molecules to be built or modified. Alteration of torsion angles allows realtime changes in conformation. A set of I/O routines enable files of cartesian coordinates and connection tables of individual molecules to be used as the input for structural displays. The program has been written in Fortran 77 with a set of graphic driver routines written in 8086 assembly language.

Chemmod provides an extremely useful tool to study chemical structures and interactions using high resolution raster graphics with a 16-bit microcomputer at a low cost. Raster graphics are ideally suited for the display of space filling representations of the molecules, which can also be manipulated in realtime.

The program is being transferred to a Motorola MC68000-based Sage II microcomputer which has considerably better performance than the 8086 system described above. A version of the graphics processor board previously mentioned, using the Thomson EF9365 chip, is commercially available from Digisolve Ltd. After minor modifications to provide double buffering and a light pen, this unit has been connected to the Sage II. This system costs approximately £9500.

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'Exploration of known and unknown active sites of proteolytic enzymes' **Marshall, G R, Naruto, S*, Schneider, C† and Labanowski, J** Department of Physiology and Biophysics, Washington University School of Medicine, St Louis, MO 63110, USA. *Guest investigator, Sankyo Pharmaceuticals, Tokyo, Japan. †Guest investigator, Boehringer-Ingelheim, West Germany.

Problems facing molecular modelling can be divided into those with detailed information regarding the binding site of the drug, and those in which only structure-activity data exists. In order to evaluate various approaches, we have explored current techniques with both classes of problem in studies of proteolytic enzymes. The serine proteases have been characterized by *X*-ray crystallography, and chymotrypsin studied by molecular modelling by Pincus and Scheraga and by DeTar. Mechanism-based inhibitors for proteolytic enzymes have been developed by the groups of Abeles and Katzenellenbogen. Detailed studies of the interaction of these inhibitors with chymotrypsin have been conducted in collaboration with Professor Katzenellenbogen of the University of Illinois. A limited active site was excised from the enzyme and the severed backbone segments anchored for subsequent minimizations. Systematic search of possible productive binding modes with the active site serine were performed, and representative examples minimized. In addition, alternative binding modes for the transition state, acyl intermediate and affinity-labelling compounds were all examined. Several predictions regarding stereospecificity have resulted which are in the process of being experimentally verified. The minimization procedure used was MAXIMIN which allows the flexibility necessary for a problem of this sort. Examination of the results on the PS 330 colour graphics system confirms the interactions, and the appropriate course of minimization. Entropic terms could best be approached by molecular dynamics beginning with those coordinates and alternate modes of interaction.

Angiotensin converting enzyme (ACE) and enkephalinase are two zinc proteases of considerable pharmaceutical interest. Roques and coworkers have recently described an analogue of thiorphan in which the amide bond has been reversed which inhibits enkephalinase, but not ACE. Examination of possible geometrical arrangements of the three groups postulated for ACE interaction with inhibitors (ie the C-terminal carboxylate, the central amide carbonyl and the active site zinc ligand) has led to a single geometrical arrangement consistent with the set of ACE inhibitors in the literature. The retroamide bond analogue of enkephalinase cannot assume an appropriate conformation while thiorphan binds to this hypothetical site in agreement with the data. The methodology used to deduce the site geometry will be illustrated, including orientation and vector maps.

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'Display of the course of α-carbon chains of large proteins in 3-dimensional space without utilising stereopsis' **Milner-White, E J** Department of Biochemistry, University of Glasgow, Glasgow G12 8QQ, Scotland

Previous work[1–3] in this Laboratory has concentrated on methods of displaying features of the surfaces at the subunit–subunit interactions of large proteins. In the present work new methods are being developed for visualizing the course of their α-carbon chains without recourse to stereo pairs. It is a relatively easy matter to make drawings of polypeptide chains of proteins that show the spatial folding unambiguously. I and colleagues have written new software that achieves the same effect by computer.

The initial processing of the coordinates is carried out on an ICL 2988 mainframe computer. Colour displays are produced on a Sigma T5680 terminal attached to the mainframe, with the help of the GINO graphics package. Hardcopy is generated in two ways, either by direct photography of the screen, or by means of a Trilog colour plotter associated with the graphics terminal.

An averaging procedure is used to produce a pleasing representation of the course of the chain. Zigzags and acute angles are largely smoothed out which means that the course of the chain is much easier to follow. The lines joining the averaged α-carbon positions are thickened so that they are clearly visible in the final picture. Shading, together with hidden-line elimination, is used to show the course of the α-carbon chains of each of the six subunits (three regulatory and three catalytic) in one half of the 12-subunit aspartate transcarbamoylase molecule. The *X*-ray crystallography was carried out by others[4].

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