Chapter Nineteen

SYNCHROTRON RADIATION FOR MACROMOLECULAR CRYSTALLOGRAPHY

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PURPOSE

This study, conducted by a working group established by the Office of Science and Technology Policy (OSTP) and chaired by Marvin Cassman of the National Institutes of Health (NIH), examined how access to synchrotron beamlines for X-ray crystallographic studies could be improved. The working group analyzed funding and requirements in the following areas at five U.S. synchrotron facilities:

- Staffing
- Detectors and other equipment
- Research and development
- Improved access procedures
- Upgrades in facility operations
- Expansion of existing crystallographic capabilities.

The working group's primary goal was to stimulate interagency collaboration to produce the more efficient use of resources and improved synchrotron access for crystallographers.

BACKGROUND

The working group was established in response to several earlier reports confirming the increase in demand for synchrotron radiation beamline facilities for use in X-ray crystallographic studies of biological macromolecules. Beginning in the 1990s, the number of crystallographic structures determined (i.e., identified and understood) each year has increased rapidly, and the percentage of those structures determined using synchrotron beamline technology has increased threefold.

The increased demand for this technology has created problems for scientists who now have trouble finding open time slots on beamlines and often experience extremely long wait times before gaining access once they do obtain a slot. The demand for beamline time is not likely to subside as the possible applications of this technology continue to increase.

The Working Group on Structural Biology at Synchrotron Radiation Facilities published its report in January 1999. The working group consisted of scientists and policymakers from the NIH, the National Science Foundation (NSF), the U.S. Department of Energy (DOE), OSTP, and the National Institute of Standards and Technology (NIST) specializing in biology, physics, material science, and other related fields.[1]

Five synchrotron facilities with biomolecular crystallographic capabilities were examined in the working group report. Four of those facilities—the National Synchrotron Light Source at Brookhaven National Laboratory, the Advanced Photon Light Source at Argonne National Laboratory, the Advanced Light Source at Berkeley Lab, and the Stanford Synchrotron Radiation Laboratory—are supported by

[1]For a complete list of working group members and other contributors to the report, see Working Group on Structural Biology at Synchrotron Radiation Facilities (1999), p. 6.

the DOE. One facility, the Cornell High Energy Synchrotron Source (CHESS) in Ithaca, New York, is supported by the NSF.

The Center for Advanced Microstructure and Design (CAMD), a state-run facility in Baton Rouge, Louisiana, did not have an operating crystallography station at the time the report was written but was given consideration by the working group because of its high potential for conducting crystallographic studies. Although synchrotron radiation is used extensively in many areas of science, including other fields of biology (e.g., X-ray scattering, X-ray microscopy, X-ray spectroscopy), this report focused only on its use in crystallographic studies.

METHODS/APPROACH

The working group drew extensively from three previous publications that examined the requirements and resources of synchrotron facilities in response to the expanding need for X-ray crystallographic studies. The working group also drew from a fourth document[2] that provided a synthesis of these analyses, and from recommendations on the synchrotron needs of the crystallographic community.[3] In addition, the working group engaged several agency personnel from the DOE, NIH, NSF, NIST, and OSTP in discussions conducted in preparation for writing its report.

Using the findings articulated in the published sources and the feedback from discussions with agency personnel, the working group examined in detail the crystallographic capabilities of each synchrotron radiation source and the support each receives from federal agen-

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[2]A Structural Biology Subcommittee of the DOE Office of Biological and Environmental Research Advisory Committee produced a document using the information in the three previous reports with "recommendations as to the resources and processes that are necessary for the proper support of the macromolecular crystallographic community at the synchrotrons" (Working Group on Structural Biology at Synchrotron Radiation Facilities, 1999).

[3]Basic Energy Sciences Advisory Committee Panel (1997); Structural Biology Synchrotron Users Organization (2002); and Hodgson, Keith, and Eaton Lattman, "Survey of Structural Biology Beam Lines and Instrumentation and U.S. Synchrotron Centers—Needs and Opportunities for the Future," San Diego, Calif.: San Diego Supercomputer Center, February 1998.

cies. This effort produced findings that led to several recommendations in the six specific functional areas listed earlier in this chapter.

FINDINGS AND RECOMMENDATIONS

The findings and recommendations from the working group's report are as follows:

Staffing

Increased staffing for user support is a high priority. At the time the report was written, the working group expected that most, if not all, of the estimated requirements would be met by existing agency initiatives. The working group believed that inflationary adjustments would be needed in future years to ensure continued optimal performance.

Detectors and Other Equipment

Again, a significant part of the requirements for improved detectors appears to be met by planned agency expenditures. However, an additional $1 million may be required for spares, which can be distributed as needed. It was more difficult to assess the requirements for other equipment, but the working group believed that perhaps another $2 million to $3 million would be required. It seems likely that, in this case, planned agency expenditures would provide some or most of the necessary funds. The estimate for future years was uncertain, but, on average, $250,000 per beamline was thought to be required each year to maintain and improve capital equipment.

Research and Development

No dollar value could be estimated for the requirements in this area, especially for new detector technology. However, the committee strongly recommended that a transagency request for proposal be prepared to solicit applications for synchrotron operations in this field.

Improved Access Procedures

Changes in the application process for beamline time should be considered. The working group strongly encourages joint discussions including federal agency representatives and synchrotron operators and users to address this critical issue.

Upgrades in Facility Operations

Approximately $121 million in major upgrades for the DOE synchrotrons were recommended. The committee recommended that these funds be incorporated into the DOE's budget. It is essential that all the agencies that benefit from the availability of synchrotron resources support this effort.

Although the operation of the Cornell Electron Storage Ring (CESR), and therefore the operation of CHESS, is reasonably secure for the next five years, the situation beyond that time is much less certain. There are several possible developments that could have an impact on the continued operation of the CESR. It is essential that an expert group be assembled to assess the future viability of CESR and the consequences of various actions for CHESS and the crystallographic community. Possible shortfalls in near-term CESR/CHESS operating costs should also be examined.

Expansion of Existing Crystallographic Capabilities

Because it is unlikely that additional synchrotrons will be built in the near future, proposals for expansion of the facilities at the Advanced Light Source and CAMD, which currently have little or no crystallographic capacity, should be carefully evaluated. Additionally, new beamlines at other facilities should be considered on a case-by-case basis. It is difficult to assess how much additional capacity will be needed in the next five to ten years, but it seems certain that additional capacity will be required. Considering the three- to four-year time lag for construction of new beamlines, plans must be developed well in advance of anticipated requirements.[4]

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[4]Working Group on Structural Biology at Synchrotron Radiation Facilities (1999), Summary.

The working group, through its findings and recommendations, reiterates the need to address the documented growing scientific yield from and increasing demands by users of synchrotron radiation beamlines. Increasing accessibility to beamlines at these facilities, and therefore maximizing the facilities' scientific output, will require ongoing attention to and maintenance of each of the six areas addressed in the working group's report. Additionally, the working group strongly recommends that the interagency model used to conduct its examination be applied to other aspects of research at national facilities.