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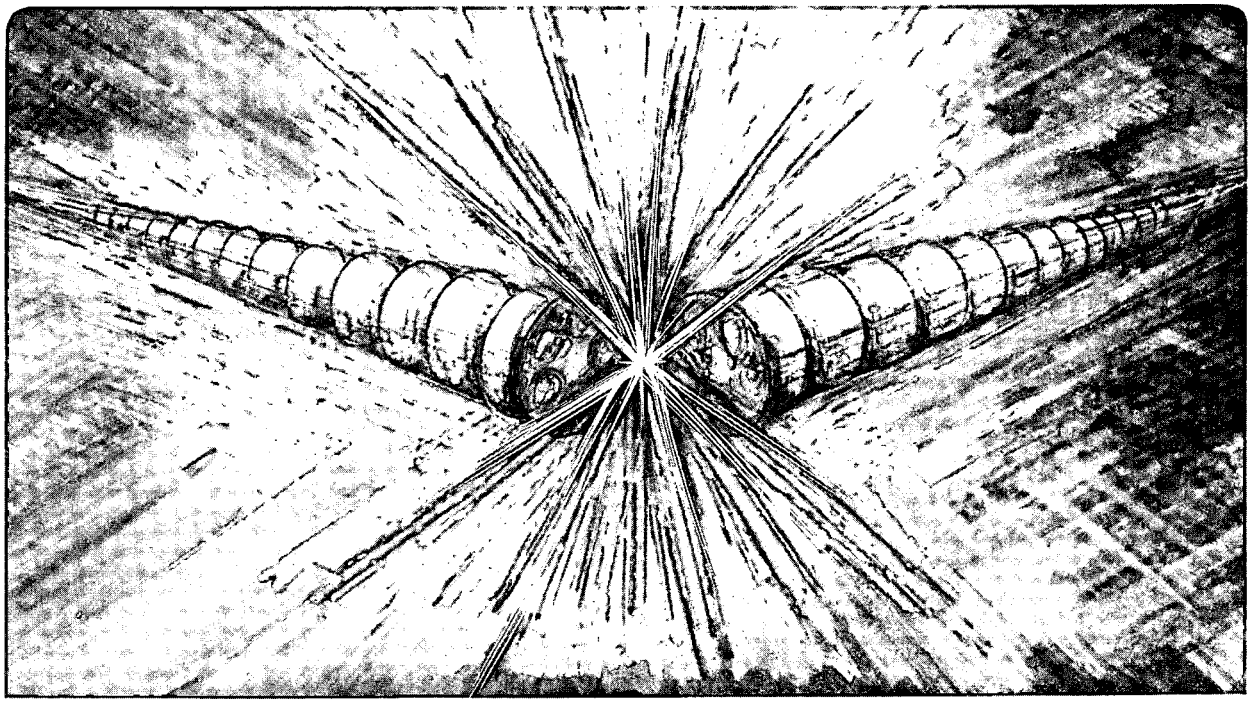

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THE MACROMOLECULAR CRYSTALLOGRAPHY FACILITY AT THE ADVANCED LIGHT SOURCE*

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THE MACROMOLECULAR CRYSTALLOGRAPHY FACILITY AT THE ADVANCED LIGHT SOURCE

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ABSTRACT

Synchrotron radiation offers several advantages over the use of rotating anode sources for biological crystallography, which allow for the collection of higher-resolution data, substantially more rapid data collection, phasing by multiwavelength anomalous diffraction (MAD) techniques, and time-resolved experiments using polychromatic radiation (Laue diffraction). The use of synchrotron radiation is often necessary to record useful data from crystals which diffract weakly or have very large unit cells. The high brightness and stability characteristics of the Advanced Light Source (ALS) at Lawrence Berkeley National Laboratory, along with the low emittance and long straight sections to accommodate insertion devices present in third generation synchrotrons like the ALS, lead to several advantages in the field of macromolecular crystallography. We are

presently constructing a Macromolecular Crystallography Facility at the ALS which is optimized for user-friendliness and high-throughput data collection, with advanced capabilities for MAD and Laue experiments. The x rays will be directed to three branchlines. A well-equipped support lab will be available for biochemistry, crystal mounting, and sample storage, as well as computer hardware and software available, along with staff support, allowing for the complete processing of data on site.

INTRODUCTION

The design of biological crystallography facilities based on synchrotron radiation (SR) must consider the stringent requirements needed to optimally acquire x-ray data from crystals of biological materials, which diffract rather weakly. The ability to make accurate intensity measurements is especially important when measuring the small differences in intensity of Friedel pairs in order to determine anomalous scattering contributions for multiwavelength anomalous diffraction (MAD) and isomorphous replacement experiments. The high brightness and beam stability of third generation synchrotrons, such as the Advanced Light Source (ALS), will allow for further improvements in the field of synchrotron-based biological crystallography, which already has shown a great deal of success in solving otherwise intractable problems.

Synchrotron radiation has several advantages over other x-ray sources in biological crystallography including very high flux, high brightness, and broad bandpass [1]. The high flux (photons per second per milliradian at 0.1% bandpass) usually leads to higher resolution, higher quality data. In some cases SR is required to observe any measurable diffraction and the time of data collection is greatly reduced. The advantages of high brightness (photons per second per square milliradian per square millimeter at 0.1% bandpass) allow data collection from crystals with large unit cells due to the increased collimation, and from microcrystals. The broad bandpass allows for the selection of energies needed for MAD experiments, which can be used for obtaining phases, and polychromatic Laue diffraction for time-resolved experiments. In this paper the design of the Macromolecular Crystallography Facility (MCF), which is presently

under construction at the Advanced Light Source at Lawrence Berkeley National Laboratory, is described.

FACILITY DESIGN

Insertion device

At the ALS which operates at energies of 1.5 or 1.9 GeV, the bending magnets have a critical energy of around 1.5 keV, which is too low for macromolecular crystallography. Also the undulators at the ALS have harmonic spectra at energies that are too low. Thus a hybrid permanent magnet, wiggler was chosen. The high field magnetic structure of this device can produce substantial flux and brightness down to 0.9 Å wavelengths. To optimize the parameters of the wiggler we maximized the horizontal phase space density as the number of poles was varied using a fixed length of three meters [2]. The phase space is defined by the crystal size and maximum angular divergence (related to the unit cell dimensions). The vertical source size and divergence is small enough to be completely accepted by the crystal, thus only the horizontal phase space needs to be considered. The phase space density is then calculated for differing numbers of poles using phase space acceptances from between one and eight mm-milliradian. By this process a 38-pole device was chosen with optimum flux integrated into the phase space acceptance of the crystal. Comparison of this source with several other crystallography sources presently in use is shown in Table II. From this table it is seen that an improvement of approximately a factor of three is achieved when the operating energy of the ALS is 1.9 GeV versus 1.5 GeV. The ALS will operate at 1.9 GeV primarily

beginning in 1996. Also it can be seen that this source does very well compared to all existing sources.

Beamline optics

In order to make efficient use of the fan of radiation produced by the wiggler, we plan to build three branchlines and end stations. The central branchline will be capable of performing MAD and Laue, as well as standard monochromatic, experiments, with a wavelength range extending from 4.0 to 0.9 Å, and two side branchlines will be utilized for standard monochromatic crystallography or single isomorphous replacement with anomalous scattering at wavelengths from 1.6 to 0.9 Å. The beamline optics must be designed to preserve the brightness to the greatest degree possible and to deliver the brightest beam onto the sample. This requires great attention to dealing with power loading on the optical elements (mirror, monochromator crystals, apertures, etc.), and to monitoring and steering the photon beam.

The overall layout of the beamlines is shown in Figure 1. The central station has a vertically collimating mirror, a double crystal, fixed exit monochromator, and a second vertically focusing mirror with a toroidal cut to supply some horizontal focusing as well. The first mirror and the monochromator were designed to capture the central 1.5 milliradians of the horizontal fan of radiation from the wiggler and let pass the adjacent radiation from -4.5 to -1.5 milliradians and 1.5 to 4.5 milliradians, which will be used for the two side stations. This is achieved by using a downwardly deflecting mirror for the central fan and upwardly deflecting mirrors, located downstream, for the side beams. The side stations will utilize sets of asymmetrically-cut curved crystal monochromators which will achieve beam compression ratios (thus increased flux) by a factor of from two

to four. The first mirror for each branchline will require integral water cooling. This is also true for the first crystal of the double crystal monochromator and the asymmetrically-cut curved crystal monochromators.

End stations

The end stations will be equipped with kappa-geometry diffractometers, which allow for maximal reciprocal space coverage while maintaining a compact form. This is especially important, when performing MAD experiments, for observing Friedel pairs on the same exposure and for using the reverse beam approach. In order to match the detector readout time to the exposure time (10 - 30 seconds per degree oscillation will be typical), a fast readout device must be used. At present detectors based on charged coupled devices (CCDs) with phosphor-treated, demagnifying fiber optic front ends, are becoming available in sizes sufficient for performing high resolution macromolecular crystallography. This requires arrays of fiber optic/CCD modules to be tiled together in order to achieve a sufficient aperture. CCD-based detectors presently offer the only approach to a fast readout system, and our stations plan to utilize an array of these modules. Equipment for freezing crystals and maintaining them at cryogenic temperatures will also be available.

Control systems

With a highly bright source of x rays and fast readout detectors, data transfer rates will be extremely high. Furthermore there are approximately forty motors in the central beamline alone which need to be integrated together, with the diffractometer and detector, and to the internal and external computer environments. The design of the software should allow for maximum flexibility and modularity of the code, and

compatibility with the necessary software tools. For this reason we have chosen Sun workstations as our beamline control and primary data acquisition computers. The Solaris operating system supports a distributed operating environment using CORBA which can be overlaid on the EPICS system used at the ALS for accelerator control. This is shown schematically in Figure 2.

SUMMARY

The Macromolecular Crystallography Facility at the Advanced Light Source is presently under construction and will begin operation as a national user facility for biological crystallography by September, 1996. The design calls for the efficient utilization of the fan of radiation produced by a wiggler to illuminate three experimental stations which can be used for monochromatic, multiwavelength, and polychromatic experiments. The experimental stations are designed for high throughput and to be user friendly with very fast detector systems networked to fast data processing and archiving capabilities. There will also be an extensive Structural Biology Support Facility which will be well equipped for protein purification, characterization, crystallization, and crystal alignment using a rotating anode source. Additionally there will be computer workstations for data processing and analysis, including graphics workstations.

We are also collaborating with other engineers and scientists at Lawrence Berkeley National Laboratory to develop a pixel detector for biological crystallography [3]. This two-dimensional x-ray detector is based on a highly parallelized architecture of integrated pixel electronics with a pixel size of 150 microns. This allows for a frameless readout of the data into a histogramming memory with no deadtime. Once development is complete, this detector will find many applications in biological crystallography and

material science due to its rapid readout of data and its capability in monitoring time dependent changes in diffraction patterns during the collection of Laue diffraction data.

Acknowledgments

We wish to acknowledge a number of ALS scientists and engineers who have made significant contributions to the success of this project, including Jim Krupnick, Dick Digennaro, Tom Swain, and Alan Biocca, as well as the assistance and advice from numerous members of the structural biology community.

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Facility	ALS	ALS	NSLS	SRS	APS
Energy (GeV)	1.9	1.5	2.5	2.0	7.0
Beamline	5.0.2	5.0.2	X13C	9.5	bend magnet
Field (T)	2.0	2.0	1.2	5.0	0.6
Period (cm)	16.0	16.0	bend magnet	wavelength shifter	bend magnet
No. poles	37	37	1	1	1
Current (A)	0.4	0.4	0.25	0.25	0.1
Flux @ 1Å in 1 mm-rad (photons/s)	8×10^{13}	1.5×10^{13}	0.27×10^{13}	0.45×10^{13}	6×10^{13}

Facility	APS	APS	NSLS	SSRL	SSRL	CHESS
Energy (GeV)	7.0	7.0	2.5	3.0	3.0	5.4
Beamline	wiggler A	undulator A	X25	7.1	9.2	F1
Field (T)	1.0	K=2.2, n=3	1.1	1.8	1.9	1.2
Period (cm)	15.0	3.3	12.0	45.0	25.0	19.6
No. poles	20	152	27	8	16	25
Current (A)	0.1	0.1	0.25	0.1	0.1	0.1
Flux @ 1Å in 1 mm-rad (photons/s)	30×10^{13}	50×10^{13}	5.0×10^{13}	0.72×10^{13}	1.6×10^{13}	8.8×10^{13}

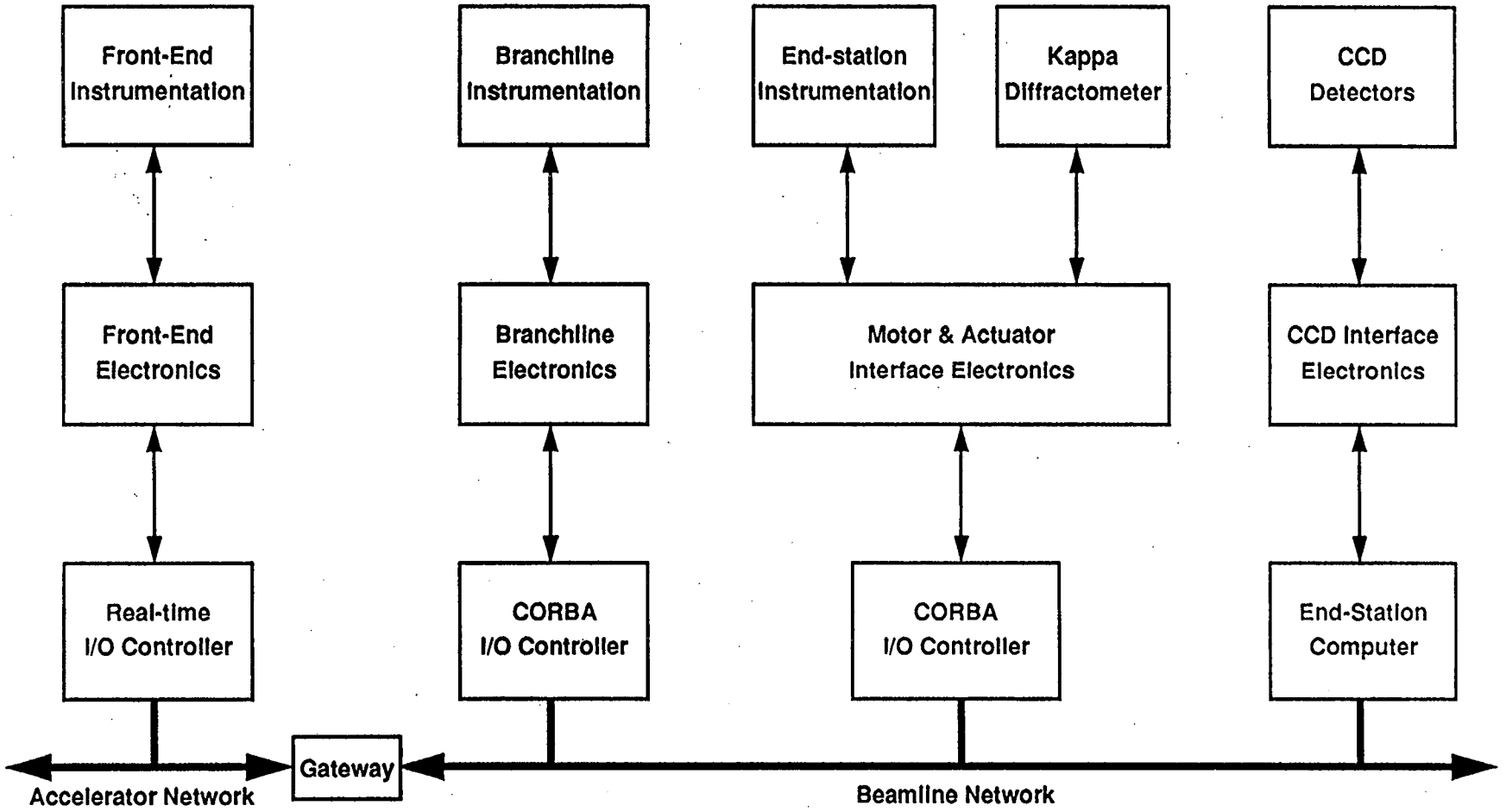
TABLE 1 - Comparison of representative synchrotron sources for macromolecular crystallography

Caption for Figure 1:

The Macromolecular Crystallography Facility at the Advanced Light Source, Beamline 5.0, includes three branchlines and experimental stations. The central station can be use for monochromatic, MAD, or Laue experiments. For the two side station, positions for the detectors are shown for the maximum and minimum wavelength positions.

9.40 M
10.60 M
27
1062.992
Meters
Inches
Station 5.0.3
Station 5.0.1
Station 5.0.2
Walkway

Beamline Control System



The front-end instrumentation is part of the accelerator EPICS control system which is based on the VxWorks real-time kernel and a distributed real-time database. The branchline and end-station instrumentation are controlled by distributed CORBA objects running on NeoSolaris-based SPARC computers. The CCD detector is directly interfaced to the experimenter's workstation.

FIGURE 2

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