

MacCHESS Director's report

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The past year has been productive for both the MacCHESS staff and the MacCHESS user community. About 50 user groups collected data on projects ranging from atomic resolution protein refinement to MAD phasing experiments. The CCD-based X-ray detectors developed in collaboration with Sol Gruner at Princeton University are now in routine operation and have produced several hundred data sets. DEC Alpha workstations are available for data analysis and many users now process their intensity data before returning home. Administratively, Dan Thiel has been appointed as Senior Staff Scientist and will oversee the day-to-day operation of the MacCHESS resource and Jon Clardy of the Chemistry Department has agreed to serve as Co-Director of MacCHESS in order to broaden the Cornell involvement in biological crystallography at CHESS.

A number of noteworthy structures, based all or in part on data collected at CHESS, have been published recently (see the list starting on page 61). A few examples include murine polyomavirus complexed to an oligosaccharide fragment (Stehle, *et al.*, *Nature* 369:160-163, 1994) from Steve Harrison's group, influenza hemagglutinin at the pH of membrane fusion (Bullock, *et al.*, *Nature* 371:37-43, 1994) from Don Wiley's group, active conformation of G α 1 (Coleman, *et al.*, *Science* 265:1405-1412, 1994) from

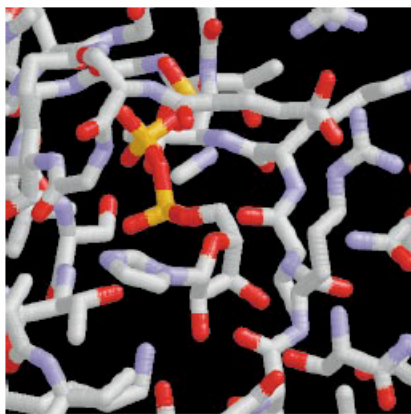
Steve Sprang's group, bacterial chaperonin GroEL (Braig, *et al.*, *Nature* 371:578-586, 1994) and NF- κ B p50 (Ghosh, *et al.*, *Nature* 373:303-310, 1995) from Paul Sigler's group, MHC-related neonatal Fc receptor (Burmeister, *et al.*, *Nature* 372:336-343, 1994) and the complex of neonatal Fc receptor with Fc (Burmeister, *et al.*, *Nature* 372:379-383, 1994) from Pam Bjorkman's group. Based on the number of successful data sets that have been collected we anticipate many more structures to be published during the coming year.

In the spring of 1994, MacCHESS organized a symposium and a workshop on applications of synchrotron radiation to structural biology. The 1 1/2 day symposium entitled "New Frontiers in Synchrotron Radiation Research and Structural Biology" was attended by about 90 participants who heard a dozen presentations from leaders in the field of macromolecular crystallography. Following the symposium a hands-on workshop entitled "Synchrotron Radiation and Structural Biology: Measuring and Processing X-ray Crystallographic Data" was attended by 16 participants who were selected from a pool of several dozen applicants. The participants learned about various aspects of experimental design, cryocrystallography and data processing. Each participant was given the opportunity to collect data on frozen crystals using station A-1 and the 1k

CCD X-ray detector and to process the data using DENZO and Alpha workstations provided by Digital Equipment Corporation.

During the summer of 1994 John and Madeleine Helliwell from the University of Manchester spent a sabbatical leave at Cornell.

Detail of the structure of G α 1, showing the bound GTP- γ S substrate analogue and surrounding protein. The structure was solved by Steve Sprang's group using data collected at CHESS. Coordinates from the Protein Data Bank, rendered using the RasMol program.



John was located in the Biotechnology Building and spent many hours interacting with the MacCHESS and CHESS staff, postdocs, and students in the Ealick laboratory. Madeleine was located in the Baker Laboratory (Chemistry) and worked in Jon Clardy's laboratory. Both John and Madeleine took advantage of their visit in Ithaca to use the MacCHESS and CHESS facilities. John used several different stations and the MacCHESS CCD-based X-ray detectors to measure ultrahigh resolution data for concanavilin A (see article on page 11) and Madeleine used CHESS for several chemical crystallography projects.

MacCHESS has completed several instrumentation projects during the past year. The 1k x 1k CCD-based X-ray detector provided by Sol Gruner at Princeton has now been in operation for more than a year and has been used by dozens of research groups. The detector has proved reliable and robust while the 50 x 50 mm² active area has provided sufficient active area for most of the macromolecular crystallography projects brought to CHESS. More recently, a 2k x 2k CCD detector with an active area of 80 x 80 mm² was built through a collaboration with Princeton, Robert Wood Johnson Medical School (Eric Eikenberry) and Princeton Scientific Instruments (John Lowrance). This detector is now in routine operation and is available to all macromolecular crystallography users (see page 56). Future detector needs will benefit from the commercialization efforts by Ron Hamlin at San Diego Area Detector Systems.

MacCHESS now has three complete liquid nitrogen cooling systems purchased from Molecular Structure Corporation. Crystal freezing is strongly encouraged because of the benefits realized by reducing or eliminating radiation damage. The experimenter can use the cooling system with either a vertical or a horizontal cold stream. Users generally work out freezing conditions at home and in many cases freeze and test crystals in the home laboratory before transporting the frozen samples to CHESS. In order to assist users, MacCHESS has prepared a cryocrystallography video that

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describes methods and procedures for sample preparation and experimentation (see article page 55).

We are continuing to improve the standard MacCHESS rotation camera. A new CCD optical imaging system has been purchased for use with the camera so that the user can more easily see and align mounted samples. MacCHESS is also in the planning stages of designing a new oscillation camera that will provide greater stability and precision, faster motor speeds and better accessibility for low temperature devices, telescopes, scintillation counters and other accessory equipment. Once data has been measured, MacCHESS provides DEC Alpha workstations for data processing. Both DENZO and MOSCO are available for data processing although some users still transport data home on tape for processing later.

MacCHESS now supports multiple wavelength anomalous diffraction (MAD) experiments on station F-2 (see pages 51 and 53). Recent structures determined by MAD phasing include lac

repressor core and gene 32 ssDNA binding protein from Tom Steitz's laboratory at Yale, interferon-g receptor complex and rusticyanin here at Cornell and most recently avian sarcoma virus integrase from Alex Wlodawer's group at the National Cancer Institute. These and other experiments demonstrate the utility of station F-2 for MAD phasing and interested users are encouraged to apply for beam time.

MacCHESS is pursuing several new research initiatives. One area of interest is ultrahigh resolution data collection for protein refinement. Experiments by Keith Wilson and Zbyczek Dauter at EMBL have shown that many proteins diffract to atomic resolution. In a non-exhaustive survey we recently identified 35 macromolecules that diffract to 1.2 Å resolution or higher. CHESS provides excellent facilities for measuring high resolution data as demonstrated by John Helliwell's work with concanavalin A (see page 11) which diffracts to 0.9 Å resolution at CHESS. Finally, atomic resolution data can be used not only to refine protein structures but also to de-

termine protein structures by direct methods. Herb Hauptman and his colleagues in Buffalo have developed a procedure called Shake-and-Bake which has been used to solve several known structures in the 300-500 atom range. We are now collaborating with the Buffalo group by developing experimental techniques to obtain the data necessary for direct methods.

In the future, users can keep up with MacCHESS developments via WWW (see page 66). The MacCHESS home page is maintained by Marian Szebenyi at address is "<http://www.chess.cornell.edu/MacCHESS/>". Users are invited to use the WWW to keep up with the latest in instrumentation, software, progress and opportunities from MacCHESS. From the CHESS home page users can learn about new CHESS developments as well as obtain beam time application forms. We hope that WWW will be an effective way for users to remain informed about MacCHESS in the time between CHESS Newsletters.