02.1-51 β-LACTOGLOBULIN: A STRUCTURE IN SEARCH OF A FUNCTION. By M.Z. Papiz and L. Sawyer, Department of Chemistry, Napier College, Colinton Road, Edinburgh, EH10 5DT, Scotland, U.K.

β-lactoglobulin is a dimer of subunit molecular weight 18000, isolated from milk. As yet no clear function has emerged but this has not prevented the accumulation of extensive experimental data in solution. Perhaps the most intriguing property is the large, pH dependent change in optical rotation centred at about pH 7 between the states N (pH 6) and R (pH 8) (Tanford, et al. [1959] J. Am. Chem. Soc. 81, 4032). The conformational change so reflected involves an aspartic acid and, more controversially, the free cysteine (Lyster, R.L.J. [1972] J. Dairy Res. 39, 279). The sequence of 162 residues is known and of the several crystal forms reported for the cow protein, four of those obtained from high salt have had their crystal structures solved at 6 Å resolution (Green, et al. [1979] J. Mol. Biol. 131, 375). Two of these, grown at pH 6 correspond to the N state of the protein, whilst of the other two, grown at pH 7.6, data for the orthorhombic form ($B22_12$; a = 55.4 Å; b = 66.7; c = 81.5 Å; Z = 4) have been used to produce an electron density map at 2.8 Å resolution phased by the MIR technique using monochloromercuriacetate and $HgI_4^=$. Although the mean figure of merit was a disappointing 0.73, we have obtained a main chain trace which has allowed us to correlate some of the solution data with the structure. Based upon the polypeptide chain fold, some speculation as to the function may be possible.

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02.1-52 THE STRUCTURE OF γ-CRYSTALLIN IIIb FROM CALF LENS. By Yu. N. Chirgadze, Yu. V. Sergeev, N. P. Fomenkova, V. Yu. Lunin* and A. G. Urzhumtsev*, Institute of Protein Research and *Research Computer Center of the Academy of Sciences of the USSR, 142292 Poustchino, Moscow Region, USSR

γ-Crystallin is a water-soluble protein from eye lens of vertebrates and has a molecular mass of ~20,000. In contrast to other crystallins, it contains a large amount of cysteine which apparently shows its importance in the processes of aging and cataract development. Crystals of γ-crystallin IIIb belong to space group $P2_12_12_1$. Unit cell has dimensions 58.7 × 69.5 × 116.9 Å, its asymmetric part contains two molecules. At the first stage of structure analysis we applied the method of isomorphous replacement with five derivatives, using anomalous scattering for three of them. Phases at 3 Å were determined for about 6,800 reflections with mean figure of merit 0.72. At the second stage we used the phase extension technique of Agarwal and Isaacs (Proc. Natl. Acad. Sci. USA (1977) 74, 2835). Phases were estimated for about 12,500 reflections at 2.5 Å. Electron density maps obtained at both stages allow to trace the main chain. In general structure of γ-crystallin IIIb seems to be similar to that of γ-crystallin II (T. L. Blundell et al., Acta Cryst. (1978) A34, S58). The molecule of γ-crystallin IIIb consists of two similar domains. Each domain has the same type of chain folding with the topology of two "simple Greek keys". The structure of domain can be described as a gable roof formed by two right-handed twisted pleated sheets, each of them consists of four antiparallel segments. The total amount of the ordered structure in the molecule is about 40%. An important feature of γ-crystallin IIIb structure is the internal pseudosymmetry: the first 2-fold rotation axis relates to both domains each to other, and the second one of the same type connects two semidomains.

02.1-53 THE STRUCTURE OF BOVINE γ-CRYSTALLIN II. By T. L. Blundell, P. F. Lindley, L. R. Miller, D. S. Moss, C. Slingsby, I. J. Tickle, W. G. Turnell and G. J. Wistow, Department of Crystallography, Birkbeck College, University of London, Malet Street, London WC1E 7HX, UK.

γ-crystallin II is a monomeric structural protein of MW 20K. An electron density map from MIR data to 2.6Å resolution has been interpreted using computer graphics techniques to give the first three-dimensional structure of an eye lens protein.

The molecule consists of two similar domains with a single polypeptide connection. Each domain is folded into two four-strand "Greek key" motifs. Three strands from one motif and one from the other form a β-sheet and the two β-sheets of each domain pack together as a wedge-shaped sandwich. With this fourfold repeat, related by intra- and inter-domain pseudo diads, the Cα backbone of the structure shows the highest internal symmetry of any known protein. However, except for residues at particular structural positions, the amino acid sequence does not have the same striking internal homology.

γ-crystallins have been implicated in human lenticular cataract in which oxidised, cross-linked protein aggregates accumulate. From the model, the environments of sulphur-containing and aromatic side-chains can be examined. It is clear that, under the appropriate conditions, the formation of intra- and inter-molecular disulphide bonds is possible.

The model also shows many of the surface side-chains to be highly ordered and capable of ionic interactions. This may contribute to the extraordinary stability of this long-lived molecule and the way in which it interacts with water and other crystallins. Further information will be available when the refinement of the γ-II structure to 1.9Å resolution by restrained least-squares methods is completed.

Sequence studies indicate that other γ-crystallins (Slingsby, C. and Croft, L. R., Exptl. Eye Res. 26, 1978), monomeric β_S-crystallin (Croft, personal communication) and the monomer of dimeric βBp-crystallin (Driessen, H. P. C., Herbrink, P., Bloemendal, H. and de Jong, W. W., Exptl. Eye Res. 31, 1980) are related to γ-crystallin II and may have similar tertiary folds. Computer graphics model building is being used to predict the interactions responsible for the dimerisation of βBp.