VISAR — Visual Interactive Structural Analysis Reporter

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VISAR is a visual graphics tool created for the purpose of facilitating analysis of structural molecular data that is generated by an optimization program.

Typically, an optimization program runs on a supercomputer. The results of the calculations are numeric, and interpretation of the data obtained is very difficult due to the vast data amounts.

VISAR lets users see the result of a calculational step as a frame in a "movie." It displays the molecule structure resulting from each step in perspective. VISAR then proceeds to show all calculational steps, thereby creating a "movie" that cuts result analysis time greatly, as well as giving the viewer a clear feel for where particular atomic interactions are taking significant effects.

Along with each frame, VISAR displays a window of information pertinent to the frame, such as the total potential energy of the system.

Interaction with the user takes place via a mouse and pop-up menus. The viewer can stop VISAR at any frame of interest. The interesting molecule's data can then be stored into a file for further analysis, if necessary. In addition, VISAR allows each frame to be rotated in three dimensions so as to allow better visual access to initially hidden parts.

VISAR allows the viewer to jump back and forth to any desired frame in the movie, and also allows a feature of gentle rocking motions for each frame in any direction, so as to give a better three-dimensional (3D) feel.

VISAR also has a stereo mode. Using green-red stereo separation coupled with the appropriate polarized eyeglasses, it is possible to get quite a realistic 3D view at a very low cost (the cost of the glasses).

Further features now being applied to VISAR include the facility for the viewer to point to any pair of atoms and see certain desired parameters about their interactions being displayed, even as the molecule is in motion. These parameters will change values in accordance with the state of the molecule in each frame (e.g., if the parameter is the electrostatic force between two atoms, it will be displayed continuously, with the figure changing to reflect the actual force as it varies from frame to frame). In addition, various statistics are gathered and will be displayed in separate windows.

VISAR was created on a Silicon Graphics IRIS model 3030 graphics workstation, and it makes extensive use of the windowing environment available on that machine.

Modeling Nucleic Acid Hydration

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Recent improvements in crystallographic data for oligonucleotides have enabled reliable identification of many individual solvent molecules. Ordered patterns of hydration have been observed and constitute an important element in stabilizing specific sequences and specific secondary structures of DNA.

A simple approach to understanding solvent structure around a macromolecule is the hydration site method, which determines the primary local minima of the interaction energy of one solvent molecule with the whole macromolecule. This method ignores the cooperative effects between hydrogen-bonded water molcules, but does not require such large computer power as computer simulation techniques. Qualitative and quantitative information about the possibility of hydration of the polar and ionic groups of the molecule can be obtained very rapidly.

In order to get insight into the influence of interactions of water with oligonucleotide conformations, we used this approach to initiate a systematic survey of solvation of the phosphate backbones, the bases, the minor and the major grooves for DNA in the different helical forms.

In a first step, we tried to quantify the effect of sequence variations on the hydration of the classical averaged helical forms (A, B, Z). The A form favors the formation of bridging sites on the phosphate groups and on the bases. For B structures, the water bridges connect atoms of the bases, while the phosphate groups are individually hydrated. Conversely, for the Z forms, water molecules bridges adjacent phosphate groups and phosphate groups to the bases, which can be also individually hydrated. These results are consistent with the concept of economy of hydration; however, other factors, such as entropic effects, may be important in stabilizing specific sequences.

In a second part we studied the effect of local variation in structure by comparing hydration sites for oligonucleotides in crystal forms and classical helical forms. It appears that these local variations of structure are associated with rather large differences in the hydration potentiality, favoring the formation of ordered structures. More specifically, we showed that the B dodecamer d(CGCGAATTCGCG) adopts in the crystal a conformation with a narrow minor groove in which all its hydrogen bond possibilities with water are satisfied, leading to the formation of the famous spine of hydration.

Rendering Volumetric Data in Molecular Systems

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A ray-tracing method of rendering sampled scalar functions has been layered over RMS,[1] an existing z-buffer-based program for the representation of molecular van der Waals surfaces. Calculation of a raster image is performed directly from three-dimensional volume data,

without the intermediate calculation of surface primitives. Two algorithms for the rasterization process have been implemented. In the integrative approach, partial opacities are assigned to a range of scalar data values, which are summed along rays cast from each pixel away from the viewer through the data space. Opacities are summed until the pixel is totally opaque, or until an atomic surface is reached. Shading is performed using local gradient vectors as shading normals, and antialiasing of silhouettes is performed easily during the assignment of partial opacities. These images appear as colored clouds surrounding a solid van der Waals molecular surface. The second approach yields a series of transparent isovalue surfaces, shaded by the method of Phong,[2] with an option for fully self-consistent cast shadows. Antialiasing of the surfaces is performed as a post-process. These images are much more interpretable, due to the presence of well-defined edges and highlights. The programs have shown utility in the visualization of molecular electrostatic potentials, molecular mobility and crystallographic electron density.

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1 Goodsell, D. *J. Mol. Graph.* (in press)
2 Phong, B. T. *Comm. ACM.* 1975, **18**, 311–317

Approximating Molecular Surfaces by Spherical Harmonics

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Smoothed molecular surfaces can be used to analyze the general shapes of proteins and as reference surfaces for locating clefts and projections. The radius of the surface in a given direction is defined by a polynomial or spherical harmonic function on the unit sphere. Starting with equally spaced points on a solvent-accessible molecular surface, generated by an algorithm of Connolly, we can either evaluate the spherical harmonic coefficients by a summation over the surface points, or by the "QR" least-squares algorithm. The resulting surface can be drawn with randomly spaced dots, or by ray tracing after conversion to an implicit polynomial equation.

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A Real-Time Malleable Surface for Molecular Modeling

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The use of surfaces in molecular modeling and drug design is well documented.[1–3] The two most common surfaces for these applications are the solvent-accessible[1,4,5] and the van der Waals[6,7] representations. In drug design studies, we require a surface that is both dynamic and interactive in real-time, with multiple visual cues, such as color and density, and efficient global and local manipulations to provide the user with additional feedback. We have recently described a method for generating a molecular surface using a parametric patch representation based on three-dimensional (3D) molecular structures.[8] Unlike previous methods for representing molecular surfaces, this algorithm produces a parametric patch surface that is *smooth* and *continuous* and can be manipulated in real-time. Crucial to our approach is the creation of a net of approximately equilateral triangles from which we generate the control points used as the basis for describing the surface.

A molecular surface model can be described as a continuous surface that envelopes a set of intersecting spheres. The algorithm that generates the surface must be able to generate a surface about a simple volume. Required properties include smoothness of the surface (i.e., continuity of position and tangent to the surface). Our algorithm provides for a dynamically manipulable surface based on a set of control points. For example, a user can interactively select a control point on one of the surface patches with a pointing device and move the control point outward along the surface normal. After the control point data has been modified, the graphics interface recalculates and redraws the patches of the surface model based on the new data.

Our algorithm provides for the generation of control points in such a fashion that we are able to generate a net of approximately equilateral triangles about a given surface. These equilateral triangles then become the basis for triangular parametric patches. Triangular patches, which are better at describing free-form shapes, can be described using nonpolynomial Gregory patches.[9] Gregory patches are interpolated between cubic boundaries.[10]

Our method for smooth and continuous surface generation uses cubic Bézier curves for the boundaries between patches. Quartic Gregory patches are joined with tangent-plane continuity to provide a smooth interpolated surface. Gregory patches are used as opposed to Bézier patches because Gregory patches provide twice as many interior control points and guarantee tangent-plane continuity between patches. To determine which points define which patches, a triangular net is calculated from atomic coordinates and radii. The triangular net is then converted to a parametric representation in three steps, as described by Shirman. The first step calculates the vertex normals based on the vertices of the triangles and the angles associated with these vertices. The second step involves the determination of Bézier control points