- space-filling
- ball and stick
- secondary structure
- solvent accessible surface

The objects can be coloured conventionally, or to represent some property of interest.

An extension of the same basic method has been used to construct pictures showing the variation of electrical properties on the surface of molecules. For this purpose, instead of using a constant colour for the object, the surface colour at every point is determined by computing the value of the property and mapping this on to a suitable colour range.

The technique of constructive solid geometry will be described, together with examples of its use for displaying molecular properties.

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'Towards fifth generation molecular modelling' **White, D N J and Pearson, J E** Ciba-Geigy, R1046, CH-4002 Basel, Switzerland

The advent of minicomputers of an order of magnitude more powerful than the VAX-11/780, and realtime raster scan displays whose facilities are not possible on calligraphic systems, has made the design of molecular modelling software necessary which uses these new devices.

The software described in this abstract is a preliminary, development version of the COGS (Chemically Oriented Graphics Software) package. It was developed on a VAX-11/750 minicomputer and Whizzard 7295 display but is targeted for a Norsk Data ND-570 minicomputer and a display yet to be announced (both of which will be delivered in July 1984).

In terms of performance the ND-570 relates to an ordinary minicomputer in the same way that a Cray-1 relates to an ordinary mainframe. The ND-570 is a realtime virtual memory machine which executes both scalar and vector instructions with none of the drawbacks of ordinary virtual memory architectures (eg thrashing). In addition to its advanced computational features the ND-570 has an extremely 'user friendly' operating system with features such as multiple window screen editing, built-in scientific word processing software, foolproof command abbreviations and prompts, query language etc.

The display for which COGS was designed is a colour raster scan display with an effective resolution of 3000 × 2000, 4096 colours and the following realtime picture transforms implemented in hardware:

- xyz-axis rotate
- xyz-axis translate
- xyz-axis scale
- xyz-axis clip
- perspective
- depth cueing
- area fill
- backface testing
- Phong shading
- Gouraud shading
- hidden line removal
- hidden surface removal

With all transforms active and all vectors non-trivially clipped the system can draw 100 000 medium length vectors/s. The display list memory can be up to 4.7 Mbytes long and all of this is simultaneously displayable without the flicker or other effects associated with calligraphic displays. Display list datatypes may be 16- or 32-bit integer or 32-bit floating point. The new display generates the following primitives in:

- hardware
- vectors
- polygons
- meshes
- circles
- generalized conics
- circular conic arcs
- splines
- surface patterns

New attributes such as programmable line width are supported as are a range of graphics peripherals and host minicomputer interfaces.

The design philosophy for COGS, with such powerful hardware available, is to provide all molecular modelling features, for both small- and macromolecules on the host minicomputer. In other words calculations such as molecular orbital, large molecule molecular mechanics, and large molecule conformational search are performed on the molecular modelling minicomputer and not on a mainframe. The only exceptions to this strategy are, eg the use of a FPS-164 array processor for quantum chemical and full-matrix molecular mechanics calculations requiring double precision arithmetic, and the use of the indexed sequential file access method of VAX/VMS in conjunction with Dr Murray-Rust's software for accessing the Cambridge crystallographic database. Furthermore, COGS is designed to make maximum use of graphics peripherals. Almost all operations are performed by pointing at atoms, molecules or menus using a puck and graphics tablet. A few options use valuator dials and minimum use is made of the keyboard.

The standard and novel features of COGS are too numerous to mention, but include a full range of 3D model building facilities such as model definition from 2D sketches, amino-acid sequence, and databases of standard internal coordinates. User supplied internal coordinates are also featured along with user-supplied crystal or cartesian coordinates and databases of standard molecular fragments. Easy back and forth swapping between a range of default picture types is provided. Current picture types include coloured stick models, red/green stereo pairs, Pearl/Honnegger molecular surfaces and molecular mesh surfaces. Other representations such as space-filling models may be drawn but are not used as picture types because of the difficulty of pointing at individual atoms in these types of pictures. Hydrogen atoms may be added to medium weight atoms automatically. Bond lengths, angles, and torsion angles may be measured by pointing, and may be dynamically altered in realtime. Single or collections of atoms or molecules may be removed from the screen without individual specification, bonds may be made

and broken, and rings may be closed automatically. Molecules may be least-squares superimposed with fixed geometries or the conformation of the moving molecule may be adjusted to optimize the superimposition. Docking of molecules may be done manually or via an automatic constrained optimization procedure. Sections of molecules (eg the active site of an enzyme) may be interactively edited out in realtime by using '3D cheesecutters' or by a realtime interactive amino-acid editor. Wipke and Gund steric congestion, Delre charges, and surface areas and volumes may be calculated. Attributes of the pictures and molecules may be changed and/or highlighted.

A full range of facilities is provided for both local and global energy minimization. Two molecular mechanics procedures are available: pattern search for models which are very far from a local minimum, and block diagonal Newton-Raphson for models which are close to optimum. One novel aspect of these procedures is that the force-field is completely orthogonal. In other words there is a *complete* set of force constants for all 30 atom types recognized by COGS, in any combination. COGS has facilities for global minimization and the location of low energy structures. It can locate linear molecules by the SITAR (Sequential Iterative Torsion Angle Refinement) procedure and cyclic molecules by CYCLOGLOMIN (Cyclic molecule global minimization). There are also facilities for Monte-Carlo calculations for location of low energy structures by simulation of thermal perturbation. There are facilities for calculating potential energy maps as a function of one or two torsion angles. The 1D plots are presented as graphs. The 2D plots are presented either as coloured contour maps (the 'bluer' the colour of the contour the lower the energy it represents), coloured area maps where areas of the map are colour filled with the same colour code as for contours, or surface mesh maps.

Finally, there is a suite of molecular orbital programs for EHT, MINDO, MNDO, CNDO, PCILO and *ab-initio* calculations with or without geometry optimization.

COGS is now being used in a variety of drug design projects. These include the docking of inhibitors with macromolecular enzyme receptors and the inductive design of active compounds via a database of analogues with greater and lesser activity.

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