MSURF: a rapid and general program for the representation of molecular surfaces

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A program for the generation of shaded surface images of molecular structures is described. The program has been specifically designed to be readily implemented on modern raster work stations and the new generation of microcomputers. The high level of device-independence is obtained by generating images in the memory of the computer and then transferring them to the display device. Use of graphical primitives gives excellent performance. Hidden surface removal is obtained with the depth-buffer algorithm. Molecular structures can be illustrated either with shaded spheres or with shaded cylinders directed along chemical bonds.

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INTRODUCTION

The development of microcomputers and low-cost raster work stations has greatly increased the accessibility of molecular graphics hardware to the chemist and biochemist. To date, however, implementations of graphics on microcomputer systems have generally been at the level of relatively simple stick figure drawings.[1,2] With progress in microcomputer technology rapidly removing some of the hardware limitations on the complexity of molecular graphics displays, there is a growing need for programs that will make efficient use of this new technology. In the present paper, a program is described that allows the generation of complex and aesthetically pleasing molecular graphics. The program, MSURF (Molecular Surfaces Using Rasters Faster), has been designed to be both rapid — without the need for special graphics processors — and general enough to be implemented on a wide variety of computers with only minimal changes in the source code.

Most microcomputers generate graphic images using a raster display. These systems are generally used for the display of molecular surfaces rather than line drawings of bonds as commonly depicted with calligraphic (vector) displays. With a molecular surface display, the overall shape of the molecule is readily discernible, and variability in the resolution allows one to emphasize the structural information of choice.[3] Surface topography, including the area for interaction with other molecules, is clearly seen in the surface display. Coloring of the surface can readily depict regions with characteristic values of such properties as electrostatic potential,[4] hydrophobicity[5] or solvent accessibility.[6] MSURF provides the ability to generate rapidly cylindrical surfaces that reveal details of internal structures in a manner that combines this advantage of vector displays with that of the surface display.

PROGRAM DESCRIPTION

Device-independence and acceptable speed without the use of special graphics hardware were the main criteria in the specific design of MSURF. Device-independence was largely obtained by doing all image generation in the memory of the computer. Once the image is generated, it is transferred to the memory of the raster display device. This minimizes the requirements for special display hardware and reduces the amount of device-specific code that needs to be written. The image is generated by "drawing" into a color matrix stored in RAM memory of the host computer. Each matrix element corresponds to a pixel on the display screen. The values stored in the matrix correspond to the color number that appears on the display device as determined by the display's color lookup table. Hidden surface removal is obtained by using a depth buffer algorithm.[7,8] When image generation is complete, the color matrix is transferred to the display memory.

Several advantages, in addition to device-independence, accrue from the use of the depth buffer in MSURF. Unlike methods that rely on hidden surface removal by sorting the points to be drawn according to z value, new portions of the structure can be added in any order. Thus the structure can be viewed at any stage of completion. Furthermore, the depth and color buffers can be stored either in RAM or on disk. Thus, once the structure is drawn, a variety of small molecules (such as substrates for an enzyme) can be added without redrawing the whole surface.

By avoiding the use of specific graphics hardware to ensure that the program is readily transportable, a high premium is placed on the speed of the algorithm. The key principle involved in ensuring the speed of the program is the use of graphic primitives. The primary primitive used is the sphere. As also noted by Hubbard

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and Fincham,[9] the use of the sphere as a graphic primitive provides significant advantages in that the surface shading is independent of translation and rotation. The combination of the graphic primitives and the depth buffer means that time-consuming mathematical operations (multiplies, square roots) take place only during the initial generation of the graphic primitive.

In MSURF, the primitive is represented as a $4 \times n$ array. The value n is dependent on the radius of the sphere and a scaling factor. The scaling factor relates the number of pixels per Ångstrom and is generally chosen so that the figure fills the available area of the display. Each column of the matrix contains the x, y and z coordinates and a shading factor for one pixel on the screen. The x and y values in the matrix are in pixel units, so that the array can be mapped directly into the depth and color buffers. The x and y values are chosen to include all pixels within the chosen atomic radius. For each pixel, a z value is calculated that corresponds to the surface of the sphere at that point. Given the coordinates of each point, and a vector representing the direction of illumination, the shading (0 to 15) can be calculated according to the diffuse reflectance model.[7] As noted by Hubbard and Fincham,[9] more complicated routines such as specular reflection,[7] need not slow the program down significantly, since they are calculated only once for each size sphere. Once the sphere array is generated, it is mapped to the correct location in the depth buffer by adding the x, y and z values of each element of the sphere array to the coordinates of the current atom. The z value is compared to that in the depth buffer, and if the new value is greater than the previous value, the point is visible and therefore the depth and color buffers are updated.

One disadvantage of the depiction of molecules by their surfaces is that interior structures are obscured; however, the use of undersized atoms can allow some details of interior portions to be seen.[3] Nevertheless, below a certain size the atoms become disconnected, and the ability to perceive the continuity of bonding is lost. Replacement of the spherical model with cylinders directed along the bond axes allows for a reduction in radius while retaining the appearance of connectivity. Using cylinders rather than reducing the radius to the point where simple vectors are drawn provides a significant advantage. This is because the use of cylinders allows for shading of the surface, which aids significantly in the perception of the directionality of the bond. This is particularly important when the structure is not depicted stereoscopically.

Unfortunately, however, the shading of cylinders is not invariant to rotation. Thus, the ability to use the graphical primitive as done for spheres is more limited. At a lower level, however, significant time savings are achieved by recognizing that each cylinder can be constructed from a graphical primitive that is a line. MSURF generates a cylinder by first calculating a circle with the desired radius for the cylinder. Then the circle is rotated in three-dimensional space so that a normal to the plane containing the circle is parallel to the axis of the cylinder. For each point on the circle, the shading value is calculated as was done for the spheres. Next the x, y and z coordinates of a line parallel to the cylinder axis are calculated. The coordinates of each element in the line array are added to the coordinates of each point in the circle and then mapped into the depth and color buffers as described for the spheres. Time is saved at this step because the line needs to be calculated only once for each cylinder. Furthermore, the shading is the same for every point on the line.

RESULTS AND DISCUSSION

MSURF has been implemented in FORTRAN-77 on a VAX 11/750 with a Lexidata color graphics display. The device-independence is exemplified by the fact that only a few lines of code are particular to this system. This device-specific code consists of calls to the Lexidata subroutines that initialize the display, load the color table and transfer the image from VAX memory to Lexidata memory.

The requirements that are placed on the computer system are in the areas of display type, resolution, colors and memory. The program is by design limited to raster graphics systems, as this is the only type that is commonly found on microcomputer systems and is more suitable for display of molecular surfaces. Most images generated in the course of this work were at a resolution of 512×512 pixels, which provides an approximate minimum hardware requirement for realistic display of complex structures. Microcomputer displays with nearly this resolution are now available, and higher resolutions should be available soon. The use of higher resolution displays allows for both multiple views of the structure in different windows or a single higher resolution display. The program is currently implemented on a system with 256 colors from a palette of 16 million. This number of colors allows for 16 distinct colors each with 16 intensities for shading. This number of colors is less commonly available but again should be more common soon. The main requirements for memory are for two image buffers. At 512×512 resolution, with 256 colors, the color buffer requires 256K bytes. To provide at least 512 resolution on the z axis requires the use of two bytes storage per pixel for the depth buffer; hence, an additional 512K bytes are required for the depth buffer. With current memory prices such storage is well within a reasonable price range. Color Plate 1 illustrates a typical image generated with the MSURF program. The structure illustrated is that of the small metal-binding protein, metallothionein.[10] The peptide backbone is depicted as a cylinder 0.8 Å in radius. The colors used change gradually from yellow at the amino terminus to orange at the carboxyl terminus. This sequential coding readily allows the eye to follow the path of the peptide backbone.[3] Use of the cyclinder mode is particularly valuable with this protein because it allows one to view the metals that would otherwise be obscured by surface residues. Color Plate 2 gives an alternate depiction of the metallothionein structure. In this image the individual atoms of the structure are represented as spheres 1 Å in radius.

The speed of the program is dependent on several factors, which are illustrated by the information in Table 1. This table gives the total CPU time and CPU time in milliseconds per atom required to draw the atoms of the peptide backbone of the protein metallothionein, and its β-fragment, which consists of only the first 31 amino acid residues. Generation of cylinders takes approximately twice as long as the generation of spheres. This is actually quite good in that the use of graphic

Table 1. Image generation times for spherical and cylindrical representations of the 91 C and N atoms comprising the peptide backbone of the β-fragment of the protein metallothionein, and for the 171 backbone atoms of the whole protein

Radius	Spheres	Cylinders	Both
		91 atoms	
0.8 Å	4.2 (48)	11.6 (133)	14.4 (165)
1.6 Å	10.9 (125)	17.9 (206)	26.7 (307)
		171 atoms	
0.8 Å	3.0 (17)	9.3 (54)	11.4 (67)
1.6 Å	8.2 (48)	16.2 (95)	22.9 (134)

Values are total seconds of CPU time to generate the matrix containing the image of the molecule. Times in parentheses are CPU time per atom in milliseconds.

Table 2. Surface generation times for several similar programs

CPU time/atom (msec)	Reference	Comments
0.8	9	a
50	11	b
84		c
180	12	d
5000	6	e

[a]Surface generated on parallel computer with 4096 processors
[b]Including time for interior atom removal
[c]MSURF, Color plate 2 of this paper
[d]Timing from reference 11
[e]Surface generated is solvent accessible. Timing from reference 11

primitives with the cylinder model is less efficient than for the spherical model. Normally, when using the cylinder mode one also generates spheres to fill in the gaps between cylinders. It can be seen that the total time for generating both is less than the sum of the individual times. This is because when drawing in the second of the two modes many of the pixels are already drawn and their entries in the depth and color buffers need not be updated. Table 1 also shows that the drawing time is approximately proportional to the size of the atoms drawn: doubling the size of the atoms approximately doubles the time required to generate an image. Larger structures thus require proportionally less time per atom since the atoms must be drawn at a smaller scale to fit in the display window. This can be seen in the comparison of the drawing time for the fragment and whole metallothionein (Table 1).

Doubling the number of pixels in both the horizontal and vertical directions leads to the expected fourfold increase in time required to generate the image. In practice we generally display trial images at the 512 × 512 resolution, making use of the extra display area for multiple windows. Then the desired final view is drawn at 1024 × 1024 resolution by making use of the full display area.

Table 2 lists timings for several other graphics programs that generate molecular surfaces. While it is hard to make direct comparisons among these programs because of differences in how the surfaces are depicted and in the molecules drawn, it is clear that MSURF is quite competitive with them. It should be noted that no particular effort, other than the use of the graphic primitive algorithm described above, has been made to optimize the program for speed.

The images described here were generated with a VAX 11/750. While this is not a microcomputer, the requirements of resolution and memory are readily met by current raster work stations, as well as by several recently released microcomputers. The current generation of microcomputers, based on the Intel 80386, Motorola 68020 and comparable processors, generally have performances that exceed that of the VAX 11/750. Thus the goals of producing a program for generating shaded molecular graphic images using inexpensive computers and without compromise of resolution, color and speed has been met.

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