MacCHESS Director's Report

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"MacCHESS" stands for "**Mac**romolecular Diffraction at **CHESS**" (or "son of CHESS" if one is Scots like Keith Moffat, the founder of MacCHESS). It was founded more than 20 years ago, when the potential of synchrotron sources for macromolecular structure determination was just becoming apparent, and was one of the first organizations dedicated to welcoming structural biologists into what had heretofore been a physicists' domain. Funding was obtained, and has continued to this day, from the National Institutes of Health under its National Center for Research Resources program, which mandates both service and R&D activities by supported facilities. MacCHESS has been among the leaders in the development and implementation of the beamline hardware – detectors, goniometers, cooling systems, cameras – and software – for alignment, data collection, processing – that have made synchrotron work so routine that users can concentrate on biology and not details of the structure determination process. Today, MacCHESS continues to provide excellent user support, while its research activities have branched out into new paths which will enhance opportunities for structural investigation beyond the traditional crystallographic experiment.

Support is provided by MacCHESS for all biological crystallography at CHESS, i.e. almost all experiments at stations A1, F1, and F2, and about half the use of F3, as well as occasional experiments at other stations. The typical MacCHESS user visits for a 24-hour period and collects 5-20 data sets during this time. In the last year for which statistics are available (April 2007 – March 2008), there were approximately 500 badges issued to MacCHESS users and nearly 100 MacCHESS-related publications released. Important work by users includes Eddy Arnold's ongoing studies of drugs to treat AIDS[1], Kate Ferguson's investigation of anti-cancer drugs[2], Gino Cingolani's study of how a bacteriophage punctures a cell membrane[3], and many more.

Our facilities for crystallographic data collection are always being improved; some recent upgrades include: motorized CCD detector motion, enhanced crystal centering interface, private networks at each station for data transfer, and robust automatic safety shields. More details are given in the report on page 25. Mail-in data collection is available; it has been used roughly half a dozen times per year and is working well. A number of collaborations between MacCHESS scientists and other investigators are active and have produced excellent work such as the elucidation of the active site structure in the multifunctional enzyme CD38[4]. Additionally, experiments that are not standard crystallography can now be carried out at CHESS:

- Small angle x-ray scattering (SAXS) and wide-angle x-ray scattering (WAXS) of solutions, at G1 (or F2) and F1, respectively. A new sample cell with a disposable insert, and temperature control between 4 ºC and 60 ºC, is available. Staff are knowledgeable in data collection and processing techniques.
- Pressure cryocooling of crystals or other samples. This technique can produce better quality crystals than those cryocooled at ambient pressure, and can also stabilize ligands which are otherwise disordered. Apparatus for pressurizing samples with helium, and cooling them to liquid nitrogen temperature under pressure, is installed at CHESS, and trained staff will process users' samples, on request. Pressure-cooling using other gases is also possible using equipment in the Gruner lab, located in nearby Clark Hall.
- Microbeam, produced by focusing x-rays with a glass capillary. Capillaries with focal spot sizes of 18 and 5 µm are routinely available, and custom capillaries can be produced if needed. Microbeams have been used to examine small crystals, small good regions on heterogeneous crystals, and non-crystalline samples such as plant fibers.

Research projects at MacCHESS are focused on 5 initiatives: Microcrystallography, Pressure Cryocooling, SAXS and Envelope Phasing, X-ray Optics (at F3), and Automation. More detailed reports are found elsewhere in this Newsmagazine; here I will just mention a few highlights:

- Dan Schuette (a graduate student of Sol Gruner) and MacCHESS staff demonstrated that a prototype Pixel Array Detector (PAD; one of several being developed by the Gruner group) could be used to collect crystallographic data, of a quality comparable to that from a CCD, but with a much shorter readout time. This PAD is small compared to current CCD and image plate detectors, but work is in progress at Area Detector Systems Corp. to produce a large, tiled, device for crystallographic use. See report on detectors on page 54.

- Xinguo Hong, Visiting Scientist, designed and constructed the improved sample cell for SAXS experiments, and also developed a method for avoiding radiation damage by stepwise translation of the cell between exposures. Moreover, he has demonstrated the feasibility of combining SAXS and WAXS data to obtain information about the internal structure of macromolecules.
- Sterling Cornaby (a graduate student of CHESS Associate Director Don Bilderback) collaborated with MacCHESS staff to show that Laue data collected from many small crystals, using a tailored 30% bandpass beam, could be used to solve structures. See full report on page 63.
- Chae Un Kim has used the pressure-cryocooling technique, and lots of beamtime, to collect data on samples cooled at various pressures and examined at various temperatures, to improve our understanding of that most common but most complex material – water. See page 71.

In a recent competitive renewal process, the MacCHESS proposal received an excellent rating from NIH, and funding is assured through 2013. MacCHESS personnel tend to stay with the organization for a long time, but there have been some changes in recent years. Quan Hao, Director since 2001, has moved on to a faculty position at Hong Kong University; he continues a connection with MacCHESS as a collaborator. Marian Szebenyi has taken over as Director. Xinguo Hong has been in residence as a Visiting Scientist for the last few years and has been a great asset to the MacCHESS SAXS program; he is now at Brookhaven Lab. Long time technical support person Chris Heaton has retired to the sunny South and been replaced by Scott Smith as the local CompuMotor expert (among other talents). We welcome Chae Un Kim as a new Staff Scientist; as the principal developer of the pressure cryocooling technique, he is uniquely qualified to advance research in this area.

References:

1. K. Das, J.D. Bauman, A.D. Clark, Jr., Y.V. Frankel, P.J. Lewi, A.J. Shatkin, S.H. Hughes, and E. Arnold; *"High Resolution Structures of HIV-1 Reverse Transcriptase/TMC278 Complexes: Strategic flexibility explains potency against resistance mutations"*, PNAS **105**, 1466-1471 (2008)
2. J. Schmiedel, A. Blaukat, S. Li, T. Knöchel, and K. M. Ferguson; *"Matuzumab Binding to EGFR Prevents the Conformational Rearrangement Required for Dimerization"*, Cancer Cell **13**, 365-373 (2008)
3. A. S. Olia, S. Casjens, and G. Cingolani; *"Structure of Phage P22 Cell Envelope-penetrating Needle"*, Nature Struct. Mol. Biol. **14**, 1221-1226 (2007)
4. Q. Liu, I. A. Kriksunov, H. Jiang, R. Graeff, H. Lin, H. C. Lee, and Q. Hao; *"Covalent and Noncovalent Intermediates of an NAD Utilizing Enzyme, CD38"*, Chemistry & Biology **15**, 1068-1078 (2008)

MacCHESS is pleased to welcome Staff Scientist, Chae Un Kim

Chae Un Kim hails from South Korea, where he majored in physics at Seoul National University and graduated *summa cum laude* in 1999. Following a 2-year stint in the Korean army, he arrived at Cornell in 2001 as a graduate student in Sol Gruner's lab. After completing the required coursework, he quickly became interested in proteins under pressure, an interest of Gruner's for many years, but one that involved tricky experiments whose results were not widely applicable. Together with fellow grad student Raphael Kapfer, Chae Un developed a new apparatus (much easier to use than the old one) for cryocooling crystals under pressure, and determined that crystals cooled in this way, and subsequently handled at room pressure, were often of better quality than those cooled in the normal way. After Raphael's untimely death in a bicycle accident, Chae Un continued as the principal developer of pressure cryocooling, and proceeded to elaborate a series of extensions to the technique. Publications reporting these developments, beginning with the initial report in 2005, have generated great excitement in the crystallographic community. Chae Un is now recognized as the number one expert in pressure cryocooling, and has made numerous presentations on the topic. In 2005, he received the Oxford Cryosystems Prize for his poster, *"High Pressure Cooling of Protein Crystals without Cryoprotectants"*, presented at the Annual Meeting of the American Crystallographic Association. In 2007, he received the Ph.D degree in the Field of Biophysics, with a thesis entitled *"High Pressure Cryocooling for Macromolecular Crystallography".* Wishing to continue working with Gruner, and CHESS, Chae Un stayed on at Cornell, first as a post-doc, and now as a MacCHESS Staff Scientist. He is continuing to explore the ramifications of pressure cooling, and the advances that it makes possible in protein crystallography and the understanding of the physics of proteins, water, and other materials in cryocooled crystals. Besides conducting exciting research, which he is always willing to explain to anyone who is interested, Chae Un is a very helpful guy: when people heard about the pressure-cooling technique, many of them were eager to try it; since the method requires special high pressure apparatus and is a little tricky to learn, Chae Un volunteered to pressure-cool (many!) collaborators' crystals. When a pressure-cooling apparatus was installed at CHESS, it was he who approved its design and trained MacCHESS staff in operating it. MacCHESS is pleased to welcome Chae Un Kim as its newest Staff Scientist.