structure, act as a filler to match the irregular protein surfaces, or are simply formed by the juxtaposition of the solvent structures present around the isolated protein molecules in solution.

The analysis suggests that the ordered solvent positions are determined largely by short range electrostatic and van der Waal's interactions with the protein surface. The position prediction algorithm has been developed on this basis. The energy of the molecular dipole and van der Waal's sphere of a water molecule interacting with the dipoles, charges and van der Waal's surface of the protein is calculated, assuming the water dipole to be optimally oriented. This energy is determined for points on a grid around the protein, and energy minima in the grid are then identified. Minima positions may then be compared with observed solvent molecule positions. Tests of this method on the refined 1.5 Ångstrom resolution crystal structure of the serine protease SGPA using the 100 most strongly ordered solvent molecules found crystallographically yields 55 of these minima within 1 Ångstrom of an experimental position, using a 0.5 Ångstrom grid. Relaxing the minima criteria to produce about 50% over-prediction increases this score to 77 of the 100. Inspection of the energy surface suggests the undetected molecules lie in minima defined by the detected ones and the protein surface together. This hypothesis is currently being tested.

02. 12–5 SOLVENT INTERACTIONS IN B12 COENZYME CRYSTAL HYDRATE by F. Vovelle[a], J.M. Goodfellow, J.L. Finney, H.F.J. Savage[b], and P. Barnes, Department of Crystallography, Birkbeck College, Malet Street, London WC1E 7HX, UK.

The structure of Vitamin B12 coenzyme crystal hydrate has been determined at better than 1.0Å resolution using both X-ray and neutron diffraction data[1]. A highly refined experimental model involving several alternative hydrogen bonding networks, has been obtained for both the ordered pocket and disordered channel regions. For this reason, we have chosen to study these solvent regions using Monte Carlo computer simulation in order to predict both the ordered and disordered regions. The results using several different water models have been compared with experiment using a detailed analysis of hydrogen bonded solvent networks in terms of both average predicted atomic positions and atomic positions est imated from the maxima of probability density maps from all four asymmetric units for this crystal. The solvent molecules are allowed to move independently without crystal symmetry constraints.

The following was found:

(i) Within each asymmetric unit only one hydrogen bonded network was predicted although there were several possible hydrogen atom positions for any one solvent molecule (defined as maxima of probability density).

(ii) Reasonable agreement was obtained between predicted and experimental positions in the ordered solvent region whatever the potential function used. It should be possible to improve this level of agreement as the agreement between experimental and predicted results was always larger than the agreement between the different predicted asymmetric units.

(iii) The positions of the probability density maxima were different in different asymmetric units for the disordered channel region. This led to different hydrogen bonded networks which were not always consistent with the experimentally determined alternative (lower occupancy) sites. This implies that it is essential to simulate more than one asymmetric unit if one wishes to look at disorder in solvent regions.

(iv) Probability density maps were qualitatively very useful for picturing these disordered regions. However, there were no significant differences between quantitative results predicted using either average atomic positions or maxima of the probability density distributions.

Although it is difficult to quantify the best agreement between experimental and predicted disordered solvent networks, the potential which included hydrogen atoms explicitly (EMPWI)[2] seemed to give overall best agreement possibly because it was successful in predicting some of the unusually short hydrogen bonds (less than 2.6Å) which are found in this crystal system.

1) H.F.J. Savage, PhD Thesis, University of London, 1983

2) F. Vovelle and M. Ptak, Int. J. Peptide Protein Res., 435-446 (1979)

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02. 12–6 SOLVENT INTERACTIONS IN NUCLEOTIDE CRYSTAL HYDRATES by Julia M Goodfellow and P. Lynne Howell, Department of Crystallography, Birkbeck College Malet St., LONDON WC1E 7HX, UK.

Since the earliest fibre diffraction patterns it has been known that solvent plays an important role in the stability and transitions of the different helical forms of nucleic acids. With the accumulation of a number of dinucleotide structures and a few oligonucleotide structures, it is now possible to look theoretically at the molecular nature of the interactions of nucleic acids with solvent (both water and counterions) and with drugs(which may also act as counterions). We have used two techniques to study these interactions at the molecular level. Firstly, computer simulation techniques have been used to predict solvent networks in crystal hydrates. This involves the use of 'realistic' potential energy functions i.e. those which give close agreement with experimental data, if meaningful predictions are to be made. Secondly, we have used accessibility calculations to look at the variation of contact and accessible areas in (a) di- and oligo-nucleotide sequences in the classical helical and crystal forms and (b) dinucleotide and dinucleotide-drug complexes for which there are three-dimensional atomic coordinates. Differences in solvent exposed areas may be important for both the stability of the different helical forms and for sequence specific recognition processes.

In the study of small nucleotide crystal hydrates, computer simulation techniques are being used to predict structural details of the solvent networks using potential energy functions derived for water-amino-acid interactions[1]. A detailed comparison of predicted and experimental results on the structure of the solvent networks has been made and includes an analysis of both