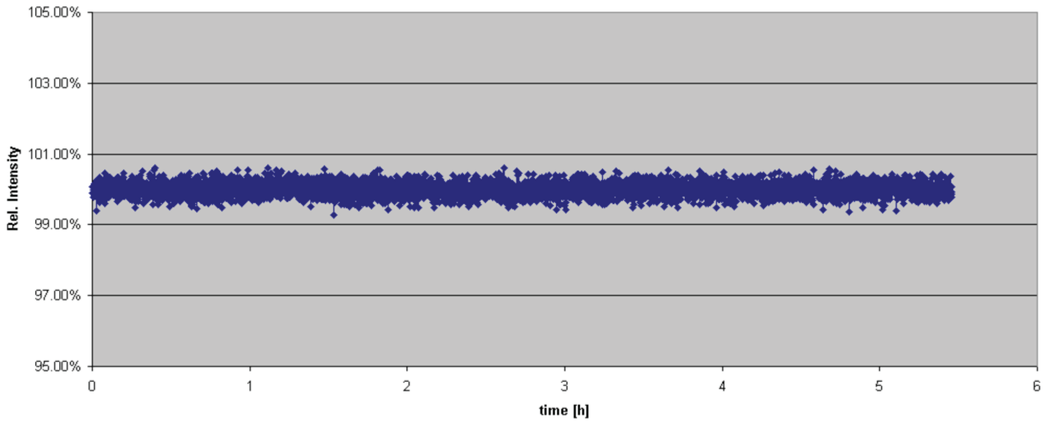
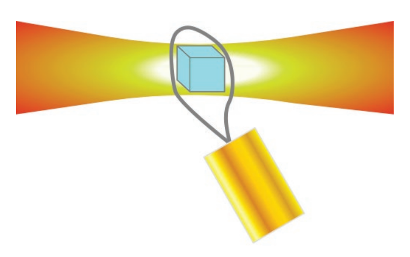
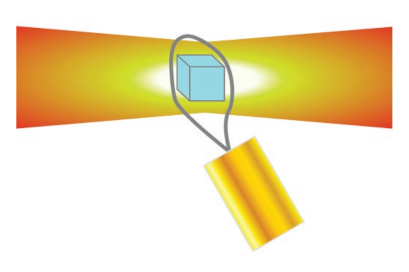


Figure 4: The intensity from the IμS is stabilized with respect to changes in ambient air temperature, showing less than 0.19% variations over 5.5 hours with a temperature change of 3° Celsius per hour.

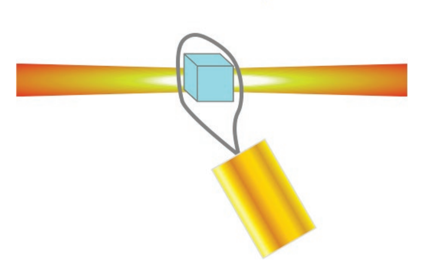
Matching the beam size to the sample size



a) The optimal beam size should match the sample size.



b) Though this is seldom achieved in practice as the size of the beam cannot be adjusted easily for most sources, a larger beam is inefficient since the X-rays that do not hit the sample will not be diffracted but will only contribute noise from scattering.



c) A beam which is smaller than the sample is not ideal but in most cases is acceptable if reasonable redundancy can be collected to allow the data to be accurately scaled.

Figure 5: Matching of the beam size to the sample size.

It is, of course, much easier to design a tube cooling system using water cooling because the water temperature is externally stabilized. However, water chilling has a number of disadvantages. Firstly, the need for a water chiller obviously increases installation and operating costs, requires routine maintenance, and also increases background noise in the laboratory. Secondly, and more importantly, if the cooling water is not kept extremely clean, ions in the water can attack the cooled anode surface and lead to the buildup of a thermally-insulating corrosion layer. This can occur in any water-cooled tube, but it is a particular danger for microfocus tubes that require cooling of a small, localized spot on the anode. This can compromise the cooling of the tube and lead to decreased tube lifetimes.

Higher-powered sources like the TURBO X-RAY SOURCE (TXS) microfocus rotating anode generator do require water cooling, since the heat load is too high to be handled by air cooling. As noted above, water cooling of a microfocus source requires the highest water quality, so the TXS incorporates a patented water deionization system to prevent corrosion of the anode surface (which could lead to reduced anode lifetimes).

In short, for low-power sources, air cooling offers a number of compelling advantages including higher reliability, lower costs, and lower noise. High power sources absolutely require water cooling; in this case, it is crucial to maintain the hygiene of the cooling water to prevent damage to the source.

Optimization of the beam size

Ideally, the size of the X-ray beam at the sample should approximately equal the size of the sample. If the beam is much larger than the sample, X-rays are wasted by not hitting the sample. Also, the beam that does not hit the sample contributes to air scatter and scatter from the entrained liquid and the loop.

If the beam is much smaller than the sample, the changes in diffracted intensity as a function of the sample's angular position will typically be larger since the intersection volume between the beam and the sample will change. However, this is tolerable in many cases since modern scaling algorithms are so powerful (as long as a reasonable multiplicity of observations can be achieved).

Therefore, in general, the optimal case is to have a beam that matches the sample size, but in most cases having a beam somewhat smaller than the sample is also acceptable.

These considerations—together with the fact that the "average"-sized crystal is steadily becoming smaller—have driven source designers to adopt ever-smaller beam sizes. While the "classic" rotating anode typically featured a beam size of about 300 microns at the sample, modern sources typically feature beam sizes of about 100-150 microns.

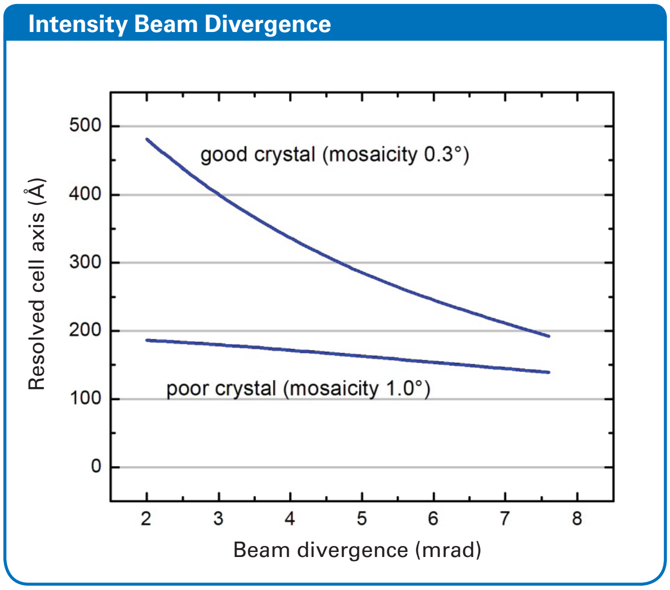


Figure 6: The typically resolvable cell axes versus the divergence of the X-ray beam. By changing the divergence, the beam can be tailored to the sample.

Optimization of beam divergence

As noted above, the use of optics allows one to increase the X-rays focused onto the sample (and thus the diffracted X-ray signal) but at the cost of increasing the divergence (and thus also, the size of the diffracted spots). If the divergence is too high, spots will overlap and the Bragg diffraction pattern can no longer be indexed or integrated. How much divergence is acceptable is obviously sample-dependent since crystals with longer units cells will have more spots (which are therefore more closely spaced and more prone to overlap).

Thus, the divergence of the beam must be optimized for the sample of interest. For samples with shorter cell axes, it is advantageous to use a higher divergence (in order to focus more intensity onto the sample as per Equation (1) above). For longer cell axes the beam divergence must be decreased in order to avoid spot overlap (at the cost of decreased intensity).

To first order, the maximum resolvable cell axes can be quantified by the equation

$$d_{max} = \frac{\lambda}{\sqrt{\alpha_{div}^2 + \alpha_{mos}^2}} \qquad (2)$$

where d_{max} is the maximum unit cell axis that can be resolved for a crystal with a mosaicity of α_{mos} and α_{div} is the divergence angle of the beam. This expression is plotted in Figure 6 for samples with typical good mosaicity (0.3°) and relatively poor mosaicity (1°). It can be seen that a beam divergence of about 7.6 mrad allows good samples with unit cells up to about 200 Å to be resolved. However, longer unit cells require a reduction in beam divergence: 5 mrad to resolve cell axes up to 300 Å and 3 mrad to resolve cells up to about 400 Å.

It is possible to adjust the divergence of a source through the use of adjustable slits or collimators. Bruker optics typically use pre-aligned collimators (although adjustable slits are optionally available as well) with pinholes designed for 7.6 mrad (for units cells up to about 200 Å), 5 mrad (for unit cells up to about 300 Å) and 3 mrad (for unit cells up to about 400 Å) and 2 mrad (for unit cells up to about 500 Å). These collimators are designed to be switched in seconds without tools and without realignment. A collimator change is sensed automatically, and the divergence is stored in the frame file headers. In this way, one always knows exactly the experimental configuration that was used for a particular data set.

D8 VENTURE with METALJET source.

Table 2: Comparison of typical performance of Bruker laboratory sources (microfocus sealed tube, microfocus rotating anode, and METALJET) for macromolecular crystallography.

Source	Power (W)	Cooling	Beam size at focus (μm)	Max divergence (mrad)	Relative Intensity
Classic Rotating Anode					
RU 300 BLUE optics	5400	water	380	2.7	1
Microfocus Source					
Bruker IμS 3.0*	50	air	110	7.6	10
Microfocus Rotating Anode					
Bruker TXS*	2500	water	180	7.6	45
Liquid-Metal Source					
Bruker METALJET (Ga)	200	air**	90	7.6	120

* With HELIOS Cu MX optics

** Internal water cooling with a water-air heat exchanger

Conclusions

Three different types of laboratory X-ray sources—differing in performance and cost—are now available for laboratory protein crystallography systems. The characteristics of these sources are summarized as follows:

Microfocus sealed tubes offer up to 10 times the intensity of a classic rotating anode. This type of source is the most economical option for the home laboratory. Installation is simplified, because 3-phase power and cooling water are not required. No routine maintenance is required beyond a tube exchange (typically every 3-5 years). This source is most suitable for screening and structure solution of medium- to strongly-diffracting samples (typically larger than 100 microns, depending on diffraction quality).

Microfocus rotating anode generators offer significantly higher intensity (more than 45 times the intensity of a classic rotating anode), comparable to second-generation synchrotron beamlines. This source is more expensive and also requires more routine maintenance (typically filament changes 2-3 times per year and annual anode refurbishment). This source is most suitable for screening, *de novo* structure solution, and high-resolution data collection of weakly-diffracting samples (typically as small as 50 microns, depending on diffraction quality).

The liquid-metal-jet source offers the highest available intensity in the home lab, with more than 120 times the intensity of a classic rotating anode. This type of source has routine maintenance requirements similar to those of a microfocus rotating anode (filament changes 2-3 times per year, changing a graphite radiation window once per year). The metal-jet source is suitable for all types of crystals, including very weak diffractors.

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