strongest reflections to $2\theta = 130°$ (or .56 Å resolution) were identified. These were then collected, resulting in a total of 6619 reflections with $I/\sigma > 1$ after background averaging. Further analysis will continue with these data which initially have an R-factor of .094 without further refinement.

02.8-04 COMPUTER SIMULATION OF SOLVENT STRUCTURE AROUND BIOMOLECULES. By J. M. Goodfellow, J. L. Finney and P. Barnes, Department of Crystallography, Birkbeck College, Malet Street, London WC1E 7HX, United Kingdom.

Monte Carlo computer simulation techniques have been used to investigate water-protein interactions at the molecular level. By extending the polarisable electropole model for water we have developed a set of interatomic potentials describing water-protein interactions. This model specifically accounts for non-pair-additive (cooperative) effects which are thought to be important in hydrogen-bonded systems. Small amino acid crystals have been used as test systems in which all the solvent molecules are well defined. The following parameters were used to compare the predicted structure with the observed structure: (a) average final positions of water oxygen atoms; (b) root-mean-square deviation about these final positions; (c) number and type of molecules coordinating the solvent molecules; and (d) the length and directionality of each hydrogen bond.

We have found that the final predicted water structure is very sensitive to non-bonded parameters, partial charges on the atoms and also to the polarisability of both the water molecules and the amino acid atoms. The magnitude of the increase in dipole moment of the water molecules depended on the system under investigation. We emphasise the need for: (1) adequately testing potential functions before extending the simulations to larger systems, and (2) the importance of including non-pair-additive effects in water-protein systems. Using these optimised interatomic parameters, we are extending this method to look at solvent-related effects in larger systems of biological interest including Vitamin B_{12} coenzyme, aPP, cyclodextrins, calcium-containing drugs and nucleic acids.

02.8-05 WATER STRUCTURE AROUND VITAMIN B_{12} COENZYME : A CHARACTERISATION BY NEUTRON/X-RAY DIFFRACTION AND COMPUTER SIMULATION. By H. F. J. Savage, J. L. Finney, P. F. Lindley, P. Barnes, Department of Crystallography, Birkbeck College, Malet Street, London, WC1E 7HX, UK.

This paper describes the results of neutron and X-ray refinements of the solvent organisation around the coenzyme of vitamin B_{12} and compares them with the hydration structure derived from computer simulation methods. The coenzyme is being used as a test system for further work aimed at understanding the structure and dynamics of larger aqueous macromolecular systems.

The diffraction data were collected at low temperature ($\sim 5°C$) from crystals grown in D_2O. Both the neutron and X-ray D_2O structures have been refined by least-squares methods to the crystallographic residuals $R \sim 13\%$ and $R \sim 14\%$, respectively, at 0.9Å resolution. There are several significant differences between the present D_2O model and the early H_2O model (P. G. Lenhert, Proc. Roy. Soc. A. 303, 45 (1968)). During the initial refinement it was recognised that the coenzyme molecule differed in its position within the unit cell by a small rotation (from Lenhert's model) and one of the sidechains was rotated by $\sim 70°$, causing the water structure in some parts of the unit cell to be noticeably different.

The refined neutron model consists of 21 water oxygen sites per asymmetric unit (several with unit occupancy) and the X-ray model includes 36 oxygen sites : the $\overline{U^2}$ values range from 0.07 to $0.15Å^2$. The solvent structure is divided into at least 2 distinct regions :

(1) An ordered monolayer connecting adjacent coenzyme molecules.

(2) A partially ordered region comprising of a solvent channel and an interconnecting region. The waters in the first region appear to be generally coordinated with polar groups while those of the second region are associated with groups which are mainly apolar in character.

A Monte Carlo computer simulation (N. Metropolis et al, J. Chem. Phys., 21 1087 (1953)) in being undertaken using a whole unit cell of 4 coenzyme molecules and 68 initial water positions, selected from the X-ray and neutron sites. The interatomic potentials are based on the polarisable electropole model of water (P. Barnes et al, Nature, 282, 459 (1979)). Each water molecule-coenzyme atom interaction is defined by two non-bonded interaction coefficients and partial atomic charges (J. Goodfellow, see abstract).

The results of a fully equilibrated simulation will be presented. From the initial stages we have found that the water movements were orientational, but in the proceeding stages the following observations were made : (a) the movements of the waters in the ordered region are consistent with the crystallographic temperature factors and (b) there are significantly greater movements of the waters in the partially ordered regions. As in the bulk water case, the dipole distribution shows a relatively wide dispersion, indicating the need to take into account the non-pair additive effects within the system.