Single Crystal Diffraction and Protein Crystallography Working Group Interim Report: Remit and Initial Considerations

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Background

We have used as the basis of our initial considerations various quantitative assessments of the performance of generic single crystal instrumentation at neutron sources via detailed flux/reflection intensity/resolution calculations which have been carried out in the past, notably involving one of our group (Jauch). These comprehensive assessments have included:

- the original SNQ report in 1984, from which we note the Jauch and Dachs paper on single crystal diffraction and also a paper from Mogens Lehmann (ILL) on low resolution crystallography;
- the 1996 Jauch paper on single crystal diffraction at long pulse spallation sources;
- the original ESS large unit cell study - Working Group convened by Mogens Lehmann, and including Jauch & Wilson along with Clive Wilkinson (EMBL) and Lennart Sjolin (Stockholm). The report of this group was issued as ILL Report ILL97/JA19T.

Generic Instrument Types

We have chosen to benchmark the following generic instrument types against the pulse-moderator choices under consideration:

(i) Chemical Crystallography (*cf.* D9, SXD)
(ii) High Resolution Macromolecular Crystallography/Protein Crystallography (*cf.* D19, LADI, PX-LANSCE)
(iii) High Resolution (short d & low $\Delta Q/Q$) and (iii') Diffuse Scattering (*cf.* D9, D10, SXD)
(iv) Low Resolution Biological Crystallography (*cf.* DB21)
(v) "Single Peak" Measurements (*cf.* D10, D9, specialist instruments, e.g. at Saclay)

We have not tried to design instruments, but some consideration of the general requirements are inevitable in order to do out benchmarking.

(i) Chemical Crystallography

Standard chemical crystallography is a "high resolution" technique, typically requiring the measurement of d-spacings to as low as 0.35-0.4Å. This also requires good Q-space resolution to allow for peaks to be separated and therefore integrated accurately. A short pulse is therefore best, possibly around 30μs pulse length.

To maximise the flux in the region of interest a medium cold moderator would be best (say around 130K), with high flux at 1Å or lower but also retaining significant flux in the region up to and beyond 2-3Å. Sharp pulses are required for good Q-space resolution to high Q, so a decoupled moderator.

This instrument type can have a relatively short path length on a 50Hz source, where the band-width will be adequate.

Such an instrument type on ESS will be world-leading, and will offer the opportunity for qualitatively new science to be opened up, for example, in parametric measurements and in the use of very small crystals.

(ii) High Resolution Macromolecular Crystallography/Protein Crystallography

The definition of high resolution here implies measurements to a d-spacing of typically 1.5-1.8Å, on unit cell edges of up to 150-200Å. Once again there is the need to resolve peaks well to allow for adequate integration implies a short pulse source.

In this case once again a medium cold moderator (130K) is undoubtedly best, with optimal flux (or more particularly the "effective flux", $\phi(\lambda)\lambda^2$) in the 2-5Å region. If the instrument is relatively long, then coupling (or “partial” coupling) to a pulse width of, say, 100μs would be acceptable (though see the Aside below).

As envisaged in the original Lehmann Working Group report, a 40m instrument on a 50Hz source gives a restricted bandwidth ($\Delta\lambda$=2Å, Δd=1Å), so a reduced rep-rate target is a possibility for this instrument.

This instrument on ESS promises to be world-leading if a 130K moderator is available, but the arguments are much less clear with a cold or ambient moderator choice.

Aside – peak width and background

Coupling (or "partially" coupling) to a pulse length of up to 100 or even 200 μs offers increased flux, but the reduced resolution has consequences not only for peak separation but also for the background from “chemical” samples. The broader pulses leads to significant build up of background under Bragg peaks (incoherent scattering plus long reflection tails which becomes increasingly less ideal as the pulse is broadened/resolution lessened). It is not just sheer count rate but signal/background which is important here in determining the instrument performance. Also if peaks overlap very severely then there can be problems in separating peak from background. Even full-profile methods such as Rietveld refinements of powder data can suffer from this problem, and in cases (i) and (ii) under consideration here we have the added complication that much of our “background” is coming from hydrogen incoherent scattering; the cross-section of this is wavelength-dependent. The consequence is that even if good peak modelling/intensity extraction software is available, the underlying physics of the

scattering in the sample can make the situation more complicated.

(iii) High Resolution Diffraction

Here we consider very high Q measurements, to d-spacing of 0.2Å or less, primarily for "physics" measurements. Frequently this must also be accompanied by another high resolution aspect – high $\Delta Q/Q$ resolution to allow the examination, for example, of incommensurate or satellite reflections or of diffuse scattering close to Bragg peaks (for example critical scattering). This instrument type clearly requires a short pulse source and a pulse width of around 20μs.

The need for very high epithermal flux places us on an ambient moderator, which with the need for very sharp pulses to maintain very high resolution will be decoupled and poisoned.

The instrument would be envisaged to be of medium length on the 50Hz source; there is no problem with band-width.

This instrument type would be world-leading, and accessing very high Q values is potentially unique on a pulsed source.

(iii') Diffuse Scattering

During our discussions a diffuse scattering instrument type became separate from the high resolution instrument. This instrument type refers to diffuse scattering which is not necessarily close to Bragg peaks. It must, however, maintain good Q resolution and hence requires a short pulse source, with a pulse width of around 50μs.

The instrument, since it examines often weak non-Bragg peak scattering, requires good intensity at both high and low Q, and should couple this with extremely low (ideally "zero") background. In addition the instrument set-up must be well understood and reproducible to allow accurate corrections.

Related to this, it is clear that band width is also important, to allow reliable collection of a continuous diffraction pattern over all of reciprocal space/Q values for whole pattern modelling, for example using p.d.f. and related techniques – like those carried out by the Disordered Materials community.

Such diffuse scattering measurements would be ideally carried out on a medium-length instrument on a low rep-rate source (e.g. 10/16 Hz) as wide simultaneous band-width is needed. It would of course be possible in principle to slew choppers continuously to cover the full necessary Q-range but why do this if a good flux instrument sitting on a 10-16Hz source can yield a sufficiently wide band in a single shot with the ability to be normalised accurately and consistently? The moderator would have to be decoupled for high resolution, but the need for good flux over the whole Q-range means that medium-cold or cold moderator would be most appropriate.

This instrument type would be world-leading on ESS, with the potential for fully 3-D resolved measurements of reciprocal space volumes unique on a pulsed source.

(iv) Low Resolution Biological Crystallography

For low resolution biological Crystallography (typically to a d-spacing of 6-8Å on a 200-500Å cell edge) we require a high flux of long wavelength neutrons. A long pulse source is an option here, while if a short pulse option is chosen, we would clearly require a cold, coupled moderator. However, we must always be wary of the problems of pile-up of incoherent background (see above). Resolution is not a major issue here and so this instrument can probably be of medium length, on a 50Hz source.

Such an instrument would open up new areas of biology, for example in the study of protein-nucleic acid complexes, if fully optimised. Capacity is also important here – in the biological sciences area we must offer more instrumentation to allow us to tap into that large community. Thus we should be looking to pursue this important area on ESS even if the instrument appears not to be world-leading.

Our preliminary conclusion is that this instrument type on the ESS would be competitive with the leading existing steady state instrumentation, but probably equal at best with this.

(v) "Single Peak" Measurements

This type of measurement is an extremely important component of, for example, the programme on D10 at the ILL. We have therefore recently begun also to benchmark this instrument type.

The aim is to follow a single peak (or very limited range of reflections) as a function of some external variable (e.g. temperature, pressure, magnetic field),. Q-space resolution is not an issue if the peaks are always well separated in reciprocal space. Otherwise, if resolution is required this can be gained at the expense of flux.

Thus the requirements are for a very high point by point flux over a limited wavelength range, clearly opening up the long pulse option.

However, there is also the need to have also a more standard "chemical crystallography" capability on the same instrument to characterise important sample characteristics (such as extinction etc. under the same data collection conditions as those in which the single peak changes are followed. This can still be achieved in the long pulse case, but is less obviously favourable.

Such an instrument type can be competitive with the best steady-state options, but only if the time-averaged flux is the same.

Next steps

The work of our group will now move on to include detailed quantitative assessments of our generic instrument types. This will allow us to justify or modify our preliminary conclusions and provide more detailed input to the deliberations of the SAC.