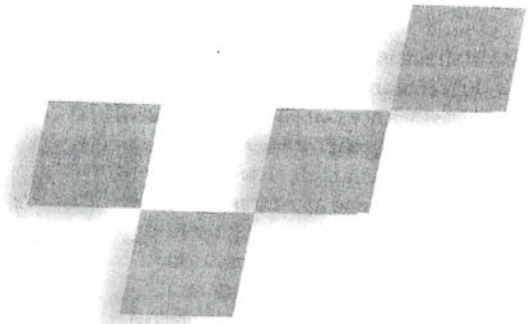
# Viewing Geometric Protein Structures from Inside a CAVE



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**New software generates both outside-in and inside-out views of geometric models for proteins. The models, computed on a remote supercomputer, were sent through the I-WAY for visualization in a CAVE.**

Biologists study proteins and other biomolecules intensely to understand how life functions on the molecular level. One application of this research is the design of drugs that can influence the mechanisms of molecular life. Common geometric representations for proteins and other molecules are the space filling (SF), solvent accessible (SA), and molecular surface (MS) models.

The SF model, introduced by Lee and Richards,[1] represents a protein as the union of possibly overlapping spheres. The SA model, introduced to study the interaction between a protein and a solvent, represents the solvent as a ball that it subsequently deflates to a point while inflating all other balls by the same radius.[2] The MS model is obtained by rolling the solvent ball over the SF model.[2] The MS model is useful in studying the structure of and interaction between proteins.

A fourth and relatively recent geometric protein model is the alpha complex—a combinatorial concept that represents the overlap pattern among the atom balls.

We developed general modeling software for a Cave Automatic Virtual Environment (CAVE); one of its applications is modeling 3D protein structures.[3] An advantage of the CAVE over other virtual environments is that multiple viewers can observe the same scene at the same time and place. Our software is scalable—from high-end virtual environments such as the CAVE, to midrange immersive desktop systems, down to low-end graphics workstations. In the current configuration, a parallel Silicon Graphics Power Challenge architecture performs the computationally intense construction of surface patches remotely and sends the results through the I-WAY (Information Wide Area Year) using very high Bandwidth Network Systems (vBNS) to the graphics machines that drive the CAVE and our graphics code.

## Software and hardware configuration

In our approach, the SF, SA, and MS models are all constructed from the alpha complex of the protein. (For details on the algorithms we used, see Akkiraju[4] and Akkiraju and Edelsbrunner.[5]) The alpha complex itself is computed as a subset of the Delaunay complex, defined for a set of atom balls. (For details on the alpha complex computation, including the relation between Delaunay complexes and Voronoi diagrams, see Edelsbrunner and Mücke.[6])

### Geometric software

The geometric software consists of two major pieces:

- a library for alpha complexes and
- a library for surface triangulations.

The geometric integrity of the alpha complex supports topologically correct surface triangulations for SF, SA, and MS models that use it as an underlying data structure.

We implemented the library for alpha complexes to provide geometric primitives that can be linked to any application software. The main two data structures built and used by our software are the Delaunay complex and the sequence of Delaunay simplices that contains all alpha complexes as prefixes.

We implemented the library for surface triangulations so that molecular surfaces are constructed based on convex polyhedral approximations of a sphere. Starting with a random distribution of a finite set of points on a sphere, the software constructs a good approximation during an iterative process that moves points in an attempt to maximize the surface area of the convex hull. Approximations of sphere patches, as opposed to spheres, are computed first by bounding the patch with cycles of arcs approximated by cycles of edges. Next, a given sphere approximation is modified so that it contains the cycles of edges in its boundary. Finally, a traversal of the modified sphere approximation accepts triangles in the patch and rejects other triangles.

### CAVE and I-WAY

The geometric software constructs the models, which are then rendered in a CAVE. The visualization software, Valvis (short for virtual alpha shapes visualizer), in many ways resembles the better known desktop version, Alvis. Valvis renders all geometric concepts and structures in the CAVE and interacts with the CAVE library to create immersive visual effects and track the



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position of a main observer.

As mentioned above, an SGI Power Challenge parallel machine performs the patch computation, while graphics and other computations are done on a workstation. The required communication between the workstation and the parallel machine uses DTM (short for data transfer mechanism), a message-passing facility designed to simplify the task of interprocess communication.

To achieve interactive performance, the I-WAY provides the communications backbone. An experimental, high-performance network based on asynchronous transfer mode (ATM) technology, the I-WAY links dozens of the country's fastest computers and advanced visualization machines. We used a specific network supported by I-WAY, the aforementioned vBNS.

## Geometric protein models

We can think of proteins and other molecules as conglomerates of atoms. If we model each atom as a spherical ball occupying space, the conglomerate might include overlapping balls—typically indicating binding forces between atoms.

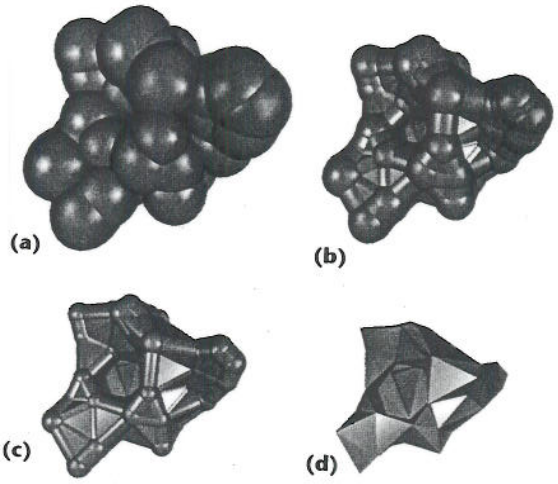
The SF model is the union of a collection of balls, where the radius is chosen equal to the *van der Waals radius*. In physical chemistry, this roughly equals half the distance between two of an element's atoms that are as close to each other as possible without being formally bonded. Because different types of atoms tend to have different van der Waals radii, our software must handle balls of various sizes.

The SA model is similar to the SF model, except that each van der Waals radius is increased by the radius of a spherical solvent. The SA model, shown in Figures 1a and 2a, is a spatial expression for how the solvent can interact with the protein without overlapping any of the van der Waals balls. More precisely, the solvent does not overlap the SF model if and only if its center lies outside the SA model.

Finally, the MS model is obtained by subtracting from the SA model the solvent balls that do not overlap the SF model (see Figure 2b through 2d). Possibly a more intuitive way of constructing the MS model is by rolling the solvent sphere over the SF model and letting the front of the rolling ball trace out the boundary of the MS model.

A representation of the molecule that is less direct than the sphere models consists of simplices connecting atom centers, as shown in Figure 1d. The simplices are derived from the Voronoi decomposition of the SF or the SA model.[7] The collection of simplices is referred to as a *simplicial complex*. The advantage of this complex over the sphere models is primarily computational. For example, with the complex you can identify cavities instantaneously, whereas software working directly on sphere models has difficulties finding the cavities at all.

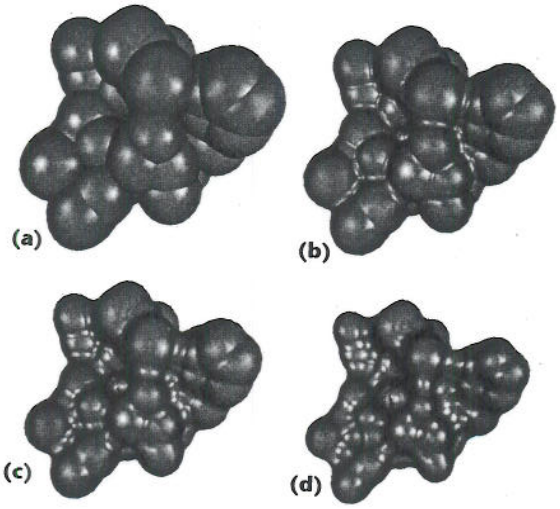
Furthermore, the complex is instrumental in the robust construction of a surface triangulation for any of the three sphere models.[4,5] In contrast to previous work (for example, see Connolly[8]), our software constructs topologically correct surface triangulations that can be exploited for such numerical computations as electrostatic potential field (for example, see Zauhur and Morgan[9]). We use surface triangulations to animate continuous deformations between sphere and complex models of a molecule. These animations are visually striking and may be the only convincing means for conveying the intricacies of the models and their relationships.



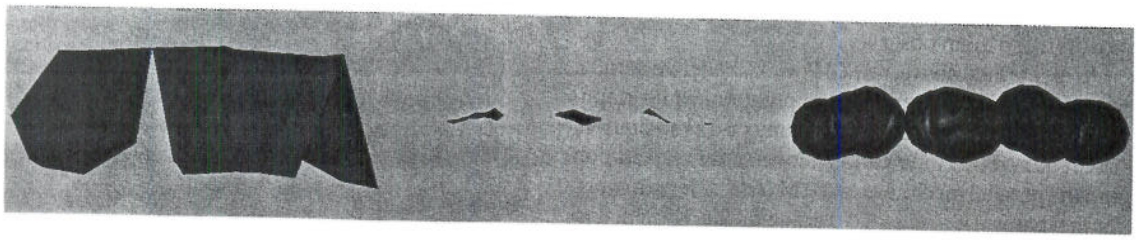

**1** Four snapshots during the deformation of the SA model into the alpha complex: (a) $t = 0.00$, (b) $t = 0.36$, (c) $t = 0.63$, and (d) $t = 1.00$.

### SA to complex deformation

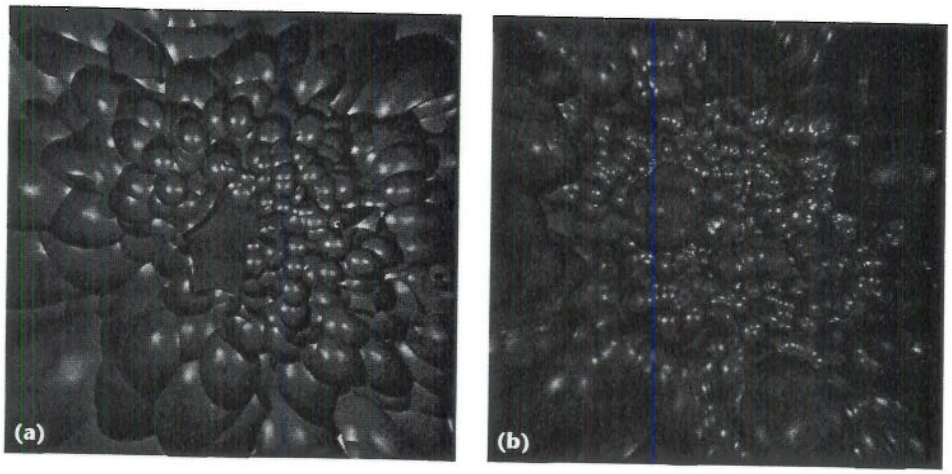
The deformation between the SA and the alpha complex models of a protein is governed by a time parameter, $t \in [0, 1]$, where $t = 0$ corresponds to the SA model and $t = 1$ corresponds to the complex. The surface of the SA model consists of sphere patches, circular arcs, and corner points. As $t$ goes from 0 to 1, each spherical patch shrinks toward a vertex of the complex. Each circular arc shrinks and widens to form a cylindrical section that eventually becomes an edge of the complex. Each corner point of the SA model grows towards a triangle of the complex. Recall that the SA surface is triangulated, so each patch is approximated by a collection of triangles, each arc is approximated by a sequence of edges,




**2** Four snapshots during the deformation of the SA model into the MS model: (a) $t = 0.00$, (b) $t = 0.36$, (c) $t = 0.63$, and (d) $t = 1.00$. The spheres shrink from left to right with one apparent exception—the growing bulge roughly in the middle of the picture, representing a self-intersection.



3 Different representations of the voids in Gramicidin A.




4 Inside views of the protein Myoglobin: (a) SA model and (b) MS model.

and each corner point is a vertex.

The deformation can be specified by prescribing the motion of the vertices in the SA triangulation. We use a straightforward linear motion determined by the starting and ending positions. Each motion follows the formula

$$(1-t)\cdot S_i + t\cdot A_j$$

where $S_i$ is a vertex of the SA triangulation and $A_j$ is a corresponding vertex of the alpha shape. The deformation progresses linearly, as shown in Figure 1.

### SA to MS deformation

The surface of the MS model consists of sphere patches, torus patches, and inverse sphere patches. As the time parameter $t$ goes from 0 to 1, each sphere patch of the SA surface shrinks toward a smaller but otherwise identical sphere patch of the MS surface. Each arc of the SA surface shrinks and widens to a torus patch. Each corner point of the SA surface grows toward an inverse sphere patch. Again we use a straightforward linear motion that deforms the SA triangulation into a triangulation of the MS model. The motion of each vertex is determined by its starting and ending positions, and follows the formula

$$(1-t)\cdot S_i + t\cdot M_j$$

where $S_i$ is a corresponding vertex of the SA triangulation and $M_j$ is a vertex of the MS triangulation. Figure 2 illustrates the process.

### Voids

The combinatorial nature of the alpha complex allows for fast algorithms that detect and compute voids in proteins. Technically, a *void* is a component of the complement space that cannot be accessed from outside the protein. It is represented by a connected collection of Delaunay simplices that do not belong to the alpha complex.[10]

Figure 3 illustrates different representations of the voids in the antibiotic Gramicidin A. The voids in the SA model tend to be tiny and difficult to see. Each SA void is enclosed by the corresponding alpha complex void and also by the corresponding MS void.

### Clipping

A unique feature of our software is the possibility of generating uncluttered inside views of SF, SA, and MS models. Other software packages can generate high-quality renderings of views from the outside, but they cannot generate uncluttered views from the inside unless all spheres and tori are appropriately clipped. With our software, users can detect voids and tunnels by walking into the model and viewing the surface from the inside. In the CAVE, the user feels complete immersion in the model.

Figure 4 shows views from the inside of an SA and an MS model. Molecular structure is just one application where information available from such inside views is crucial. Solid modeling and medical imaging are two others.

## Discussion

There is an ongoing debate regarding the extent to which the high cost of virtual environments can be justified in the face of very affordable high-quality graphics interfaces. We wish to contribute a piece of anecdotal evidence to this debate, in support for the claim that the immersive experience generates new insights and discoveries.

The molecular surface of a protein can exhibit self-

intersections, which are sometimes referred to as "degeneracies." It was only in the CAVE that we noticed the seriousness and frequency of such self-intersections. The easily imagined first type of self-intersection involves pieces that are fairly far apart along the surface—the solvent ball peeking inside-out and outside-in through a narrow window. Figures 2 and 3 reveal such self-intersections, for example, in the growing bulge roughly in the middle of Figure 2.

There is another and apparently more frequent type of self-intersection resulting from torus-sweeping motions of the solvent ball. If the sweeping circle is larger than the circle swept by its center, then the torus has a self-intersection. In most cases, only a small patch of such a torus is part of the surface. Locally, the surface folds sharply backward and again forward.

The folds and self-intersections originate in the MS model definition, which should possibly be altered. The biology community has recognized shortcomings of this model, but only in the CAVE visualization of our software have we realized how serious and frequent these shortcomings are. ■


## Acknowledgments

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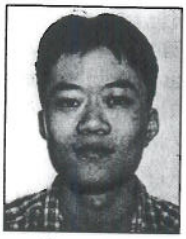


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