Equi-Density Surface Method. In both methods, emphasis is placed on the illustrations of three-dimensional (3D) images of the density and the relations between the molecular skeleton and the distribution.

The procedures of the first method are as follows: (1) Planes that cut the molecule are introduced and the values of the density are calculated on the planes; (2) the planes are reconstructed in a 3D way by evaluating the refrectance coefficients and then are displayed along with the molecular skeleton; (3) the molecular skeleton is illustrated by the ball-and-stick model and is overwritten on the density figure, keeping their 3D relations; (4) outside parts of the planes, which have lower electron density, are removed to get a better perspective view of the whole system.

The procedures to draw the density by the second algorithm are: (1) The equidensity surfaces are searched, starting from the given lattice density data, and the surfaces are drawn by using nets; (2) so-called hidden-line treatments are taken to make the relative position of each surface clear; (3) the molecular skeleton drawn by the ball-and-stick model is overwritten on the figure of the nets. To see the change of the inner shell electron distribution, the nets are adapted here instead of using the ray-tracing method, since the algorithm requests less CPU time.

VIEW — Visualizations Impromptu Evaluations Workbench

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There is no single "best" way to represent molecular structure data. The best visualizations are the ones that provoke the most profound insights, and which those are depends on what is being studied and who is studying it. To find the best visualizations, the scientist needs to try many different views.

The VIEW system is a workbench for experimenting with various molecular visualizations. The system provides a set of geometric primitives and visual attributes, such as color, transparency and glossiness. The user can make impromptu assignments of parameters from the molecular data to the geometric primitives and visual attributes. The system allows an experienced user to build complex visualizations, while the novice user can build simple views easily.

A VIEW visualization is built in two steps. First, one builds a model of a molecule. A model is a three-dimensional (3D) entity that represents the molecule. Brass stick-figure or plastic CPK models are familiar examples, realized in brass or plastic. VIEW models are realized in the computer's memory only, but they have all the other attributes of real 3D models. For example, we might choose to represent the backbone atoms of an insulin molecule as spheres, colored by atom type, and the side chains of the molecule as stick figures, colored by residue hydrophobicity.

Once one has a model, it can be looked at from any direction, at any zoom, and under a variety of lighting conditions, just as with a real model. The model is built independent of the display device and can be viewed on any of several displays. Depending upon the power of the display machine, the viewing can be done interactively or dynamically.

One can save views on film or tape. One can also save all or part of the model parameters and easily make other variants. For example, we could take our insulin model and change the residue hydrophobicity coloring scheme, or decide not to color the side-chain sticks by residue hydrophobicity after all, but rather color them all white. That would not require recalculating the stick-figure structure, or any part of the backbone model. Such a simple change can be done very quickly. Changes to the underlying geometric structure, such as changing the backbone representation to a ribbon, can take the system more time to rebuild the model, but it is still a simple change for the user.

The initial VIEW prototype is implemented on a Sun 3 workstation, using X-windows for the user interface, and the database facility of the Sybyl system from Tripos Associates. Supported display devices are Adage Ikonas 3000, Evans and Sutherland PS330 and UNC Pixel-Planes.

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RSPACE — A Reciprocal-Space Modeling Tool for Planning Area-Detector Collection Strategies

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When collecting data with area detectors, crystallographers are faced with the question of how best to sweep out a volume of reciprocal space for their particular crystal. An analytical solution to maximizing coverage and minimizing X-ray exposure time is not feasible because of the large number of poorly defined variables involved — how sensitive to radiation damage a crystal is, how useful the collection of redundant data might be and how significant the loss of some low-resolution data would be. To questions of this sort, it is hard to give quantitative answers, or to imagine all the permutations. Currently strategies are planned with back-of-the-envelope calculation, mental visualizations and hard-

won intuition, usually by experienced crystallographers.

Our approach has been to provide crystallographers with an interactive graphical model of the diffractometer and to allow them to try out various collection strategies while graphically indicating the volume of the reciprocal space swept. The Biochemistry department at UNC has been using the program for several months and is now processing data collected with strategies planned with it. Use of the program has improved the efficiency of collection, reduced the chance of erroneous scanning and enabled inexperienced users to plan their own collections.

During a session, the user is prompted for information about his detector system and his particular crystal, and the program uses this information to draw an Ewald-like construction depicting the real and reciprocal cell axes, the laboratory axes, the goniometer, and the area detector, along with a sphere representing the chosen resolution limit and the boundary of a volume of unique data characteristic of the crystal's space group. The goniometer model can then be manipulated interactively, and the volume of reciprocal space swept is displayed at the end of each scan. Gaps and redundant collections in the strategy can be identified readily from the display.

For practical reasons, such as mechanical limits on the movement of the goniometer, it is sometimes impossible to collect a complete data set in a continuous region of reciprocal space, and collections from symmetry-equivalent positions have to be made. To address the difficulty in judging how such noncontiguous volumes complement each other, RSpace can optionally map all swept volumes to equivalent regions of a single unique volume.

The current version is a C-language program that runs under UNIX or VMS on Masscomp or VAX processors, driving Evans and Sutherland PS300 series displays.

RSpace can model any data collection based on rotation methods, including those using the Xuong-Hamlin, Centronics and FAST detector systems. It can be used for teaching or as a research tool.

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Force Display in Molecular Docking

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We have developed a real-time system that uses the master station of a remote manipulator system as a force and torque display in interactive modeling. The force system is integrated with interactive computer graphics and a high-speed calculation of the interaction forces between a drug and its receptor site to form a tool for molecular docking. When the drug molecule is maneuvered by the user's hand, the manipulator serves both as an input device for six-dimensional manipulation and as an output device for displaying forces.

The GROPE-III molecular modeling system consists of the Argonne E-3 Remote Manipulator (ARM) for force and torque presentation to the user, a graphic system (Evans and Sutherland's PS300 or Fuchs's Pixel-Planes, a very fast raster graphics engine developed at UNC-Chapel Hill) for displaying proteins and drugs, a Tektronix alternating polarization plate for stereo images and software for energy and force calculations. The system operates under Unix, with Ethernet connections between the graphic systems and a Masscomp 5500 workstation, whose digital-to-analog (D/A) and analog-to-digital (A/D) converters control the ARM. At present we achieve 4.5 updates/second.

Real-time force and torque evaluation is achieved by precalculating electrostatic and van der Waals forces on a grid, using the technique of Pattabiraman.[1] Most of the update time is spent doing image generation and the A/D, D/A sampling.

Considered as descendants of force-feedback remote manipulators, GROPE-III and a conventional robot are opposites. A conventional robot is a master-slave remote manipulator with a computer model assuming the role of the master station and its user. Grope-III is a remote manipulator with a computer model assuming the role of the slave station and its task-world.

We have simulated the interaction forces between dihydrofolate reductase enzyme (DHFR) and the inhibitor trimethoprim, which contain 1500 and 21 atoms, respectively. Even at the present slow update rate, we have found that chemists can reliably dock the drug into the crystallographically determined docking position, starting from arbitrary undocked positions and guided by their chemical intuition and a combination of visual and force feedback. Experienced chemists can dock trimethoprim into DHFR accurately in about 20 minutes. Docking with visual feedback alone is much more difficult, and we conclude that force feedback can be a useful tool.

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References

1 Pattabiraman, N., Levitt, M., Ferrin, T. E., Langridge, R. Computer grahics in real-time docking with energy calculation and minimization. *J. Comput. Chem.* 1985, **6** 1985, 432-436

CHAIN — A Crystallographic Modeling Program

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