Published in final edited form as:

Nucl Instrum Methods Phys Res A. 2007 November 11; 582(1): 233–235.

An X-ray microsource based system for crystal screening and beamline development during synchrotron shutdown periods

Mitchell D. Miller^{*} and **Ashley M. Deacon**

Joint Center for Structural Genomics and Stanford Synchrotron Radiation Laboratory, SLAC, MS 69, 2575 Sand Hill Road, Menlo Park 94025, USA

Abstract

Crystallographic end-stations require a significant investment in state-of-the-art equipment, as well as a significant effort in software development. The equipment often sits idle during annual maintenance shutdowns. In order to utilize the existing hardware and software during these shutdowns, we installed a sealed-tube microsource X-ray generator in the beamline 9-2 hutch at Stanford Synchrotron Radiation Laboratory. A multi-layer optic provides good flux and spectral purity. The small physical size of the source, the long optic to focus distance (635 mm) and the short source to optic distance (65 mm) allowed the use of existing beamline components, without any significant modification. The system replaces a short section of beam pipe upstream of the beam conditioning slits and shutter. The system can be installed and removed from the beamline in less than 1 day.

The Joint Center for Structural Genomics (JCSG) and SSRL Structural Molecular Biology group developed the Stanford Automated Mounting (SAM) system and installed it on beamlines at SSRL. The JCSG relies on this system to test crystals for diffraction. The installation of the X-ray microsource in beamline 9-2 allowed crystal screening to continue during SSRL shutdowns. Using a standard screening protocol of two 10 minute exposures, separated by a 90° phi rotation, the system was capable of screening up to 400 crystals per week and was left to run unattended for up to 4 days. Over 8200 crystals were screened during the last four SSRL shutdown periods.

An X-ray generator can also be useful for ongoing beamline development. Shutdown periods provide easier access to the experimental hardware, however, some tests require beam. The X-ray microsource offers the ability to conduct these tests during periods when users are not scheduled.

Keywords

Protein Crystallography; Crystal Screening; X-ray Generator

1. Introduction

Synchrotron end-stations for macromolecular crystallography represent a significant investment in both hardware and software [1–2]. The equipment is utilized continuously by the user program throughout the run. However, each year there is a period of several months without user beam. These annual shutdowns of the ring are necessary to maintain and upgrade the storage ring and beamlines, in order to ensure reliable operation of the machine for the next

^{*}Corresponding Author. E-mail: mmiller@slac.stanford.edu, Phone: 650-926-5036, FAX: 650-926-3292.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

user run. During years in which there is no upgrade to the endstation, the detector, goniostat, and automated sample changing equipment sit idle.

Large scale projects like structural genomics generate a steady supply of new crystals to be evaluated [3]. The demand for crystal screening results does not diminish during the synchrotron shutdowns. When the ring is down for maintenance, all users must analyze and collect their samples elsewhere.

Here we describe the installation of a compact sealed-tube X-ray generator in the SSRL BL 9-2 hutch. The system allows us to make continued use of the endstation equipment for crystal screening and beamline development work during extended shutdown periods.

2. X-ray microsource

The X-ray generator system we selected for installation during the SPEAR-3 upgrade shutdown (Summer 2003) was the Rigaku (The Woodlands, TX) MicroMAX-002. This system comprises two main components, a Bede (Durham, UK) Microsource microfocus sealed tube generator and an Osmic (Auburn Hills, MI) microfocus Confocal Max-Flux (CMF) multilayer optic. The generator consists of a 3U 19" rack mount chassis that contains the high voltage power supply and control electronics and a tube head assembly that houses the copper target, electron beam focusing optics and safety shutter. We typically operate the unit at 28 W (45 kV/0.6 mA) with a 20 m focal spot. An external water chiller supplies the required cooling water (15° C at 200–400 ml/min).

The -CMF optic is an 80 mm long multi-layer with graded d-spacing and radii of curvature. The d-spacing of the optic varies from 21–43 Å. The optic has two elliptical mirrors in a Kirkpatrick-Baez side-by-side arrangement with matched foci [4]. The spectral purity of the doubly-reflected beam is greater than 97% Cu K.

The key benefits of the MicroMAX-002 system for our installation are the compact size of the unit and the long optic to focus distance. This simplified the installation and integration on the beamline. The only moving parts are the safety shutter and the water chiller pump. This results in a reliable system with low yearly maintenance requirements.

3. Beamline installation

Since 2003, we have installed the X-ray source in the BL 9-2 hutch at SSRL during the annual shutdown. The installation requires the removal of a section of beam pipe, an ion chamber and some attenuation filters. We then mount X-ray tube and optic assembly to a fixed support at the front of the beamline table. We can then align the table to the beam using the same table motions we use to align to the synchrotron beam. The support rails were designed to facilitate easy installation and removal of the system. We can install or remove the system in less than a day.

Provided the environmental and cooling water temperatures are maintained, the beam intensity and position remain constant. We have not found it necessary to realign the system after the initial alignment at the start of each shutdown.

4. Results

As one of the large-scale production centers for structural genomics under phase II of the NIH Protein Structure Initiative (<http://www.nigms.nih.gov/Initiatives/PSI/>), the JCSG (www.jcsg.org) has built a high-throughput pipeline, which automates all of the major experimental steps in the structure determination process from target selection through

submission to the Protein Data Bank (PDB). The JCSG currently screens approximately 570 crystals per week. The joint development with the SSRL SMB group of the SAM system for automated screening has been essential for handling this large number of samples [5–6].

The installation of the X-ray generator allowed the JCSG to continue screening during the shutdowns. A summary of the number of crystals screened with the microsource during the shutdowns is shown in Table 1. Of the 8282 crystals screened from 339 different targets, 220 later had data collected at a synchrotron. Data from 105 of the crystals (97 targets) have been deposited in the PDB. This represents 20 % of the crystals screened by JCSG and nearly 25 % of the JCSG targets deposited in the PDB.

Prescreening the crystals before data collection trips to the Advanced Photon Source (Argonne, IL) and the Advanced Light Source (Berkeley, CA) has proven to be much more efficient than screening on beamlines without automated sample changers, greatly reducing the amount of beamtime needed.

The microsource screening system has also been used for several user training workshops during the shutdowns. It allowed users to become familiar with the operation of the new sample changing hardware and software interfaces prior to the start of the user run.

5. Future plans

With the high demand for macromolecular crystallography beamtime, it is often difficult to find time for beamline development during the user run. Maintenance and shutdown periods allow development work to take place without impacting the user schedule. However, some beamline testing absolutely requires the use of X-rays. The availability of an X-ray generator at a beamline can enable testing of new components during synchrotron down times. Utilizing the system for hardware development work that requires beam during shutdown periods allows more beamtime to be allocated to users. Plans are underway to build an off-line simulator beamline that can house the microsource for beamline development and screening during the user run. We are also planning to purchase a second microfocus X-ray generator for installation at beamline 1-5.

6. Conclusions

The X-ray generator has been beneficial for the ongoing crystal screening required for JCSG. The reliability and ease of use have minimized the operational overhead of the system. Microfocus X-ray generators provide a means to utilize existing equipment that would otherwise remain idle during the annual shutdown.

Acknowledgements

We would like to thank the other members of the SMB-PX group and JCSG for developing beamline infrastructure and providing samples. We thank Ron Reyes for machining components and help with installation and removal of the system each year. The JCSG is supported by NIGMS/PSI (U54 GM074898). Portions of this research were carried out at the Stanford Synchrotron Radiation Laboratory, a national user facility operated by Stanford University on behalf of the U.S. Department of Energy, Office of Basic Energy Sciences. The SSRL SMB Program is supported by the Department of Energy, Office of Biological and Environmental Research, and by the National Institutes of Health, National Center for Research Resources, Biomedical Technology Program, and the National Institute of General Medical Sciences.

References

1. Kuhn P, Soltis SM. Nucl Instrum Methods Phys Res A 2001;467:1363–1366.

2. McPhillips TM, McPhillips SE, Chiu HJ, Cohen AE, Deacon AM, Ellis PJ, Garman E, Gonzalez A, Sauter NK, Phizackerley RP, Soltis SM, Kuhn P. J Synchrotron Radiat 2002;9:401–406. [PubMed: 12409628]
3. Lesley SA, Kuhn P, Godzik A, Deacon AM, Mathews I, Kreusch A, Spraggon G, Klock HE, McMullan D, Shin T, Vincent J, Robb A, Brinen LS, Miller MD, McPhillips TM, Miller MA, Scheibe D, Canaves JM, Guda C, Jaroszewski L, Selby TL, Elsliger MA, Wooley J, Taylor SS, Hodgson KO, Wilson IA, Schultz PG, Stevens RC. Proc Natl Acad Sci U S A 2002 Sep 3;99(18):11664–11669. [PubMed: 12193646]
4. Micromax-002 Service Engineer Manual. Rigaku/MSK; The Woodlands, TX: 2002.
5. Cohen AE, Ellis PJ, Miller MD, Deacon AM, Phizackerley RP. J Appl Crystallogr 2002;35:720–726.
6. Cohen AE, McPhillips SE, Song J, Miller MD. Synchrotron Radiat News 2005;18:28–35.

Figure 1.

The MicroMAX-002 installation on beamline 9-2. The tube head and optic are mounted in a 176 (w) × 226 (l) × 245 (h) mm housing. The existing beam conditioning slits are used with the microsource. The beam transport pipe that was removed for the installation normally connects from the flange protruding through the upstream wall of the hutch. (Note: Color on Web, Grayscale in print)

Table 1

Screening usage summary for the MicroMAX-002 system on BL 9-2

Run Dates	Days Installed	Days Screening	Number of Crystals	Number of Targets
07/09/2003 – 03/14/2004	249	131	3350	117
09/03/2004 – 10/11/2004	38	33	867	57
01/10/2005 – 01/31/2005	21	20	668	59
08/25/2005 – 11/06/2005	73	63	1441	74
08/17/2006 – 10/16/2006	60	55	1956	89
Total	441	302	8282	339