



## MacCHESS Director's Message

Daniel Thiel - *Dept. of Molecular Biology and Genetics, Cornell University*

As the reins of MacCHESS were passed to me in the fall of 1999 I found myself full of excitement. I also found myself facing a real challenge. MacCHESS has a history of prominence in the international macromolecular community. This stature has been achieved in part by the leadership of effective Directors starting with Keith Moffat who created the entity back in the early 80's. After Keith moved to the University of Chicago, Don Bilderback, the CHESS Associate Director, took over as Interim Director for MacCHESS. In 1991, Steve Ealick joined the Cornell faculty and became the second full-time MacCHESS Director and gave 8 years of dedicated service. Now I have been asked to take over as the Director. I do not take the task of MacCHESS Director lightly. My predecessors labored to keep MacCHESS at the frontier in a field of science that has seen phenomenal growth, assisted, in no small part, by developments which came out of MacCHESS itself. The challenge is to continue in the spirit of my predecessors making contributions by exploiting the unique opportunities we have in the Cornell environment.

The story of MacCHESS (and CHESS for that matter) has been described as one of David and Goliath. In terms of funding, we are small compared to all of the other US synchrotron facilities with crystallography facilities (we are the only U.S. hard X-ray synchrotron facility that is not supported by the Department of Energy). But, in terms of output we are very significant. Our users are responsible for a large percentage of the world's publications in structural biology. Our internal developments in areas such as cryocrystallography, X-ray detectors, and phasing methodologies are quite substantial.

Continuing the story, some of you may know that MacCHESS is the acronym coined by Keith Moffat, a Scotsman, who used the old-world nomenclature in naming his arm of CHESS. The expanded name is a mouthful - the Macromolecular Diffraction Facility at CHESS; we like to stick with the shorter name MacCHESS. For the entire 17 years of its existence, MacCHESS has been supported by the National Center for Research Resources (NCRR), one of the 25 institutes making up the National Institutes of Health. At the risk of sounding self-serving, we are proud that the NCRR and the NIH have allowed Cornell to play a major

role in the area of synchrotron-based macromolecular crystallography. Their support has been crucial to our existence.

The MacCHESS Resource has a clearly defined two-fold mission: develop technology that enhances biomedical related research using synchrotron radiation and crystallography; and ensure that our technology enables scientists in carrying out frontier science in the area of macromolecular research. What I personally find most satisfying with the structure set forth by the NIH is that we must balance a strong in-house research program with a healthy and active service component which allows the U.S. scientific community (as well as the international community) access to our resource. The key is balance. My objective as the new Director is to keep a proper balance and to settle for no compromises in the quality of each. This is very much a part of the spirit of combined in-house research and dedicated user service which characterizes the entire CHESS operation.

The MacCHESS resource utilizes three insertion-device beamlines, stations A-1, F-1, and F-2, devoted to macromolecular crystallography. In addition, it supports additional bending magnet stations for part-time macromolecular experiments. The resource also specializes in large unit-cell diffraction, ultra-high resolution diffraction, MAD phasing, rapid throughput crystallography (with particular applications in structure-based drug design and structural genomics), microdiffraction, multiple-beam diffraction, and software development.

Although rich in instrumentation, it is the people who work on the MacCHESS team that make the operation tick. Our team of four Research Support Specialists, Bill Miller, Chris Heaton, Mike Cook, and Irina Kriksunov, provide excellent user support as well as instrumentation development and crystallographic research. Our other team members are Dr. Marian Szebenyi and Dr. Arthur Weaver. Both provide support with data processing and other aspects of crystallography while carrying out basic crystallographic research as well. Soon, we expect to hire several new people to enhance the operation. The MacCHESS staff works hand-in-hand with the rest of the CHESS staff to develop new techniques and to provide the best user service possible.

In terms of instrumentation, we now have large-area mosaic CCD detectors on all three wiggler stations. The smaller CCDs continue to service the bending magnet stations. For the largest area coverage, a dual image plate system replaces the mosaic CCD detector at F-1, the station presently certified for handling biohazardous materials at the BL-2 level. Our upgraded rotation camera has been implemented at the three wiggler stations allowing efficient data collection. Anticipating additional projects with cell dimensions in excess of 1000 Å, we are developing a custom dual-plane CCD detector system to accommodate all large-cell projects as well as ultra-high resolution experiments. Additional information on the CCD detectors is presented by Marian Szebenyi on page 14.

The past year has brought new benchmarks in the performance of the MacCHESS facility. A recent survey of the field showed that almost a quarter of the structures published in the high-profile international journals involved data obtained at CHESS. To get a taste of the breadth of macromolecular publications coming out of CHESS I encourage you to browse our publication list. The A-1 beamline, the last station to receive a large CCD detector, has seen an increase in user efficiency on the order of 25%. Unit cells as large as 1400 Å have been resolved on the F-1 beamline (Reinisch, Nibert, & Harrison, *Nature* **404**, 960-967, 2000). The largest Selenium sub-structure determination to date is from our F-2 station – a remarkable accomplishment where 70 sites were located using the Shake-and-Bake algorithm, SnB (Deacon & Ealick, *Structure* **7**, R161-166, 1999). This work also leads the field in terms of the largest MAD structure ever solved (see Deacon article, page 46); the protein formed a dual pentameric ring structure of 370 kDa. We have been honored to see a second MacCHESS user receive the Albert Lasker Basic Medical Research Award: The 1999 award went to Prof. Rod MacKinnon of Rockefeller University for his determination of the potassium ion channel. This work was also recognized by *Science* magazine as one of the top 10 scientific discoveries of 1998.

During the summer of 1999 we hosted a workshop on membrane protein crystallography as part of the 1999 CHESS Users Meeting. Seven outside speakers, all experts in the field, presented informative lectures to an audience approaching 125 in number, making it one of the most popular workshops CHESS has hosted. This year we had good attendance and stimulating discussion at the structural genomics workshop organized in conjunction with the 2000 CHESS Users Meeting, having over 70 in attendance.

Our capabilities continue to expand. We now have crystal growing expertise and facilities including an on-site

cold room, 3-D graphics computers, and a new beamline under development. Exposure times at CHESS typically vary from 5 to 60 seconds; the new 50-pole wiggler and the increasing ring currents will continue to reduce these times. With a rich history behind us and with excellent programs in place at CHESS, MacCHESS, and LNS, the future of our facility could not be more promising.

In closing, I encourage scientists interested in biological macromolecular research to contact us. Although we host hundreds of scientists each year, we are not fixed in our agenda; we always want to see the user base expand, and we welcome potential collaborations.