02. 2–8 COMPUTER GRAPHICS MODELLING OF MOUSE AND HUMAN RENINS BASED UPON THE HIGH RESOLUTION STRUCTURE OF ENDOTHIAPEPSIN. By B. L. Sibanda, L. H. Pearl, A. M. Hemmings and T. L. Blundell, Laboratory of Molecular Biology, Department of Crystallography, Birkbeck College, University of London, London WC1E 7HX, UK

The aspartic proteinase, renin, catalyses the first, and rate-limiting step in the conversion of angiotensinogen to angiotensin II, a hormone important in the regulation of blood pressure. A detailed structure of renin is required as a basis for designing inhibitors which may be of pharmaceutical value. We have modelled both mouse submaxillary and human kidney renins based upon their sequences and the three-dimensional structure of the homologous aspartic proteinase, endothiapepsin. The procedures for modelling using an Evans and Sutherland colour calligraphics system and schemes for using structural data from other proteins in the modelling will be described. The renin models demonstrate that the catalytically active aspartates (Asp 32 and Asp 215) are conserved at the active sites but the specificity subsites differ between renins and other aspartic proteinases, and to a lesser extent between human and mouse submaxillary renins. The absence of Asp 304 in renins may be related to their more neutral optimal pH for catalytic activity. The surface regions adjacent to the active site clefts contain several interesting features which are uniquely found in renins and may be involved in recognition of the globular angiotensinogen molecule.

02. 2–9 THE APPLICATIONS OF COMPUTER CALLIGRAPHICS IN PROTEIN ENGINEERING AND DRUG DESIGN. By L. H. Pearl, I. J. Tickle, A. Honegger*, G. L. Taylor#, D. J. Barlow, J. M. Thornton, I. Haneef, W. R. Taylor, T. L. Blundell and B. Busetta+, Laboratories of Molecular Biology and Molecular Graphics, Department of Crystallography, Birkbeck College, University of London, London WC1E 7HX, UK.

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Industrial interest in protein crystallography has been stimulated by the development of colour computer calligraphics for the manipulation and display of proteins, and the determination of structures which may be relevant to drug receptors or protein engineering. In the case of drug receptors software is required to design inhibitors complementary to a protein, whereas in protein engineering the protein is often modified to be complementary to the transition state of a chemical reaction. Software developed at Birkbeck includes computer programs to display proteins in general (MIDAS), surfaces (BILBO), charge distributions (HAMMER), thermal motions (HANSET) and to represent globular proteins as ellipsoids (ELLIPSE). Molecules may be compared (BILBO and FITZ) and docked together (MIDAS, BILBO, DOCKER). Examples of applications to enzymes, hormones and other proteins will be described.

02. 2–10 DETERMINATION OF THE POSITION OF THE ZINC ION IN A SMALL PROTEIN EXPLOITING ANOMALOUS DISPERSION BY USING MULTIWAVELENGTH MEASUREMENTS WITH SYNCHROTRON RADIATION. By I. D. Glover, I. J. Tickle, S. P. Wood, J. E. Pitts and T. L. Blundell, Laboratory of Molecular Biology, Department of Crystallography, Birkbeck College, University of London, London WC1E 7HX, UK.

Single crystal X-ray intensity data at 1.8Å resolution on photographic film have been collected at the synchrotron DESY for the 36 amino acid protein aPP at three wavelengths near the zinc absorption edge. A new heavy atom coefficient computed from the Bijvoet means allows determination by the Patterson method and refinement by least-squares of the position of the anomalously scattering zinc ion. Phase calculation by the conventional isomorphous/anomalous replacement method will be discussed. It confirms the position of the zinc ion but underlines the importance of accurate measurement of the intensities (better than 5%) and the wavelengths (within 0.001Å).

02. 2–11 THE STRUCTURE OF FUNGAL CATALASE AT 2 Å RESOLUTION. By B.K.Vainshtein*, W.R.Melik-Adamyan*, V.V.Barynin*, A.A.Vagin*, A.I.Grebenko*, V.V.Borisov*; K.S.Bartels"; M.G. Rossmann+, I.Fita+. * Institute of Crystallography of USSR Acad.Sci.,Moscow,USSR. " EMBL, c/o DESY, Hamburg, W.Germany. + Department of Biological Sciences, Purdue University, West Lafayette, USA.

Catalase (EC I.II.I.6) is an enzyme that decomposes hydrogen peroxide to molecular oxygen and water. X-ray study has been carried out for fungal catalase from Penicillium vitale, a tetrameric heme-containing protein of mol.weight 280000. The crystals belong to space group $P3_12I$, a=I44,4 Å and c=I33,8 Å. Asymmetric unit contains two subunits of 222 tetramer. Amino acid sequence for this catalase is unavailable.

X-ray intensities were collected to 3 Å resolution on a four-circle diffractometer and to 2 Å resolution with an oscillation camera using synchrotronous X-ray beam. Phases of structure factors to 3 Å resolution were determined and refined by isomorphous replacement and molecular averaging technique. 3 Å-electron density map was used for generation of a preliminary atomic model including all backbone and some side chain atoms. Phases derived from this model were calculated to 2 Å resolution and a new model was generated using $(2F_o-F_c)$ map. The model was based on "X-ray sequence" of 670 residues deduced in fitting process. Hendrickson-Konnert restrained refinement was performed to R-factor 0.3I (5-2 Å, 68000 reflections). The hydrogen bonds, intersubunit contacts and structure of the active site have been analysed.