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Diffraction Methods for Biological Macromolecules

Part B

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R. Stroud. A wholly digital version of the device, which allowed coordinates to be both read out and entered through a control console (e.g., for model building from coordinates), was constructed at the University of California at San Diego, and subsequently at the University of Arizona.[4] The motorized versions of this superposition device produce coordinates of comparable precision to the optical and acoustic devices described previously (at least ±1 mm), and similarly allow for very rapid measurements (one atomic position per 30 sec). However, construction of the former device is more complicated than either the AIMS (which can simply be rented) or acoustic coordinate measuring devices.

With the advent of computer graphics and associated software for both map fitting and coordinate readout (this volume [12]), it appears only a matter of time before graphics obviates either building physical models of proteins in optical comparators or devising means for measuring their coordinates. Nevertheless, the techniques described here will undoubtedly continue to prove effective aids in determining crystal structures for some time to come. In addition, many modeling studies of protein conformation and interaction continue to be most readily investigated in their initial stages by the construction of physical models. Subsequent model development and analysis by computer necessitates having accurate coordinates, so that the technical feasibility of such studies depends on having an accurate and easy way of measuring model coordinates.

[4] F. R. Salemme and D. G. Fehr, *J. Mol. Biol.* **70,** 697 (1972).

[12] Interactive Computer Graphics: FRODO

By T. ALWYN JONES

Introduction

Computer graphics provides an elegant method of controlling the protein crystallographer's interaction with his model. The graphics display allows the model to "show" the crystallographer a part of its electron density such that he can decide how a molecular fragment best fits. Once the crystallographer has made his decision, the computer merely does the bookkeeping and minor improvements. The aim of the molecular fitting program, therefore, is to create the necessary environment to allow the crystallographer to decide what atoms he wants in what piece of density.

A great deal of effort has been spent to develop the necessary control software and, in some cases, to build the hardware. At present there are approximately 10 density-fitting program systems in active use. Most laboratories are not able to build the necessary hardware, but high-performance equipment is available from a number of vendors. The program FRODO[1,2,3,4] is presently implemented on the Vector General 3400 (with DEC, VAX, or PDP-11 computers), MMS-X, Evans & Sutherland PS 2 (PDP-11), MPS (VAX or PDP-11), and PS300.

The man–machine interface in FRODO varies with the available equipment. All systems use a data tablet to pick menu items and to identify atoms shown on the screen. The VG3400 and Evans & Sutherland PS300 systems use analog-to-digital converters to define the view direction, and other picture-related functions such as clipping, zooming, and intensities. Commands that invoke dihedral angle rotations, single atom, and fragment shifts are also coupled to the A-Ds. On the Evans & Sutherland PS2 and MPS equipment, pseudo A-Ds are drawn on the screen and can be activated by the data tablet pen. The MMS-X version uses the standard user control panel.

Program Flow

The following is strictly applicable to only the VG3400 version of FRODO. Other versions have some minor differences.

After starting the program the user must specify a control data set. This data set contains all of the important parameters needed by FRODO. It includes, for example, the data set name for the user's coordinate file and the regularization zone. It is a source file and can be edited (at one's own risk). The user then gets to the CHAT interface, which has a large number of menu items activated from a terminal keyboard. Every exit from CHAT causes an update of the control file. Control normally then passes to the display loop.

To make the system easier to use an effort has been made to keep the display menu options to a minimum, and to a single "page." The data tablet pen position is marked on the screen by a cursor, and a menu item is activated by moving the pen so that the cursor is positioned over the

[1] T. A. Jones, *J. Appl. Crystallogr.* **11**, 268 (1978).
[2] T. A. Jones, *in* "Computational Crystallography" (D. Sayre, ed.), p. 303. Oxford Univ. Press, London and New York, 1982.
[3] B. L. Bush, *in* "Computers & Chemistry," vol. 8, p. 1. Pergamon, Oxford, 1984.
[4] J. W. Pflugrath, M. A. Saper, and F. A. Quicho, *in* "Methods and Applications in Crystallographic Computing" (S. Hall and T. Ashida, eds.), p. 404. Oxford Univ. Press, London and New York, 1984.

item and then pushing the pen into contact with the tablet. In principle, any number of commands can be activated and each is polled in turn. This means, for example, that an atom can be moved and have its contacts updated at the same time. In practice some care has to be taken, since there are a number of mixed options which may be disagreeable to the user. For example, if a group of atoms is being moved and the user activates the SAVE command, then the current fragment coordinates will get written to disk. The active commands can be seen at a glance because each has a star drawn next to it. To exit from the display loop, the user must pick a suitable menu item to either terminate the session or enter one of the utilities. Reentering the display loop causes a new loading of coordinate information from the disk.

The vectors drawn on the display are constructed from three data sets and normally show some of the atoms in the coordinate data set superimposed on a "chicken wire" representation of some sort of electron density.

The coordinate data set contains more than just atomic coordinates. The atoms are grouped together to form a residue. There are residue records to describe the type of residue (e.g., PHE, MPD), the name of the residue (e.g., A2, 10G), the position in the data set of the atom records for this residue, the center of gravity, and the radius of the residue. The residues are grouped together to form a sequence. As far as the display loop is concerned, the sequence is only important when defining viewing zones, i.e., it does not necessarily force any chemical connectivity between residues (although it may exist). The data set can also contain extra information such as lattice type (P, I, R, F, A, B, C), unit cell constants, and crystal symmetry information. This information is optional but may be required for certain commands. The user must decide at the CHAT interface how he wishes to access this data set. There are three possibilities: (1) Define the start and end residues of a zone. The program then displays all the atoms in the residues within the zone as defined by the sequence. (2) Define a point in space and a radius, and then display all of the atoms in the data set which are within the volume. (3) Define a mixture of 10 display zones plus a sphere.

In the sphere mode the user can choose an option to display any symmetry-related atoms which may fall within the volume. Both the sphere and symmetry options make use of the residue center of gravity information to decide what appears in the volume. Another option allows one to define by name which atoms are to be displayed; e.g., one can define just C_α to see the fold of a protein.

After picking which atoms are to be displayed, one must decide on a connectivity, i.e., which atoms should have a line drawn between them.

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