site. On a different aspect of structure, a study of disulphide bridges in proteins has recently been completed. Their distribution, topology, conformation and conservation were analysed. Several general patterns emerge which to some extent dictate disulphide bridge formation. For example, there is a strong preference for shorter connections, with half-cystines separated by less than 24 residues in 50% of all disulphides. This analysis of the covalent disulphide bridges led to a consideration of the weaker electrostatic salt-bridges between charged amino acid side chains. Preliminary results derived from a survey of salt bridges in high resolution protein structures will be presented.

02.X-07 WATER AND PROTEIN FOLDING. By J. M. Goodfellow, Department of Crystallography, Birkbeck College, University of London, Malet Street, London WC1E 7HX, UK.

Solvent effects are known to play a significant role in many important aspects of protein interactions including folding. The contributions to the free energy of folding which involve water interactions include :

(i) the entropy on release of water molecules hydrogen-bonded to the unfolded conformation, and

(ii) the relative strengths of hydrogen bonds between polar-polar and polar-water groups.

Estimates of these terms are difficult to make as they depend critically on the geometry and energy of weak, not always well-characterised hydrogen bonding interactions. Finney *et al* (1980) have attempted to estimate these contributions and to compare them with other terms including the so-called hydrophobic interaction.

If more detailed calculations are to be made, we must improve our knowledge about the relevant interactions especially those between water molecules and groups on the protein. Such intermolecular potential energy functions are being developed based on the polarisable electropole model for water which allows us to incorporate the known cooperative effects in hydrogen-bonded systems. After extensive testing against experimental data on amino acid hydrate crystals, these potentials are being used to examine the state of water around biomolecules using Monte Carlo simulation techniques.

Although *potential* energies are easily extracted from these simulations *free energies* require special methods. Such methods have been used successfully on small, homogeneous systems and are being extended to look at free energy differences in the much larger and heterogeneous protein-solvent systems. In principle, it is possible to calculate the free energy difference between the native and fully extended conformations of a protein using these methods.

Finney, J. L., Gellatly, B. J., Golton, I. C. and Goodfellow, J. M., Biophysics J. 32, 17 (1980).

02.X-08 LAMBDA REPRESSOR. By Carl Pabo and Mitchell Lewis, Department of Biochemistry, Harvard University, Cambridge, Mass. USA

The crystal structure of an amino-terminal fragment of lambda repressor has been determined at 4.5 Å resolution. This fragment, which was generated by cleaving repressor with papain, contains the first 92 amino acids of repressor and binds specifically to the lambda operators. (The intact protein contains two domains. The amino-terminal domain recognizes the operators, and the carboxy-terminal domain allows the protein to dimerize.) The amino-terminus crystallized in space group $P3_121$ with cell dimensions of a=b=65 Å, c=150 Å. These crystals diffract to 2.5 Å resolution. An unusual pattern of weak reflections and the observation that related crystal forms show planar disorder allowed us to deduce that there were three layers of molecules along the c axis. (When h and k are both even, reflections that would be absent in a rhombohedral cell tend to be weak.) Each layer has six molecules, which are related by a crystallographic twofold axis and a non-crystallographic threefold axis. A single isomorphous derivative, $PtCl_4$, with anomalous measurements was used to produce a preliminary set of phases. Molecular averaging improved the quality of these phases, and a detailed image of the molecule was produced. A model is being built, and the experimental phases are being extended to 2.5 Å resolution.

We have also grown some crystals of a carboxy-terminal fragment of lambda repressor, but the current crystals do not diffract to high resolution. Further crystallization attempts are in progress.