tile is limited. Then a simple hidden-surface algorithm can be used on the limited data.

For example, if a van der Waals surface picture is being prepared, there might be, say, 50 atoms impinging on a given tile in projection on the screen. The specifications of the atoms are initially sorted by closeness to the viewer, and the new algorithm can then perform a very fast hidden-surface elimination for any given pixel within the tile. The algorithm starts with the atom closest to the viewer and works its way down the list until it gets to an atom that cannot possibly have a surface point closer to the viewer at the given pixel position than the closest atom yet chosen. In the language of computer graphics, this algorithm is said to use a priority list combined with z-buffering.

Once the hidden surfaces have been eliminated, and it is known which parts of the molecule are in shadow, the shading computation is straightforward and in the present case is based entirely on Chapter 16 of Foley & van Dam,[1] with specular reflections approximated using the Phong model.

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1 Foley, J. D., and van Dam, A. *Fundamentals of Interactive Computer Graphics*. Addison-Wesley, Reading, MA, 1982

Protein Surface Analysis: Qualitative Approach Using B-spline Functions and Quantitative Comparison

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A new way to describe protein surfaces is suggested, bringing out the interesting potentially functional features to facilitate their analysis and comparison. The classical representation of molecular surfaces (often calculated with the algorithm of M.L. Connolly[1,2] is very efficient for detailed surface examination but is unsuitable for an overall view, the few significant features being buried in many small amplitude bumps. In order to improve this representation of protein surfaces, we use B-spline functions,[3] smoothing the surface iteratively from atomic details to overall shape.

The program SURSPLIN uses, as starting data, the solvent-accessible surface of M.L. Connolly and is interfaced with the general-purpose molecular modeling software MANOSK.[4,5] It could be added easily to other software.

Up to now, SURSPLIN has been employed to study and compare more than 50 macromolecules, mainly proteins. In addition to the well-recognized active sites, a small number of conical pits, about 7Å in diameter and depth, are often encountered among interesting and repetitive topological features observed on protein surfaces.

The above comparison also shows that the rugosity of protein surfaces is variable. Several proteins, such as Azurin, are particularly smooth; others, such as Ferredoxin, possess very complex and uneven surfaces.

Currently, the splined surface is displayed by three-dimensional (3D) grids with a 50% reduction of memory occupancy, in comparison with the corresponding solvent-accessible surface displayed as dots. Large macromolecule complexes, such as the icosahedral face of a virus, can therefore be handled. Using fine grids, the splined surfaces are also valuable in displaying features of small molecules.

To complement the SURSPLIN program, we have developed a program (SURSCOP) for the analysis and comparison of quantitative aspects of surfaces. SIRSCOP allows a count of the distribution in size of topological features at the surface of molecules, which is especially useful for proteins. Typical examples of results obtained with SURSPLIN and SURSCOP programs will be presented.

The programs SURSPLIN and SIRSCOP are available upon request to the authors.

1 Connolly, M. L. Solvent-accessible surfaces of proteins and nucleic acids. *Science* 1983, **221**, 709–713
2 Connolly, M. L. *Quantum Chem. Prog. Exchange Bull* 1981, **1**, 75
3 Dube, P. Preliminary specification of splines curves. *IEEE Trans. on Comput.* 1979, **C–28**, 4
4 Vaney, M. C., Surcouf, E., Cherfils, J., Morize, I., and Mornon, J. P. MANOSK, a new graphics program designed for macromolecular modeling. *J. Mol. Graph.* 1985, **3**, 123–124
5 Cherfils, J., Vaney, M. C., Morize, I., Surcouf, E., Colloc'h, N., and Mornon, J.P., MANOSK: a general-purpose graphics program for analysis of molecular and macromolecular structure and functions. *J. Mol. Graph.* 1988, **6**, 155–160

The Quantitative Measurement of Molecular Shape and of Binding Interfaces Using Molecular Shape Descriptors

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Within the field of molecular graphics, much effort has been devoted to displaying the molecular skeleton of complex biomolecules, providing an elegant demonstration of the way in which these molecules are constructed. There is, however, a need for displaying surfaces, especially if one is interested in carrying out docking or drug design studies. Here, too, some elegant methods exist; foremost among these is the method due to Connolly,[1,2] but these methods are of use primarily for display purposes and do not give any quantitative measure of shape or of differences in shape.

The molecules of interest in biological processes are characterized *inter alia* by well-defined but apparently

highly irregular surfaces, but where certain surfaces features endow the molecule with the property of specifically recognizing and binding to other molecules. In the case of globular proteins, these recognition phenomena include the binding of specific ligands that may alter the properties of the protein or of the ligand itself, and the association of the protein with other proteins, with sugars, nucleic acids, or lipids. In order to understand these phenomena fully, a complete audit of the various energetic contributions to the interaction is required, but it cannot have escaped the notice of anyone studying these processes that the shape of the complementary binding regions of two molecules participating in the binding is an important feature. The natural explanation for this is that the shape of a region on the surface implies a specific spatial distribution of the atoms, electrons, etc., which are responsible for the energetic contributions to the interaction, be it charge, van der Waals interactions, polarizabililty, and so on.

A new type of shape descriptor has been developed for use in the study of biomolecules, which is a three-dimensional (3D) version of a Fourier shape descriptor technique already developed for pattern recognition of 2D objects, such as machine parts and radar images of aircraft. The 3D version, which employs spherical harmonics, has been used to describe the surfaces of globular proteins[3] and the contact interfaces of protein-protein and enzyme-substrate complexes.[4] The coefficients obtained in the expansion in spherical harmonics represent the shape descriptors themselves, and their magnitude allows one to make a quantitative estimate of shape similarity between two shapes or between contingent surfaces on interacting molecules.

In the early stages of this work, only van der Waals surfaces have been considered, but the method is easily adaptable to the case of charge or other kinds of interaction.

Fourier methods lend themselves naturally to a consideration of spectral analysis. The methods employed here enable one to construct "shape spectra" of molecules. From such spectra for two molecules known to bind to each other, it is possible to extract the common features that correspond to their congruent surface binding regions. In this way it is even feasible to contrive routines for "automatic docking" of two molecules in cases where it is not known how they associate with one another.

1 Connolly, M. L. Solvent-accessible surfaces of proteins and nucleic acids. *Science* 1983, **221**, 709–713
2 Connolly, M. L. *J. Appl. Cryst.* 1983, **16**, 548–558
3 Leicester, S., Bywater, R. and Finney, J. L. *J. Mol. Graph.* 1988, **6**, 104
4 Leicester, S., Bywater, R., and Finney, J. L. (in preparation)

Molecular Graphics Software on a Raster Device

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Most recent developments in molecular graphics software attempt to drive raster device hardware. High-resolution and fast three-dimensional (3D) local transformations have been achieved in new graphics processors. At the Microbiology Lab, University of Liège, a Megatek 9300 is linked to a VAX 11/780 through an Ethernet interface.

On the same bus are connected several local processors with specific functionalities, such as real-time manipulations of 3D wire-frame and shaded objects and z–buffering with hidden-surface removal.

Through the Local Task Language, graphic objects refer to host entities that can be organized into a hierarchical database by FORTRAN-callable subroutines (APPRENTICE). Moreover, the communication protocol allows a full dialog between the application program running on the host and the graphic processor.

To begin with, two well-known programs have been adapted to the 9300:

- PAKGGRAF, from the Department of Biological Sciences of Columbia University, has extensive facilities for handling protein data sets, including connectivity changes, rigid motion of the whole molecule, or "jiggles," energy calculation and minimization. We have improved this last feature and written the visualization tools using interactive devices.
- FRODO, first written by Alwyn Jones (Wallenberg Laboratory, University of Uppsala, Sweden), is used worldwide by protein crystallographers as well as in molecular modeling applications. The graphic part of the E&S MPS (B.L. Bush, MSD and Co.) was converted into MEGATEK software, giving rise to an efficient real-time version.

At last, we have developed software for calculating and representing 3D electrostatic potential maps at the quantum chemistry level.

These graphic developments are the first step of a wider project that has to be seen as a more general program in the molecular interaction study.

Extracting Conformational Information from Molecular Dynamics Trajectories Using Digital Signal Processing Techniques

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New techniques will be presented that allow conformational information from molecular dynamics trajectories to be analyzed and displayed on interactive computer graphics systems.