01.X-05 PROTEIN REFINEMENT IN THE ADVANCED STAGES. By Wayne A. Hendrickson and John H. Konnert, Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, D. C. 20375, U.S.A.

Several protein structures have now been refined to R-values appreciably under 0.20. However, the ultimate goal of generating a model that is compatible with prior stereochemical knowledge and which reproduces the diffraction pattern to within the accuracy of measurement is yet to be achieved. Large vibrational amplitudes and structural variability in protein crystals usually greatly limit the extent of measurable data, and models for the highly anisotropic and anharmonic character of such displacements must have many variables. Thus, perversely, where higher order effects are most pronounced they tend to become indeterminate.

The incorporation of stereochemical information into the refinement process as restraints on parameters has proved to be an effective means for improving the degree of overdetermination for macromolecular crystals. We have extended the use of restraints to permit meaningful refinement of anisotropic thermal parameters (Konnert and Hendrickson, Acta Cryst. A36, 344, 1980). Recently, we have also included hydrogen atoms in the restrained refinement procedure and have investigated methods for treating the problem of discrete disorder.

We will report on our experience in the advanced stages of refinements. Initial tests were performed on carp parvalbumin at 1.9A resolution. Crambin has been refined to R=0.104 for all data in the 10 to 1.5A shell of spacings. This model is typified by an rms deviation of 0.018A from bond ideality and an rms bond-length fluctuation of 0.05A due to thermal parameter variations. Bovine pancreatic trypsin inhibitor (data kindly provided by J. Deisenhofer) has been refined to R=0.142 for the most significant 86% of the 1.5A data with geometry restrained as for crambin. Further work on these and other anisotropic protein refinements is in progress.

01.X-06 JOINT REFINEMENT OF MACROMOLECULAR STRUCTURES WITH X-RAY AND NEUTRON SINGLE-CRYSTAL DIFFRACTION DATA. By Alexander Wlodawer[+] and Wayne A. Hendrickson[*], [+]National Measurement Laboratory, National Bureau of Standards, Washington, DC 20234, USA and [*]Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, DC 20375, USA.

We have modified the procedure for the stereochemically restrained refinement of macromolecular models (Hendrickson and Konnert (1980) in "Biomolecular Structure, Conformation, Function, and Evolution," edited by R. Srinivasan, Vol. I, pp. 43-57. New York: Pergamon Press) to enable joint refinement with two sets of diffraction data: one measured using X-ray diffraction and the other using neutron diffraction. The changes to the refinement program PROLSQ involved setting appropriate switches for reading the respective data sets, calculating structure factors and derivatives based on the appropriate scattering factors, and including the separate scale factor refinement. A new directory of amino acid standard groups, containing hydrogen positions derived mainly from neutron structures of amino acid crystals, was compiled. The procedure was tested by refining the structure of ribonuclease A with only 2.8 Å resolution neutron data, as well as jointly with 2.8 Å neutron and 2.0 Å X-ray structure amplitudes. A number of side chains of asparagine, glutamine, lysine, valine, and arginine were observed to shift by up to 1.5 Å from the original positions in separate neutron refinement, while no such movement was observed after the joint refinement. This may be caused by a small number of observations in the separate refinement case and shows why the joint refinement is preferable. The joint refinement was stable and rapid, with convergence reached in fifteen cycles.

01.1-01 PROTEIN CRYSTALLOGRAPHIC COMPUTING IN THE U.K. - A COLLABORATIVE PROJECT. By D. Akrigg, T.N. Bhat, P.E. Bourne, J.W. Campbell, E.J. Dodson, M. Elder, P. Evans, J.R. Helliwell, P.A. Machin, D.S. Moss, I.J. Tickle, K. Wilson and A.J. Wonacott, Science Research Council Daresbury Laboratory, Warrington, WA4 4AD, England.

The Science Research Council of the U.K. has set up a number of Collaborative Computational Projects for the benefit of scientists from University and other research groups. One of these projects is in protein crystallography. The basic services provided through this project are:

1) Computing Facilities
Allocations of time are made available on the IBM 370/165 and Cray 1 computers at the SRC Daresbury Laboratory.

2) Manpower
Two research assistants have been appointed to work on the project.

3) Software and Documentation
The project aims to assemble and document a comprehensive suite of protein crystallography programs which may readily be adapted to include new programs and to which all users may contribute. To this end, standards for file structures and documentation have been defined.

4) Distribution of Information
An informal newsletter, the Informational Quarterly for Protein Crystallography gives details of the project together with articles of more general interest contributed by the various groups.

5) Organisation of Meetings
The project organises study weekends, workshops and other smaller meetings.

A major interest of the groups involved in the project has been protein structure refinement and this topic was the subject of a study weekend held at the Daresbury Laboratory in November 1980. The advent of the vector processing Cray 1 computer has given added impetus to the refinement of protein structures. The Oxford group, using a version of the Hendrickson-Konnert restrained least squares program, has been particularly active in this area. Fast Fourier refinement techniques, extensively used at York, have also opened up new possibilities for refinement.

A working group from the project has, after much preliminary work, agreed on standards for file structures and documentation to be used in building up a system of programs. A new reflection data file format has been developed for the project at Imperial College. The process of systematically implementing the standards in the basic programs used by protein crystallographers (film processing, data reduction, phasing, Fourier calculations, plotting, structure refinement etc.) is now well under way.