Seventh Annual Report
Interactive Graphics for
Molecular Graphics System

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6. PRINCIPAL INVESTIGATOR:

6a. NAME: Dr. Frederick P. Brooks, Jr.

6b. TITLE: Kenan Professor of Computer Science and Chairman

6c. SIGNATURE:

7. DATE SIGNED (Month, Day, Year): March 5, 1981

8. TELEPHONE (Include Area Code): 919-933-2148

1. Summary of Research Progress

We have built, and operate as a service resource, an effective interactive computer resource for seeing, manually manipulating, and computationally modifying mathematical models of complex molecules. We believe that our present resource, called GRIP-75, has been shown to be as complete and useful as any in existence. One impressive measure of the power and utility of GRIP-75 is that at least five of our clients have obtained their own graphics systems as a direct result of their successful work here.

Our resource has dual objectives. We are a service center providing powerful computer graphics facilities and expert computer assistance to chemists studying macromolecular structure. We are also computer scientists dedicated to advancing the art of interactive computation and interactive, three-dimensional graphics. The objectives are complementary. Our chemist clients provide the essential focus and a real, complex, and interesting driving problem for our computer science research; our computer science research in turn provides our clients with more powerful tools to improve the accuracy of their results and, most importantly, improve their insight into very complex structures.

Our goals for the 1980-81 grant year were to obtain the equipment and personnel necessary to build a completely new version of our system, using more powerful hardware and consolidating the knowledge gained from five years of experience with GRIP-75, our present system; and to continue production use of GRIP-75 for our clients. Some specific achievements during the past year were:

1. Complete refitting of Conconavalin-A by Dr. K. Hardman; of an immunoglobulin fragment by S. Bryant (Dr. M. Amzel, Principal Investigator); of superoxide dismutase by E. Getzoff and J. Tainer (Dr. D. Richardson, Principal Investigator); and solution of the three-dimensional structure of a fish hemoglobin at low resolution by E. Getzoff and J. Tainer using molecular replacement and partial structure techniques, aided substantially by our graphics system.
2. Development of a method for semi-automatic, computer assisted interpretation of electron density maps by T. V. Williams.
3. Procurement, installation, and checkout of all of the major hardware components of our new system — a VAX 11/780 computer, 300 MB disk storage unit, and a Vector General 3303 graphics system; and installation, customizing, and checkout of our operating system software (the Berkeley version of the UNIX† operating system).
4. Research in high performance raster graphics. We have transferred our results on depth cues for three-dimensional images of macromolecules from the stick models of vector displays to the solid surface models of raster displays. We find that smooth motion kinetic depth cues are effective in raster displays, and that kinesthetic feedback greatly enhances both kinetic depth cues and highlighting depth cues.
5. Substantial progress on the design of GRIP-X, our new system. An overall architecture has been developed in conjunction with our collaborators in the U.K. under Dr. W. V. Wright, the molecular data structure is defined, an adjunct language for specifying system commands has been proposed, and we are now designing intermediate level data structures. We have also obtained a wide range of crystallographic programs which will run with GRIP-

†UNIX is a Trademark of Bell Laboratories.

X to provide our clients with a much wider range of tools with which to attack their problems.

These results all relate specifically to our overall objectives, which are:

1. To help our client biochemists obtain the most accurate structural information their data will support; and
2. To advance the art of interactive graphics to the point that our clients are able easily to perceive the significant *chemical* information in their structures, at all levels of detail.

We believe that the use of our system substantially improves a chemist's understanding of the molecules with which he is working. Our most valuable product is insight.

We have four goals for the 1981-82 grant year.

1. Complete a test implementation of GRIP-X. We do not expect to complete the production version, but hope to test most of the new concepts in the design.
2. Incorporate full color raster graphics into GRIP-X.
3. Produce efficient programs for least-squares refinement of macromolecular crystal structures.
4. Produce a program for computer-aided semi-automatic fitting of molecular models to experimental electron density maps.

Five years of experience with GRIP-75 have shown us a number of inadequacies. We are now building a second-generation version of this system, called GRIP-X, designed to be more comprehensive in the biochemical problems that can be attacked, more powerful in the mathematical tools available, smoother in the user interface, and constructed as product-quality, documented, exportable software.

Fundamental to our approach are the following objectives:

- The GRIP system is designed to help chemists get results from their research, and its success is measured only by theirs.
- GRIP is designed to help the chemist visualize his molecules, his density maps, etc., so that he can use his knowledge to guide computational processes. That is, it is an aid to, not a surrogate for, human thinking and manipulation. Hence a strong emphasis is placed on human factors research and on human engineering of the system.
- GRIP is designed to serve many users, not one or two, so it must include an armory of alternative tools and techniques.
- GRIP is designed to interface smoothly with any batch computations its users must do, and to incorporate on-line facilities for all computations that can reasonably be done "while you wait."
- We as computer scientists are interested in GRIP as a test-bed for research in man-machine systems design, in man-machine interaction, and in the design of distributed computing systems.

A corollary of these objectives is that we are heavily dependent on observation of and feedback from real users attempting to solve real problems.

Our users are almost exclusively working on the structures of molecules of considerable biochemical interest: proteins and nucleic acids. We advance health-oriented biochemical research by enhancing the productivity of individual researchers through better tools.

1.1. Summary of GRIP Usage by year, 1975-1980

Table I summarizes the use of the GRIP system for all purposes since we began demonstrations and productive operation on July 15, 1975. We have not tried to estimate the system time spent on development before the beginning of productive operation but know it to be many hundreds of hours. Because we changed from manual to machine logging of GRIP sessions in mid-1976, we believe the true buildup of system usage to be substantially greater than suggested by these data. We have observed that users tend to overestimate the time they spend using GRIP.

Table I. GRIP Use by Year (Hours)

	1975	1976	1977	1978	1979	1980	Totals
Production	329	581	781	1034	1108	556	4389
Demonstrations	12	50	161	137	43	57	460
Development	297	186	198	213	345	109	1348
Totals	638	817	1140	1384	1496	722	6197

Table II gives the use of the GRIP system by year for each team of biochemists. These teams are identified by their principal investigators.

Table II. GRIP Production Time (Hours)

User	1975	1976	1977	1978	1979	1980	Total
Hermans	7	29	42	13	11	-	102
Kim	200	321	105	24	49	42	741
Richardson	83	79	91	188	384	297	1122
Lipscomb	12	-	-	102	-	-	114
Carter	27	21	-	4	5	16	73
Jensen		46	62	-	-	-	108
Tsernoglou		85	11	-	-	-	96
James			19	-	-	-	19
Low			55	191	65	-	311
Davies			85	92	-	-	177
Schiffer			35	28	26	28	89
Amma			163	35	-	-	198
Wright			41	-	96	-	137
Hendrickson			72	80	34	-	186
Schevitz				74	-	-	74
Love				94	-	-	94
Kartha				109	-	-	109
Taylor					89	45	134
Rich					78	-	78
Sarma					188	-	188
Olson					20	-	20
Bugg					39	-	39
Premilat					24	-	24
Amzel						98	98
Hardman						27	27
Eggleston						3	3
Total Hours	329	581	781	1034	1108	556	4389

Table III is a list of the biochemists whose research teams have used the GRIP system and their institutions. These are listed in the order of their first use of GRIP. For groups sending more than one biochemist to use our system, the principal investigator is given first and the names of his colleagues follow indented. The institutions of these colleagues are given only where they differ from the principal investigator's. In five cases, Sarma, Rich, Love, Sigler, and Amzel, the principal investigator has made little or no direct use of GRIP himself.

Table III. GRIP Users (1975-1980)

J. Hermans	University of North Carolina
D. R. Ferro	Istituto di Chimica delle Macromolecole
J. E. McQueen	
T. Kuntz	University of California School of Pharmacy, San Francisco
M. Vacatello	Institute of Chemistry, University of Naples, Italy
S. H. Kim	Duke University
J. L. Sussman	
R. W. Warrent	
S. R. Holbrook	
G. M. Church	
W. Shin	
C. J. Alden	
D. E. Richardson	Duke University
J. S. Richardson	
E. D. Getzoff	
J. A. Tainer	
D. McRee	
W. N. Lipscomb	Harvard University
J. L. Crawford	
C. W. Carter	University of North Carolina
R. A. Jones	
L. H. Jensen	University of Washington
K. Watenpaugh	
R. E. Stenkamp	Yale University
D. Tsernoglou	Wayne State University
G. A. Petsko	
M. James	University of Alberta
L. T. J. Delbaere	
G. Brayer	
B. W. Low	Columbia University
A. Sato	
M. Kimball	
D. R. Davies	National Institutes of Health
M. C. Liu	
E. A. Padlan	
M. Schiffer	Argonne National Laboratory
E. L. Amma	University of South Carolina
R. L. Girling	
R. C. Paslay	

H. T. Wright	Princeton University
W. Hendrickson	Naval Research Laboratory
P. B. Sigler A. Podjarny R. W. Schevitz	University of Chicago
W. E. Love W. E. Royer	Johns Hopkins University
G. Kartha	Roswell Memorial Institute
H. C. Taylor	Berkeley Springs Research Consortium
A. Rich N. Woo	Massachusetts Institute of Technology
R. Sarma A. Laudin	SUNY, Stony Brook
A. Olson	National Resource for Computational Chemistry
C. Bugg R. Almassy J. Fontecilla	University of Alabama
S. Premilat	Université de Nancy, France
M. Amzel S. Bryant	Johns Hopkins University
K. Hardman	IBM Yorktown Heights Research Center
D. Eggleston	University of North Carolina

1.2. Changes in Resource Direction and Problems

The 1980-81 year has been devoted primarily to getting the facilities and personnel required for the development of GRIP-X. The facilities are now in place and we are proceeding with the design of GRIP-X. Our hardware configuration is non-standard in ways which give us a great deal more capacity for our money, but which will not affect the exportability of our finished product.

Dr. Lynn TenEyck has joined the project as director and Research Associate Professor of Computer Science. Dr. TenEyck is a macromolecular crystallographer and structural biochemist, with particular research interests in computational methods for protein crystallography and interactive graphics. He plans to use our new system for research in numerical methods for macromolecular crystallography. This is a new direction for us. Previously we have been completely dependent on our clients for direction and information on the biochemical aspects of our work. We still intend to depend primarily on client information and direction. However, we now have more ability to interpret and supplement the client information, and we can interact more knowledgeably with our clients.

Because of our overriding concern with facilities and design of the new system we did not advertise the availability of the GRIP-75 system during 1980. The natural result is that we had fewer clients. We did serve three new users, two of whom completely re-fit entire protein molecules. Since our staff situation has improved we are resuming limited advertising of our facility. As soon as we finish building our new system we intend to concentrate on client service as we have in the past. We expect that the new system's unique fitting and refinement aids will attract quite a few clients. At present GRIP-75 remains a powerful and useful tool, but is no longer unique.

1.3. Core Research and Development Summaries

1.3.1. Facilities for GRIP-X

Most of our effort over the last year has been devoted to procuring and installing the facilities for our next version of GRIP. By careful configuration analysis and extensive use of second-source vendors we were able to stretch our equipment budget of $207,253 to get a VAX 11/780 with 750 KB of memory and 300 MB of disk space for only $118,067. The Computer Science Department had obtained money from NSF for another VAX for departmental use. By pooling resources we have come up with a situation in which everybody wins. In exchange for some of the currently surplus capacity of our VAX we have obtained, through the Computer Science Department and the Microelectronics Center of North Carolina, the use of 1.25 MB of memory (in addition to the 750 KB we bought) and a magnetic tape drive. We share the GRIP VAX with other graphics users in the department; in return we get the use of the Ikonas raster graphics system and the full resources of the department VAX — for example, the Versatec printer/plotter and a Hewlett-Packard four-pen plotter.

Our effective configuration is

- VAX 11/780 with UNIBUS but no MASSBUS;
- the UNIX operating system (Fourth Berkeley version for the VAX)
- 2 MB memory
- 300 MB disk storage
- 800/1600 bpi dual density tape drive
- Vector General 3303 vector graphics display
- Ikonas RDS-3000 image processing and display system
- Summagraphics data tablet
- 16-channel (expandable to 32) analog to digital converter
- serial link to department VAX, which has hard copy plotters, printer, and a dial-up connection to the national "USENET" UNIX network

Another large gain from pooling resources with the department VAX has been reduction of maintenance costs. We can use each machine to verify faults in the other machine. Rapid identification of defective circuit boards translates directly to shorter and cheaper service calls.

At present all of the major hardware components for the new GRIP system are in place and running, though not quite complete. The Vector General 3303 graphics display does not yet have the clip/zoom option installed; delivery is scheduled for mid-April. We have not completed fabrication of the interactive devices and the physical workstation which will be used to control the program. However, the computer system is running well; the operating system software is working very well; and the VG 3303 is a major improvement over the VG 3 on which GRIP-75 runs.

Two major tasks remain with respect to GRIP facilities. We need to build the GRIP workstation, and we need to plan for the future. The workstation, including the displays and interactive devices, has been designed by James S. Lipscomb. Lipscomb drew heavily on the experience we obtained from GRIP-75, including a human factors analysis of the way the system was actually used, to develop a design which should be substantially easier to use for long periods without fatigue. The new design should be easier to use than the existing system, in part because a great deal of attention was given to simplifying the layout and control of interactive devices. We are presently fabricating a test version of the new workstation.

We have been convinced for some time that a color graphics facility for GRIP would be very desirable. Color provides another dimension which we can use to encode information for our users. Unfortunately there have been no color graphics systems with the line drawing speed and update rate we require. This situation has recently improved. Color line drawing displays have been developed by several manufacturers which, although they do not have a full range of color, do have adequate speed. Raster graphics systems with color maps and internal processors are another promising avenue. The Ikonas RDS-3000 is an extremely high performance raster graphics system, and we hope to experiment with it for this purpose. These systems will be used to present more of the information inherent in the chemist's data than we can presently show. Our present program designs are reserving the parameters needed to implement this.

1.3.2. Design of the New GRIP

The field of protein crystallography has moved rapidly in the last five years. GRIP-X will have to be far more flexible and powerful than GRIP-75 if we are to lead in the field of molecular graphics. We identify three categories of users: *fitters*, *viewers*, and *movers*. *Fitters* are protein crystallographers adjusting or creating a molecular model to fit an electron density map. *Viewers* are those studying a series of structures looking for homologies or attempting to characterize macromolecular structures. *Movers* are biophysical chemists studying molecular interactions or molecular dynamics. All three categories of users place special demands on a molecular graphics system.

Fitters typically work in two stages. The first stage is obtaining a molecular model, by hook or by crook. The second stage, at least in recent years, is to refine the molecular model against the crystallographic data. Both steps require the ability to edit the molecular model conveniently. Lack of such facility is one of the deficiencies in GRIP-75. We are designing the new GRIP to include editing of the structure at several levels — the atomic level, the residue level, and perhaps the secondary and tertiary structure levels.

There is no general agreement concerning the best methods to be used during the refinement stage. Thus GRIP must not only support refinement, it must support research on refinement methods. We are proposing to make available to the user a variety of automatic and semi-automatic aids to fitting, such as bump checkers, on-line geometry idealizers, and perhaps a utility to evaluate measures of the current goodness of fit to the experimental electron density map. We are also planning to include a convenient interface to batch programs for such tasks as structure factor calculation, partial structure difference map calculation, and structure factor least squares refinement. Finally, we will support generation and manipulation of structures with non-standard geometry. (Such structures can easily arise during refinement.)

Viewers generally have very elaborate graphics requirements. They need to be able to manipulate several structures at once, with both automatic and manual control of relative orientation. They need to be able to edit the picture (as distinguished from editing the molecule) very extensively. Viewers need the ability to identify and manipulate as units various substructures within the molecule — helices, sheets, and domains, for example; to selectively display chemically significant features of the molecule; and to show various abstractions of the molecular structure. (Common structural abstractions are the α-carbon skeleton of proteins, ribbon diagrams, and representation of helices by cylinders or β-sheets by broad arrows.) Present plans for GRIP-X do not include immediate full support of all of these features, but do include the hooks necessary to install them. We will provide the ability to identify and selectively display various subsets of a structure.

We do not yet have a satisfactory analysis of the requirements of *movers*. Obviously they need some of the features required by viewers. Just as obviously, they need a wide variety of automatic aids for evaluating different conformations and interactions. We presently believe that the same features of the system design which will provide automatic aids for fitters will also be adequate to incorporate the automatic aids required by movers.

The design and implementation of GRIP-X is in progress cooperatively with the IBM United Kingdom Scientific Centre at Winchester, England. We are striving for a common architecture for our systems (that is, they should appear the same to a user) even though we will necessarily have different implementations. Dr. William V. Wright, who directed work on GRIP-75, is now at the IBM U. K.

Scientific Centre. The new design incorporates some novel human interaction concepts developed by Dr. Wright. It will also provide, in addition to the manipulation of structures by knobs and joysticks as in the present system, some very interesting ways of specifying structural manipulations from a data tablet. (We are continuing our popular tradition of providing our clients with a wide selection of techniques and strategies.) The design effort has proceeded to the specification of an adjunct language for combining system primitive operations and a data structure which we believe is sufficiently general to support all of our intended applications and is expandable for new applications. We are now designing internal data structures related to graphical operations and structural manipulations.

1.3.3. Ridge-line Methods for Initial Fitting of Models to Densities.

From a biochemical point of view the most exciting progress during the last year has been the work by Thomas V. Williams on developing methods for semi-automatic interpretation of electron density maps. Present methods for the initial interpretation of an electron density map require the construction of a contoured map which shows the probable domain of a whole molecule. This map is then examined manually and the polypeptide chain is traced. The chain tracing is used to build a molecular model, either physically or on a computer graphics system. (A few models have been built entirely on computer graphics systems, including the chain tracing; this is extremely difficult because of the limited field of view of present graphics systems.) This process takes weeks. Williams's method looks as though it might be able to obtain an initial fitting in a few days.

The approach taken by Williams is related to those explored by Jonathan Greer and by C. K. Johnson. The computer extracts ridge lines from the three-dimensional density map, connecting them to form spanning trees. The computer then examines the trees and graphically presents a tentative interpretation to the chemist. The chemist can modify the interpretation, for example, by altering the assignment of main chain and side chain at branch points, or identifying specific residues in the sequence, or reversing the direction of the main chain in a region of the map. The program then generates a new interpretation based on the chemist's assumptions and presents the results for further modification. As sections of the molecule are identified, the ridge line graph becomes a molecular model.

We expect this approach to succeed beyond previous explorations because of the insertion of human pattern recognition into the process. Ridge line abstractions of the electron density map are difficult to interpret automatically because they are noisy, contain gaps from sampling artifacts, and contain extra connections to bound solvent molecules, or cross-links following hydrogen bonds in the structure. The combination of spurious gaps and spurious connections makes the total topology of the ridge lines differ substantially from that of the molecule. However, there are many regions — in fact, most of the volume of the molecule — in which the ridge lines are a good representation of the molecular structure. The difficulties encountered by earlier attempts to solve this problem automatically are, we think, due almost entirely to the inability of programs to backtrack sensibly when they misinterpret a section of the map. A program can generate a possible interpretation of a ridge line map rapidly, but the interpretation will almost certainly be wrong — in many cases, ludicrously so. The interactive graphics system then lets the chemist pick out those areas which are correct, and alter the interpretation of those sections in which the program went wrong. For example, the chemist may decide to bridge a gap, or break a connection that seems to be spurious or weak, basing the decision on

his chemical knowledge of the properties of the molecule. The program can then preserve the correct regions and derive a new interpretation for the dubious regions based on the new assumptions.

We are particularly encouraged because this method combines the researcher's pattern recognition abilities and chemical intuition with the computer's rapid generation of trial structures. This strikes us as much more feasible and flexible than trying to come up with a set of rules which would permit the computer to do the whole job. That approach essentially requires that the program have as much knowledge of stereochemistry and density maps as a chemist has acquired through years of experience. Additionally, Williams has obtained some very encouraging results representing real electron density maps as ridge lines. The data assumptions underlying the method thus seem sound. We have high hopes for the success of this project.

1.3.4. High Performance Raster Graphics

There are aspects of molecular graphics for which raster graphics are much better suited than line-drawing graphics. Examples are space filling representations of molecules and full color displays. The Ikonas color graphics image processing system attached to our VAX has a frame buffer that can be used either for a picture 512 by 512 pixels with 24 bits per pixel, or for pictures 1024 by 1024 pixels with six bits per pixel; a color map, which can map any pixel value into 30 bits of color information; a cross-bar switch, which can arbitrarily permute the bits in each pixel before they go through the color map; an internal 32 bit processor with a 200 nsec cycle time; a multiply-accumulator module, which can multiply a pair of 16-bit numbers and accumulate a 35-bit sum in 200 nsec; a video digitizer for storing video signals into the frame buffer; and a high resolution monitor. We have begun experiments to determine how a device of this nature might be used for interactive molecular graphics.

James S. Lipscomb has continued his work on depth cues reported last year, and finds that the kinetic three-dimensional effect is a powerful aid in visualizing the structure of a complex molecule even on a full color raster graphics system. This was done by storing several images in the frame buffer at once, and switching among the images as the user moved a hand control back and forth across a data tablet. Lipscomb also confirmed his previous result that kinesthetic feedback is an important aid. With as few as four views in the frame buffer a satisfactory illusion of continuous rocking is obtained by the person operating the hand control; to other viewers the illusion is weaker.

Langridge, Ferrin, Kuntz, and Connolly at the University of California at San Francisco Computer Graphics Laboratory have demonstrated the value of representing molecular surfaces by a collection of points placed according to the reentrant surface ideas of Lee and Richards. This representation requires the drawing of some 5000 - 7000 dots, with color coding a very valuable adjunct. Such a representation is most useful when combined with a stick drawing of the molecule and dynamic motion to change the viewpoint, enlarge features of interest, etc. This sort of dynamic drawing cannot be done on a classic frame buffer system, but it appears possible on the Ikonas. We will be able to use the multiply-accumulator module to transform the points according to the current viewing transformation, and the Ikonas internal processor to selectively erase the old points, draw the new points, and generate lines between selected pairs of points. We expect these displays to be a valuable adjunct to GRIP-X.

One of the best possible depth cues, for those who can see it, is stereo. The Ikonas monitor runs at 60 Hz non-interlaced. By using the cross-bar switch to exchange images every frame and having the user view the display through an

appropriate shuttering device we expect to be able to show very stable stereo images with full color and 512 line resolution, or eight colors and 1024 line resolution. In a system of this nature the limit on the complexity of the picture is determined by the fineness of the raster, rather than by the number of vectors to be drawn. Any picture that can be stored in the frame buffer can be viewed in full stereo by this method. This raises the very interesting question of a suitable representation for an electron density map on a stereo raster graphics system.

David M. Holmes, one of the GRIP research assistants in 1980, developed an extremely creative use of the Ikonas color map. He is able to improve the three dimensional appearance of a molecular drawing by representing the molecule in conventional style as a collection of highlighted spheres. The unique feature of his approach is that the apparent position of the light source is under the direct control of the user in *real time*. As the user moves a hand control the picture changes as though that control were positioning a spotlight. Holmes accomplishes this very difficult task by storing in the frame buffer a value encoding the direction and color of the vector normal to the surface at that point. Then, given a position for the light source, he can calculate what the color value should be for each of the possible directions of the surface normal. He uses this information to set the *color map* so that each facet of the surface is shown in the correct color and brightness. Thus changing the position of the light source is reduced to the rapid operation of loading the color map, rather than the costly operation of recomputing the contents of the frame buffer. From the user's point of view, the net effect is substantially improved three dimensional perception. In any view there are areas that seem rather flat. An appropriate position for the light source can optimize the highlighting for any part of the structure. With Holmes's system that position can be found easily and rapidly for photography. More important, the *moving* highlighting enhances perception and intuition.

2. Administrative Changes

The principal administrative change during the 1980-1981 year was the appointment of a biochemist, Dr. Lynn F. TenEyck, as the project director. Dr. TenEyck is the senior full-time member of the project. Dr. Brooks, the Principal Investigator, provides overall direction. Two of the major contributors to GRIP-75, Mike Pique and James Lipscomb, have assumed full-time status with the project. Pique completed the requirements for his M.S. degree in computer science this fall; Lipscomb has completed all of the requirements except a trivial one for his Ph.D.

We have recruited two new graduate students for the project this year. Lawrence M. Lifshitz has a B.S. in physics from Harvard University, and a strong interest in scientific computing. He is in our Ph.D. program; we hope to have him with us on the project for several years. Michael Holder is in the M.S. program here. He has a B.S. in mathematics, and several years experience programming command and control computers for the U. S. Navy. We expect Holder to be with us for at least another year.

Phil Stancil, our electronics engineer hired at the end of the 1979-1980 year, has proven an invaluable asset to the project. He has proven adept at converting experimental prototype equipment into soundly engineered production devices. He has demonstrated the ability to design new equipment as we need it. Finally, without his knowledge and ability our maintenance costs would be greatly increased.

3. Highlights

The large molecules studied by our clients are extremely complex. Their properties depend in subtle ways on the specific three-dimensional arrangement of the atoms which comprise the molecule. It is difficult for a chemist to visualize in detail a structure with several thousand atoms. The only satisfactory method for learning such a structure is to study a model in three dimensions. Mechanical models are unsatisfactory. The metal and plastic get in the way, and are difficult to modify. A computer model, however, can be rotated into any position, looked through, bent, colored, and generally taken apart for study. The GRIP system enables a chemist to see new things in his molecules, and manipulate the molecule to see the consequences of hypothetical changes. These features greatly improve the chemist's insight into the properties of the molecule. This insight is our most important product. We are pleased to report on two of our projects directed straight at increasing the chemist's understanding of his data.

3.1. Ridge line map fitting

Production of a molecular model from an electron density map is a process that has vigorously resisted automation. T. V. Williams is producing a system based on artificial intelligence methods which relies on the real intelligence of the chemist when the artificial intelligence of the computer fails to interpret the map.

Williams's work is based on transforming the data into a form that looks like the stick figure pictures of molecules chemists are used to dealing with. The usual representation of electron density data on a computer graphics system is as a sort of birdcage around the space occupied by the molecule. The molecular shapes are very complex, so the density (for a good map) has the appearance of a twisting, branching tube. The "ridge line" representation of a map consists of running lines down the middle of the tubes and throwing away the tubes. The goal is to take advantage of the chemist's knowledge of molecular structure while exploiting the computer's ability to rapidly apply a lot of rules. When the computer gets confused the chemist makes the decisions.

3.2. Raster Graphics

The work of J. S. Lipscomb and D. M. Holmes has shown that it is possible to get greatly improved three-dimensional perception of images produced on a raster graphics system by changing the pixel interpretation while the picture is being displayed. Lipscomb was able to produce moving pictures of very complex objects; Holmes was able to change the highlighting (an important depth cue) at will under direct and immediate user control. In both cases the important result is much improved perception of complex information.

4. Resource Advisory Committee and Allocation of Resources

Table IV lists the members of our Advisory Committee. We currently offer the facility, and such help as we can give, free of charge to any chemist:

- who has a scientifically interesting problem, as assessed by the Committee,
- whose work is at a stage where our facility might be useful,
- who is willing to commit his time, travel money, and effort to a serious use of the facility, and
- who is willing to give us written and oral feedback from his experience.

Table IV: Advisory Committee Members

Name	Degree	Title	Department	Institution
F. P. Brooks	Ph.D.	Kenan Professor & Chairman	Computer Science	UNC-CH
J. Hermans	Ph.D.	Professor	Biochemistry	UNC-CH
D. Richardson	Ph.D.	Professor	Biochemistry	Duke U.
J. Richardson	M.S.	Assistant Professor	Anatomy	Duke U.
W. V. Wright	Ph.D.	Senior Systems Architect	UK Scientific Centre	IBM England

5. Dissemination of Information

5.1. Announcements of Availability

As explained above, during 1980 we made no effort at publicizing the resource's availability because of our limited capacity to increase our service level, and our desire to move forward in installing our new facilities.

5.2. Demonstrations

Some 57 hours of 1980 resource time were used in demonstrations. During 1980 we demonstrated GRIP to the following biochemists and computer scientists.

Dr. R. Adrion	National Science Foundation
Dr. J. D. Andose	Merck and Company
Dr. C. Bolling	Bell Laboratories
Dr. B. L. Bush	Merck and Company
Mr. C. R. Carroll	California Institute of Technology
Mr. M. Conrad	University of North Carolina
Dr. N. Einspruch	University of Miami
Dr. R. Ernshaw	University of Leeds, England
Dr. Hehner	University of Toronto
Dr. Z. Kedam	SUNY Stony Brook
Dr. E. D. Lazowska	University of Washington
Mr. J. Logue	IBM Components Division
Dr. J. Meindl	Stanford University
Mr. A. Morffew	IBM UK Scientific Centre, England
Dr. J. C. Mudge	Digital Equipment Corporation
Dr. T. P. Murtaugh	Cornell University
Dr. J. Ortega	University of Virginia
Dr. U. Shani	University of Rochester
Dr. C. Smith	University of Texas
Mr. M. Tarvid	Independent Consultant
Dr. S. G. Wasilew	Bell Laboratories
Dr. N. Weste	Bell Laboratories

PART II, SECTION A — DRR SCIENTIFIC SUBPROJECT FORM

PROJECT NUMBER: P41RR000898-07 — REPORT PERIOD: 05/01/80 TO 04/30/81 — INST: UNC

Fill out a separate Subproject Form for Core Collaborative, or Training. Check one of following:

[X] CORE RESEARCH AND DEVELOPMENT [ ] COLLABORATIVE WORK IN THE GRAPHICS [ ] TRAINING

Descriptive Title (30 characters) or less	Science Code AXIS I	Science Code AXIS II	(a) Investigator(s) Last Name First I. (b) Department (c) Another Institution	Name System 1/	Hours Used	Resource Staff-Hrs	DRR Funds Allocated
1. Ridge-Line Methods for fitting models to densities. An algorithm is being developed to partially automate the initial interpretation of an electron density map, with or without an initial amino acid sequence.	-	52	a. Brooks, F., TenEyck, L., Williams, T. b. All UNC Dept. of Computer Science	Computer Graphics System	150	1541	
2. Color Raster Graphics for Molecular Display Exploration of depth cues and dynamic motion methods appropriate for very high performance full color raster graphics systems.	256	52	a. Fuchs, H., Lipscomb, J., Holmes, D. b. All UNC Dept. of Computer Science	Computer Graphics System; VAX computer system	150	1820	
SUB-TOTALS: No. of Subprojects 2							

1/ Identify Resource Technology Used

2/ Give Hours Resource Technology Used

PART II, SECTION A — DPR SCIENTIFIC SUBPROJECT FORM

GRANT NUMBER: N 0 0 1 4 - 8 0 - C - 0 8 9 8 — 0 7 — REPORT PERIOD: 05/01/80 TO 04/30/81 — HOST: UNC

[illegible] X [illegible]

Subproject Title (40 characters)	Science Code AXIS I	Science Code AXIS II	(a) Investigator(s) Last Name First I. (b) Department (c) Associate Institution	Usage Factor: Research Technology 1/	Usage Factor: Hours Used 2/	Usage Factor: Person-Years (Std) Effort	DDP Funds Allocated
3. Design of GRIP-X Definition of user architecture, design of data base, designs of internal data structures, definitions of extended capabilities, definition of system task and goals.	-	52, 42	a. Brooks, F., TenEyck, L., Pique, M. b. All UNC Dept. of Computer Science	VAX Computer System	300	2814	
4. Facilities Development for GRIP-X Operating system implementation and extension, installation and checkout of new hardware and software, documentation of new system, procurement of new hardware.	-	52, 42	a. Brooks, F., TenEyck, L., Stancil, P., Seaver, T., Smotherman, M., Hoffman, D., Middleton, D., Colotta, J., Lifshitz, L., Holder, M. b. All UNC Dept. of Computer Science	VAX Computer System	500	7841	
SUB-TOTALS: No. of Subprojects 2							

1/ Identify Resource Technology Used
2/ Give Hours Resource Technology Used

PART II, SECTION A — DOE SCIENTIFIC SUBPROJECT FORM

PROJECT NUMBER: P 4 1 P P 0 0 8 9 8 – 0 7 — REPORT PERIOD: 05/01/80 TO 04/30/81 INST: UNC

Subproject Title (80 characters)	Science Code AXIS I	Science Code AXIS II	(a) Investigator(s) Last Name, First I. (b) Telephone # (c) Name of Institution	Users Facility Research Technologies 1/	Users Facility Hours Used 2/	Users Facility Person-Hours 2/	DOE Funds Allocated
1. Conconavalin A	8,13	76b	Hardman, K., IBM Yorktown Heights Research Center	Computer Graphics System	27	47	
2. Bence-Jones Protein		76b	Amzel, M., Bryant, S., Dept. Biochem. Biophys. Johns Hopkins University	Computer Graphics System	98	118	
3. High Potential Iron Sulphur Protein			Carter, C., Jones, R., Dept. of Biochemistry Univ. of North Carolina Chapel Hill, NC	Computer Graphics System	16	0	
4. Ribonuclease - S			Taylor, H. Berkeley Springs Research Consortium, Berkeley Springs, West Virginia	Computer Graphics System	45	0	
5. Phenylalanine tRNA		74j, 74k	Kim, S., Alden, C., Dept. of Biochemistry Duke University	Computer Graphics System	42	0	
6. Mcg Bence-Jones Protein	8, 13	76b, 64	Schiffer, M., Biological and Medical Research, Argonne National Lab.	Computer Graphics System	28	48	
SUB-TOTALS: No. of Subprojects	6						

1/ Identify Resource Technology Used
2/ Give Users Resource Technology Used

PART II, SECTION A — DRR SCIENTIFIC SUBPROJECT FORM

GRANT NUMBER P41RP00898-07 — REPORT PERIOD: 05/01/80 TO 04/30/81 — INST: UNC

Fill out a separate Subproject form for Core, Collaborative or Training. Check one of following:

☐ CORE RESEARCH AND DEVELOPMENT ☒ COLLABORATIVE RESEARCH AND SERVICE ☐ TRAINING

1 Descriptive Title (80 characters) Abstract	2 Science Code AXIS I	2 Science Code AXIS II	3 (a) Investigator(s) Last Name, First I. (b) Department (c) Non-Host Institution	4 Usage Factor: Resource Technologies 1/	4 Usage Factor: Hours Used 2/	5 DRR Funds Allocated: Resource Staff Hours
7. Superoxide dismutase	17	50, 74d	Richardson, D., Richardson, J., Tainer, J., Getzoff, E., Dept. of Biochemistry Duke University	Computer Graphics System	260	0
8. Spot hemoglobin	1, 17	74d, 74c	Richardson, D., Richardson, J., Getzoff, E., Tainer, J. Dept. of Biochemistry Duke University	Computer Grahpics System	25	0
9. Reciprocal space data analysis	—	74	Richardson, D., Richardson, J., McRee, D. Dept. of Biochemistry, Duke University	Computer Graphics System	12	0
10. Thrombin	13	90	Eggleston, D., Dept. of Chemistry Univ. of North Carolina Chapel Hill	Computer Graphics	3	30
SUB-TOTALS: No. of Subprojects	4					

1/ Identify Resource Technology Used

2/ Give Hours Resource Technology Used

PART II, SECTION B	GRANT NUMBER	P	4	1	R	R	0	0	8	9	8	—	0	7
INSTITUTION UNC - Chapel Hill	REPORT PERIOD 05/01/80 TO 04/30/81													

Fill out a separate form for each of the following categories: Check one

☒ CORE RESEARCH & DEVELOPMENT ☐ COLLABORATIVE RESEARCH & SERVICE ☐ TRAINING

Number Published:	BOOKS		PAPERS	1	ABSTRACTS		
Number IN Press	BOOKS		PAPERS	1	ABSTRACTS		

Author(s)	Title of Article, Journal, Volume, Number, Pages (e.g., 44-48), Year Published
*Lipscomb, James S.	"Reversed Apparent Movement and Erratic Motion with Many Refreshes per Update," Computer Graphics, 15, #2 (in press)
*Pique, Michael E.	Nested Dynamic Rotations for Molecular Graphics, M.S. thesis, Department of Computer Science, University of North Carolina at Chapel Hill, 1980.

Indicate by an asterisk (*) that the resource was given credit.

See Instructions, Page 6.

PART II, SECTION B	GRANT NUMBER	P	4	1	R	R	0	0	8	9	8	—	0	7
INSTITUTION UNC - Chapel Hill	REPORT PERIOD 05/01/80 TO 04/30/81													

Fill out a separate form for each of the following categories: Check one

☐ CORE RESEARCH & DEVELOPMENT ☒ COLLABORATIVE RESEARCH & SERVICE ☐ TRAINING

Number Published:	BOOKS		PAPERS	1	ABSTRACTS	1	
Number IN Press	BOOKS		PAPERS	1	ABSTRACTS		

Author(s)	Title of Article, Journal, Volume, Number, Pages (e.g., 44-48), Year Published
*Fontecilla-Camps, J. C., Almassy, R. J., Suddath, F. L., Watt, D. D., and C. E. Bugg	"Three-dimensional Structure of a Protein from Scorpion Venom: A New Structural Class of Neurotoxins," Proc. Natl. Acad. Sci. USA, 77, #11, pp. 6496-6500, 1980.
*Taylor, H.C., Richardson, D.C., Richardson, J.S., Wlodawer, A., Komoriya, A., and I. M. Chaiken	"'Active' Conformation of an Inactive Semisynthetic Ribonuclease - S." submitted to J. Mol. Biol.
**Wright, H.T., Manor, P.C., Beurling, K., and J.R. Fresco	"A Crystal Structure of Yeast $tRNA^{gly}$. Possible Solvent Effects on tRNA Conformation," 7th Katzir-Catchalsky Conf, Israel

**Conference presentation only; conference director requested no discussion of methods; therefore use of resource not acknowledged.

Indicate by an asterisk (*) that the resource was given credit.

See Instructions, Page 6.

PART II

GRANT NUMBER: P41RR00898-07 REPORT PERIOD May 1, 1980 TO: April 30, 1981 UNC

SECTION C RESOURCE SUMMARY TABLE — BIOTECHNOLOGY RESOURCES

RESOURCE COMPONENT	1 Number Subproj	2 Number Publica	3 Number Investigators	4 Usage Factor: Resource Technologies 1/	Hours Used 2/	Resource Staff Hrs	5 BRP Funds Allocated $	6 Resource Fees ($) Collected	7 Other Funds $
CORE RESEARCH & DEVELOPMENT									
TOTAL:	4	2	15	Computer graphics system	1200*	13936			
COLLABORATIVE RESEARCH & SERVICE									
TOTAL:	10	3	14	Computer graphics system	556	243			
TRAINING									
TOTAL:									
ADMIN/MISC									
TOTAL:	XX	XX							
DOWN TIME									
TOTAL:	XX	XX	XX	Computer graphics system	(336**)	-		XX	XX
GRAND TOTALS:	14	5	19		1756	14179		-0-	-0-

* Estimated; our new systems do not yet have automatic accounting.

** Two weeks scheduled downtime to move the system to a neighboring room and rebuild the interactive devices, not included in grand total.

1/ Identify Resource Technology Used
2/ Give Hours Resource Technology Used
See Instructions, Page 6.