LMX – A Diffractometer for Large Molecule Crystallography

…An innovative high flux cold neutron solution for problems in supramolecular chemistry and biological structure

1. Introduction

Structure determination by single crystal neutron diffraction has been a highly successful enterprise for perhaps three decades and with spallation sources for some 20 years. The SXD diffractometer is typical of that success, producing world-leading science for crystals with small unit cells. In the past 20 years there have been enormous advances in the study of large molecular systems, including naturally occurring biological systems, synthetic supramolecular assemblies and network materials, all aided enormously by advances in single crystal X-ray diffraction - via better detectors, higher flux/brilliance sources and associated software improvements. Neutron crystallography, with much to offer in these areas, has by contrast seen only modest success until very recently since most instruments do not possess sufficient flux and resolution for precise studies of inherently small crystals.

The LMX design includes a long incident beam path and novel neutron optics, allowing the diffractometer to be highly optimised to deliver a high flux of cold neutrons and to resolve low *d*-spacing Bragg reflections from very large unit cell crystals. The instrument will be a world-leading single crystal diffractometer, ideally suited to ISIS TS2, and will access the large structures that play a crucial role at the forefront of modern molecule-based materials and molecular biology.

2. Outline Design Specification

LMX will provide qualitatively different capability to the existing SXD and strong complementarity with the LADI diffractometer at the ILL over a wide range of materials. The basic design aims of the instrument will be to allow the study of large unit cell structures (20-30,000 $Å^3$) to good resolution (d_{min}~1-1.2Å), larger unit cells (1-2 x 10^6 $Å^3$) to medium resolution ~2.0-2.5 Å, and to routinely use relatively small samples of maximum dimension of 1mm or less for these studies. Detailed comparisons with the LANSCE Protein Crystallography Station (PCS) indicate that LMX should be comparable in neutron flux and exceed in brilliance. An estimated flux gain of at least 40 over the current SXD in the wavelength range of interest to LMX provides the necessary capabilities in terms of performance and, together with retention of good time-of-flight and angular resolution, ensures competitiveness with the best available instrumentation world-wide. LMX will also allow the study of substantially smaller single crystals of smaller unit cell materials, an area where demand is very high, and we anticipate enabling the study of, for example, ~0.05mm^3 crystals of unit cell volume ~2000$Å^3$.

2.1 Description of design

The science described in this proposal requires time-of-flight (TOF) Laue neutron diffraction measurements on small single crystals with large unit cells to good resolution. At high *Q*, these samples will produce closely spaced Bragg peaks of low intensity on a high diffuse background. In this regime, the parameter to maximise is not flux, but effective brilliance, *i.e.* flux x reflectivity / 3D resolution element. Hence a diffractometer with high long-wavelength flux (to optimise reflectivity in the *d*-spacing range of interest), good instrumental resolution and high detector pixellation (to exploit the inherently high brilliance of the TS2 moderators) is needed. Low instrumental background is an obvious requirement when dealing with small crystals, and a large detector solid-angle is necessary to maximise reciprocal space coverage at long wavelengths. As the signal-to-background increases at longer *d*-spacings, effective flux becomes the key parameter even for very large unit cell crystals, and we must be able to maximise it, at the expense of some resolution. In a TOF diffractometer, this is accomplished by making the incident beam divergence tuneable. Our design will attain these characteristics by optimally exploiting the broad-pulsed coupled cold hydrogen moderator on ISIS TS2. This moderator, with a high flux of neutrons in the long neutron wavelength range, possesses the ideal incident neutron spectrum and is intrinsically very brilliant. Modern, low-loss neutron optics enables us to achieve excellent resolution from a relatively broad pulse shape by using a long flight-path, made possible with the 10Hz repetition rate of TS2. The specifics of the outline design are summarised in the table.

Moderator	Cold coupled Hydrogen 10Hz
Primary flight path	80 m
Secondary flight path	0.25-0.75 m (Dependent on size of available detector pixels)
Choppers	2 Disc, 1 Nimonic (Nimonic chopper would only be needed if the sample has a direct view of the moderator)
Guide	WISH design elliptical guide with variable in-guide collimation; possible further ellipsoidal beam transport to sample.
Maximum wavelength bandwidth, $\Delta\lambda$	4.9 Å
Useful wavelength range	~1-8 Å
Divergence	Tuneable (1.5° max)
Neutron flux (1-5Å, 0.24° divergence)	4.1x10^6 n cm^{-2} sec^{-1} (Peak at 3.5 Å)
Detectors	Aiming for psds with 1mm^2 pixels; >2π sterad (but within budgetary constraints).
Beam size at sample	3x3mm^2 (max); collimated down to 0.1x0.1mm^2 for smaller samples
Sample tank	Open, with χ–ϕ sample goniometer; option for vacuum or other gases around sample
Sample environment	Cold stage to 5 K, moderate pressure

The elliptical guide will transport a larger flux than the equivalent straight guide; albeit with increased divergence

(see below). Insert collimation along the guide, with motor-controlled variable apertures, will then reduce the divergence as necessary on a sample-by-sample basis to match the sample's size and scattering characteristics. In order to minimise background, the design will also incorporate either a background suppression 't_0' chopper or the guide will be curved to prevent direct line-of-sight viewing of the target by the sample or an additional ellipsoidal guide will transport the useful neutron beam to an off-axis sample. The latter approach may remove the need for insert collimation and has the benefit of increased flexibility (see below).

The instrumental resolution in the 'longitudinal' (TOF) direction will be ~0.2% at backward scattering angles, becoming progressively worse at lower angles (depending on detector pixel size etc.). This resolution is sufficient to separate successive Bragg reflection orders around (100,0,0) for a sample with a=150Å (i.e. d=1.5Å). The instrumental resolution in the 'transverse' (angular) direction will vary depending on the choice of collimation, directed by the mosaic spread of the sample and the required d_{min} resolution. This choice will also have an impact on the neutron flux.

The detector array is a key part of the instrument design. In fact, the high incident-beam brilliance would be dissipated by coarse detector elements. Simulations have shown that this is true both at high and at low divergence. Small solid angle pixels are needed to maximise signal to noise and to software focus Bragg intensities in TOF to further improve separation of closely spaced reflections. Large overall solid angle coverage and high efficiency is needed for these inherent count-rate limited applications. LMX will aim for a pixel resolution ~1 mm^2 and it will be the first megapixel instrument at ISIS. SXD-type detector modules provide a base-line specification, but there are a number of developments underway at ISIS to improve detector efficiency and reduce pixel size using scintillator technology. Work is also progressing elsewhere on detectors based on Anger camera and gas chamber designs. We will utilise the best detector technology available.

2.2. Comparing LMX with SXD on ISIS TS1 and PCS at LANSCE

LMX is a cold neutron single crystal diffractometer with a resolution, flux profile and a highly-pixellated detector array ideally matched to the complex, large unit cell chemical, biological and materials science problems outlined below. As such it is distinct from thermal neutron diffractometers such as SXD or VIVALDI at the ILL which serve a different purpose. PCS, which operates at a spallation neutron source, is akin to the LMX diffractometer although it operates as an exclusive nPX instrument. To compare relative performance the effective brilliance is a better measure of the effective count-rate than the neutron flux for cases where the signal to noise (S/N) is around unity. This function (see Figure 1a) takes into account the Bragg peak reflectivity and the differences in instrumental resolution (Figure 1b) and shows that the effective brilliance of LMX will be much higher than PCS. Furthermore, still faster count-rates may be achieved on LMX by increasing the beam divergence (for systems when S/N >>1) and from the greater detector solid angle proposed for LMX. Increased beam divergence to increase flux will be an effective way of permitting analysis of very small crystals (ca. 0.05mm^3) with smaller unit cells (e.g. 2000 Å^3), improving on capabilities at SXD, albeit it with slightly greater d_{min} than attainable on SXD.

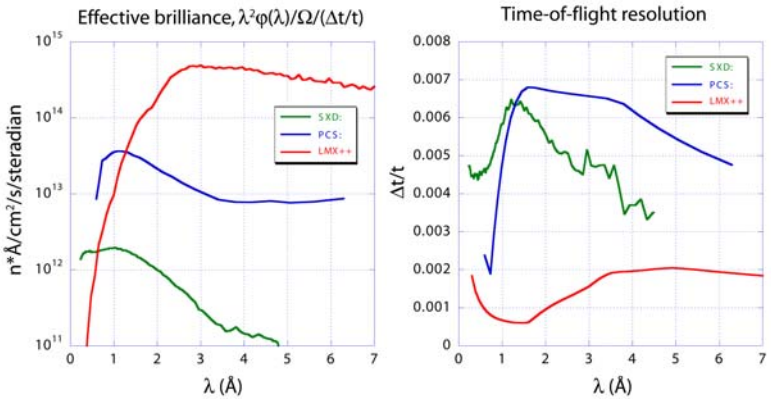

Figure 1: Comparison of (a) the effective brilliance and (b) instrumental resolution measured on SXD at ISIS, PCS at LANSCE and from calculations of the proposed LMX instrument on ISIS TS2.

3. Outline Science Case

LMX will contribute substantially to two of the TS2 science themes, namely advanced materials and biomolecular sciences, with a significant but smaller contribution in the third area of soft condensed matter. Thus, an outstanding opportunity is presented which tackles some of the exciting and leading edge areas in chemistry and structural biology which are currently not within the scope of existing ISIS instrumentation and not yet well catered for at neutron facilities internationally. The common features of the science areas to benefit from LMX can be summarised as follows:

(i) neutron diffraction adds significant value to information offered by other techniques, notably X-ray diffraction;
(ii) the materials to be studied will often have larger unit cells; and/or
(iii) available crystal size will be limited;
(iv) the problems are beyond the scope of the current ISIS TS1 instrument SXD.

3.1 Large scale chemical systems

3.1.1 Supramolecular chemistry

• Identification and characterisation of 'unconventional' hydrogen bonding within supramolecular systems: 'Mesoscale' crystallography is highly topical – i.e. characterising systems which are larger than conventional 'small molecules' yet smaller than most biological macromolecules whilst still displaying many 'protein-type' experimental problems. Supramolecular chemists will

be able to examine the detailed nature of unusual and surprising hydrogen bonds *in their macromolecular context*. Applications range from large supramolecular capsules for molecular encapsulation and as nano-reaction chambers, hydrogen bond-mediated anion sensors and framework materials for chemical separations.

• Characterisation of framework atoms (incl. H), cavities and molecular guests within metal-organic supermolecules and framework materials: Recently a number of systems have been designed based upon metal centres of well-defined coordination geometry as nodes linked together by fairly rigid ligands to produce either nanoscale (1-10 nm) supermolecules or infinite framework materials with large cavities for encapsulation of guest molecules. The potential applications of these materials range from chemical sensors, porous materials for separations, to novel heterogeneous catalysts with designed active site cavities and some very promising candidates for gas sorption, including hydrogen storage.

3.1.2 Molecular magnets and single molecule magnets

• Element specific diffraction: Much current work involves synthesis of large complexes, including single molecule magnets containing more than one type of 3d-metal. Accurate and reliable identification of metal sites including the degree of disorder at these sites is vital for understanding the physics. In some cases, e.g. design of two Qubit gates based on heterometallic wheels, the unit cells are extremely large (cell edges > 50 Å).

• Identification of protonation states: In clusters of 3d-metals the oxidation state of the metal is vital in understanding the magnetic structure. This can be difficult to assign based on X-ray data, as structures can contain structural motifs, e.g. "lone" oxygen atoms, which could be assigned as a variety of species, e.g. oxide/hydroxide/water. As more large clusters are reported this problem is encountered more frequently.

• Photomagnets: Multifunctional molecular magnets offer the possibility of controllable switchable magnets. Use of light is an attractive alternative, and diffraction studies of photo-excited states are important. Although such experiments are possible with X-rays, the small crystals that can be studied at LMX means that neutron studies of photoexcited states become feasible.

3.1.3 Zeolites and other framework materials

Microporous solids such as zeolites find widespread use in the chemical industry as molecular sieves and catalysts. The scope of microporous materials has been extended by the development of aluminophosphates (AlPOs) and more recently by metal-organic hybrid materials (section 3.1.1). Zeolites can be thought of as inorganic analogues to biological enzymes. To rationalise their properties and predict new uses for specific materials it is necessary to determine the location of extra framework cations (e.g. Ca and K), guest molecules (including low-Z D and Li), the ordering of framework (Si/Al) atoms and accurate site occupancies.

To date only 27 zeolite structures have been determined by single crystal neutron diffraction, several associated with the same parent zeolite, a small minority of the 139 known structure codes (framework topologies). Using the small crystal capability of LMX, key features of many more zeolites can be determined. For example: (i) the structure of stable hydrated intermediates during dehydration during catalyst activation, (ii) the location of protons at catalytic centres, (iii) the location of polarising cations of low atomic mass e.g. Li^+ used in gas separation, (iv) the location and occupancy of guest species (catalysis and gas separation) and (v) the determination of as-synthesised materials showing the location of templating organic molecules, important for understanding the nature of host-guest interactions in the synthesis of new framework compounds. All of these can be determined in an in-situ manner, further making use of the relative transparency of environmental cells to neutrons.

3.1.4 Organometallic chemistry and homogeneous catalysis

Characterising molecular geometries and intermolecular interactions that involve light atoms, predominantly hydrogen, in the presence of d- and f-block metals has led to vital contributions to the elucidation of the many coordination modes of hydrogen to metal centres in mono- and multi-metal complexes. The coordination and activation of dihydrogen at metal centres, activation of C–H and more generally X–H bonds, even hydrogen bonding involving metal centres X–H···M and $X–H^{\delta+}\cdots H^{\delta-}–M$ have also been studied, enhancing our understanding of key processes, especially those important in metal-based catalytic transformations of organic molecules. LMX will be used to study very small crystals with relatively small unit cells and larger unit cell systems designed with larger and more complex ligand sets to impose chirality on the metal reaction centre or very large weakly interacting anions to stabilise cationic catalysts.

3.2 Biomolecular science

Neutron protein crystallography (nPX) more completely defines biological structures, by including hydrogen and hydration details, and thus helps explain important biomolecular functions, as exemplified by studies of aspartic proteinases, concanavalin A and rubredoxin. Furthermore, comparisons of ultra-high resolution synchrotron X-ray and nPX studies of concanavalin A show that the neutron approach is capable of delivering many more bound water details at medium diffraction resolutions (~2.4 Å) and at room temperature, which is physiologically relevant. The LMX instrument on ISIS TS2 will bring a second instrument to Europe, besides LADI at the ILL, suitable for single crystal neutron diffraction from biological macromolecules. At PCS at LANSCE, an instrument similar to LMX but with lower brilliance, 50kDa in the asymmetric unit is within reach (indeed promising data from a 220kDa protein have been reported). There is also fresh impetus from associated deuteration laboratories; samples from the new biological perdeuteration facility (D-LAB) have produced significant increase in capability from LADI, particularly from small samples. Taken together these new results tell us that the molecular weight ceiling we can expect to study with nPX on LMX will

cover much of the molecular weight histogram of genomes including the multi-macromolecular complexes and molecular machines where further Nobel prizes must surely lie.

Biomolecular science also encompasses liganding small molecules, on their own as well as complexed with protein receptors. The study of these is a major interest of pharmaceutical protein crystallographers engaged in new drug discovery. Typically hundreds of such complexes are surveyed at SR X-ray beamlines. This sort of work can be expected to spin into nPX use of LMX. The nPX results from LMX will contribute to fundamental knowledge of biology at the molecular level and hence inform new biotechnologies.

3.3 Partially ordered systems at low and high resolution

Knowledge of the location of water and hydrogen atom positions is of critical importance in understanding the molecular basis of the physical/biological properties of polymer molecules such as DNA, hyaluronic acid, filamentous viruses, silk and Kevlar©. While X-ray fibre diffraction is well suited to definitive structural studies of filamentous molecules, the extraction of information on water and hydrogen is often difficult. Neutron fibre diffraction, especially with selective deuteration, provides a reliable method of accessing this information.

Importantly, LMX will be unique in that it could allow one single instrument to collect both high- and low-resolution data simultaneously, offering a neutron (SANS/WAND) analogue of the SAXS/WAXS capability that has had such a major impact in X-ray synchrotron studies. Such a capability will be important for the study of many polymer systems that have important diffraction features both at low resolution (typically from 500 – 80 Å) and at very high resolution (in favourable cases at atomic resolution).

4. Outline Business Case

Immediate demand for LMX will be high since LMX will be one of the few instruments worldwide offering nPX capability and it will be unique in targeting large chemical systems, notably in supramolecular and materials chemistry. Demand will also be high because LMX will offer new scientific opportunities to numerous scientists who have previously been unable to benefit from neutron diffraction studies. The broad science base, contained in a large number of supporting letters, also demonstrates high demand. There is also strong synergy with the instruments being built at Diamond, notably the macromolecular beam lines, and beam line I19, for innovative studies of single crystals of molecular and materials systems.

It is significant that both the US and Japanese governments are investing in time-of-flight neutron diffractometers for large molecule crystallography (MaNDi at the SNS and BIX-P1 at J-PARC, respectively). MaNDi is designed exclusively for nPX, whereas BIX-P1 has a very similar remit to that proposed here, albeit with a shorter primary flight path. This growth shows that there is a worldwide appreciation of the benefits of cold neutron diffraction for large molecule crystallography. This stems from results from LADI at the ILL and, more recently, from PCS in Los Alamos, the only time-of-flight neutron diffractometer currently handling large unit cells and operating as a dedicated nPX instrument. Although it is hard to make a direct comparison with the Laue diffractometer LADI, our calculations suggest that LMX will outperform LADI for a given problem by a factor of 2-3 with significantly better performances in cases where tight resolution (both longitudinal and transverse) and high brilliance are required.

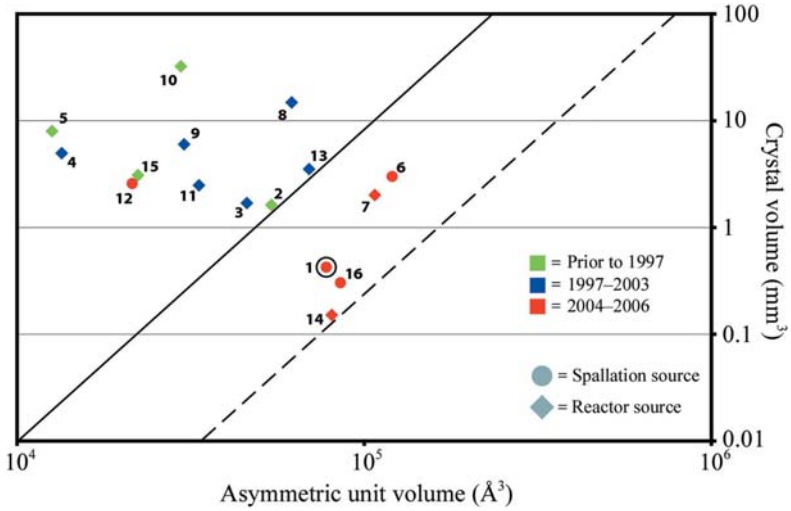

Figure 2. Scatter plot of asymmetric unit cell volume versus crystal size, based on published neutron protein structures (see Table 2). The dashed line represents a guideline for current and near-future neutron structures. (Reproduced from Blum *et al Acta Cryst* F **63** 42 (2007); see article for further details).

It is also very encouraging that the range of accessible problems is increasing with improved instrumentation (see figure 2 and table 2). Structures with asymmetric unit volumes up to 100,000Å^3 are being studied successfully on crystal volumes <1mm^3. This overlaps with a large number of (although not including the largest) proteins currently being studied using X-ray diffraction and exceeds the largest of current chemical systems being studied. LMX will count more rapidly than PCS, thus reducing counting times, but it is inevitable that this will lead to users wanting to address still more challenging problems. The limitations will therefore be twofold: when is an experiment too long to be acceptable and at what point will a crystal's signal be too low with respect to the LMX background? The first is relevant to the business case; in a scenario where LMX might concentrate on the most challenging—and potentially highest impact—systems (i.e. beyond those listed in table 2), is it acceptable to only have ~2-3 protein experiments per ISIS round? The second point comes down to the instrument

	Spacegroup	V_u(Å^3)	V_a(Å^3)	V_c(mm^3)	MW (Da)	Time (d)	d_{min}(A)	Inst.	Cit.	Reference
1. DFPase	$P2_12_12_1$	310503	77626	0.43	35000	37	2.2	PCS	1	Blume et al (2007)
2. Trypsin	$P2_12_12_1$	216761	54190	1.62	23300				218	Kossiakoff & Spencer(1981)
3. DsrD	$P2_12_12_1$	183143	45786	1.70	8840	70	2.4	BIX-3	7	Chatake et al. (2003)
4. Rubredoxin	$P2_12_12_1$	53600	13400	5.00	5900	35	1.5	BIX-3	14	Kurihara et al. (2004)
5. BPTI	$P2_12_12_1$	50111	12528	8.00	6530				369	Wlodawer et al. (1984)
6. d-Xylose isomerase†	$I222$	962934	120367	3.00	160000	?	1.8	PCS	3	Katz et al. (2006)
7. Rasburicase†	$I222$	814080	101760	1.80	135000	35	2.1	LADI	4	Budayova-Spano et al. (2006)
8. Concanavalin A	$I222$	493697	61712	15.00	25600	34	2.5	LADI	17	Blakeley et al. (2004)
9. Lysozyme	$P4_32_12$	242213	30277	6.00	14300			(T=15K)	79	Niimura et al. (1997)
10. Ribonuclease A	$P2_1$	59444	29722	30.00	13700				206	Wlodawer & Sjölin (1981); Wlodawer (1980)
11. Myoglobin‡	$P2_1$	66735	33368	2.50	17200				32	Shu et al. (2000)
12. Amicyanin	$P2_1$	43127	21564	2.60	11500	21	1.9	PCS	5	Sukumar et al. (2005)
13. Endothiapepsin	$P2_1$	138925	69463	3.52	35000				36	Coates et al. (2001)
14. Aldose reductase‡	$P2_1$	161663	80832	0.15	36000	93	2.0	LADI	10	Hazemann et al. (2005)
15. Insulin	$H3$	200409	22268	3.00	5790				27	Wlodawer et al. (1989)
16. DHFR §	$P6_1$	516990	86165	0.30	36100	23	2.2	PCS	3	Bennett et al. (2006)

† Tetramer. ‡ Perdeuterated. § Dimer.

Table 2. Sample volume (V_c), unit-cell volume (V_u), asymmetric unit volume (V_a) and molecular weight (MW) from neutron protein structural studies included in Figure 2 (from Blum *et al Acta Cryst* F **63** 42 (2007)). In addition, measurement time, resolution and instrument are included for post-2003 measurements and the number of citations is given.

design and the vital importance of focussing *without* substantial background increases; extreme focussing on its own may not increase the effectiveness of the instrument for these low-signal systems.

It is also important to note that perdeuteration is having/will have a significant impact on nPX (see item 14 in the table) and groups are getting much better at growing larger deuterated crystals. This is a really key aspect for reducing background and is why there is a strong world-wide effort in this area. LMX will therefore access a wide range of scientifically relevant PX problems. The relevance of nPX to the wider PX community is reflected in the average citation of the papers in the above table which is a healthy 5.2 per year (or 4.1 per year for those papers less than 10 years old). Furthermore, the science problems identified within the chemical crystallography community are much less challenging experimentally than those of nPX and this community will be served very well by LMX and within much shorter measurement time-scales.

Looking forward, the science on which the LMX beamline is focused is undergoing rapid growth. Illustrative indicators are the exponential growth in numbers of published crystal structures (see Figure 3) of biological macromolecules and of coordination framework materials, one of a number of research strands yielding large structures within the field of supramolecular chemistry. Such growth suggests that the success of LMX will inevitably and perhaps quite rapidly lead to demand for a second beam line to cover the needs of the science within the LMX remit. This aspect should be carefully monitored and used to assess demand for a second instrument for inclusion within the TS2 Phase 3 suite.

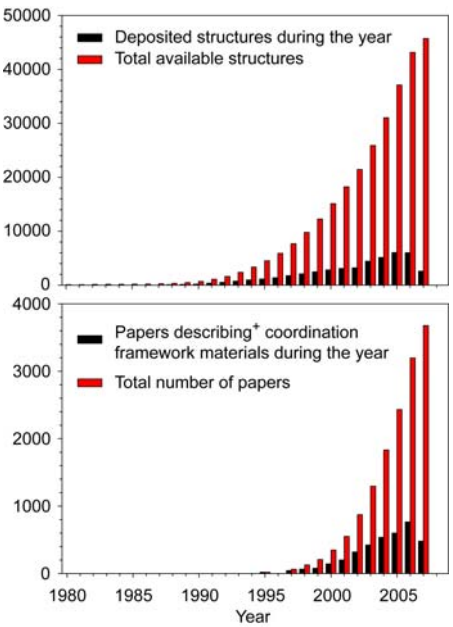

Figure 3. Growth of (a) biological macromolecular crystal structures (Protein Data Bank (www.rcsb.org/pdb/) and (b) coordination framework materials. ($^+$from papers containing 'coordination polymer' or 'metal-organic framework' in their title, abstract or keywords in the Web of Knowledge database, wok.mimas.ac.uk/, see S L James, *Chem. Soc. Rev.* **23** 276 (2003)).

5. Development Needs

The experiments on LMX will be challenging and as such the instrument must incorporate a number of innovative developments:

• ***Neutron beam transport:*** This will be dependent on advanced neutron optics including a long elliptical guide and an ellipsoidal mirror for further variable beam focussing. The focal point of the elliptical guide, defined with a variable aperture, will act as the object for an ellipsoidal mirror whose image will be at the sample position. This mirror can be used to de-magnify the beam to produce a more concentrated (and more divergent) beam at the sample and vice-versa. In addition, the mirror will steer the beam, in principle without losses, out of the direct beam path to aid background suppression and reduce geometrical constraints around the sample. Although the elliptical guide can benefit from the WISH guide design and the HRPD new guide design, the ellipsoidal mirror is new territory—more akin to synchrotron X-ray optics and engineering—and will require substantial development and possibly even proof-of-principle experiments on a neutron test beam. We note however, that the design is not dependent on the development of an effective ellipsoidal mirror; other more

established focussing devices (such as, for example, K-B mirror systems) will deliver much of the required functionality.

• ***Sample manipulation and beam location:*** With the very small samples being used on LMX, work is required to ensure that the samples are placed in the beam and rotated with much greater reproducible precision than currently used at ISIS. Techniques such as laser alignment and micro-rotation stages must be developed in order to ensure that LMX achieves the level of signal to noise etc. needed for successful experiments. This becomes even more important when using highly focussed beams.

• ***Large two-dimensional position-sensitive detectors:*** Current SXD-type designs do not have small enough pixels for LMX to operate at its most effective. Developments are underway at ISIS to design 2D psds with smaller pixels (e.g. a ZnS module with 65,536 $1mm^3$ pixels is in design). Other alternatives include making use of developments at SNS with Anger cameras which are currently delivering 150x150 pixels, each pixel slightly larger than $1mm^2$ and excellent neutron detection efficiency, or basing psds on ^{3}He technologies (e.g. the D19 detector at the ILL). There are two further restrictions on the design for LMX; they should be easily tessellated with minimal gaps between psds (this may discount ^{3}He designs) and they should ideally be low-cost (since the cost of the detectors will be a substantial component of the total).

• ***McStas simulation:*** The parameter space which must be optimised during the LMX design is very large. Developments are needed to facilitate this, especially in terms of optimised single crystal modules and advanced optical components. The development of ellipsoidal mirrors may require additional ray-tracing modelling tools and associated expertise.

• ***Fast electronics:*** LMX will collect a very large amount of data, with a detector array ~1Mpixels and ~2000 TOF channels. The electronics systems must be able to accommodate this, both in terms of data-rates during collection and to minimise data download times.

• ***Software:*** Data reduction will have a significant time overhead using currently available routines. Developments are needed to optimise these routines for increased speed and to cope with the increased amount of data from each experiment. Furthermore, work is required to adapt routines for input into existing protein crystallography software.

6. Further Requirements for Successful Science

• ***Development of suitable sample cells:*** LMX will need specialist sample cells and holders for the small crystals which will be run on the instrument. In addition, some of these samples will require specific environments, all with a minimal increase in background. Examples of this might be to maintain hydration and/or deuteration of proteins, inert atmospheres for sensitive chemical systems or specific gas atmospheres, the latter being especially pertinent for studies of hydrogen or methane storage in framework materials. In tandem with these cells, facilities for safe transfer of samples from dry box or vacuum to the beam line without sample degradation must be included.

• ***Facilities for deuterated single crystal PX growth:*** It has been clearly shown that the most effective way to optimise nPX results is to produce fully deuterated crystals. This allows results of comparable quality from much smaller samples than could be obtained from a hydrated crystal. There are a number of deuteration laboratories in operation or being developed world-wide (e.g. the D-LAB on the ILL-ESRF site) and it is vital that we establish good working contacts with these facilities and encourage our potential users to do the same. We will also need to establish what additional local resources are needed in this area to optimise the effective use of these facilities.

• ***Facilities for producing deuterated crystals of large chemical systems:*** It is likely that the most challenging problems in this area will benefit from deuteration (or even site-selective deuteration). This will benefit from the recent Facilities Development Advisory Board funding of the Isotope Facility once it is fully operational.

Outline Case for the first stage of the TS2 Phase 2 process
David Keen
3rd Dec 2007

[Updated from the TS2 SAC Autumn 2005 submission as prepared by the LMX working group: L Brammer (Sheffield) J B Cooper (Southampton) V T Forsyth (Keele/ILL) J R Helliwell (Manchester) J A K Howard (Durham) R H Jones (Keele) D A Keen (ISIS) P G Radaelli (ISIS) J W Steed (Durham) C C Wilson (Glasgow) and R E P Winpenny (Manchester)]