Three Biomedical Beamlines at NSLS-II for Macromolecular Crystallography and Small-Angle Scattering

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Abstract. We report on the status of the development of three beamlines for the National Synchrotron Light Source-II (NSLS-II), two for macromolecular crystallography (MX), and one for wide- and small-angle x-ray scattering (SAXS). Funded by the National Institutes of Health, this suite of Advanced Beamlines for Biological Investigations with X-rays (ABBIX) is scheduled to begin operation by 2015. The two MX beamlines share a sector with identical canted in-vacuum undulators (IVU21). The microfocusing FMX beamline on the inboard branch employs a two-stage horizontal source demagnification scheme, will cover an energy range of 5 - 23 keV, and at 12.7 keV will focus a flux of up to $10^{13}$ ph/s into a spot of 1 µm width. The companion AMX beamline on the short outboard branch of the sector is tunable in the range of 5 – 18 keV and has a native focus of 4 µm (h) x 2 µm (v). This robust beamline will be highly automated, have high throughput capabilities, and with larger beams and low divergence will be well suited for structure determinations on large complexes. The high brightness SAXS beamline, LIX, will provide multiple dynamic and static experimental systems to support scientific programs in solution scattering, membrane structure determination, and tissue imaging. It will occupy a different sector, equipped with a single in-vacuum undulator (IVU23). It can produce beams as small as 1 µm across, and with a broad energy range of 2.1 - 18 keV it will support anomalous SAXS.

1. Introduction

Biomedical research is well represented among the thirty early beamlines [1] at the National Synchrotron Light Source-II (NSLS-II), consistent with the prominence of structural biology at the NSLS. Three of them are being constructed with funding from the National Institutes of Health (NIH) and include two macromolecular crystallography (MX) beamlines and one for small- and wide-angle x-ray scattering (SAXS). In addition, the New York Structural Biology Consortium is developing a microdiffraction MX beamline and DOE will support relocation of a correlated spectroscopy and macro-molecular crystallography program from NSLS to the new synchrotron. Several other early beamlines will offer capabilities useful in biological research [2], including x-ray absorption spectroscopy and microprobe fluorescent imaging. Current plans are to position several of these beamlines together at NSLS-II to nucleate formation of a Biology Village.

Here we summarize the preliminary design of the three NIH-supported ABBIX (Advanced Beamlines for Biological Investigations with X-rays) beamlines. The optical layout of the FMX microdiffraction instrument and its AMX mini-beam companion has evolved from an early concept [3]
to achieve even smaller beams and more lateral separation of the pair on canted undulators. Similarly, the optical concept of the LIX small-angle instrument was refined to improve beam collimation and versatility.

2. Undulators for FMX, AMX, and LIX
Owing to the advantage enjoyed by structural biologists in genetically engineering Se-methionine substituted proteins for phasing by anomalous diffraction [4], undulators for FMX and AMX were optimized for high flux at the Se K-edge at 12.7 keV. Further, to achieve optimal microfocusing on FMX, its undulator is located in the 17-ID low-β straight of the NSLS-II ring where the source size is smallest [5]. For a pair of canted identical in-vacuum undulators in this straight, optimizations yielded 1.5 m long insertion devices with a magnetic period of 21 mm. Flux spectra were calculated with the SRW programs [6] for this IVU21 and are shown in figure 1.

For the scattering beamline, the insertion device will be located in a long straight section, where the default high-β source is optimal for measurements that require low source divergence. Reduced horizontal β is optional during operations for experiments that prefer smaller source size. Considering that planned anomalous small-angle experiments can be carried out at the Ca edge, the LIX undulator was optimized to have its third harmonic provide flux to 3.7 keV. This led to an insertion device of 23 mm period and 2.8 m length. Its flux spectrum is shown in figure 1. Located in the 16-ID straight along with ring diagnostic components, the LIX undulator will be the only device in this sector, which benefits the unencumbered layout of this high-brightness multi-purpose SAXS beamline.

3. The FMX and AMX pair of MX beamlines
The FMX microdiffraction beamline is laid out to achieve a focal spot size of 1 μm or less with an expected flux approaching $10^{13}$ ph/s at 12 keV and covering a photon energy range of 5 – 23 keV. The highly automated AMX will exceed this flux in a native focal spot of 4 μm width and have an energy range of 5 – 18 keV. The size of the focal spots on each station can be expanded by up to a factor of 20, and beam divergence can be reduced, at the expense of flux, up to five fold from a native 1 mrad to obtain optimal conditions for data collections on large complexes. Thus, the pair of MX beamlines, while specialized in their native microfocusing or high flux configurations, will have overlapping capabilities in their mid focal ranges. Figure 2 gives a cartoon of the optical concept of the pair.

**Figure 1.** Calculated flux spectra for canted IVU21s for AMX and FMX (lower curves) and for the IVU23 undulator for LIX (upper curves). The solid lines are the sum of the flux from odd and even harmonics, and the dashed lines represent odd harmonics only. Collection apertures for the IVU23 are 70 μrad (h) x 50 μrad (v) and for the IVU21 120 μrad (h) x 50 μrad (v) and encompass all of the available undulator radiation within their central cones. Focused beam on all three beamlines will exploit part of this flux and emphasize odd harmonics.

**Figure 2.** Cartoon of the optical concept of the FMX and AMX pair of MX beamlines.
To obtain at FMX a beam of 1 µm cross section with a beam divergence that is small enough for MX, the x-ray beam is demagnified in two stages in the horizontal direction and in one stage in the vertical direction. In the first stage, a horizontally focusing mirror, set at a glancing angle of 2.5 mrad, illuminates a secondary source aperture with a 3.25 fold demagnified source image. The second optical stage consists of a Kirkpatrick-Baez pair of mirrors set to reduce the beam width 23:1 to achieve an overall demagnification of 75:1. Owing to the small vertical size and divergence of the undulator source, it can be focused directly. The native focal spot, simulated through SHADOW [7] becomes 1 µm (h) x 0.5 µm (v).

The AMX optical configuration is optimal when the beamline’s optics and experimental station interdigitate the first optical stage of FMX. For beam focusing a Kirkpatrick-Baez mirror system suffices when positioned to demagnify the photon source by 25:1. With high quality mirrors of figure errors of 0.1 µrad SHADOW ray tracings yield an intense beam of 4 µm (h) x 2 µm (v). The principal optical challenge for AMX is achieving sufficient lateral separation from the adjacent FMX beam path. A pair of flat side-deflecting mirrors, inserted immediately after the monochromator and set at glancing angles of 3.5 mrad, are sufficient to gain space for a fully functional experimental station and a large detector.

4. The LIX small- and wide-angle scattering beamline
The scientific scope of the LIX beamline includes three components: (1) static high throughput solution scattering and time-resolved solution scattering using microfluidic continuous flow (10 µs - 1 ms time resolution) as well as stopped flow (1 ms and slower) mixing cells; (2) diffraction and scattering from multi-layered and single-layered lipid membranes containing membrane-active peptides and membrane proteins; and (3) scattering-based scanning-probe imaging and tomography of biological tissues.

These experiments require adjustable beam size on the sample down to 1 micron, within a wide x-ray energy range of 2.1-18 keV. We therefore will utilize a two-stage focusing scheme with beryllium compound refractive lenses (CRLs) for secondary focusing. Compared to mirrors, the CRLs are more promising to achieve the 1 micron beam size at working distances of 1 m or longer, which is necessary to minimize the parasitic scattering from the focusing optics. However, secondary focusing using CRLs will be limited to 6 keV and above due to the low x-ray transmission and the difficulty to adjust the focal length for these devices at lower energies. This is acceptable since the low energy x-rays are to be used only in anomalous scattering measurements that will not require very small beam sizes. At x-ray energies of 4 keV and lower, a pair of small mirrors will replace the CRLs to provide harmonic
rejection as well as modest focusing in the vertical direction in grazing incident scattering measurements on membrane samples.

The CRLs do not alter the beam direction after the secondary source. Therefore one can either remove the CRLs from the beam path, or incorporate additional optics to add imaging capabilities in future upgrades, without needing to re-arrange the downstream instrumentation.

Figure 3. Layout of the LiX beamline, which also employs a two-stage focusing scheme. The primary focusing KB mirrors focus to the secondary source aperture, with a fixed demagnification of ~3:1. Secondary focusing is accomplished by CRLs, at variable distances from the sample, to adjust the demagnification in the range of ~4 - 7:1.

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