

24.X-1 STRUCTURES OF ENGINEERED DIHYDRO-FOLATE REDUCTASE. By J. Ernest Villafranca, E. E. Howell, S. J. Oatley, M. S. Warren, C. David, J. Hirai and J. Kraut, The Agouron Institute and University of California, San Diego, La Jolla, California USA.

Thirty mutants of *E. coli* dihydrofolate reductase(DHFR) have been made by site-directed mutagenesis. The variants were designed to probe the structure-function relationships in DHFR with respect to the catalytic mechanism, coenzyme specificity, structural stability and inhibitor binding. The high resolution (1.9Å-2.0Å) crystal structure of a dozen of these variants is now known. This makes possible a detailed structural analysis of the effects of these specific amino acid substitutions. In general, few changes are observed in the enzyme structure. Some significant changes are found, however, in the case of Gly 95-ala where a cis-peptide bond is converted to the trans conformation and in the case of Asp 27-glu where the backbone shifts to accommodate the additional methylene group of the glutamate side chain. Where large van der Waals gaps are formed by the amino acid substitution, highly ordered water molecules fill the space. The effects of these amino acid substitutions on the enzymes' function will be presented.

24.X-2 INTERPRETATION OF MOMENTUM DENSITIES. By W. Weyrich, Faculty of Chemistry, University of Konstanz, F.R.G.

In terms of their Fourier transform, the reciprocal form factor  $B(s)$ , the momentum densities  $\rho(p)$  are related to the off-diagonal part of the first-order matrix  $\gamma(r,r')$  by a projection. Coulson's charge and bond-order matrix is an example of such a matrix, and generally chemical bonding is reflected by strong off-diagonal features of the density matrix of the electrons. The power of the interpretation of momentum densities by this concept can be demonstrated for the electronic structure of a number of molecules.

The density matrix contains the position density of the particles as its diagonal as well, and in fact the matrix is a representation of the phase-space density. Therefore, the challenging goal in electron density work, first formulated by Pauli in 1933 for the wave function, is the determination of the density matrix from experimental data. While previous work by Clinton, Massa, Frishberg, Pecora *et al.* is restricted to Hartree-Fock representable systems and is handicapped by slow iteration, a new approach combines full generality with favourable convergence properties. It is shown that thus the synthesis of position and momentum density data to a quantum mechanically correct unified description of systems has become feasible.

24.X-3 MOLECULAR GRAPHICS ON MICROCOMPUTERS. By George M. Sheldrick, Institut für Anorganische Chemie der Universität, Tammanstrasse 4, D-3400 Göttingen, F.R.G.

Recent developments in micro-computer technology, especially in raster graphics hardware and user-friendly programming languages, enable highly realistic displays of crystal and molecular structures to be produced at modest effort and cost. Some simple algorithms will be discussed, with emphasis on the possibilities for user interaction.

The "graphical editing" of potential atoms from direct methods or difference Fourier's provides a good example of the benefits of user interaction, and is particularly effective if red-green or other stereo techniques are employed. An automatic procedure for isolating a molecule to be plotted must take into account that there may be more than one molecule or ion in the asymmetric unit, that atoms may need to be moved to symmetry equivalent positions, and that if the molecule lies on a symmetry element extra atoms may need to be generated; appropriate action is needed if the structure turns out to be polymeric. The user may wish to edit the resulting connectivity table, change bond types, etc

Real-time rotation of a "wire model", in which the three-dimensional effect is provided by the interplay of motion with red-green stereo or depth cueing, enables a suitable orientation to be found quickly. If the graphics console is connected to the computer by a (relatively slow) serial line, it is still possible to "download" a series of orientations into the local VDU memory, then play them back fast, causing the molecule to "rock". Alternatively a molecule may be displayed oriented on its inertial axes, with the axis of largest moment perpendicular to the screen, and the axis of smallest moment horizontal.

Stereo diagrams are much more effective if perspective is taken into account in generating the principal ellipses or shading, so that atoms appear solid rather than as flat discs. A particularly simple and effective method is to use random dots to represent a spherical surface. "Highlighting" (e.g. by varying the dot density), hidden line removal and exaggerated bond perspective also augment the three-dimensional effect. Dots may also be used to represent the van-der-Waal's surface of the molecule, and the common or difference volumes after a least-squares fit of two structures. Dot surfaces are particularly informative if presented in stereo with interactive "clipping" of the front and back planes.

Some user interaction is essential in automatic atom labelling procedures, which should provide for the generation of stereo labels and allow the user to change his mind. In packing plots the user may intervene to delete superfluous atoms, bonds, molecules or (automatically generated) intermolecular (hydrogen) bonds. A general "plotfile editor" provides a convenient method of annotating the various types of diagram.

Simple and effective algorithms will be presented for the production of "solid" raster-graphics space-filling models, in which the intersection lines of the atoms do not need to be calculated analytically, and the highlighting is generated using (pseudo-) random numbers. A simple algorithm for "solid" polyhedral display of inorganic and mineral structures will also be discussed.

Many of these algorithms are employed in the Nicolet SHELXTL-PLUS system for the Microvax II / Tektronix 4207 and in the new Nicolet PC-based crystallographic workstation.