SMILE—shaded molecular imaging on low-cost equipment

D. Eufri and A. Sironi

Instituto di Chimica Strutturistica Inorganica, Milano, Italy

The SMILE program runs under MS-DOS on IBM PC AT-compatible computers equipped with the SM640 or the PG640 Matrox graphic board. The program allows real-time three-dimensional (3D) animation and modeling of several isolated molecules that can be built from scratch, manipulated interactively and compared by superimposition.

SMILE enables users to compute atomic partial charges, molecular surface area, molecular volume, electrostatic and nonbonded potential energies. PLUTO, ORTEP, and MMP2 input files are set up automatically. The program also provides simple access to crystal packing by real-time animation of the unit cell contents, interactive inspection of the relevant stereochemical parameters and fragment manipulation within the unit cell. SMILE animates stereo views and produces beautiful shaded 3D images (8 colors, 32 shades each) of molecules in many different styles—stick, ball-and-stick, CPK (space filling), and transparent CPK with backbone.

Keywords: molecular computer graphics, visualization, modeling, shaded molecular models, small molecules, crystal packing

INTRODUCTION

Computer graphics is a powerful tool for both analyzing and presenting molecular structures. Several excellent programs exist[1] and are presently running on very expensive computers and graphic devices. Such programs are often confined to the top biochemical laboratories, where they have been proved invaluable.

Reasonably cheap hardware, with the related software, would make molecular computer graphics (MCG) and computer-aided molecular design (CAMD) available to the whole chemical community. Although programs have been developed recently on Apple, Macintosh, IBM PC and compatible computers,[2] none of them couples versatility of modeling with the beauty of shading. SMILE satisfies the chemist's need for efficient molecular modeling in a low-cost environment. The program is capable of creating pictures that convey maximum structural information.

Address reprint requests to Prof. Sironi at the Instituto di Chimica Strutturistica Inorganica, Via Venezian 21, 20133 Milano, Italy.

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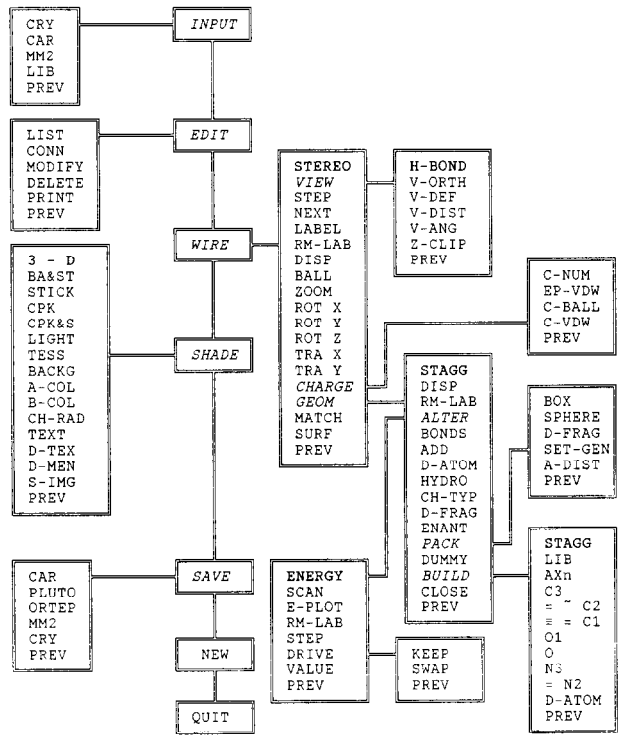

Figure 1. The flux diagram of SMILE, exemplified by the hierarchy of menus. Bold and italic characters represent flags and menus, respectively

THE PROGRAM

SMILE is a menu-driven program with no complicated command strings to learn or remember; commands and their parameters are entered by pointing with a mouse on the appropriate area. Figure 1 shows the hierarchy of available menus, while Table 1 lists the principal commands.

The present version of the program handles a maximum of 1024 atoms, 9 fragments, all the chemical elements and all the crystallographic space groups. The program is written in the C language using the Microsoft 4.00 compiler under MS-DOS 3.20, and no external library is required. The program listing contains more than 15 000 lines, and the executable code occupies about 430K bytes of memory.

Table 1. List of the commands available to the user

	FLAGS	
	ON (enlightened)	OFF (not-enlightened)
ENERGY	Activates energy calculations	Deactivates energy calculations
H-BOND	Doesn't draw C–H bonds	Draws C–H bonds
STEREO	Draws red/green couples	Draws normal pictures
STAGG	Joins staggered fragments	Joins eclipsed fragments
3-D	Uses SM640 3D primitives	Uses PG640 2D primitives

	MENUS
ALTER	Access to the conformations editor
BUILD	Access to the molecular builder
CHARGE	Access to the displaying partial charges menu
EDIT	Access to the coordinates editor
GEOM	Access to the geometry editor
INPUT	Access to the input menu
PACK	Access to the packing analysis menu
SAVE	Access to the output menu
SHADE	Access to the shaded 3D image builder
VIEW	Access to the view selection
WIRE	Access to the real-time animation of molecules

	INSTRUCTIONS
ADD	Adds a new atom by entering distance, bond angle and torsion angle with selected atoms
A-DIST	Finds "short" intermolecular contacts
A-COL	Changes atom's color
AXn	Substitutes a selected terminal atom with an $AX_{(n-1)}$ group (A,X any kind of atom; $n \leqslant 12$; many geometries)
BACKG	Changes interactively background color
BALL	Adds colored circles (atoms) to wire frame representation
BA&ST	Draws shaded ball-and-stick representations
BONDS	Creates or destroys bonds
B-COL	Changes bond's color
BOX	Draws all the molecules inside a box
C-BALL	Displays partial charges as red(−) and blue(+) balls
C-NUM	Displays partial charges numerically
C-VDW	Displays partial charges as red(−) and blue(+) dots on the van der Waals surface
CH-RAD	Changes sphere radius in ball-and-stick representation
CH-TYP	Changes atom type
CLOSE	Imposes constraints, such as the closure of a ring or a desired intramolecular contact, by altering systematically pertinent torsion angles
CONN	Redetermines connectivity
CPK	Draws shaded van der Waals surfaces
CPK&S	Draws shaded van der Waals surfaces with backbone
C1	Substitutes a selected terminal atom with a CH (sp)
C2	Substitutes a selected terminal atom with a CH_2 (sp^2)
C3	Substitutes a selected terminal atom with a CH_3 (sp^3)
D-ATOM	Deletes selected atom
D-FRAG	Deletes selected fragment
D-MEN	Clears the screen from the menu
D-TEX	Deletes last written text
DELETE	Deletes a list of atoms
DISP	Displays bond distance or angle between selected atoms
DRIVE	Scans interactively the selected degree of freedom
DUMMY	Defines a dummy-atom (baricenter of selected atoms)
EL-VDW	Displays electrostatic potential as red(−) and blue(+) dots on the van der Waals surface
ENANT	Generates the enantiomorph of a selected fragment
E-PLOT	Plots potential energy profiles produced by SCAN

Table 1. List of the commands available to the user — continued

INSTRUCTIONS	
HYDRO	Adds hydrogens to a selected atom
KEEP	Keeps the actual conformation
LABEL	Labels selected atoms
LIB	Substitutes a selected terminal atom with a library fragment
LIGHT	Sets light source for shading (3D must be ON)
LIST	Lists atom's coordinates and connectivity
MATCH	Superimposes two fragments
MM2	Prepares MMPMI input file for the selected fragment
MODIFY	Edits atom's coordinates, radius, color
NEW	Restarts SMILE, deleting all the present atoms
NEXT	Changes the active fragment (circular)
N2	Substitutes a selected terminal atom with a NH_2 (sp^2)
N3	Substitutes a selected terminal atom with a NH_3 (sp^3)
O	Substitutes a selected terminal atom with an O atom
O1	Substitutes a selected terminal atom with an OH (sp^3)
ORTEP	Prepares ORTEP input file for the selected fragment
PLUTO	Prepares PLUTO input file for the selected fragment
PREV	Returns to the previous menu
PRINT	Prints a list of coordinates
QUIT	Returns to DOS
RM-LAB	Removes all the displayed labels
ROT X (Y, Z)	Rotates the active fragment around X (Y or Z)
S-IMG	Saves on hard disk the displayed shaded image
SCAN	Produces a potential energy profile along the desired torsion angle
SET-GEN	Redetermines packing generators
SPHERE	Draws all the molecules inside a sphere
STEP	Sets the rotation step
STICK	Draws a shaded picture of the molecular backbone
SURF	Computes surface, volume, globularity and draws van der Waals dot surfaces
SWAP	Swaps the moving residues
TESS	Sets accuracy degree (0–7) on drawing shaded surfaces
TEXT	Adds comments or labels to shaded images
TRA X (Y)	Translates the active fragment parallel to X (Y)
VALUE	Sets the selected degree of freedom to the specified values
V-ANG	Sets the viewing angle
V-DEF	Returns to the default view
V-DIST	Sets the viewing distance
V-ORTH	Sets orthogonal view
Z-CLIP	Allows clipping on the Z axis
ZOOM	Interactive rescaling of screen pictures

SMILE operates on all IBM PC AT-compatible computers with 640K bytes of memory, an 80286 CPU and an 80287 mathematical coprocessor. It requires a Microsoft mouse and the SM640 or PG640 Matrox graphic board (256 colors from a pallette of 16.8 million, 640 × 480 pixel resolution). In principle, the program could run on the less expensive (but slower) IBM Professional Graphics Controller (PGC), but it has not yet been implemented in this environment. For very fast high resolution work, the SM1281 or PG1281 Matrox graphic boards (1280 × 1024 pixel resolution) can be used, although these are more expensive.

INPUT/OUTPUT FILES

At the beginning of a SMILE session, the user can choose to either build a new molecule from scratch (selecting the WIRE option) or display a known molecule (selecting the INPUT option). In the latter case, free format input files are used to supply title, cell parameters, space group number (or symmetry operations) and crystallographic (or Cartesian) coordinates. Connectivity is automatically determined from the stored covalent radii.

SMILE recognizes a range of different file types and formats. It determines their nature from the directory in which they are stored. The subdirectories and the corresponding file type and format are listed in Table 2.

*See note on page 184.

By selecting the SAVE menu, the user can generate future input files for the current fragment in Cartesian or crystallographic coordinates, and ORTEP, PLUTO or MM2 "ready to run" input files.

Table 2. The directories and the relative input/output file structure

CRY	Fractional cordinates data directory	
	TITL	(optional)
	CELL a b c alpha beta gamma	
	SYMM	(as in SHELX)
	SPAC[a] (space group number) X Y Z [b]	
	atom f_1 f_2 f_3	
	U_{11} U_{22} U_{33} U_{12} U_{13} U_{23}	(optional—not used)
	. . . . .	
	. . . . .	
	[a] SPAC and SYMM are mutually exclusive instructions	
	[b] XYZ means that f_1 is X, f_2 is Y and f_3 is Z; all the permutations are possible	
CAR	Cartesian coordinates data directory	
	TITL	(optional)
	atom x y z	
	. . . . .	
	. . . . .	
MM2	MMPMI format coordinates data directory	
LIB	Library coordinates (Cartesian) data directory	
	atom x y z	
	. . . . .	
	. . . . .	

"REAL-TIME" ANIMATION

The molecular backbone is drawn using a double-buffering technique to avoid flickering. The redrawing frequencies are 10.9, 7.8 and 1.6 Hz for molecules of 10, 100 and 1 000 atoms, respectively. Stereovision is obtained by displaying green and red overlaid images and delivering them to the proper eye with a pair of red and green glasses.

Several fragments can be simultaneously displayed and then zoomed, rotated, translated, compared, joined or splitted. Fragments can be quickly altered, or built from scratch, by using the mouse to select predefined groups of atoms (CH_4, . . .), or library fragments (C_6H_6, . . .) and the user can expand the library. Bonds can be made or broken and atoms can be deleted or created in the desired positions. Fragments can be compared by superimposition (least-squares minimization of distances between selected atom pairs). Bond lengths and angles can be modified, and it is possible to sample the conformational space by altering the torsional degrees of freedom.

MODELING WITHIN CRYSTALLOGRAPHIC SPACE

When the SPAC instruction is present in the input file, all the modeling operations are allowed, but the bulk of the molecule is kept tied to its original crystallographic position. This allows the user to edit or to build a molecule in a desired position of the crystallographic cell, which is useful for crystal structure resolution and interpretation. The program has many functions devoted to packing analysis, such as the automatic recognition of chemically meaningful packing-generator fragments, the ability to build the molecular environment around a chosen site and the automatic listing of anomalous intermolecular interactions (those shorter than the van der Waals radii sum of the pertinent atoms).

ENERGY AND RELATED COMPUTATIONS

Atomic partial charges are computed within the PEOE (Partial Equalization of Orbital Electronegativity) framework,[4] parameterized as in Ref. 4(c), and then represented on the molecular van der Waals dot surface. Molecular surface area and volume are computed with the OEPP (One Element Per Point) method.[5] Electrostatic potential and electrostatic interactions are computed on the basis of the above-mentioned partial charges. Nonbonded interactions are computed using the MM2 force field.[6] Nonbonded potential energy calculations are available only for the atoms parameterized in MM2 (H, B, C, N, O, F, Si, P, S, Cl, Br and I), but the user can define his or her own parameters.

SMILE lets the user analyze potential energy profiles for one torsional degree of freedom at a time and allows only a rough, step-by-step, energy minimization. When a full energy minimization is necessary, the program generates the whole MM2 input file, which will, of course, be meaningful only in the presence of MM2-supported atom types. Unsupported atoms are marked and their parameterization left to the user. MM2 atom types, assigned on the basis of the atom connectivity, are those of MMPMI,[6b] which runs on the IBM PC.

SHADED IMAGES

Two different shading approaches are actually implemented. The first exploits the full 3D capabilities of

the SM640 or the SM1281 boards, that is, Boolean operations on volumes, hidden-surface remotion, Gouraud shading, translucency and selection of light direction. The second shading approach uses only 2D primitives (filled circles and polygons) and a temporal priority algorithm similar to that developed in Ref. 2(i). The latter approach is faster and enables the program to run on the less sophisticated and less expensive PG640 and PG1281 graphic boards, but the light source is tied to the observer and pictures can be affected by color Mach bands when a part of the molecule is inspected from nearby. Both approaches afford 8-color (32 nuances each) pictures, fully exploiting the 256 colors, out of the 16.8 million available on these graphic boards.

SMILE can produce four different shaded-picture styles: ball-and-stick, in which atoms are represented by spheres of fixed radius and bonds by "cylinders" (see Figure 2); stick, in which the molecular backbone only is represented; CPK, in which atoms are represented as spheres of dimensions proportional to van der Waals radii (see Figure 3); and CPK and stick, in which the CPK and stick models are drawn together in transparency. Shaded images can be edited by changing atoms, bonds and background colors or by adding/deleting text strings. Moreover, shaded images can be stored on and retrieved from the hard disk. A shaded picture for a 1 000-atom molecule can be produced in a matter of minutes with the faster temporal priority algorithm (2 minutes for ST&BA, 3 minutes for CPK on our system).

CONCLUSIONS

SMILE is an integrated molecular modeling program that can be used in either the Cartesian or the crystallographic space. It allows users to produce real-time animation of complex molecular models and beautiful shaded 3D pictures. Many different interactions with the model are quickly addressed by using the mouse to select screen menus, and the minimization of the molecular potential energy can be achieved through the interface with MMP2.

The simple system discussed here demonstrates that a molecular computer graphics program with rather advanced features can run with acceptable time performance on inexpensive graphics workstations. Our own system, consisting of a 20-MHz/80386/80387 Compaq Deskpro 386/20, a Microsoft serial mouse, a PG640 graphics controller and an EIZO 8060S Flexscan 14-inch monitor, is available to academic institutions on the Italian market for less than $10,000 (U.S.). Standard display devices used in this field are typically 10 to 20 times more expensive.

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