Recent major improvements to the ALS Sector 5 Macromolecular Crystallography Beamlines

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Introduction

Although the Advanced Light Source (ALS)) was initially conceived primarily as a low energy (1.9GeV) 3rd generation source of VUV and soft x-ray radiation it was realized very early in the development of the facility that a multipole wiggler source coupled with high quality, (brightness preserving), optics would result in a beamline whose performance across the optimal energy range (5-15keV) for macromolecular crystallography (MX) would be comparable to, or even exceed, that of many existing crystallography beamlines at higher energy facilities. Hence, starting in 1996, a suite of three beamlines, branching off a single wiggler source, was constructed, which together formed the ALS Macromolecular Crystallography Facility[1]. From the outset this facility was designed to cater equally to the needs of both academic and industrial users with a heavy emphasis placed on the development and introduction of high throughput crystallographic tools, techniques, and facilities - such as large area CCD detectors, robotic sample handling and automounting facilities[2], a service crystallography program, and a tightly integrated, centralized, and highly automated beamline control environment for users.

This facility was immediately successful, with the primary Multiwavelength Anomalous Diffraction beamline (5.0.2) in particular rapidly becoming one of the foremost crystallographic facilities in the US - responsible for structures such as the 70S ribosome[3]. This success in-turn triggered enormous growth of the ALS macromolecular crystallography community and spurred the development of five additional ALS MX beamlines all utilizing the newly developed superconducting bending magnets ("superbends") as sources[4-8]. However in the years since the original Sector 5.0 beamlines were built the performance demands of macromolecular crystallography users have become ever more exacting; with growing emphasis placed on studying larger complexes, more difficult structures, weakly diffracting or smaller crystals, and on more rapidly screening larger numbers of candidate crystals; all of these requirements translate directly into a pressing need for increased flux, a tighter beam focus and faster detectors.

With these growing demands in mind a major program of beamline and detector upgrades was initiated in 2004 with the goal of dramatically enhancing all aspects of beamline performance. Approximately $3 million in funding from diverse sources including NIH, LBL, the ALS, and the industrial and academic members of the beamline Participating Research Team (PRT), has been employed to develop and install new high performance beamline optics and to purchase the latest generation of CCD detectors. This project, which reached fruition in early 2007, has now fulfilled all of its original goals – boosting the flux on all three beamlines by up to 20-fold - with a commensurate reduction in exposure and data acquisition times for users. The performance of the Sector 5.0 beamlines is now comparable to that of the latest generation ALS superbend beamlines and, in the case of beamline 5.0.2, even surpasses it by a considerable margin. Indeed, the present performance of this beamline is now, once again, comparable to that envisioned for many MX beamlines planned or under construction on newer or higher energy machines.

Overview of the Sector 5.0 beamlines

The suite of three adjacent branchlines, 5.0.1, 5.0.2 and 5.0.3 (figure 1) at Sector 5.0 of the Advanced Light Source, Lawrence Berkeley National Laboratory is operated by the Berkeley Center for Structural Biology (BCSB; http://bcsb.lbl.gov), which also operates beamlines 8.2.1 and 8.2.2 for the Howard Hughes Medical Institute. The Sector 5.0 beamlines are funded primarily by the members of a PRT which is comprised of pharmaceutical and biotech companies and non-profit research groups. Additional funds are provided by the National Institutes of Health (NIGMS) and have been provided in the past by the Department of Energy (OBER). The PRT members are collectively allocated 50% of the available beamtime on 5.0.1 and 5.0.2, whilst the majority of the remaining beamtime is made available to General Users through the ALS beamtime proposal system. Beamline 5.0.3 is funded jointly by the Genomics Institute of the Novartis Research Foundation and Takeda Pharmaceuticals - who together receive 75% of the 5.0.3 beamtime - with the remainder again being made available to General Users. For reasons of efficiency many of the industrial users often elect to have their data collected for them by their own third-party “service crystallography” provider(s).

The three Sector 5.0 beamlines share a common 1.96 Tesla, 56 pole, 11.5cm period, permanent magnet wiggler source from which beamline 5.0.2 accepts the central 1.5mrad of the emission fan and beamlines 5.0.1 and 5.0.3 each accept a 2.7mrad wide sidefan. The central beamline, 5.0.2, is a full capability Multi-wavelength Anomalous Diffraction (MAD) beamline with an energy range of 4-16keV. The optics comprise a downwardly deflecting plane parabolic collimating mirror, a liquid nitrogen cooled Si(111) double crystal monochromator with a flat second crystal, and a toroidally bent M2 focusing mirror with a 2:1 horizontal demagnification. All the optics in this beamline were recently replaced as part of the major upgrade program and beamline 5.0.2 now achieves a source size limited focus of 350μm x 120μm (h x v), from which a pinhole collimator (typically 100μm in diameter) is used to select the central portion, and define the beam shape, for experiments.

The two sidestations, 5.0.1 and 5.0.3, share essentially identical optical characteristics and both currently operate at a fixed wavelength of 1Å. Vertical focusing is achieved solely by the M1 mirrors; these are upwardly deflecting to provide enhanced spatial separation from the downwardly deflected 5.0.2 beamline (figure 1). Horizontal focusing - and additional horizontal separation of the beamlines - is provided by the sidestation's curved Si(220) monochromator crystals. The asymmetric offcut angle of the crystal Bragg planes provides 10:1 horizontal demagnification of the wiggler source size; allowing a source limited focus of 500μm x 120μm (h x v) to be achieved. Again, a pinhole collimator of, typically, 100μm diameter is used to define the final beam size.

Beamline Optics Upgrade Program

The recently completed program of major beamline optics upgrades was initially launched in 2004. The first step of this project was to develop a thorough theoretical understanding of the existing beamline performance. Dual independent theoretical models (one analytical, the second using "Shadow" ray-tracing) were developed for each beamline and these were cross-validated with models of the already well understood superbend beamlines to provide a solid theoretical baseline of achievable beamline performance. Extensive FEA analysis of the water cooled optical components were also undertaken to fully characterize the effects of the high thermal loads from the wiggler on both the existing components and upon a broad spectrum of potential replacement designs. These FEA models were also used to quantify the effects of the increased thermal loads stemming from the pending introduction of ALS "top-off" operation in 2007. Top-off will raise the ALS ring current from a maximum of 400mA to a steady 500mA, resulting in a 25% increase in peak thermal load and a 100% increase in time averaged thermal loads due to the elimination of the gradual beam decay to 200mA and consequent re-fills.

The second stage of the upgrade project was then to undertake a rigorous experimental investigation of critical beamline performance parameters such as flux, focused spot size, beam profile, divergence, and beam stability and to compare these measurements with the predictions derived from the theoretical models. To facilitate accurate quantitative flux measurements a methodology was developed for the absolute calibration of PIN Diodes using the ALS white-light beamline 8.3.2 as an absolute radiometric X-ray source. As a result of the analytical and experimental investigation of Sector 5.0 beamline performance a number of critical issues were identified as high priority upgrade targets.

Firstly, thermal overload of the water-cooled beamline 5.0.2 monochromator stemming from the large (400W) applied power load was shown to be very significant. This problem had already been suspected for some time but it is only in recent years that a viable alternative to water cooling has emerged in the form of commercial liquid nitrogen cooling systems for monochromators. Hence the original water-cooled monochromator was replaced in the summer of 2005 by an internally cooled liquid nitrogen design from Oxford-Danfysik - with an immediate tripling in the beamline 5.0.2 flux.

Secondly, significant performance deficiencies were identified with the M1 mirrors. These mirrors were temporarily removed for more detailed analysis during the 2004 ALS shutdown and this analysis enabled a number of specific issues to be identified. The M101 and M301 mirrors (from beamlines 5.0.1 and 5.0.3 respectively) exhibited significant surface damage that is believed to have been caused by a plasma discharge within the vacuum chamber at a very early stage in beamline operation. This damage reduced their reflectivity and increased their thermal absorption, affecting both absolute flux and achievable focal spot size. The M201 mirror (from beamline 5.0.2) was undamaged but was found to have structural shortcomings that would limit its ability to achieve the slope error tolerances demanded by the upgraded beamline performance goals. Furthermore the FEA models of all three M1 mirrors suggested that their internal water-cooled Glidcop designs would not be able to deliver optimal performance under the anticipated absorbed power loads (250W per mirror) during top-off operation.

These observations lead to the decision to replace all three existing M1 mirrors with new, higher tolerance, Si mirrors. These new mirrors are cooled by immersing a Ni-plated water-cooled Cu cooling-fin into a slot in the upper face of the mirror that is filled with a liquid Indium/Gallium eutectic alloy to provided good thermal transfer between the mirror and the cooling fin. Our FEA analysis had demonstrated that this cooling scheme could deliver a performance that was far superior to that of the original internally cooled Cu mirrors.

The new mirror designs also benefited substantially from experience gained by the ALS during development of the more recent superbend beamlines, from which a number of important design elements were adopted including the mirror mounting system and the choice of reflective coatings. The original mirrors were Rhodium (Rh) coated, effectively limiting the maximum useable energy of beamline 5.0.2 to approximately 13.5keV due to reflectivity cut-off of the Rh. The new mirrors have a bi-layer coating[4] with a thin (8nm) Rh layer atop a secondary Platinum (Pt) layer. As the Rh layer becomes increasingly transmissive at energies above 13keV the X-rays are able to penetrate through it and reflect off the underlying Pt layer, effectively extending the useable energy range of beamline 5.0.2 by an additionally 2.5keV for no additional cost whilst avoiding the unwelcome Pt absorption features that would be present at energies below 13keV if a solely Pt coated optic were used. However in order to obtain the maximum benefit from this bi-layer coating it was also necessary to replace the second Rh coated M2 mirror in beamline 5.0.2 with an otherwise identical Rh/Pt coated mirror; even though no other specific performance issued had been identified as stemming directly from the M2 optic. Although beamlines 5.0.1 and 5.0.3 are designed to operate at a fixed energy their M101 and M301 mirrors also received the new bi-layer coating; this allows for future additional flexibility in the choice of their operational energy.

All four new X-ray mirrors and their associated vacuum, mirror bending, beam steering and control system hardware were installed during the major ALS shutdown at the end of 2006 and the beamlines were re-commissioned in January 2007. The immediate results from this program of upgrades can be clearly seen in the comparison of 2004 and 2007 beamline performance shown in figures 2 through 4. Flux on all three beamlines has been increased by 15 to 20-fold with much larger gains realized at energies above 13keV on beamline 5.0.2. It should be noted that the pending introduction of ALS top-off operation (currently scheduled for late 2007) will lead to an additional gain in flux of 25% over and above the values presented here (which are measured at 400mA ring current) and a doubling in the time averaged flux delivered to users (since the ring current will no longer decay to 200mA over time between refills).

The final element of the beamline optics upgrade program will be concluded in the fall of 2007 with the replacement of the 5.0.1 and 5.0.3 monochromators. This upgrade is not anticipated to have a dramatic impact on beamline performance; rather it will raise the output energies of 5.0.1 and 5.0.3 from their current set value of 12.4 keV (1Å wavelength) to 12.7 keV. This new energy is slightly above the Selenium K-edge which will significantly improve the capability for conducting Selenium based Single Wavelength Anomalous Diffraction (SAD) experiments on 5.0.1 and 5.0.3 and thus greatly expands the experimental options available to our users.

Detectors and endstation facilities

The detectors in use on the Sector 5.0 beamlines have undergone a number of major revisions since the very first CCD detector to be built by ADSC was installed on beamline 5.0.2 in 1996. Both beamlines 5.0.2 and 5.0.3 have now been upgraded to ADSC Q315 and Q315r 3x3 CCD detectors respectively; the latter was recently provided by Takeda Pharmaceutical. These detectors combine a large (~ 100,000mm^2) detector area with a sub-second readout time at full un-binned resolution - up to an order of magnitude faster than the detectors they replaced. The beamline 5.0.1 detector is a smaller ADSC Q210 2x2 CCD detector array, but it has similar performance characteristics. The smaller footprint of the Q210 detector permits a closer approach to the sample - allowing resolutions better than 1Å to be reached. The fast read-out times of all the detectors are crucial for industrial users who typically must screen, and collect datasets on, a large numbers of crystals from many disparate projects in a limited time period.

The second key component in high throughput crystallography is automated robotic sample mounting, which allows users to mount a new sample without having to enter the experimental hutch. The time saved increases data acquisition efficiently by 5 to 6-fold, reduces the risk to samples from manual mishandling, and allows for further development of automated and remote data acquisition techniques. The Berkeley Automounter system[2] was developed at LBNL by Thomas Earnest and colleagues and installed on all three beamlines. It was one of the first such systems to be deployed in the world and the design has since been adopted by several groups at other synchrotron beamlines. The major features of the Berkeley Automounter system are described in detail elsewhere[2] but it provides immediate access to 96 samples stored in standardized shipping “pucks” under liquid nitrogen in an attached dewar (figure 5). Since the automounters were first introduced to the beamlines in 2000 they have been in continuous frequent use, each mounting and unmounting an estimated 10,000 crystals per year, and they are now used by the majority of the Sector 5.0 users. Recent BCSB upgrades to the automounter system include; redesigned lids with improved sample access, a low-pressure liquid nitrogen feed with improved level sensing, and laser-based status monitoring of sample location.

The robotic automounter control system, data acquisition software, and MySQL sample tracking database are tightly integrated into the newly developed Beamline Operating System (BOS) environment which provides users with a simple unified GUI interface for all their necessary beamline and data acquisition functionality. The modular, (Java and XML based) nature of the BOS framework makes it straightforward to incorporate new features as users require them and the system is currently being integrated with Web-Ice[9], which is being developed in a collaboration between SSRL and LBNL, to introduce a remote data analysis capability. This will eventually permit users to mount samples with the robot, control the beamline, and collect and analyze their data without leaving their home institution or company.

Summary

The completion of a major $3 million program of optics and detector upgrades has delivered substantial performance improvements to all of the Sector 5.0 beamlines and restored beamline 5.0.2 to its former position as the highest performance Macromolecular Crystallography beamline at the Advanced Light Source. Furthermore, the time averaged performance of the beamlines, in common with all ALS beamlines, will be doubled again in late 2007 when the ALS moves to implement “top-off” operation.

A number of additional upgrades are still underway, or are in the process of being developed which will deliver significant new functionality such as Selenium SAD capability or remote access data collection. The completion of these projects will further enhance the scientific capability of the beamlines and introduce new experimental options for Sector 5.0 users.

If you are interested in becoming a Sector 5.0 user please contact Stacy Ortega (SLOrtega@lbl.gov) for further information.

Acknowledgments

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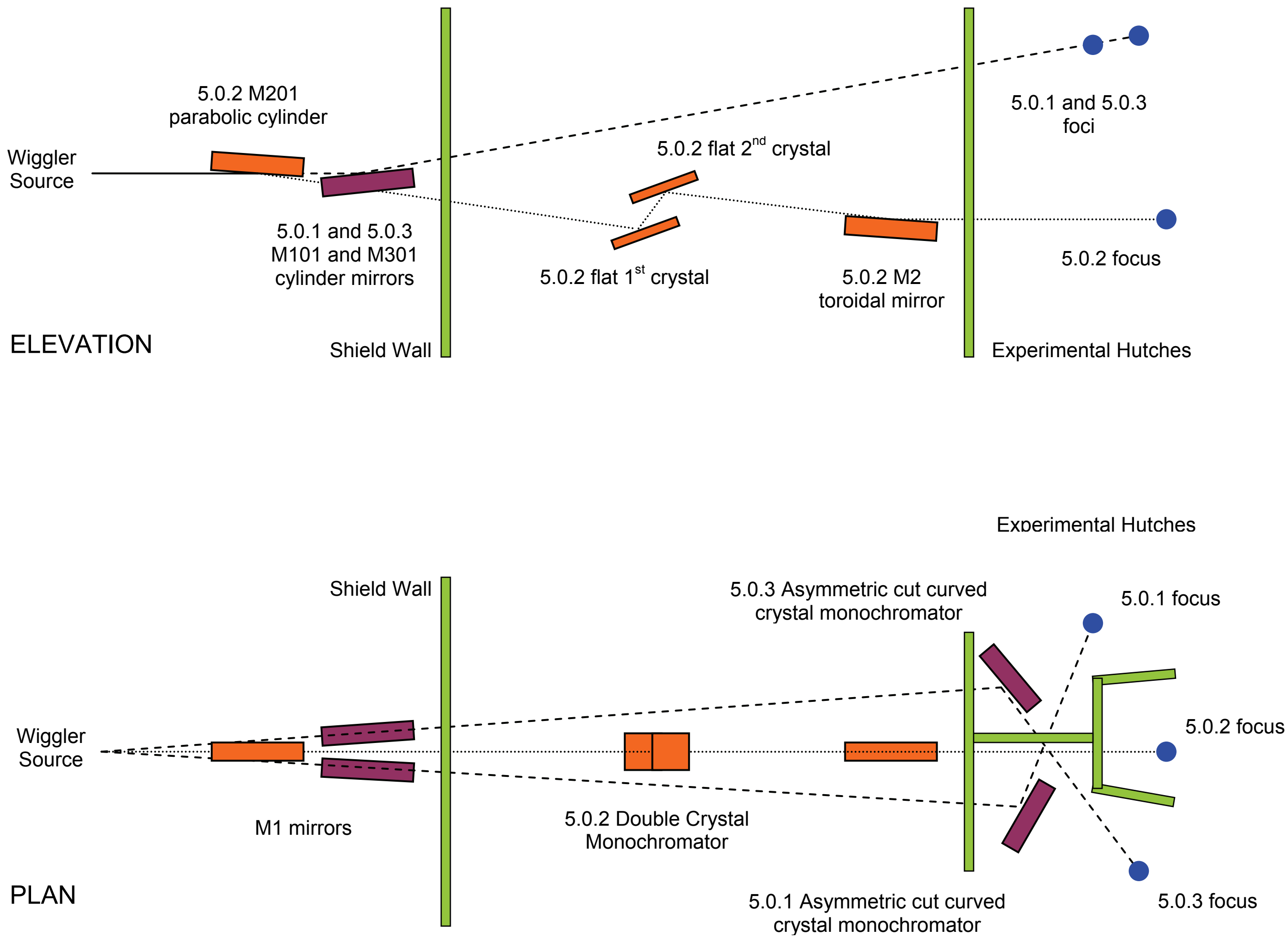

Figure 1

Schematic layout of the Macromolecular Crystallography Facility suite of beamlines at the Advanced Light Source

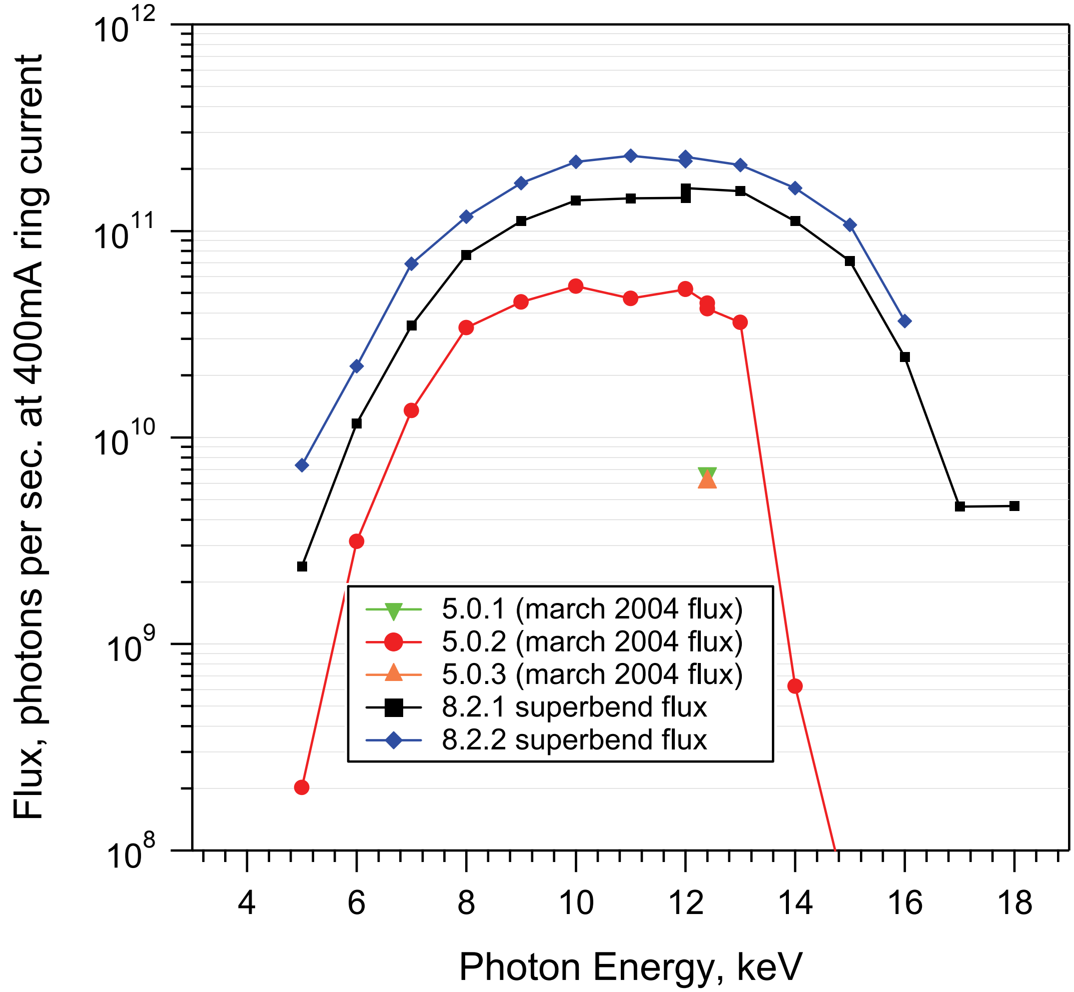

Figure 2

Flux as a function of photon energy for the ALS Sector 5.0 beamlines measured in March 2004 before the start of the beamline upgrade program. All flux measurements were taken under typical user operational conditions of 1.5mrad beam divergence using a 100µm diameter beam defining pinhole collimator. *(Flux curves for the superbend based MX beamlines 8.2.1 and 8.2.2 are included for comparison)*

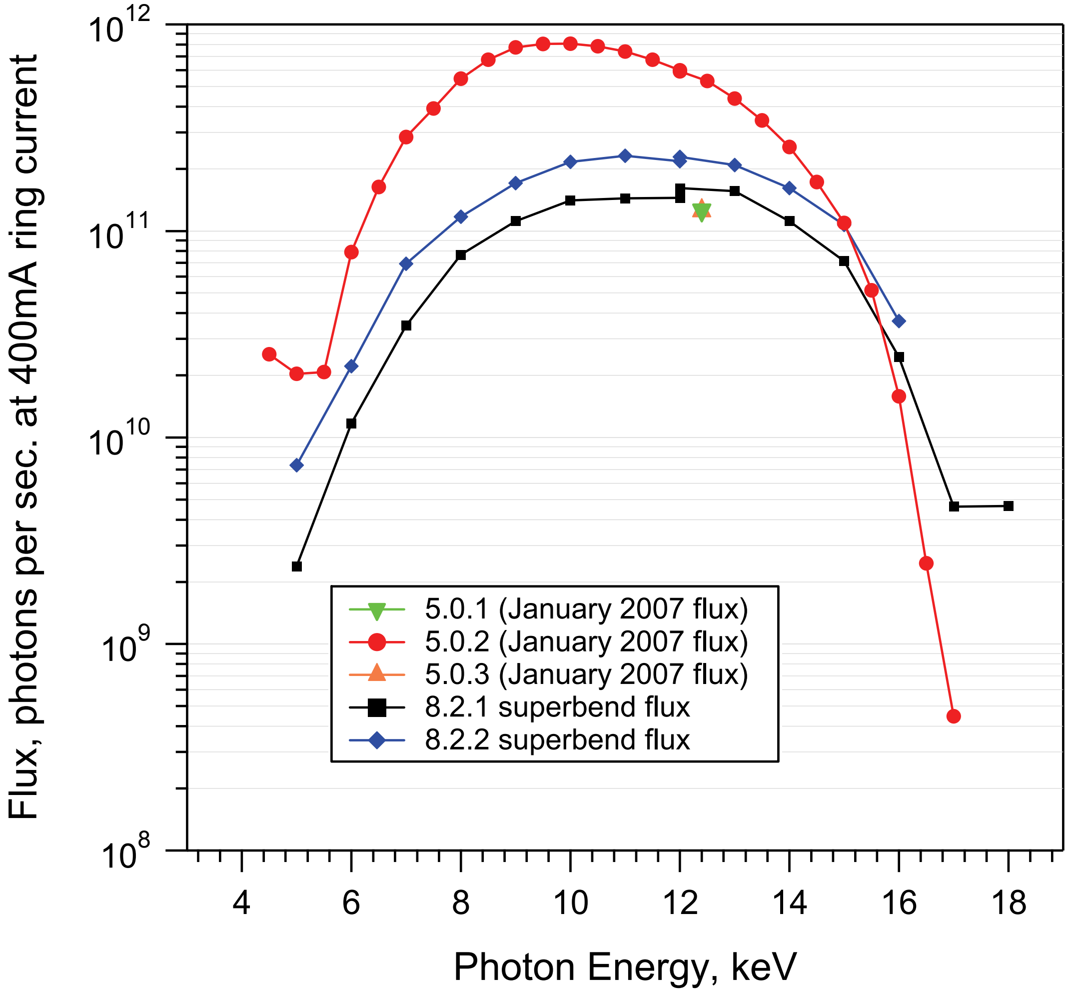

Figure 3

Flux as a function of photon energy for the ALS Sector 5.0 beamlines measured in January 2007 upon completion of the beamline upgrade program. All flux measurements were taken under typical user operational conditions of 1.5mrad beam divergence using a 100µm diameter beam defining pinhole collimator. *(Flux curves for the superbend based MX beamlines 8.2.1 and 8.2.2 are included for comparison)*

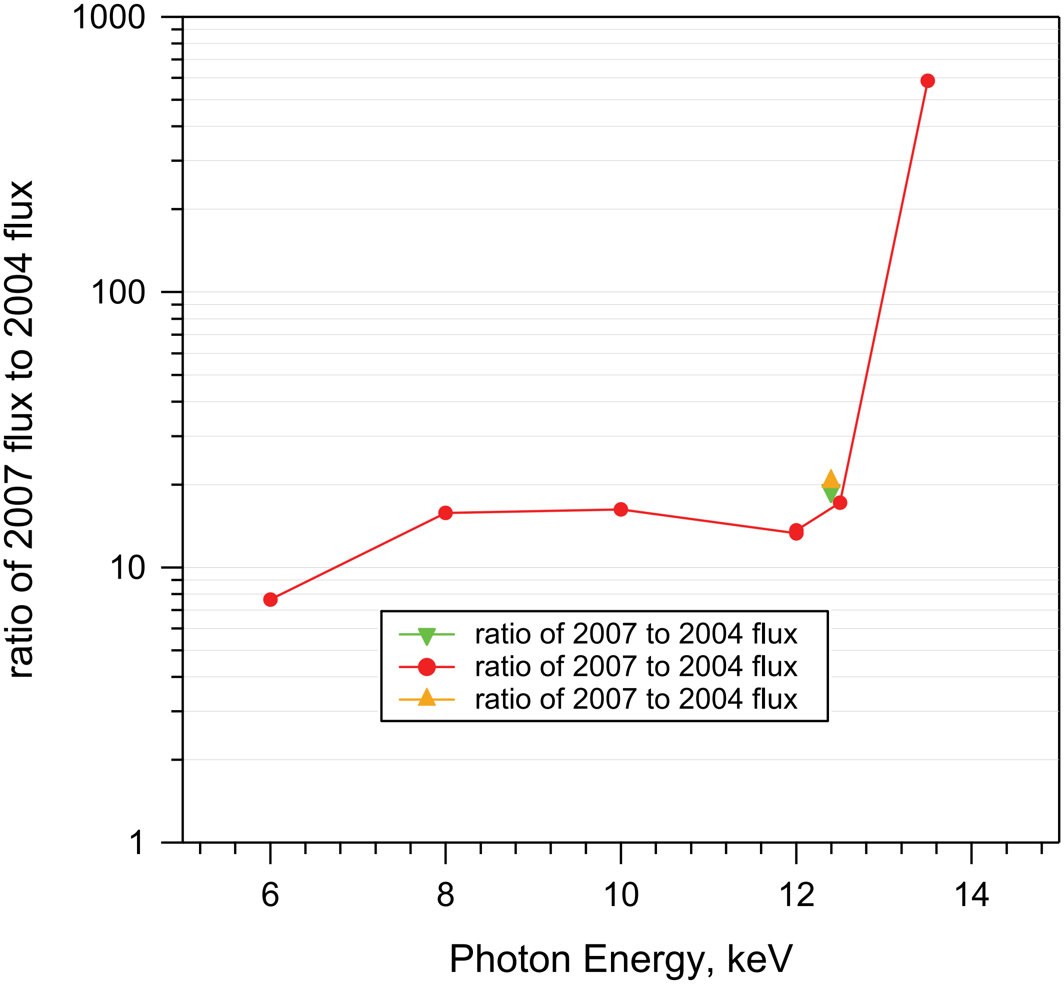

Figure 4

Ratio of flux measurements from 2004 and 2007 for the ALS Sector 5.0 Macromolecular Crystallographic Facility beamlines. Completion of the beamline optics upgrade program has boosted performance of the Sector 5.0 beamlines by typically 15 to 20-fold. All flux measurements were taken under typical user operational conditions of 1.5mrad beam divergence using a 100µm diameter beam defining pinhole collimator.

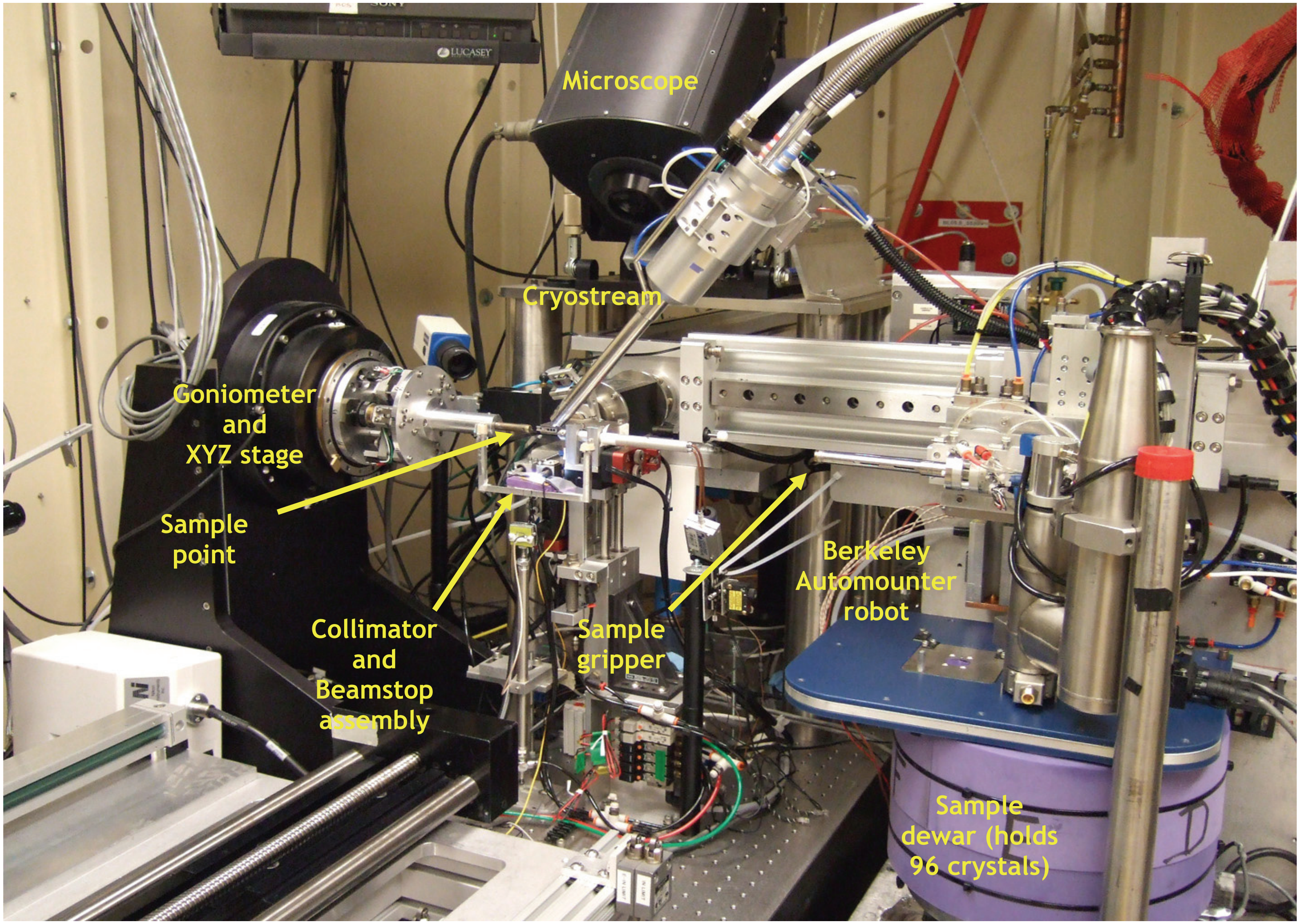

Figure 5

Sample environment of beamline 5.0.2 showing the Berkeley Automounter and sample storage dewar