# NanoVision—molecular graphics for the Macintosh

**William R. Light* and Bruce Paul Gaber**

*Center for Bio/Molecular Science and Engineering, Code 6090, Naval Research Laboratory, Washington, DC*

*NanoVision is a molecular graphics program for the Apple Macintosh. The program follows accepted Macintosh design criteria, making it easy to learn by anyone familiar with the Macintosh. Molecules containing up to 32,000 atoms may be displayed. The program includes a range of molecular display options, including skeletal, ball-and-stick, and CPK. Images may be displayed using up to 240 colors. Color depth cuing is provided, as is Z-clipping. NanoVision images may be easily transferred (cut and paste) to drawing programs.*

*Keywords: NanoVision, molecular graphics, Macintosh*

## INTRODUCTION

As molecular graphics has moved out of the computer science department and into the laboratory,[1-8] several points have become clear. First, dedicated graphics systems, while extremely powerful, require machines and software which are expensive and of limited accessibility for many small laboratories.[9,10] In part because of their power, dedicated graphics computers are not easy to learn to use or particularly "user friendly." Finally, dedicated graphics computers do not support the range of desktop publishing applications which are becoming increasingly important in scientific communication.

The requirement for a low cost alternative has not gone completely unnoticed, but early attempts were hampered by inadequate hardware. These programs were generally limited to molecules of only a hundred atoms or so, and execution time was often measured in minutes.[11-16] Since these efforts, a new generation of microcomputer hardware has evolved with greatly increased capabilities. A number of commercially available programs have been written for microcomputers,[17-21] but they were primarily designed for small- to medium-sized molecules of less than 5000 atoms (*much* less in most cases).

Color Plates for this article are on page 194.

*Present address: BioPure Corporation, 68 Harrison Ave., Boston, MA 02111

Address reprint requests to Dr. Gaber at the Center for Bio/Molecular Science and Engineering, Code 6090, Naval Research Laboratory, Washington, DC 20375-5000.

Received 17 July 1991; revised 30 November 1993; accepted 10 January 1994

Our goal with NanoVision is to provide a low-cost, easy-to-learn, desktop molecular graphics package for the individual scientist which has very nearly the power of a dedicated graphics system, as well as new features not available on large machines, and which will accommodate medium- to large-sized molecular structures.

## DESIGN CONSIDERATIONS

The design specifications for NanoVision were created for the user who wants molecular graphics capabilities on his or her desktop at a price that is personally affordable. Of equal importance was the design of a user interface which is easily learned by the casual user, yet sufficiently powerful for the experienced modeler. The program was not designed to replace sophisticated modeling programs with minimization routines on workstations, but to work in conjunction with them when such facilities are available or to provide a useful subset if they are not available.

NanoVision is written specifically for the Apple Macintosh. The Macintosh was chosen because of its powerful graphics-oriented environment, large amount of addressable memory, and ease of use. Our guiding programming principle has been that NanoVision meticulously follow established Macintosh programming rules. This assures compatibility within the complete line of Macintosh hardware[22] and with all other Macintosh applications which follow Apple's guidelines. As a consequence of this approach, NanoVision runs on the Mac Plus, Mac SE, or Mac Classic (in black and white), and on the Mac II series (240 colors). Applications compatibility assures that NanoVision images can be easily transferred (cut and paste) to word processors, presentation graphics packages, and animation programs. NanoVision is designed to be straightforward and intuitive. We wanted a program with which a novice or casual user could quickly do molecular graphics. Consequently, the program maintains an uncluttered screen and makes extensive use of pull-down menus and mouse control of images. NanoVision has the look and feel of a typical Macintosh application.

Graphics features were incorporated that have been shown to aid in distinguishing features in a complex rendering. These include color (up to 256 when available), black and white patterns when color is not available or desired, depth cuing, Z depth clipping, and a variety of illustration techniques (line, shaded spheres, or CPK) that can be combined within a single molecule. Hardcopy output capabilities for easy inclusion into notebooks, presentations, and papers

was included to make NanoVision useful even for veteran molecular graphics users.

## IMPLEMENTATION DETAILS

### Hardware

Technical considerations of the Macintosh include a clean linear memory addressing scheme, consistent graphics hardware and software standards, the availability of a math coprocessor on enhanced models, the option of at least 240 user-defined colors, and the ready availability of publication quality output devices. Furthermore, the well-planned Macintosh visual user interface is consistent with our design goals.

Printer support on the Macintosh is provided by the operating system. The following hard copy output devices have been used with NanoVision: the Apple ImageWriter II (a dot matrix printer), the Apple LaserWriter (a PostScript laser printer), the Tektronix 4693 (a wax thermal printer with a resolution up to 300 dpi and 256 colors), and the SlideWriter from Image (an electronically connected slide generating device capable of 4000 scan lines and 256 colors).

### Software

NanoVision comprises over 10,000 lines of Pascal code. Most of the sophisticated ROM routines in the Macintosh operating system have Pascal interfaces, so the choice of Pascal was a matter of convenience. Currently there are a number of excellent C compilers available for the Macintosh, but this was not the case when NanoVision was started (1986). The particular programming environment included both LightSpeed Pascal and the Macintosh Programmer's WorkShop (MPW). Lightspeed was easier to use, but MPW allows for Pascal, FORTRAN, assembly, and C modules to be linked in together. This option was left available for future extensions.

Meticulous care was taken to observe Apple's recommendations on future compatibility guidelines as set forth in their programming manuals.[23] Short-term speed enhancements could have been obtained on existing technology by ignoring Apple's suggestions but this would have compromised NanoVision's compatibility with subsequent improved hardware releases. Furthermore, ignoring the programming rules may reduce the ability to coexist with other Macintosh applications. The ability to transfer a picture from NanoVision to virtually any other Macintosh graphics application has proven to be very useful.

### File structure

The Brookhaven Protein Data Bank (PDB) file format is supported for the import of large molecules. Simpler small molecule formats, Cartesian,[20] and Moldat[21] were also chosen for compatibility with other microcomputer-based programs. No preconceived notion of molecule type was assumed, however. This reflected our interest in lipids and the current lack of support from most display systems, which emphasize proteins and nucleic acids. The central philosophy in the design of NanoVision's internal data structures was that memory is relatively inexpensive and abundant; main memory was utilized whenever a useful feature required it or when it aided the execution time of the program. A feature was never discarded because of an attempt to minimize memory usage.

### Interface

The interface design decisions (but not implementation) were greatly simplified by the choice of the Macintosh. Apple has released a set of human interface guidelines[24] which most Macintosh programmers follow. This insures that all applications share a similar design philosophy. The assumption is that once a user becomes familiar with one application, learning to use other programs is simplified. The basic premise is that all functions should require one to "see-and-point" with a mouse rather than "remember-and-type." Static options, such as input and output or presentation parameters, are available through a series of logically associated menus located in a menu bar at the top of the screen. The complete menu is only seen when the user presses the mouse button in that region. Dynamic options such as rotation, scaling, or selection are located as a series of visual "tools" on the left side of a display window (Figure 1).

If a particular option requires a series of operations to be performed, or text to be entered, a dialog box is used. A dialog box may be a collection of buttons, a list of files, or text fields to be edited. Whenever possible, user input has direct visual feedback.

### Import

Files are brought into NanoVision by selecting the Open command from the File menu. The user is presented with a standard open file dialog box (Figure 2) to choose the file of interest. Several options are included for convenience; the file display can filter files by type so that the binary NanoVision files, text files, or both are presented. The binary format loads in faster, but text files are more standard with other programs. The text file formats that are supported include: Brookhaven Protein Data Bank, Cartesian, and Moldat. The program has a simple algorithm to determine the format of a text file, or the user can specify the type by using a pop up menu (Figure 2).

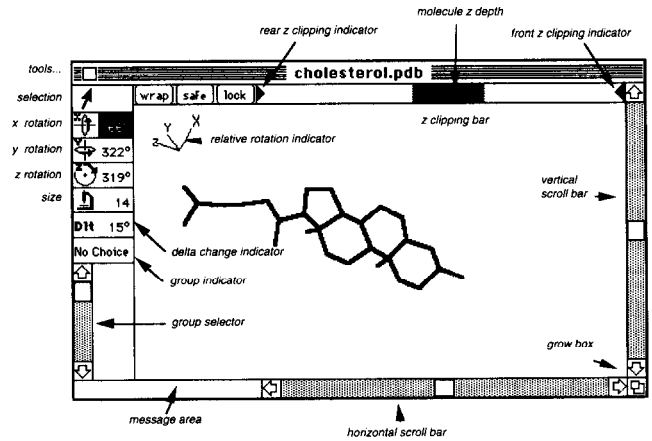


*Figure 1. The NanoVision window.*

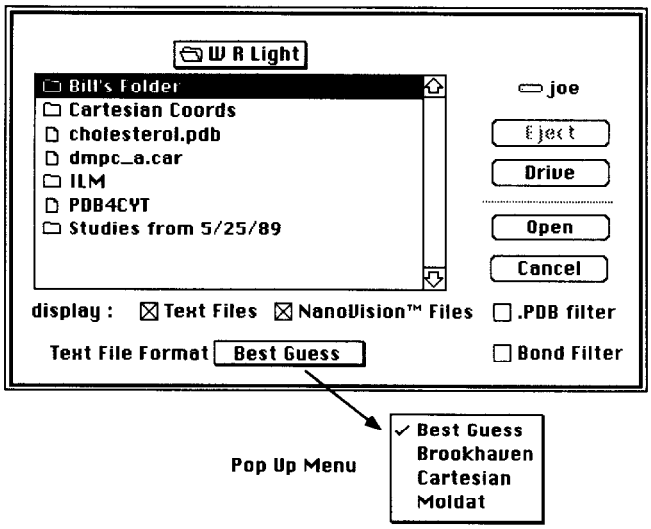


*Figure 2. Open file dialog box with pop up menu.*

## Export

Work in progress can be saved by selecting either the Save or Save As command from the File menu. The Save As command offers one the option to change the file name; the Save command simply overwrites the existing file. The file is in binary format and preserves the work state exactly as the user left it, including window sizes, display options, and orientation. Users can also export an image as a MacDraw-compatible file or "copy" the image to the Macintosh electronic clipboard to be "pasted" into another application program. The ability to cut and paste NanoVision images into sophisticated drawing programs has been found to be extremely helpful in image enhancement, and its importance cannot be overemphasized (Color Plate 1).

# DISPLAY FEATURES

## Windows

The actual images are displayed in movable, sizable, and scrollable windows. Up to four windows of 32,000 atoms each can be opened at any given time (provided there is enough memory). A window should be considered as a viewport to the drawing area. Not all of the area need be visible at once; the viewport can be moved around the drawing area by the use of scroll bars (Figure 1). Windows can be stacked for maximum display of one window or tiled so that the contents can be visually compared. The window approach was designed to create page size images (or larger) for a printer or other graphics programs independently of the actual screen size (which may be small). The use of multiple windows allow separate files to be compared and manipulated easily.

## Color

The proper use of color can clarify a complicated drawing for the viewer. Atoms can be colored by atom type, individually, or by group. This freedom allows the user to choose exactly what he wants to emphasize. For example, when combined with the rendering options, the binding site of carbonic anhydrase becomes clear when the zinc prosthetic group and associated histidines are colored differently from the rest of the molecule (Color Plate 2). Up to eight different user-defined colors are available. For each color, 30 shades are available. The different shades are used to give a three-dimensional look to the CPK figures or for depth cuing. In depth cuing, the lighter shades are used in the foreground, and the colors get progressively darker with distance. This assumes a dark background. The converse can be used when the background is light.

## Monochrome gray scale patterns

Color is not always an option: a color output device may not be available, and some journals accept only black and white figures. For these situations NanoVision provides seven patterns: black, white, stripe, checkerboard, light, medium, and dark gray, which may be used in much the same way as color. They are not as effective as color for large objects, and do not provide enough variation to allow for depth shading. When a true gray scale is used (a series of very fine patterns ranging from solid white to solid black on high resolution printers), there is enough variation for only two colors, white and black, to provide depth cuing.

## Rendering options

There are three rendering modes which can be mixed within a single molecule; wire frame, hollow sphere, and filled sphere (Color Plate 3). A fourth option, CPK space-filling, currently operates only on the total model. Molecular bonds are drawn from one atom to the next in the wire frame mode. Bond color and width are menu options. In the hollow sphere mode a circle is drawn around the atom to represent the van der Waals radius. The filled sphere mode is similar, except the sphere is solid. When color depth cuing is selected the sphere color has one shade representing the depth; otherwise, it is a graduated shaded sphere. In both the hollow and filled sphere modes, the radius is a function of the van der Waals radius. However, for clarity it can be instructional to use only a fraction of the radii in drawing the spheres. This is a menu option. For example, when the filled spheres mode is mixed with the molecular bond mode, a ball-and-stick model is created.

## Stereo

Both the divergent and convergent stereo models are supported in NanoVision. Spacing between the images can be set as a function of window size, page size, or can be user defined.

## Z clipping

Depiction of large three-dimensional objects on a two-dimensional screen can lead to complex and crowded images. It can be difficult to see the area of interest. A common data reduction technique is to view only a slice of the molecule along the $z$-axis. Atoms outside the $z$-clipping region are simply not displayed. The $z$-clipping region controls are located near the top of the active window in

NanoVision (Figure 1). The depth of the molecule is indicated by a horizontal green bar which is constantly updated as the molecule is rotated. The front and rear clipping limits are indicated by two red arrows or by a single red rectangle. To set the limits, the indicator is dragged into the green depth bar and everything outside of the indicator is not displayed. The combination of the green depth indicator and the red clipping controls is a visual image that both assures and informs the user when and where $z$-clipping is in effect, even when the molecule is subsequently rotated.

Along the $z$-clipping bar are three buttons (*lock, safe,* and *wrap*) used to simplify some clipping operations (Figure 1). Clicking on the lock button causes one red rectangle to replace the two arrows by spanning the distance between the arrows. The rectangle can then be moved as a single clipping region through the molecule; this maintains a single slice size as one changes the molecular view. Alternatively, the rectangle can be unlocked by clicking on the button again. The two red arrows return, and the front and rear clipping limits can be set independently. Clicking on the button labeled *safe* sets the clipping limits to values that will never clip the molecule regardless of orientation. This is not always the optimal setting, however. The color depth cuing option discussed earlier sets its limits to the $z$-clipping limits. The scaling is based on the distance between the indicators. Hence, maximum depth cuing, or the greatest change in shading from the front of the molecule to the rear, will occur when the indicators just barely span the entire $z$-depth. This can be set automatically by clicking on the *wrap* button.

## Animation

A problem common to all computer graphics is that eventually the model becomes too large to manipulate in real time. Specific performance figures for a common operation, rotate and redraw of a wireframe model, are given for a variety of Macintosh computers in Table 1. The time required for the generation of a CPK image is also given in Table 1. The solution to a slow redraw time is the same for all hardware platforms, the rapid playback of *precomputed* images. Of course, the problem is more obvious on a personal computer than on a dedicated graphics workstation, and so it was imperative that animation be implemented in NanoVision. With animation, model rotation of relatively large molecules can be observed in real time on even the slowest machine in Table 1. For example, 6 separate rotations of the protein myoglobin can be observed in under a second on the Macintosh SE using the animation feature. A full 360° degree rotation can be observed with a stepsize of 15° in under 4 seconds. This is independent of model complexity (a CPK image takes a similar amount of time as a simple wireframe model).

Animation requires at least two steps, creation and display. Images are created by choosing the *Make Movie* menu command. The user is presented with a dialog box asking for a root name for the images, the rotation axis, and the step size in degrees (Figure 3). The options are set to a default based on the user's past operations. The requested images are then calculated in the current drawing mode and saved to disk to be viewed later, either with NanoVision or by any graphics program that reads the standard PICT format (or PICT II for color files). The operation can be canceled at any time by pressing the command period keys. It is not necessary for the user to remember this, as a visual prompt is displayed in the message area.

A prerecorded sequence of images can be played by

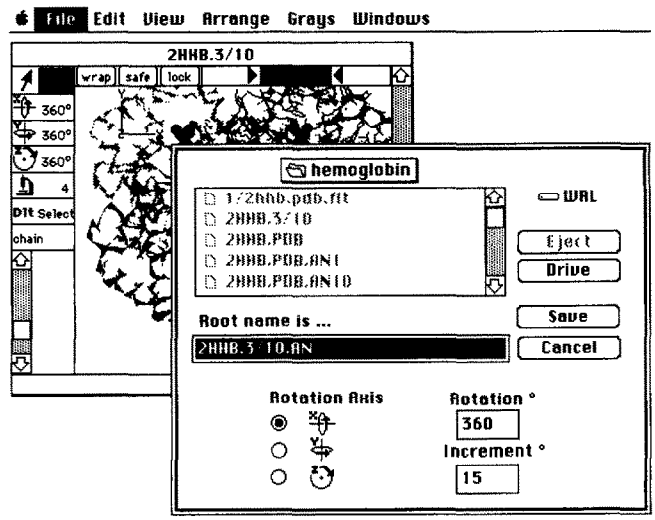


*Figure 3. Animation dialog box.*

**Table 1. Performance indicators for wire frame and CPK representations on various models of the Macintosh computer**

| Model | Test | Number of atoms | Time (sec) |
|---|---|---|---|
| SE (bw) | DMPC, rotate and redraw (once) | 46 | 1.0 |
| | Myoglobin, rotate and redraw (once) | 1258 | 27 |
| II si (with math chip & color) | DMPC, rotate and redraw (once) | 46 | 0.133 |
| | DMPC, CPK representation | 46 | 9.0 |
| | Myoglobin, rotate and redraw (once) | 1258 | 2.1 |
| | Myoglobin, CPK representation | 1258 | 57 |
| Powerbook 170 (bw with math chip) | DMPC, rotate and redraw (once) | 46 | 0.115 |
| | Myoglobin, rotate and redraw (once) | 1258 | 1.75 |

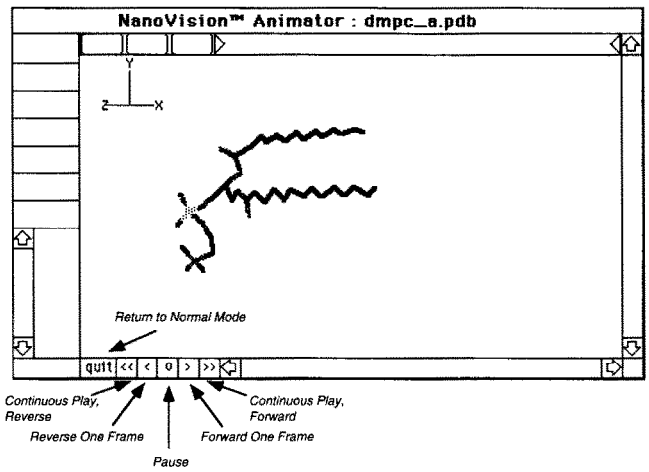


*Figure 4. Animation control buttons.*

selecting either the *Movie from Memory* or *Movie from Disk* menu options. A standard window must first be opened. Selection of these menu options evokes an open file dialog box so that the user can select the first image in the sequence to be viewed. Selection of the *Movie From Memory* option results in all the images being loaded directly into memory before subsequent playback, while the *Movie From Disk* option will read a file, display the image, close the file and then get the next file in the sequence. The latter option conserves memory usage, but it is slower. Six buttons specific to animation control are located on the bottom portion of the animation window (see Figure 4). The sequence can be paused, viewed continuously in forward or reverse, or viewed one frame at a time by clicking on the appropriate button. The default is continuous play, forward. The images will playback in a continuous loop. An animation image cannot be manipulated by the normal NanoVision tools.

## INTERACTIVE TOOLS

### Movement

There are two ways to rotate a molecule with NanoVision: by mouse or by keyboard. With the keyboard, one can choose the axis about which to rotate ($x$, $y$, or $z$) by typing the corresponding key. The selection is indicated in the window side indicators (Figures 1 and 5). The molecule will then rotate when the left or right arrow key is pressed. The amount of rotation will depend on the value shown in the delta change indicator. This is increased or decreased by pushing the up or down arrow key. To move by mouse, the user chooses a rotation tool by selecting the appropriate indicator and then clicks and drags in the main window in the desired rotation direction. The amount of change is displayed in the delta change indicator. The molecule rotates after the mouse button is released, and both the $z$-clipping bar and relative rotation indicator are updated (Figure 1). A rotation about the $z$-axis occurs by dragging along the diagonal. An $x$-axis rotation accompanies an up and down mouse motion and a $y$-axis rotation is caused by a horizontal dragging motion. The relative size of the molecule can be changed by first selecting the size tool (by mouse or by typing $m$) and then using the arrow keys as described above.

### Highlighting

Most of the menu options for the various rendering choices work on the currently selected portion of the molecule. The default value is all atoms. However, it is sometimes desirable to highlight a portion of a molecule; this is done with the selection tool (Figure 1). The delta change indicator will display *select* when the selection tool is chosen. An atom becomes highlighted when the user clicks on it with the mouse (Figure 6). When a structure is imported into NanoVision various levels of group hierarchy are determined. For example, NanoVision recognizes individual atoms, amino acids, and subunits in a protein. These levels of organization are accessed with the group selector (Figure 6, steps a–f). The exact information will depend on the file and molecule type. The rendering commands work only on the selected level.

The first step in the group selector (step a, Figure 6) always indicates the file name. This indicates that all of the atoms can be worked on. Step b is reserved for future use. Step c indicates the subunit name; in this case, the DNA strand has two subunits, A and B. Step d indicates the

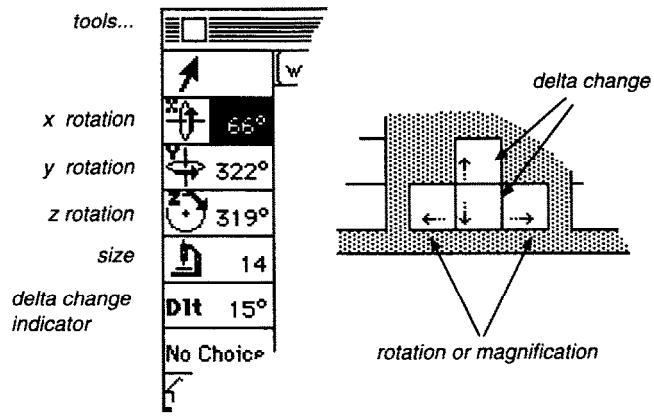


*Figure 5. Movement tools.*

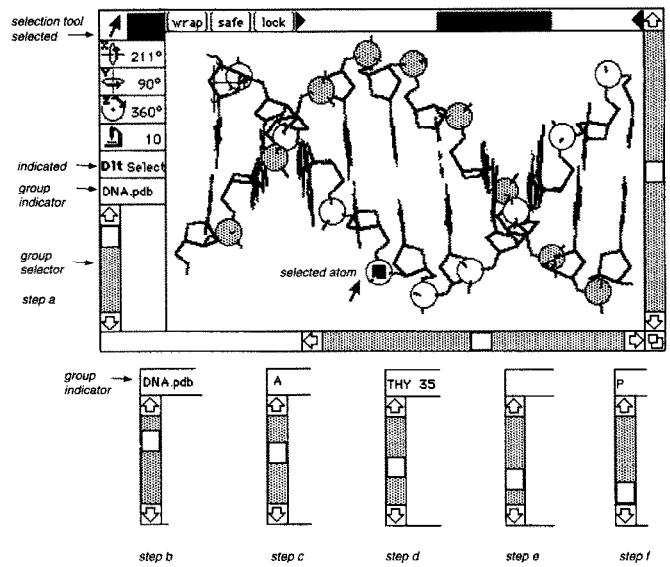


*Figure 6. Selection tool and group indicator.*

residue type, if available. Step e is useful only for proteins; it indicates if a particular atom is part of the alpha chain. Step f is the actual atom type. In Figure 4, each P was selected and changed from bond rendering to sphere to highlight the DNA twist.

## CONCLUSION

NanoVision is a straightforward, yet powerful molecular display program for the Apple Macintosh. The very large number of atoms which NanoVision can handle makes the program particularly useful for the display of biomolecules. An array of display options offers considerable flexibility in viewing molecular attributes. A useful feature of NanoVision is the ability to cut and paste images directly into drawing programs for the preparation of presentation graphics.

## ACKNOWLEDGMENTS

Our early work with desktop molecular graphics began with the program Spock, written by Ronald Brown and ported to the Amiga by Reed Omary. We thank Drs. Brown and Omary for their continued interest in the development of NanoVision. Dr. Light was the recipient of an NRL–National Research Council Research Associateship. This work was supported by the Molecular Biology Program of the Office of Naval Research. This paper describes a research version of NanoVision (version 0.42) and should not be confused with the significantly enhanced version commercially released by the American Chemical Society.

## REFERENCES

1 Langridge, R. and MacEwan, A.W. *Proceedings, IBM Scientific Computing Symposium on Computer Aided Experimentation.* IBM, Yorktown Heights, NY, 1965, 305
2 Levinthal, C. Molecular model-building by computer. *Sci. Am.* 1966, **214,** 45–52
3 Feldman, R.J. The design of computing systems for molecular modeling. *Annu. Rev. Biophys. Bioeng.* 1976, **5,** 477–510
4 Ferrin, T.E., Huang, C.C., Jarvis, L.E., and Langridge, R. The Midas display system. *J. Mol. Graph.* 1988, **6,** 13–27
5 Ferrin, T.E., Huang, C.C., Jarvis, L.E., and Langridge, R. The Midas database system. *J. Mol. Graph.* 1988, **6,** 2–12
6 Namba, K., Caspar, D.L.D., and Stubs, G. Enhancement and simplification of macro-molecular images. *Biophys. J.* 1988, **53,** 469–475
7 O'Donell, T.J. and Olson, A.J. GRAMPS—A graphics language interpreter for real-time interactive three-dimensional picture editing and animation. *Computer Graphics* 1981, **15,** 133–142
8 Connolly, M.L. Solvent-accessible surfaces of proteins and nucleic acids. *Science* 1983, **221,** 709–713
9 Langridge, R., Ferrin, T.E., Kuntz, I.D., and Connolly, M.L. Real-time color graphics in studies of molecular interactions. *Science* 1981, **211,** 661–666
10 Bash, P.A., Pattabirman, N., Huang, C., Ferrin, T.E., and Langridge, R. Van der Waals surfaces in molecular modeling: Implementation with real-time computer graphics. *Science* 1983, **222,** 1325–1327
11 Egan, J.T., and MacElroy, R.D. Interactive display of molecular graphics using a microcomputer system. *Comput. Prog. in Biomed.* 1980, **12,** 203–211
12 Keat, R. Graphics display of molecular structures from crystallographic data. *J. Chem. Ed.* 1982, **59,** 128–129
13 Hull, L.A. Animated 3-dimensional graphical display of line drawings of molecules. *J. Chem. Ed.* 1983, **60,** 96–97
14 Nakano, H., Sangen, O., and Yamamoto, Y. Drawing of ball-and-stick-type molecular models with hidden line elimination. *J. Chem. Ed.* 1983, **60,** 98
15 Brumby, S. Moldot: Space-filling perspective diagrams of molecules. *J. Chem. Ed.* 1986, **63,** 326–327
16 Cozzini, P., Pavesi, P., and Andreetti, G.D. Computer graphic tool for color display on personal computers. *J. Mol. Graph.*, 1985, **3,** 90–92
17 *Promodeler I.* New England BioGraphics, Peacham, VT 1988
18 *Alchemy.* Tripos Associates, St. Louis, MO, 1988
19 *Desktop Molecular Modeller.* Oxford University Press, Oxford, England, 1988
20 *Chem3D.* Cambridge Scientific Computing, Cambridge, MA, 1988
21 *Ball & Stick II.* N. Muller and A. Falk, 1988.
22 *Technical Introduction to the Macintosh Family.* Apple Computer, Inc. Addison-Wesley, Reading, MA, 1987
23 *Inside Macintosh. vol 1–5* Apple Computer, Inc. Addison-Wesley, Reading, MA, 1985–1987
24 *Human Interface Guidelines: The Apple Desktop Interface.* Apple Computer, Inc. Addison-Wesley, Reading, MA, 1987