Technical Note SC-XRD 20

X-ray Detectors for Home Laboratory Macromolecular Crystallography: Does Size Matter?

Synchrotron beamlines optimized for macromolecular crystallography typically employ large area detectors with active areas of 40,000 mm^2 or larger. However, the high cost of the latest generation of pixel array detector technology has meant that, for home lab use, much smaller detectors are often used, typically on the order of only 6,000 mm^2 aperture or less, an order of magnitude *smaller than the detectors typically used at beamlines.*

Why are large detectors used at beamlines? What are the advantages of large active area for macromolecular crystallography? What are the disadvantages of a small detector?

2Θ Resolution

The first, and most obvious advantage of a larger detector is that it can be operated farther away from the sample while still achieving useful angular resolution.

For example, as shown in Figure 1, a detector with an aperture of 20 cm achieves 1.1 Angstrom resolution at a sample-to-detector distance of 10 cm while a smaller detector with an aperture of 7.5 cm achieves only a resolution of 2.2 Angstroms at the same distance. The smaller detector must operate much closer to achieve the same resolution: a detector with an aperture of 7.5 cm achieves a resolution of 1.1 Angstroms at the sample-to-detector distance of 4 cm.

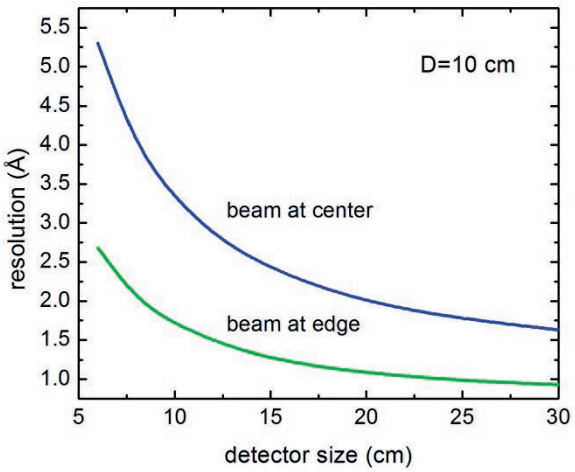

Figure 1. Maximum resolution versus detector size at a sample-to-detector distance of 10 cm with the detector centered at 2θ=0 (blue) and with the beam at the edge of the detector (green) for Cu-Kα.

Spot separation

One of the principle disadvantages of operating closer to the sample with a smaller detector is that it is more difficult to resolve closely spaced reflections. That is, the minimum angular spacing between adjacent reflections, α, scales inversely with the maximum unit cell length of the sample, d:

$$\alpha = \frac{\lambda}{d}$$

For large unit cells, the reflections are thus closer together. The reflections have a finite minimum size due to the size of the sample. Therefore, if the detector is too close to the sample, these spots can overlap [1]. The farther the detector is moved away from the sample the farther the spots move away from each other to allow the reflections to be accurately indexed and integrated.

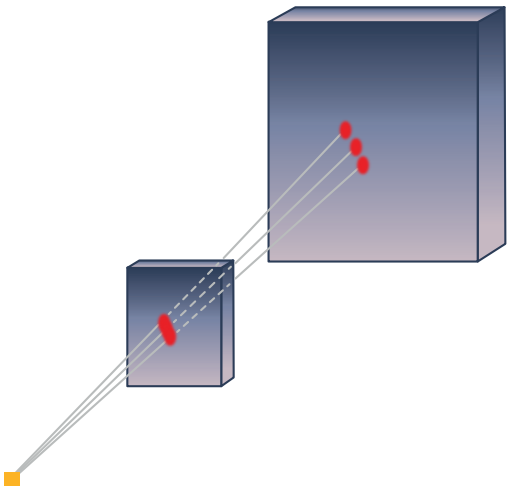

Figure 2. A larger detector, operated at a longer sample-to-detector distance can separate closely spaced reflections that would overlap on a smaller detector operated closer to the sample.

Thus, in order to resolve such closely spaced reflections the detector must be moved farther away from the sample. However, in the case of a smaller detector multiple shells of data must then be acquired to reach the same resolution as a larger detector can achieve with a single shell.

Background noise

Biological samples have amorphous solvent content which leads to incoherent X-ray scatter. This results in a diffuse background of scatter X-rays underlying the Bragg reflections. The quantum statistics of this scattered background is a source of noise, indeed, in many cases this is the dominant source of noise.

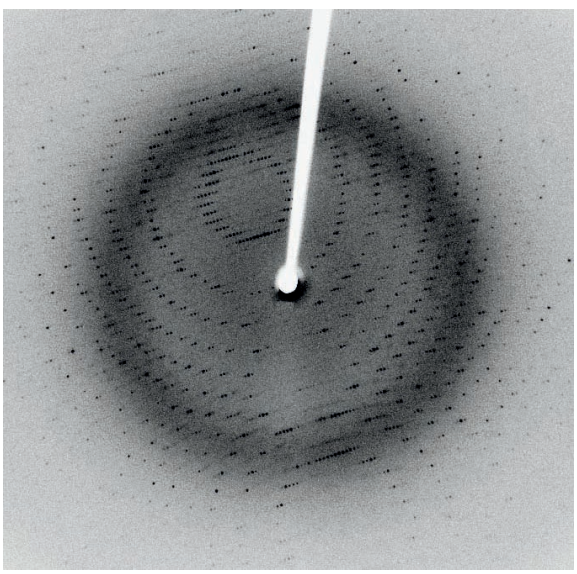

Figure 3. The X-ray diffraction pattern of protein crystals typically shows a significant background from solvent scattering. The quantum noise in this scatter background is often the dominant noise source in a diffraction image.

If the mean scatter background is I_b, then the noise associated with the quantum statistics of this background is $(I_b)^{1/2}$. For example, if the scatter background is, say, 400 X-rays per pixel, this adds a noise of 20 X-rays. In modern X-ray detectors the detector noise is typically less than one X-ray, and thus the noise contributed from the scattered X-ray background is often the dominant source of noise in the experiment.

The scattered X-ray background can be minimized by careful sample preparation (e.g. removing excess solvent before cryofreezing). However, as water is an intrinsic component of proteins, diffuse scatter cannot be completely eliminated.

The impact of the scattered X-ray background can be reduced in two ways: fine slicing data collection and by moving the detector farther away from the sample [1]. In both cases the goal is to isolate a given Bragg reflection in the smallest volume of reciprocal space possible, which in turn minimizes the scatter background that is recorded along with the Bragg signal. Thus, the ideal detector for macromolecular crystallography is fast (to facilitate fine slicing) and large (to operate at large sample-to-detector distance while still achieving the requisite resolution).

A large detector is advantageous since this background scatter is diffuse and thus is reduced by the square of the distance from the source. So, for example, if the mean scatter background at 6 cm is, say, 700 X-rays per pixel (with an associated noise of 26 X-rays), and the detector is moved back to 16 cm then the scattered background is reduced to 100 X-rays per pixel and the associated noise is reduced to 10 X-rays. That is, for weak reflections the I/σ will be improved by approximately a factor of three. As shown in Figure 4, moving the detector back improves the signal-to-noise ratio and allows weaker signals to be observed that would otherwise be buried in the scattered X-ray noise.

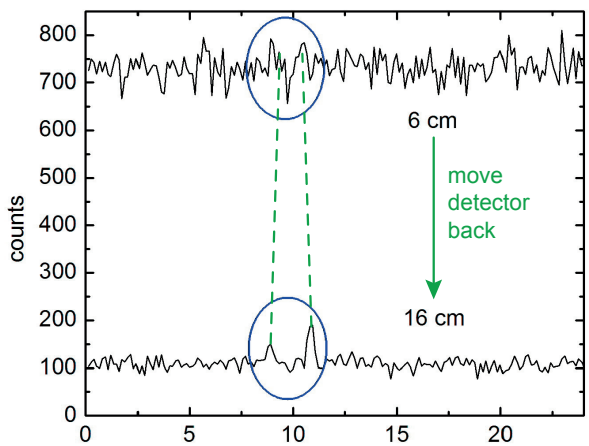

Figure 4. Two weak reflections at a sample-to-detector distance of 6 cm cannot be reliably distinguished in the noise of the scattered X-ray background. Moving the detector to 16 cm significantly improves the signal-to-noise ratio. Thus, for weakly diffracting samples there is very significant improvement in data quality at larger sample-to-detector distances.

Radiation damage

As noted above, in principle, a smaller detector can achieve the same resolution and the same I/σ as a larger detector if it is operated at the same sample-to-detector distance. However, as noted above, this requires that the smaller detector take multiple shells of data to acquire a data set to the same resolution, as shown schematically in Figure 5.

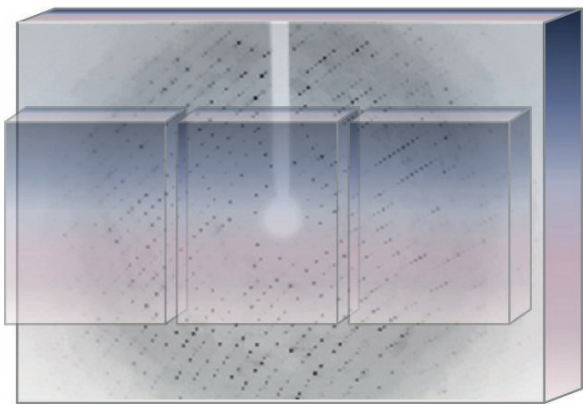

Figure 5. A small detector can collect data to the same resolution as a larger detector by acquiring multiple shells of data at different 2θ settings. However, this extends the experiment time and thus subjects the sample to a larger radiation dose. The smaller detector also records fewer reflections due to its smaller chi coverage which results in lower redundancy.

This of course extends the experiment time considerably, which impacts the productivity of the instrument. However, more importantly, it also significantly increases the radiation dose to the sample.

In modern X-ray sources such as the METALJET, the total dose to the sample can be comparable to the dose seen at synchrotron beamlines and thus radiation damage is a serious consideration, even in the home laboratory. Acquiring multiple shells of data can thus be problematic as it exposes the sample to several times the radiation dose.

Redundancy

As shown in Figure 5 above, even when a smaller detector achieves the same resolution (by collecting multiple shells of data) a larger detector will, in general, collect more reflections due to its larger chi coverage. Thus, all things being equal, the larger detector will achieve a higher redundancy and thus, in general, better data quality.

PHOTON III: a very large pixel-detector for the home laboratory

In principle the same large detectors designed for macromolecular crystallography at synchrotron beamlines such as the EIGER 9M or the PILATUS 2M [2], would also be excellent detectors for home laboratory applications as they fulfill exactly the requirements of high Detective Quantum Efficiency (DQE), fast readout and large size demanded by this application [1, 2].

Unfortunately, the cost of these large beamline detectors makes them impractical for most home laboratory applications. For this reason, most detectors offered for home laboratory use are a very small fraction of the size of the detectors employed at synchrotrons. Indeed, remarkably, the latest HYPIX 6000 pixel array detector [3] for macromolecular crystallography is not only an order of magnitude smaller than synchrotron detectors, it is even smaller than the home laboratory versions of CCD detectors that were available over a decade ago such as the SATURN 944 (see Figure 6). As noted above, this reduction in size in laboratory pixel array detectors is primarily driven by cost constraints. However, these very small detectors are highly suboptimal for macromolecular crystallography.

Bruker has worked to change this. With an active area of 20 cm × 14 cm, the new PHOTON III M28 is by far the largest detector designed for macromolecular crystallography in the home lab. Not only is the PHOTON III large, but it is also fast with a frame rate of 70 frames per second and zero readout dead time between frames. Finally, the PHOTON III boasts single photon counting readout for the highest possible DQE with no detector noise.

The PHOTON III thus allows the same type of optimal operation in the home lab as one would enjoy at the most advanced synchrotron beamlines. The PHOTON III reduces the impact of scattered X-rays both via superfine slicing and by allowing operation at larger sample-to-detector distances. The size of the PHOTON III also allows higher redundancy while reducing the radiation damage to your sample.

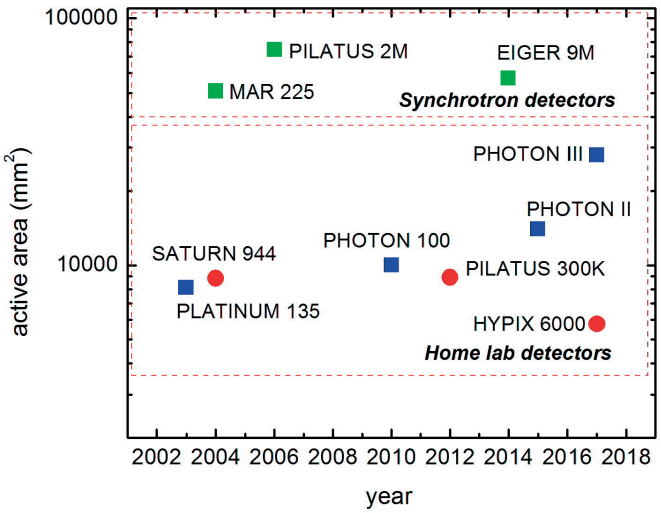

Figure 6. Synchrotron beamlines typically use detectors with active areas of 200 × 200 mm² or larger. However, in the home laboratory much smaller detectors have been typically used, primarily due to cost constraints. Now, for the first time the PHOTON III offers a pixel array detector for the home laboratory with a very large active area comparable to beamline detectors.

References

[1] C. Nave, Matching X-ray source, optics and detectors to protein crystallography requirements, Acta Crystallographica Section D 55, 1999, 1663-1668.

[2] www.dectris.com.

[3] www.rigaku.com.

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