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Remote access to crystallography beamlines at SSRL: novel tools for training, education and collaboration

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For the past five years, the Structural Molecular Biology group at the Stanford Synchrotron Radiation Lightsource (SSRL) has provided general users of the facility with fully remote access to the macromolecular crystallography beamlines. This was made possible by implementing fully automated beamlines with a flexible control system and an intuitive user interface, and by the development of the robust and efficient Stanford automated mounting robotic sample-changing system. The ability to control a synchrotron beamline remotely from the comfort of the home laboratory has set a new paradigm for the collection of high-quality X-ray diffraction data and has fostered new collaborative research, whereby a number of remote users from different institutions can be connected at the same time to the SSRL beamlines. The use of remote access has revolutionized the way in which scientists interact with synchrotron beamlines and collect diffraction data, and has also triggered a shift in the way crystallography students are introduced to synchrotron data collection and trained in the best methods for collecting high-quality data. SSRL provides expert crystallographic and engineering staff, state-of-the-art crystallography beamlines, and a number of accessible tools to facilitate data collection and in-house remote training, and encourages the use of these facilities for education, training, outreach and collaborative research.

1. Introduction

The macromolecular crystallography (MX) experiment lends itself perfectly to high-throughput technologies, automation and remote experimentation. The experiment comprises a series of distinct steps, beginning in the wet laboratory with protein expression, purification, crystallization and crystal mounting using flash-cooling in liquid nitrogen, and progressing through to the screening of crystals for diffraction quality, the collection of diffraction data, data processing and structure determination. Most of these steps have been fully automated, and in many cases it is now possible to go from expressed protein to fully determined three-dimensional structure with only minimal intervention. However, several steps still require expert human intervention, including the choice of crystal for data collection. Since the ultimate goal of the experiment is to produce a high-quality high-resolution structure of the protein in question, this relies heavily upon the choice of the best possible crystal for data collection and the most appropriate data-collection strategy. In this regard, the careful training and education of students and novices is of fundamental importance to these aspects of the process and cannot be overlooked, however much automation and remote access are involved in the experiment.

Some of the most important developments in the automation of protein expression, purification and crystallization have taken place under the auspices of the NIH-funded Protein Structure Initiative (Burley *et al.*, 2008). With regard to high-throughput crystal screening and data collection, many facilities and groups worldwide have developed automated sample changers, including Abbot Laboratories in Illinois, USA (Muchmore *et al.*, 2000), DORIS in Hamburg, Germany (Karain *et al.*, 2002; Pohl *et al.*, 2004), the Spring8 synchrotron in Japan (Ueno *et al.*, 2004), the European Synchrotron Radiation Facility in Grenoble, France (Ohana *et al.*, 2004; Cipriani *et al.*, 2006) and the Advanced Light Source (ALS) in Berkeley, California, USA (Snell *et al.*, 2004). In an effort to produce a true high-throughput crystal-screening and data-collection facility, and to improve the efficiency of the synchrotron radiation resource, the Stanford Synchrotron Radiation Lightsource (SSRL) Structural Molecular Biology (SMB) Group and the Structure Determination Core of the Joint Center for Structural Genomics (JCSG) (Lesley *et al.*, 2002) worked together to develop the Stanford auto-mounting

(SAM) system (Cohen *et al.*, 2002). In addition to complete automation of the experiment, SSRL has also implemented fully remote access to the MX beamlines (Soltis *et al.*, 2008).

Notwithstanding the obvious increase in throughput and efficiency, the advent of automation and remote access at the SSRL MX beamlines has generated substantial spinoffs for the scientific user community by providing increased opportunities for collaboration between research groups and allowing scientists who might not typically have had access to a national user facility to obtain valuable beam time. It has also introduced many young scientists to synchrotron radiation science by providing educational and training opportunities for graduate students and postdoctoral researchers in user laboratories. The scientific staff at SSRL offer in-house training workshops and have run remote-access workshops around the US and at international sites. Attending one of these workshops is strongly encouraged before taking part in remote-access beamtime. Furthermore, often the most effective training is from the experiences gained during remote-access beamtime, when new researchers conduct their own experiments under the advice and encouragement of other members of the home laboratory and of SSRL User Support scientists, who are readily available *via* cellular telephone, email and a 'chat' feature (instant messaging) in the *BLU-ICE*/*DCS* beamline control system.

2. Synchrotron radiation research at SSRL

SSRL has a long history of excellence in structural biology research, including some of the first reports of X-ray absorption spectra from a biological sample (Kincaid *et al.*, 1975), the first published report of single-crystal diffraction from protein crystals using synchrotron radiation (Phillips *et al.*, 1976), fundamental studies of what would become the multiple-wavelength anomalous diffraction phasing experiment (Phillips *et al.*, 1977, 1978; Phillips & Hodgson, 1980; Templeton *et al.*, 1980) and the development of insertion devices as sources of high-intensity radiation (Doniach *et al.*, 1997).

SSRL is a national user facility funded by the US Department of Energy Office of Basic Energy Science, the National Institutes of General Medical Sciences (NIGMS) and the National Center for Research Resources, the latter two being components of the US National Institutes of Health (NIH). SSRL provides extremely bright X-ray and UV photon beams produced by the third-generation 3 GeV SPEAR3 storage ring, for applications in materials science, environmental science, chemistry and structural biology research, utilizing scientific techniques including photoelectron spectroscopy, small-angle X-ray scattering (SAXS), X-ray absorption spectroscopy (XAS), total X-ray reflection fluorescence and MX.

The SMB group at SSRL (http://smb.slac.stanford.edu) operates and maintains ten beamlines, seven for MX (BL1-5, BL7-1, BL9-1, BL9-2, BL11-1, BL12-2 and BL14-1), two for biological XAS (BL7-3 and BL9-3) and one for biological SAXS (BL4-2). All seven MX beamlines at SSRL are fully automated, employing the SAM system which has been integrated into the *BLU-ICE*/*DCS* beamline control system and graphical user interface developed earlier at SSRL (McPhillips *et al.*, 2002). Up to 288 crystals can be screened in a matter of hours without manual intervention using this reliable and robust robotic system. The use of the SAM system has not only seen an increase in throughput by research groups but also an improvement in the overall quality of the diffraction data being collected. Researchers are now able to screen all their crystals reliably and take advantage of the automated image-analysis tools developed at SSRL, prior to choosing the best quality crystals for subsequent diffraction data collection. These tools include the Crystal Analysis server, which will automatically analyze test images and feed relevant parameters and statistics back to the researcher *via BLU-ICE*, and the browser-based *WEB-ICE* interface (González *et al.*, 2008), where diffraction and video images of the samples can be viewed, crystals ranked and data-collection strategies calculated.

2.1. Automation

The seven SSRL MX beamlines are all very similar, in that the experimental table, front-end beam-conditioning system, kappa goniometer, cryosystem and detector positioner are nearly all identical. The undulator micro-focus beamline (BL12-2) differs somewhat in design to meet the more demanding hardware requirements for microbeam and microcrystal experiments, but is still compatible with the SAM system and standard beamline control software. Every aspect of beamline control inside the experimental hutch, and also on the upstream optics elements (mirrors, monochromators and slits), is motorized to the extent that it is unnecessary to enter the hutch to change any of the experimental parameters (X-ray energy, beam size, X-ray detector position, fluorescence detector position, beamstop position, attenuation and lighting), to mount or dismount samples, or to anneal or wash ice from samples. This degree of automation of the beamlines is absolutely critical to the implementation of fully remote access; if there remains a single task that requires human intervention inside the hutch during the normal course of crystal screening and data collection then remote access is not practical.

Automated sample mounting was made available to general experimenters during the first SPEAR3 run of 2004 on three beamlines. Since its inception, use of the SAM system has accelerated such that, during the last scheduling period (2009), 110 out of 121 research groups (91%) were using SAM during their experiments. The SAM system has been described in detail previously (Cohen *et al.*, 2002; Smith & Cohen, 2008; Soltis *et al.*, 2008). During the first year of operation (2004), 30 research groups used the automated mounter and over the course of 60 experimental starts mounted over 3500 crystals. The JCSG, one of the original SAM test user groups, mounted an additional 2000 or more crystals from 125 target proteins that year, and were successful in solving 30 new structures from 36 unique proteins (Smith & Cohen, 2008). The number of crystals mounted using the SAM system has also increased dramatically since it was first introduced, such that currently

well over 300 000 crystals have been screened by researchers (Fig. 1).

2.2. The remote-access experiment

Fully remote access was made available to research groups during the 2005 scheduling period. During the first two years the number of research groups choosing to conduct their experiments remotely rose from 24 to 44%, and has continued rising each year (Fig. 2*a*) until the last scheduling period, which saw 105 of the 121 groups (87%) screening their crystals and collecting their data using remote-access tools. Most noticeably, the total number of remote starts saw an almost exponential growth in 2007 (Fig. 2*b*), which can be primarily attributed to an increase in beamline efficiency (fewer beam-hours per start) as the coupled use of the SAM system and remote access became more popular. This increase in beamline efficiency can also be seen in the total number of crystals mounted *via* the SAM system since its inception, which also experienced a dramatic rise in 2007 (Fig. 1).

The remote-access experiment at SSRL has been described previously (Smith & Cohen, 2008; Soltis *et al.*, 2008). Scientists ship their cryo-cooled samples to SSRL in 96-port cassettes custom-designed at SSRL for use with the SAM system, or in 16-port Uni-pucks (http://smb.slac.stanford.edu/robosync/Universal_Puck). The cassettes have been designed such that two can be shipped in a standard dry shipper (192 crystals in total). Up to seven Uni-pucks (112 crystals in total) may be shipped in a standard dry shipper. The Uni-pucks have been designed as part of a collaboration between developers at synchrotrons throughout the United States, allowing research groups to take advantage of automated sample-mounting systems at different synchrotron facilities (http://smb.slac.stanford.edu/robosync/). The Uni-pucks are based upon the ALS-style puck, and are currently used with the SAM robot at SSRL, with many ALS-style robots at the three other large DOE-funded synchrotrons in the US (ALS, the Advanced Photon Source and the National Synchrotron Light Source), with the ACTOR robot (Rigaku, USA), and with various other sample-mounting robots in Europe, Australia and Asia. At SSRL, four Uni-pucks are mounted in an adaptor cassette such that the sample pins can be accessed by the SAM system in the same way as it accesses sample pins in an SSRL cassette.

During their allotted beam time, the remote researchers connect to the beamline computers *via* an NX server/client application (http://www.nomachine.com). The NX client is downloaded for free onto the researchers' home computers, and they can then connect to an NX server running on an SSRL computer. The client uses minimal CPU and memory resources on the host computer, with the entire computational load on the SSRL server. Once connected, the researchers see a remote desktop (Fig. 3*a*), identical in all aspects to the environment they would see on a computer at the beamline. They can then use the *BLU-ICE* control interface (McPhillips *et al.*, 2002) and/or the *WEB-ICE* interface (González *et al.*, 2008) to screen their crystals and obtain results directly back into the *BLU-ICE* screening interface (Fig. 3*b*), collect

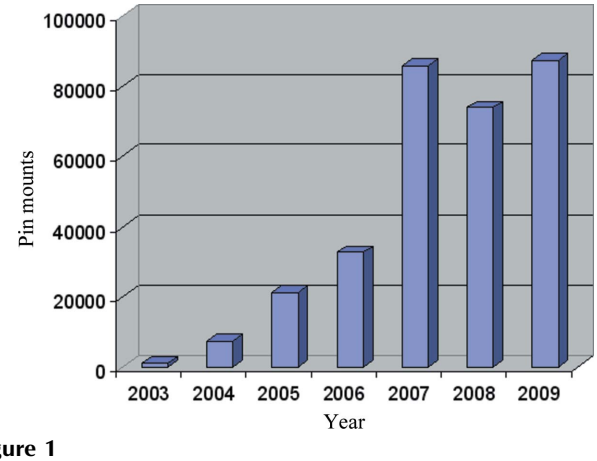


Figure 1
Total number of samples mounted each year with the SAM system since its release in 2003. To date, over 300 000 samples have been screened by more than 100 research groups.

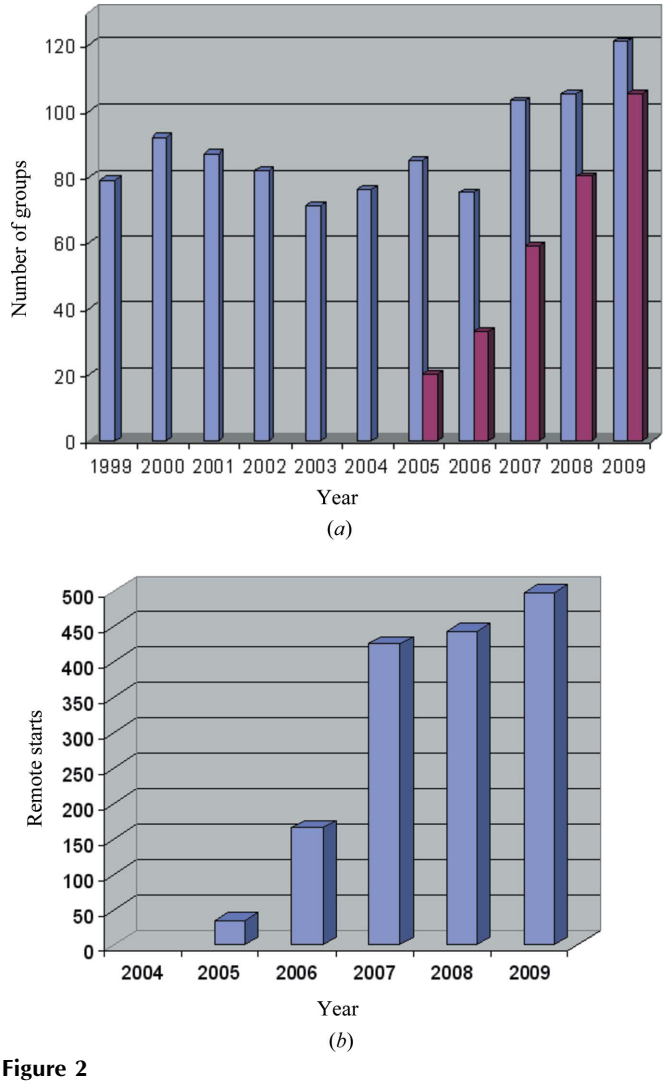
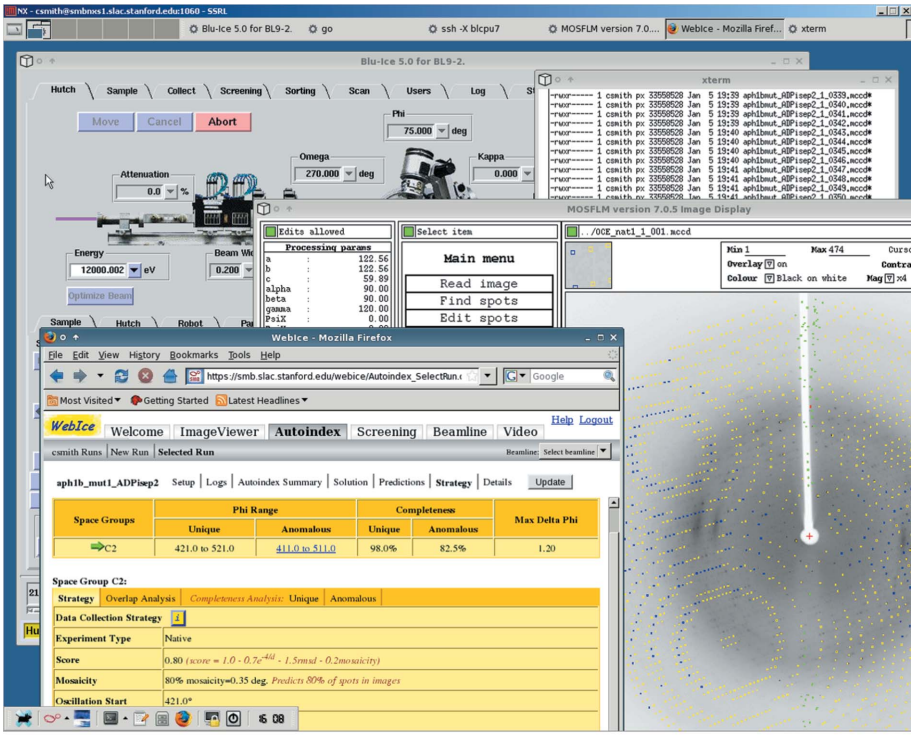
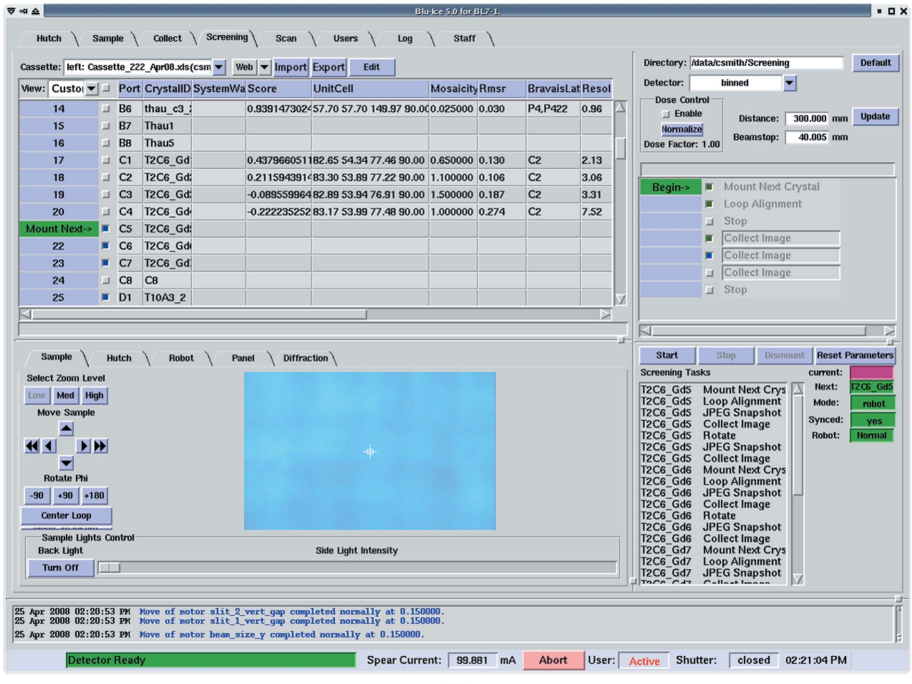


Figure 2
(*a*) The total number of groups with active proposals at SSRL (blue bars) and the number of research groups using remote access since its release in 2005 (purple bars). (*b*) The total number of remote starts (user groups starting a remote data-collection run) since 2005.

monochromatic diffraction data, measure absorption edges prior to multiple- (MAD) or single-wavelength anomalous diffraction (SAD) data collection, monitor all aspects of the experiment, and connect to User Support staff and collaborators *via* a real-time chat feature. In fact, everything that a crystallographer would typically do during a synchrotron data-collection visit can be achieved in the remote-access experiment.



(*a*)



(*b*)

Figure 3
(*a*) Screen capture of a typical remote-access NX session showing multiple windows open, including *BLU-ICE* in the top left background, the *MOSFLM* graphical user interface on the bottom right, *COOT* (Emsley & Cowtan, 2004) at the top right and a *WEB-ICE* session in the left foreground. (*b*) Screen capture of the *Screening* tab from the *BLU-ICE* software. The spreadsheet at the top left has been loaded by the experimenter, and during initial screening the Crystal Analysis server updates the table with results, as shown.

The remote desktop also gives researchers access to all the crystallographic software installed on the SSRL computers, for data processing, structure solution and analysis. Although experimental control, decision making and strategy calculation are carried out in the home laboratory by the researchers and their students, research associates, postdoctoral fellows and/or collaborators (Soltis *et al.*, 2008), SSRL User Support staff are available to troubleshoot experiments, help analyze the screened crystals or advise on data-collection strategy if required. This contrasts with the options that other synchrotrons offer, known as 'service', 'mail-in' or 'FedEx' crystallography, whereby researchers send their cryo-cooled samples to the synchrotron but the decision making and data collection are carried out solely by beamline staff (Robinson *et al.*, 2006), or the more limited telepresence described for a small-molecule crystallography beamline at Daresbury (Warren *et al.*, 2008).

3. Training and collaboration

Based upon feedback from recent SSRL remote-access workshops, remote-access demonstrations at national and international meetings and conferences, anecdotal evidence from informal discussions with research groups, and a recent remote-access survey sent to research groups who regularly use SSRL, the remote-access capabilities have not only revolutionized the way in which diffraction data at synchrotrons are collected but also changed the way in which graduate students and postdoctoral researchers, new to crystallography or synchrotron data collection, are introduced to the area and trained. The general consensus is that the remote-access capabilities at SSRL are a useful tool in training graduate students and postdoctoral fellows in the collection of good quality diffraction data.

Table 1
Cost comparison between a visit to SSRL and remote-access data collection.

Costs are in US dollars.

	US domestic†	International‡	Remote access
Airfares	432.90	1210.00	0
Sample shipping	0	0	200§/1000¶
Meals	191.25	191.25	0
Accommodation	195.00	195.00	0
Taxes	19.50	19.50	0
Rental car	148.00	148.00	0
Parking	24.00	0	0
Communications††	0	200.00	20/200
Total per person	1010.65	1763.75	0
Total (3 people)	2735.95‡‡	5195.25‡‡	220/1200

† Three-day data-collection trip from Huntsville, Alabama, USA. ‡ Three-day data-collection trip from Auckland, New Zealand. § US domestic Dewar shipping by FedEx from Huntsville. ¶ International Dewar shipping by FedEx from New Zealand. †† Includes telephone calls, internet and ftp data backup. ‡‡ Total includes three times the airfare, meals, accommodation and taxes only.

Prior to automation and remote access, a research group comprising, on average, three laboratory members (perhaps one or two experienced people and some graduate students) would undertake a synchrotron data-collection trip and spend 48–72 h continuously screening crystals and collecting diffraction data. Since the first beamlines were developed and made available to the general scientific community, a synchrotron data-collection trip has almost been viewed as a rite of passage for scientists, young postdoctoral fellows and graduate students. It is quite likely that most, if not all, synchrotron beamline users can remember the first time they set foot in one of these laboratories. In recent years, with the increased pressure on funding, the use of research grants to take a large group of scientists to a synchrotron beamline has become uneconomical, particularly given the trend towards increased numbers of crystals being produced in some laboratories, which necessitates more and more access to beamlines. Although the use of a national user facility such as SSRL has no direct cost associated with it (it is mandated that such facilities give free access to US and international scientists at academic institutions), there are still significant costs involved with travel and accommodation (Table 1). With the advent of remote-access data collection, new students or other laboratory members who would not normally be sent on a data-collection trip are now exposed to the synchrotron resource, and this access provides valuable experience for their future careers in science.

Fatigue from travel and prolonged presence at the beamline form a hurdle which has, on occasion, given rise to errors and mistakes during mounting of the crystals, analysis of the diffraction or determination of the optimum collection strategy. Prior to the incorporation of the robotic sample mounter, the screening of flash-cooled crystals typically involved manual mounting using cryo-tongs pre-cooled in liquid nitrogen, which enclose the crystal (mounted in a fiber loop at the end of a sample pin) inside a hollow cavity (Parkin & Hope, 1998; Rodgers, 2001; Pflugrath, 2004; Smith & Cohen, 2008) to maintain the crystal at cryogenic temperatures during transfer into the experimental hutch and onto the goniometer. Although this method has proved to be very reliable since its inception in the 1990s (Pflugrath, 2004), it becomes laborious and tedious when repeated many times. The skill and patience of the experimenter, rather than the number of samples available, have often dictated the quality of the crystal selected for data collection; crystals were screened manually until a crystal deemed 'good enough' to collect a complete diffraction data set was found. In cases like this, other crystals from the same project would go unscreened; if a better quality crystal were among those which were unscreened, it would go undetected and uncollected.

The process of crystal screening, crystal selection and data-collection strategy determination has become significantly easier with the implementation of the SAM system, the Crystal Analysis server and *WEB-ICE*. As noted above, useful crystal parameters and statistics [including the Bravais lattice, the unit-cell parameters, the estimated mosaicity, the predicted resolution, the r.m.s. fit from *MOSFLM* (Leslie, 1992) and an overall score] are continually fed back into the *BLU-ICE* spreadsheet (Fig. 3*b*), and these are also accessible through *WEB-ICE*, where researchers can also inspect the diffraction images and crystal video images. The availability of screening results and the crystal analysis have provided a new resource for training novice crystallographers during the experiment. Researchers can easily access and compare diffraction images, video images of each crystal and the results of the Crystal Analysis server to decide how best to proceed. For example, a crystal may need to be rescreened because the best part of the crystal was not in the beam, or perhaps the crystal may need washing as it was covered with surface ice (visible on the crystal images and as strong ice rings on the diffraction images), or the automated strategy may be confirmed as a good approach for subsequent data collection. Access to all this information through *WEB-ICE* makes it easier to teach novice crystallographers when to use automated results and when to question them.

It is undeniable that hands-on experience with the control systems of a synchrotron beamline, and the ability to analyze and monitor the data as they come off the detector in real time, are vital not only to the collection of the best possible diffraction data (which will ultimately lead to the best possible structures) but also in the training of the next generation of synchrotron beamline users. Our contention, which is thoroughly backed up by the feedback we have received over the past five years, is that the training being received by students and novices *via* SSRL User Support staff and the SSRL remote-access tools is fully comparable with the on-site training they would have received had they made an actual trip to SSRL or other synchrotron facilities. In most cases this is a guided participation approach, whereby an experienced researcher, principal investigator (PI) or SSRL User Support person will demonstrate the fundamental aspects of the system to perhaps a small group of students or novice group members, and then guide them through the experiment as they take control of the *BLU-ICE* or *WEB-ICE* interface. It is well

understood that people learn by different methods, whether it be through observation, analysis, discussion or activity, or a combination of these. The remote-access tools available to the SSRL user groups offer something to all types of learner and therefore provide a very effective method of teaching the new user the best possible ways in which to collect the highest quality diffraction data, this being the ultimate goal of any X-ray diffraction experiment.

Direct contact with SSRL User Support staff is strongly emphasized as being the important first step in remote training for any research group. The User Support staff have a vast amount of knowledge and expertise with the SSRL beamline systems, the SAM robot and the remote-access capabilities, and can direct researchers to the appropriate information and resources to make their group training, and ultimately their valuable beam time, a most effective and efficient process. Moreover, SSRL User Support staff can effectively facilitate remote training with a research group over the telephone, employing all the remote-access tools available to the research group. These tools include (i) access to the *SSRL User Guide*, (ii) access to a number of video tutorials which illustrate various steps in a remote-access data-collection experiment, (iii) connection to a 'simulated' beamline, facilitated through SSRL User Support staff, (iv) information on software packages installed and supported on SSRL computers (http://smb.slac.stanford.edu/public/facilities/software/), (v) access to test images and data sets so that the processing software and structure-solution software and scripts can be tested by or demonstrated to students and novices, (vi) use of the chat feature in *BLU-ICE*, and (vii) use of the shared desktop capabilities of the NX server/client interface, whereby SSRL support staff can demonstrate the *BLU-ICE* or *WEB-ICE* interfaces while a remote research group follows on their local computers. The full capabilities of the NX desktop-sharing tools are described on the developer's website (http://www.nomachine.com).

3.1. SSRL User Support

The SSRL User Support staff are a group of expert crystallographers and engineers who are available before, during and after beam time for consultation and practical help. Typically, one staff member is responsible for a given beamline for a specified period, and research groups can determine who their particular support person will be from the online User Support schedule (http://smb.slac.stanford.edu/schedule/sch_staff.cgi). As noted above, research groups are strongly encouraged to contact the responsible staff member by either telephone or email prior to upcoming remote-access beam time to discuss beamline characteristics, sample preparation, and experimental design and strategy, to gain access to the simulated beamlines, to test connectivity through the NX server/client system, and to organize either pre-beam remote training or training once their beam time starts. The use of remote training as a teaching tool in research laboratories assumes the presence in the research group of an experienced user of the SSRL beamlines and the *BLU-ICE* or *WEB-ICE* interfaces who can facilitate this training. If the research group is new to SSRL then this may not be the case, and under these circumstances we strongly recommend that the group send at least one representative to either an on-site or a remote SSRL workshop to gain hands-on experience with *BLU-ICE* and *WEB-ICE*, the SSRL computing systems, and in the use of the cryo-tools associated with the SAM system, the storage and transport options available, and the proper sample preparation techniques. Sample preparation is absolutely critical to the success of the experiment, irrespective of whether it is on-site or remote. These trained scientists can then return to their laboratories and facilitate the training of group members in the use of these systems, with the assistance of SSRL User Support staff. A comprehensive description of the tools and their use, along with correct sample-pin selection and preparation, is also available through the SMB website (http://smb.slac.stanford.edu/public/users_guide/manual/Using_SSRL_Automated_Mounti.html).

Once screening and data collection are underway, staff are also on hand to help with connectivity problems or beamline troubleshooting, to give *BLU-ICE* or *WEB-ICE* help, and to give direct experiment-related advice regarding crystal selection, data-collection strategy determination, processing software help and data backup. Staff can contact remote scientists by telephone, by email or using the chat feature in *BLU-ICE*, and researchers can contact staff using the same methods. SSRL User Support staff contact details are available on the SMB website (http://smb.slac.stanford.edu/public/staff/index.shtml).

3.2. *SSRL User Guide*

The SMB group website (Fig. 4; http://smb.slac.stanford.edu) contains up-to-date information for research groups on the state of the MX beamlines, the beamline schedule and the SPEAR accelerator status, with links to the computing and software resources available (through the *Facilities* tab), and to the *User Guide* (http://smb.slac.stanford.edu/public/users_guide/index.shtml). The *User Guide* is available online to all users at any time, irrespective of whether they have beam time, and can be downloaded as a PDF file. The guide gives a detailed description of all aspects of MX experiments at SSRL, from becoming an SSRL user, to detailed instructions on the use of the SAM system and the preparation of samples, and how to use the *BLU-ICE* and *WEB-ICE* interfaces effectively to set up and carry out a crystal-screening and data-collection experiment. The differences between an on-site and a remote experiment are clearly defined, such that novices and first-time remote-access users have all the information at hand prior to the start of their beam time. Information specific to the collection of MAD data and high-resolution monochromatic data are presented, and the data-processing software packages available to researchers are described, along with short tutorials on the most effective use of these programs. A set of detailed answers to frequently asked questions (FAQs) is also included at the end of the *User*

Guide to aid users in their experiments, and to help with programs and with questions should they arise.

3.3. Video tutorials

The video tutorials can be accessed from the *User Guide* page of the SMB website as given above, or *via* the link http://smb.slac.stanford.edu/public/users_guide/tutorials/). This project is constantly being developed and updated as new beamline capabilities and tools become available. Current tutorials include those that give information on tasks that can be carried out prior to beam time, such as (i) downloading and installing the NX client software, (ii) the best ways to fill in the *Excel* spreadsheet with crystal information for a remote-access or on-site SAM-assisted experiment, and (iii) instructions on how to upload the completed spreadsheet to the crystal database prior to or at the beginning of the user beam time. Three additional videos describe (iv) the SAM-assisted remote-access experiment in detail, demonstrating how to use the SAM system to screen crystals in a cassette, (v) how to interpret the screening results subsequently to select crystals for data collection and (vi) a simulated *WEB-ICE* strategy calculation. A strategy calculation for a MAD or SAD data collection is also demonstrated.

3.4. Simulated beamlines

Prior to the start of beam time, the members of a research group can connect to the SSRL computers and gain access to a 'simulated' beamline. The seven SSRL beamlines each have a simulated counterpart which can be accessed in exactly the same way as the 'real' beamlines. Access is only possible by contacting one of the SSRL User Support staff beforehand and asking for authorization on one of the simulated beamlines. Following authorization, the remote user connects to the simulated beamline through a *BLU-ICE* interface indistinguishable from the one that will be used later to screen crystals and collect data. All the motors that control experiment variables, such as beam size, detector distance, X-ray energy and the beamstop position, can be moved. Since the remote user is not actually connected to a real beamline, this does not affect experiments currently being carried on the real counterpart of the simulated beamline. The cassette spreadsheet can be uploaded and new users can then be taken through the steps involved in crystal screening by the experienced users in the group.

The simulated beamlines are an extremely valuable resource for a research group that may be new to remote-access data collection, the SSRL beamlines or synchrotron data collection in general. The best use of these simulated beamlines involves the inclusion of a member of the SSRL User Support staff in the remote training exercise, whereby the use of the *BLU-ICE* interface on the simulated beamline can be fully described and discussed in detail with all members of the group. This can be facilitated by a telephone call or by use of the desktop-sharing tools available with the NX server/client software (http://www.nomachine.com).

3.5. Multiple NX connections

In most remote-access experiments, there are generally several experienced people in the home laboratory responsible for the data collection. Because the NX client system allows multiple connections with the same user account, experienced users can passively monitor the screening and data collection being carried out by students or postdoctoral researchers, which still allows the students their independence and involvement in the decision-making process, yet allows for the correction of mistakes or the suggestion of alternative strategies. This capability also makes it easy for SSRL User Support staff to monitor the screening and data collection, and to step in if they see a potential problem. Multiple connections under the same user account can have the name and telephone number of the scientist associated with each one in the *Users* tab of *BLU-ICE*, making it easy to identify who is currently active should User Support staff wish to contact the researcher.

This can be extended beyond the home laboratory to the laboratories of

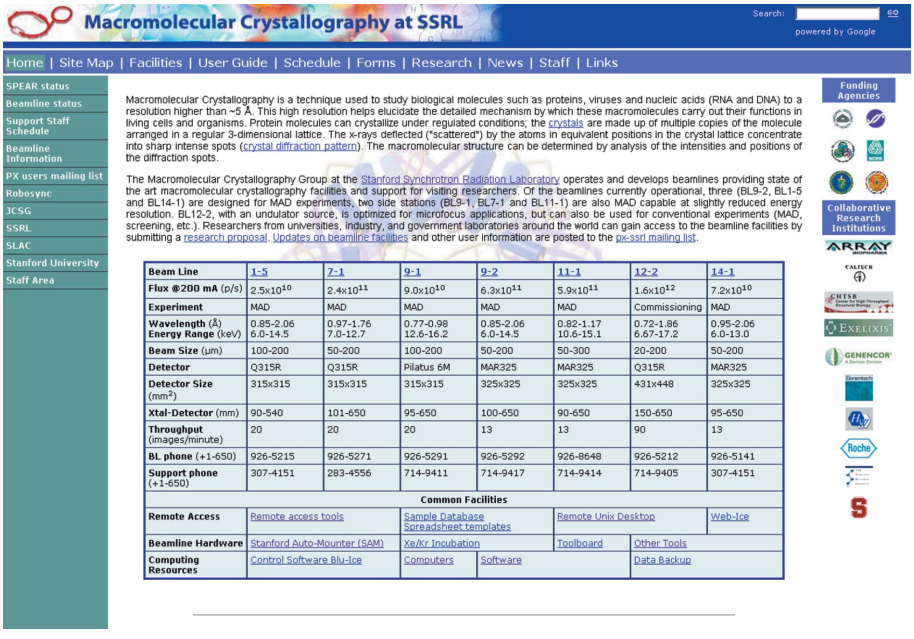


Figure 4
Screen capture of the SMB home page. The main tabs across the top give access to a secondary page for *Facilities* (computing, software and the remote desktop), the *User Guide* plus video tutorials, the beamline schedule, forms for shipping Dewars and research-related links. The left-hand side menu changes to list specific links as each secondary page is uploaded. Some fundamental characteristics of the seven available beamlines are tabulated, along with quick links to commonly used web pages.

Table 2
A selection of the many remote-access workshops, seminars, lectures and demonstrations facilitated or presented by SSRL scientific staff.

Type	Meeting/workshop	Location	Date	Notes
Workshop	SSRL	Menlo Park, California, USA	October 2004	In conjunction with the Annual SSRL Users' Meeting
Workshop	SSRL	Menlo Park, California, USA	October 2005	In conjunction with the Annual SSRL Users' Meeting
Workshop	Canadian eScience Workshop	Saskatoon, Saskatchewan, Canada	November 2005	
Lecture/demonstration	MBC 1	Fullerton, California, USA	June 2005	Sponsored by the Center for Workshops in Chemical Sciences
Seminar	ACA Annual Meeting	Honolulu, Hawaii, USA	July 2006	
Workshop	HWI	Buffalo, New York, USA	August 2006	
Seminar	NoBUGS 2006	Berkeley, California, USA	October 2006	
Workshop	Joint SSRL/ALS Workshop	Menlo Park, California, and Berkeley, California, USA	October 2006	Uni-Puck and *WEB-ICE*
Workshop	MacCHESS, Cornell	Ithaca, New York, USA	December 2006	Led from SSRL with participants at CHESS in a conference room
Workshop	University of Melbourne	Melbourne, Australia	February 2007	
Demonstration	Rotorua Proteins Meeting	Rotorua, New Zealand	February 2007	
Demonstration	BSR9	Manchester, UK	August 2007	Biology and Synchrotron Radiation Meeting
Seminar	RAMC	San Diego, California, USA	September 2007	Recent Advances in Macromolecular Crystallization
Seminar	Laboratory Automation	Palm Springs, California, USA	January 2008	
Seminar	CLS	Saskatoon, Saskatchewan, Canada	June 2008	In conjunction with the Canadian Light Source Annual Users' Meeting
Seminar	Protein Crystallography Europe	Amsterdam, The Netherlands	June 2008	
Lecture/demonstration	MBC 2	Fullerton, California, USA	June 2008	Sponsored by the Center for Workshops in Chemical Sciences
Lecture	ACA Summer Course	Indiana, Pennsylvania, USA	July 2008	
Seminar	GRC, Bates College	Lewiston, Maine, USA	July 2008	Diffraction Methods in Structural Biology, Gordon Research Conference
Workshop	CEI2008	Arlington, Virginia, USA	July 2008	Cyber-Enabled Instruments 2008 Strategic Planning Workshop
Workshop	SSRL	Menlo Park, California, USA	October 2008	In conjunction with the Annual SSRL Users' Meeting
Workshop	University of Pittsburgh	Pittsburgh, Pennsylvania, USA	October 2008	In conjunction with the Pittsburgh Diffraction Society Annual Meeting
Lecture/demonstration	AstraZeneca/MedImmune Research Meeting	Gaithersburg, Maryland, USA	February 2009	
Workshop	NIGMS Workshop	Bethesda, Maryland, USA	March 2009	Enabling Technologies for Structural Biology
Lecture/demonstration	ACA Summer Course	Indiana, Pennsylvania, USA	June 2009	
Workshop	CalTech	Pasadena, California, USA	June 2009	
Seminar	SRI	Melbourne, Australia	September 2009	10th International Conference on Synchrotron Radiation Instrumentation
Lecture	CSHL Course	Cold Spring Harbor, New York, USA	October 2009	Cold Spring Harbor Laboratory, X-ray Methods in Structural Biology Course
Workshop	SSRL	Menlo Park, California, USA	October 2009	In conjunction with the Annual SSRL Users' Meeting
Seminar	BSR10	Melbourne, Australia	February 2010	Biology and Synchrotron Radiation Meeting
Workshop	NSLS	Brookhaven, New York, USA	May 2010	Frontiers in Automated Crystal Handling, in conjunction with the NSLS Users' Meeting
Lecture/demonstration	ACA Summer Course	Indiana, Pennsylvania, USA	June 2010	

collaborators, who can also connect during active beam time, again with a name and telephone number associated with the connection on the *Users* tab, either passively to monitor the data collection, or actively to play a role in the screening, analysis and choice of crystals, or the data collection. The general consensus amongst SSRL research groups is that providing beamline access to collaborators under the auspices of their proposals has given these collaborating scientists and their group members exposure to synchrotron beamlines that they would never have been able to obtain without remote access. In some cases, this exposure has led to these collaborating scientists writing their own successful proposals for synchrotron beam time. A prime example of this is the beamtime proposal submitted by the Center for Molecular Structure (CMolS) at the California State Polytechnic University Pomona campus, which is part of the California State University (CSU). This was not a single-user proposal, as are the majority of proposals, but a wide-ranging one encom-

passing at least five CSU campuses and several different co-PIs. The CSU campuses are traditionally undergraduate institutions which have not typically had access to synchrotron resources in the past, either because of a lack of funding or because it was not something that was ever thought of as being a possibility. Remote connection to the MX beamlines at SSRL is now giving these researchers and their undergraduate students continued access to state-of-the-art facilities, and is having a positive impact on their approach to science and research.

4. Education and outreach

4.1. Remote-access workshops

Scientific staff from the SMB group not only are regularly involved in one-to-one user support *via* email and telephone (before, during and after the experiment), but also facilitate remote-access workshops to train new researchers in the use of *BLU-ICE* and *WEB-ICE*, and in the practical aspects of sample mounting and cryo-cooling, synchrotron data collection, and data processing. Several of these remote-access workshops have been held locally at SSRL, and scientists from the group have also traveled both nationally and internationally to hold remote-host workshops (Table 2).

The SSRL local workshops started in June 2006. They are usually scheduled at the start of the user run, or more often, depending on demand. Occasionally, these workshops also take place in conjunction with the Annual SSRL Users' Meeting (see Table 2). A typical workshop lasts half a day and includes a thorough introduction to the experimental facilities for MX users, including hands-on tutorials on the optimal use of the SAM robot tools, data collection with *BLU-ICE*, analysis and strategy calculations with *WEB-ICE*, and data processing with the available locally installed software packages.

The remote-host locations have included the Hauptmann–Woodward Medical Institute (HWI) in Buffalo, New York, USA (August 2006), the University of Melbourne, Australia (February 2007), the University of Pittsburgh, Pennsylvania, USA (October 2008), and the California Institute of Technology (CalTech), Pasadena, USA (June 2009). During the University of Melbourne workshop, one of the participants screened crystals that had previously been shipped to SSRL, identified the best quality crystal, collected a MAD data set and solved a novel protein structure (Schmidberger *et al.*, 2008), completely remotely, fully utilizing the computational resources made available to researchers at SSRL. SSRL remote access has also been incorporated into two workshops sponsored by the Center for Workshops in Chemical Sciences (http://chemistry.gsu.edu/CWCS) at CMolS, which were aimed at faculty from predominantly undergraduate institutions. Additional workshops at which SSRL staff have presented the remote-access tools and capabilities are listed in Table 2.

4.2. Remote-access demonstrations, seminars and lectures

Another important method of disseminating information regarding the SSRL remote-access tools to the user community is through seminars and live remote-access demonstrations at conferences and meetings (Table 2). This turns out to be a perfect test of the capabilities of the NX client system, because generally at conference locations the wireless internet access can be somewhat intermittent and with variable speed or bandwidth, particularly as conference participants continually connect and disconnect to the system. Since the NX client system is designed to run on only 20 kbps of network bandwidth, good performance is generally maintained in the seminar locations, even on a busy wireless network. The use of a remote-access connection to either an SSRL MX beamline or a simulated beamline, when combined with conference lectures or seminars, workshop presentations, or in a formal university teaching environment, is a powerful pedagogical tool. We strongly encourage and support such use of the SSRL systems by the scientific community.

5. Conclusions

The SAM system has been used to screen a total of over 300 000 crystals for diffraction quality in the past seven years, and has most certainly proved its worth. When coupled with the remote-access capabilities that have been available to scientific user groups (general users) for the past five years, this system has led to the MX beamlines at SSRL becoming a true high-throughput facility. The efficiency of the research groups who use remote access has increased remarkably, which has in turn given synchrotron access to more user groups than ever before and resulted in a surge in the number of user starts at SSRL. Researchers are now easily able to screen all crystals being grown in the laboratory, in order to choose the best possible crystals for data collection, whereas before they may have limited themselves to the crystals that simply appeared to be the best, or else spent innumerable hours on a home source screening crystals. It has become increasing clear that many user groups are forgoing in-house screening, and simply cryo-cooling as many crystals as they can fit into a cassette or Uni-pucks and letting the robust efficient SAM system do the work for them. This is exactly the vision the developers of the Stanford auto-mounter had in mind for the system: to provide a true high-throughput platform for the screening of large numbers of protein crystals.

The ways in which remote access to the SSRL beamlines can facilitate training and collaboration have most certainly not gone unnoticed by the scientific community. All research groups who collect their data remotely use the available tools provided by SSRL to train and educate their laboratory members in the most effective ways to collect the best possible diffraction data. Approximately 60% of researchers with active proposals and current beam time have at some point had collaborators participate in remote-access data collection, where they take either a passive or an active role, and in some cases have even used the time to train or educate members of their own laboratory. The way in which remote access to SSRL beamlines serves to bring collaborators together is one of the most fundamental examples of what has been described as a 'cultural community', as noted by the Director of the NSF

report *Cyberinfrastructure Vision for 21st Century Discovery* (NSF Cyberinfrastructure Council, 2007). This idea is something that we at SSRL will continue to foster and promote. At SSRL we are dedicated to making the remote-access experience as easy, efficient and instructive as possible, and making a synchrotron beamline accessible to anyone in the scientific community who has a need for a high-intensity X-ray beam and expects high-quality diffraction data.

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