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SECTION I - RESOURCE IDENTIFICATION

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SUMEX-AIM Executive Committee

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Table of Contents

Section	Page
List of Figures	iv
1. Resource Identification	
2. Resource Operations	1
2.1 Progress	1
2.1.1 Resource Summary and Goals	1
2.1.2 Technical Progress	5
2.1.2.1 Facility Hardware Development	5
2.1.2.2 System Software Development	15
2.1.2.3 Network Communication Facilities	18
2.1.2.4 System Reliability and Backup	25
2.1.2.5 Core Research	26
2.1.2.6 User Software and Intra-Community Communication	33
2.1.2.7 Documentation and Education	34
2.1.2.8 Software Compatibility and Sharing	34
2.1.3 Resource Management	36
2.1.3.1 Organization	36
2.1.3.2 Management Committees	36
2.1.3.3 New Project Recruiting	37
2.1.3.4 Stanford Community Building	39
2.1.3.5 Existing Project Reviews	40
2.1.3.6 AIM Workshop Support	40
2.1.3.7 Resource Allocation Policies	41
2.1.4 Future Plans	43

Table of Contents

2.2	Summary of Resource Usage	46
2.2.1	Overall System Loading	46
2.2.2	Relative System Loading by Community	48
2.2.3	Individual Project and Community Usage	52
2.2.4	Network Usage	59
2.3	Resource Equipment Summary	61
2.4	Publications	62
3.	Resource Finances	63
3.1	Budget Information	63
3.2	Resource Funding	63
4.	Collaborative Project Reports	64
4.1	National AIM Projects	65
4.1.1	Acquisition of Cognitive Procedures (ACT)	66
4.1.2	Chemical Synthesis Project (SECS)	72
4.1.3	Hierarchical Models of Human Cognition	83
4.1.4	Higher Mental Functions Project	89
4.1.5	INTERNIST Project	92
4.1.6	Medical Information Systems Laboratory	97
4.1.7	PUFF/VM Project	98
4.1.8	Rutgers Computers in Biomedicine	108
4.1.9	Simulation of Cognitive Processes (SCP)	122
4.2	Stanford Projects	129
4.2.1	AI Handbook Project	130
4.2.2	AGE - Attempt to Generalize	133
4.2.3	DENDRAL Project	139
4.2.4	HYDROID Project	160

Table of Contents

4.2.5	MOLGEN Project	162
4.2.6	MYCIN/EMYCIN Project	169
4.2.7	Protein Structure Project	177
4.2.8	RX Project	181
4.3	Pilot AIM Projects	188
4.3.1	Communication Enhancement Project	189
4.3.2	Computerized Psychopharmacology Advisor	195
4.4	Pilot Stanford Projects	203
4.4.1	Quantum Chemical Investigations	204
4.4.2	Ultrasonic Imaging Project	209
 Appendix I		
	AI Handbook Outline	214
 Appendix II		
	Satellite Machine Evaluation	221
 Appendix III		
	AIM Management Committee Membership	224

Table of Contents

List of Figures

1.	Current SUMEX-AIM Computer Configuration	12
2.	Planned Intermachine Connections via ETHERNET	13
3.	DEC KI-10 Versus 2020 Performance Under Load	14
4.	TYMNET Network Map	21
5.	ARPANET Geographical Network Map	22
6.	ARPANET Logical Network Map	23
7.	TELENET Network Map	24
8.	Total CPU Time Consumed by Month	46
9.	Peak Number of Jobs by Month	47
10.	Peak Load Average by Month	47
11.	Monthly CPU Usage by Community	49
12.	Monthly File Space Usage by Community	50
13.	Monthly Terminal Connect Time by Community	51
14.	TYMNET Usage Data	59
15.	ARPANET Usage Data	60

SUMEX-AIM RESOURCE PROGRESS REPORT - YEAR 06

This annual report covers work performed under NIH Biotechnology Resources Program grant RR-785 supporting the Stanford University Medical Experimental Computer (SUMEX) research resource for applications of Artificial Intelligence in Medicine (AIM). It spans the year from May 1978 - April 1979.

2 Resource Operations

2.1 Progress

2.1.1 Resource Summary and Goals

The SUMEX-AIM project is a national computer resource with a dual mission: a) the promotion of applications of computer science research in artificial intelligence (AI) to biological and medical problems and b) the demonstration of computer resource sharing within a national community of health research projects. The SUMEX-AIM resource is located physically in the Stanford University Medical School and is administered jointly under the Stanford Departments of Genetics and Computer Science. SUMEX-AIM serves as a nucleus for a community of medical AI projects at universities around the country. SUMEX provides computing facilities tuned to the needs of AI research and communication tools to facilitate remote access, inter- and intra-group contacts, and the demonstration of developing computer programs to biomedical research collaborators.

Overview of AI Research

Artificial Intelligence research is that part of Computer Science concerned with symbol manipulation processes that produce intelligent action (1). By "intelligent action" is meant an act or decision that is goal-oriented, is arrived at by an understandable chain of symbolic analysis and reasoning steps, and utilizes knowledge of the world to inform and guide the reasoning. Some scientists view the performance of complex symbolic reasoning tasks by computer

(1) For recent reviews to give some perspective on the current state of AI, see: (i) Boden, M., "Artificial Intelligence and Natural Man," Basic Books, New York, 1977; (ii) Feigenbaum, E.A., "The Art of Artificial Intelligence: Themes and Case Studies of Knowledge Engineering," Proceedings of the Fifth International Conference on Artificial Intelligence, 1977; (iii) Winston, P.H., "Artificial Intelligence", Addison-Wesley Publishing Co., 1977; and (iv) Nilsson, N.J., "Artificial Intelligence", Information Processing 74, North-Holland Pub. Co. (1975). An additional overview of research areas and techniques in AI is being developed as an "Artificial Intelligence Handbook" under Professor E. A. Feigenbaum by computer science students at Stanford (see page 130 for a status report and Appendix I for a current outline).

programs as the sine qua non for artificial intelligence programs, but this is necessarily a limited view.

Another view unifies AI research with the rest of computer science. It is a simplification, but worthy of consideration. The potential uses of computers by people to accomplish tasks can be "one-dimensionalized" into a spectrum representing the nature of the instructions that must be given the computer to do its job; call it the WHAT-TO-HOW spectrum. At the HOW extreme of the spectrum, the user supplies his intelligence to instruct the machine precisely HOW to do his job, step-by-step. Progress in computer science may be seen as steps away from that extreme "HOW" point on the spectrum: the familiar panoply of assembly languages, subroutine libraries, compilers, extensible languages, etc. illustrate this trend.

At the other extreme of the spectrum, the user describes WHAT he wishes the computer to do for him to solve a problem. He wants to communicate WHAT is to be done without having to lay out in detail all necessary subgoals for adequate performance yet with a reasonable assurance that he is addressing an intelligent agent that is using knowledge of his world to understand his intent, complain or fill in his vagueness, make specific his abstractions, correct his errors, discover appropriate subgoals, and ultimately translate WHAT he wants done into detailed processing steps that define HOW it shall be done by a real computer. The user wants to provide this specification of WHAT to do in a language that is comfortable to him and the problem domain (perhaps English) and via communication modes that are convenient for him (including perhaps speech or pictures).

The research activity aimed at creating computer programs that act as "intelligent agents" near the WHAT end of the WHAT-TO-HOW spectrum can be viewed as the long-range goal of AI research. Historically, AI research has been the primary vehicle for progress toward this objective, although a substantial part of the applied side of computer research and development has related goals, if an often fragmented approach. Unfortunately, workers in other scientific disciplines are generally unaware of the role, the goals, and the progress in AI research.

Currently authorized projects in the SUMEX community are concerned in some way with the design of "intelligent agents" applied to biomedical research. The tangible objective of this approach is the development of computer programs that, using formal and informal knowledge bases together with mechanized hypothesis formation and problem solving procedures, will be more general and effective consultative tools for the clinician and medical scientist. The systematic search potential of computerized hypothesis formation and knowledge base utilization, constrained where appropriate by heuristic rules, empirical data, or interactions with the user, has already produced promising results in areas such as chemical structure elucidation and synthesis, diagnostic consultation, and modeling of psychological processes. Needless to say, much is yet to be learned in the process of fashioning a coherent scientific discipline out of the assemblage of personal intuitions, mathematical procedures, and emerging theoretical structure of the "analysis of analysis" and of problem solving. State-of-the-art programs are far more narrowly specialized and inflexible than the corresponding aspects of human intelligence they emulate; however, in special domains they may be of comparable or greater power, e.g., in the solution of formal problems in organic chemistry or in the integral calculus.

Resource Sharing Goals

An equally important function of the SUMEX-AIM resource is an exploration of the use of computer communications as a means for interactions and sharing between geographically remote research groups engaged in biomedical computer science research. This facet of scientific interaction is becoming increasingly important with the explosion of complex information sources and the regional specialization of groups and facilities that might be shared by remote researchers (2). Our community building role is based upon the current state of computer communications technology. While far from perfected, these developing capabilities offer highly desirable latitude for collaborative linkages, both within a given research project and among them. Several of the active projects on SUMEX are based upon the collaboration of computer and medical scientists at geographically separate institutions; separate both from each other and from the computer resource. The network experiment also enables diverse projects to interact more directly and to facilitate selective demonstrations of available programs to physicians, scientists, and students. Even in their current developing state, communication facilities enable effective access to the rather specialized SUMEX computing environment from a great many areas of the United States (and to a more limited extent from Canada, Europe, and other international locations). In a similar way, the network connections have made possible close collaborations in the development and maintenance of system software with other facilities.

Synopsis of Last Year's Progress

As we complete year 06, the first year of our recent 3-year continuation grant, we can report substantial further progress in the overall mission of the SUMEX-AIM resource. We have continued the refinement of an effective set of hardware and software tools to support the development of large, complex AI programs for medical research and to facilitate communications and interactions between user groups. We have worked to maintain high scientific standards and AI relevance for projects using the SUMEX-AIM resource and have actively sought new applications areas and projects for the community. Many projects are built around the communications network facilities we have assembled; bringing together medical and computer science collaborators from remote institutions and making their research programs available to still other remote users. As discussed in the sections describing the individual projects, a number of the computer programs under development by these groups are maturing into tools increasingly useful to the respective research communities. The demand for production-level use of these programs has surpassed the capacity of the present SUMEX facility and we have been investigating the general issues of how such software systems can be moved from SUMEX and supported in production environments.

(2) A recent perspective on the scientific and financial aspects of technological resource sharing can be found in Coulter, C. L., Research Instrument Sharing, Science, Vol. 201, No. 4354, August 4, 1978.

A number of significant events and accomplishments affecting the SUMEX-AIM resource occurred during the past year:

- 1) On July 1, 1978, Professor Edward Feigenbaum, chairman of the Stanford Department of Computer Science, assumed the role of SUMEX Principal Investigator following Professor Joshua Lederberg's installation as president of The Rockefeller University. We have smoothly completed the management transition and the SUMEX-AIM project and community continue to operate with the same high level of vitality. Professor Lederberg continues to maintain close ties with SUMEX activities as chairman of the SUMEX-AIM Executive Committee. Professor Stanley Cohen, Dr. Lederberg's successor as chairman of the Stanford Department of Genetics, assists in the coordination of project activities with medical research.
- 2) We have continued development of the SUMEX facility hardware and software systems to enhance throughput and to better control the allocation of resources. We also completed installation and evaluation of a connection to TELENET as an alternate source of communications services for our community.
- 3) A first version of the AGE system, partially supported under the SUMEX core research effort, has been completed. It uses the "blackboard model" for coordinating multiple expert sources of knowledge for the solution of problems. This system provides the general control structure and an interactive facility for implementing representations of expert knowledge sources and is being used experimentally by one of the new SUMEX-AIM projects to design a program for modeling aspects of human cognition.
- 4) We successfully completed the design and a demonstration of the MAINSAIL language system as a tool for software portability. A common compiler and code generators and runtime support for TENEX, TOPS-10, TOPS-20, RT-11, RSX-11, and UNIX have been developed as part of this demonstration system and numerous applications programs written by collaborating research groups. Further work past this demonstration phase will be done independently of SUMEX through a private company being formed to continue the development, dissemination, and maintenance of MAINSAIL.
- 5) We have completed plans for a satellite machine that will be able to support more operational demonstrations of mature AI programs and help alleviate system congestion for on-going program development. A proposal for acquiring a DEC 2020 system meeting our requirements is pending approval by the NIH-BRP. We have also assisted the DENDRAL project in planning an independent system suitable for further development and export of chemical structure elucidation programs into the biochemical community.
- 5) The progress of SUMEX-AIM user projects in the development of their respective programs is reported by the individual investigators. We have worked hard to meet their needs and are grateful for their expressed appreciation.

2.1.2 Technical Progress

The following material covers SUMEX-AIM resource activities over the past year in greater detail. These sections outline accomplishments in the context of the resource staff and the resource management. Details of the progress and plans for our external collaborator projects are presented in Section 4 beginning on page 64.

2.1.2.1 Facility Hardware Development

Over the past year, the SUMEX KI-10 configuration, shown in Figure 1, has changed little and continues to operate effectively within its capacity limitations. We completed the procurement of the Systems Concepts SA-10 channel adapter including all parts outstanding as of the last report. This subsystem, with the Calcomp disks and tapes, has functioned very reliably over the past year.

Our primary new facility hardware development efforts this year have been directed at:

- 1) Selection of a satellite processor to allow more operational demonstrations of mature AI programs and to ease loading congestion.
- 2) Planning for the integration of the satellite machine into the KI-10 facility.
- 3) Implementing local communication line control facilities to make more efficient use of available scanner ports.

These are discussed in more detail below.

Loading Background

The SUMEX-AIM facility has been operating at capacity in terms of prime-time computing load for the past several years as documented in our previous annual reports. In spite of implementing a number of strategic facility augmentations over the years, we have not been able to satisfy the computing demands of our community. This condition has constrained the growth of the AIM community and our ability to bring AI programs nearing operational status in contact with potential external user communities while continuing to support on-going program development efforts. We have taken active steps to transfer prime time interactive loading to evening and night hours as much as possible including shifting personnel schedules (particularly for Stanford-based projects). We have also implemented tools to control the fair allocation of CPU resources between various user communities and projects and have encouraged jobs not requiring intimate user interaction to run during off hours using batch job facilities. Despite these efforts, our prime time loading has remained at saturation. Perhaps the most significant effect of the resulting poor response time is the deterrence of interactions with medical and other professional collaborators experimenting with available AI programs, whose schedules cannot be adjusted to

meet computer loading patterns. This has hampered the more extensive testing of mature programs such as INTERNIST, MYCIN, CONGEN, SECS, and PUFF.

This continuing saturation brought about serious discussion about the scope of computing needs of the AIM community and possible justification of additional PDP-10 scale machines to be added to the AIM network. Several specific proposals were submitted for additional user nodes. Only one of those has been approved to date, for a DEC 2050 system at Rutgers University which was brought on-line late in the summer of 1978. A small part of that machine's capacity is available now to support AIM community needs outside of Rutgers.

From the SUMEX viewpoint, we have attempted to do everything feasible and economically justified within available budgets to maximize the use of the existing hardware for productive work. We have effectively exhausted available avenues for augmenting the current KI-10 machines. Some advantage would be gained by additional core memory but we do not feel the improvement would be sufficient to justify the investment at this time. An upgrade to a more capable KL-10 system is beyond our budget limitations and may be premature in any case in light of projected developments in new machine architectures outlined in Appendix II.

As discussed in our renewal application for this grant term, an alternative approach to meet community computing needs is to explore the use of smaller, less expensive machines as satellites to the KI-TENEX system. Such systems have been under active development during recent years and could have several advantages including:

- 1) A relatively small investment in capital equipment is required for each incremental augmentation.
- 2) Possible closer location to individual research groups thereby allowing better human engineering of user interfaces by using higher speed communication lines and display technology.
- 3) An improved allocation flexibility by having to satisfy fewer simultaneous scheduling constraints and by being more easily dedicatable to operational demonstrations.

One disadvantage of this approach is that each such machine would have a lower capacity and it would be difficult to aggregate such dispersed capacity when needed for a single computing-intensive task. This suggests the continuing need for a spectrum of machine configurations from small "personalized" machines to large centralized resources. Nevertheless, we feel the capacity of available small machines is sufficient to support several simultaneous users and warrants serious consideration as both a means for incrementally augmenting the SUMEX resource and for dispersing computing power as justified to individual user groups.

Based on the Council approval of this approach in our renewal application, our plans for acquiring such a satellite machine and for integrating it into the KI-10 system with a local network are described below.

It should also be noted that we have encouraged projects with specific needs for more operational demonstration or export of programs to consider acquiring their own machines in order to preserve SUMEX resources for new program development and for support of projects unable to justify their own machine currently. The DENDRAL project has proposed a VAX machine for such a purpose that would be integrated into the SUMEX facility but dedicated to support of the DENDRAL biomolecular characterization community. The choice of VAX was made to provide the best match with machines increasingly available in a biochemistry laboratory environment and able to run the programs being developed by DENDRAL (including CONGEN recently converted from INTERLISP to BCPL). At the same time the choice of VAX is advantageous to SUMEX in that it would give us experience with that machine in line with current projections that VAX will become the "standard" DEC computing product and that the ARPANET AI community will implement a VAX INTERLISP system (see Appendix II).

Satellite Machine Selection

Over the past year we have spent considerable effort evaluating strategies and alternatives for implementing the planned satellite machine. The key requirement for any such machine to meet pressing community needs is that it be software-compatible with the existing INTERLISP and basic monitor functions available on the SUMEX KI-10 systems and the Rutgers DEC-2050. This will allow programs, written for the most part in INTERLISP, to move easily from development stages to demonstration trials and back with a minimum of reprogramming. A second requirement is that the system be inexpensive in order to minimize initial capital outlay and to allow other groups to purchase similar systems for their own needs.

As detailed in Appendix II, we have been in a period of transition in computing technology. More compact and inexpensive yet powerful machines have become available and new directions in machine architecture are being adopted emphasizing large address spaces and improved instruction sets for user program support. In several years, we expect the PDP-10/20 architecture to begin to be replaced by larger address space and more cost-effective systems (most likely VAX). We do not expect even early versions of these new systems that support INTERLISP to be available for at least two years, however. Thus, in order to meet the immediate needs of the SUMEX-AIM community, we feel the best approach is to acquire a PDP-10-compatible system as soon as possible.

There are two alternative systems available that meet our requirements for a satellite machine within budget limitations; the DEC 2020 and the Foonly F2. We have evaluated both of these candidate machines (see Appendix II) and have run benchmarks on the 2020 (the only one of the two machines with fully working system in the field). These data, shown in Figure 3, compare 2020 responsiveness under load against single- and dual-processor KI-10 systems. As can be seen, the 2020 is a bit more than half the speed of a single KI-10 and can be expected to support up to three active LISP users simultaneously. This upper bound is limited principally by page swapping capacity. Based on published specifications, we expect the Foonly F2 would perform comparably.

We feel that the DEC 2020 is the more advantageous solution. A used 2020 is deliverable almost immediately at a major discount from list price (pricing details have been submitted separately). It is known to be reliable, runs a

monitor compatible with INTERLISP and the most current DEC software, and will be maintainable by DEC for many years. It will also likely retain a better resale value in future years. Whereas the F2 is potentially more cost-effective (its quoted purchase price is below that of the discounted 2020), it has a highly uncertain delivery schedule and no performance track record. It also has no assurance of routine maintenance, vendor support, or resale value. In the long term we feel these uncertainties and the extra in-house effort that would be required to maintain and support the F2 offset its initial price advantage. Thus, the DEC 2020 is the better choice to provide an immediate, effective, and reliable solution to SUMEX-AIM community computing needs.

Based on benchmark performance and needs for integrating a 2020 system into the SUMEX facility, we have proposed the following configuration for the machine:

- 2020 Processor and console
- 512K words of memory
- 1 200 Mbyte disk drive (RP-06)
- 16 asynchronous communication lines
- TU-45 tape drive
- TOPS-20 software

A proposal is pending with NIH/BRP to approve purchase of this machine.

Satellite Machine Integration

The introduction of satellite machines into the SUMEX facility raises important issues about how best to integrate such systems with the existing machines. We seek to minimize duplication of peripheral equipment and interdependence among machines that would increase failure modes. We also require high-speed intermachine file transfer capabilities and terminal access arrangements allowing a user to connect flexibly to any machine of choice in the resource.

The initial design of the SUMEX system was that of a "star" topology centered on the KI-10 processors. In this configuration, all peripheral equipment and terminal ports were connected directly to the KI-10 busses. With the addition of a satellite machine, a unique focus no longer exists and some pieces of equipment need to be able to "connect" to more than one host. For example, a user coming into SUMEX over TYMNET will want to be able to make a selection of which machine he connects to. Another TYMNET user may want to make another choice of machine and so the TYMNET interface needs to be able to connect to any of the hosts. This could be accomplished by creating separate interfaces for each of the hosts to the TYMNET, each with a different address. Besides being expensive to duplicate such interfaces, it would be inconvenient for a user to reconnect his terminal from one host to another. He would have to break his existing connection and go through another connect/login process to get to another machine. Since we want to facilitate user movement between various machines in the SUMEX resource, this process needs to be as simple as possible - in fact a user may have jobs running simultaneously on more than one machine at a time.

Similarly, we need to be able to quickly transfer files between any two machines in the resource, connect common peripheral devices (e.g. printer or

plotter) to any machine desiring to use them, and allow any host to access other remote resources such as Stanford campus printers or terminal clusters. If we were to establish direct connections pairwise between machines and devices, the number of such connections would go up quadratically with the number of devices.

A more effective solution lies in the implementation of a local network in which all devices (host CPU's, peripheral devices, network gateways, etc.) are tied to a common communications medium and can thereby establish logical connections as needed between any pair of nodes. Such network systems have been under development for a number of years, taking on various topological configurations and control structures depending on bandwidth requirements and interdevice distances. A very attractive design for a highly localized system configuration from the viewpoint of simplicity, reliability, and bandwidth is the Ethernet which has been under development for several years at Xerox Palo Alto Research Center (3). The simplest form of Ethernet interconnection for a facility like SUMEX would be a single bus shared by all devices (see Figure 2). The Ethernet utilizes a fully distributed control structure in that each device connected to the net can independently decide to send a message to any other device on the net depending on the functions it is actively performing. Of course, decisions about which devices need to communicate with each other at a given time and what the precise message content is are determined by higher level system activities and requests, for example to implement a file transfer, mail forwarding, teletype connection, printer output, etc. As long as the net is not in use and only one device at a time is attempting to transmit, no problem occurs. The sending device transmits its packet of information which contains a destination address, packet type designator, and error detection codes. All other devices on the net continuously "listen" to what is being sent and the one assigned the appropriate destination address picks up the packet, acknowledges its receipt, and processes it. If the packet address is garbled by errors or no device with the appropriate address exists, the sender "times-out" and decides how to proceed based on the higher level function being performed. Packets are kept short relative to network bandwidth so that a given device cannot "hog" the net.

However, if two or more devices decide to transmit over the shared medium at the same time, a "collision" occurs and a mechanism must exist to detect the collision and to select one of the contending devices to go first. Since this contention arbitration is the fundamental characteristic of the control structure of such nets, they are commonly called "contention" networks. In the Ethernet, a collision is detected by each sending device listening to what is being transmitted on the bus. If a transmission is already in progress, the device waits until the net is quiet for a period before starting to send. When it does transmit, it continues to listen to what is going over the communications line and compares that data with what it is sending. If a disagreement is detected the device assumes that some other device has started to transmit at the same time and aborts its transmission. A time window exists between the start of a transmission and when all devices can be assumed to know that a transmission is in progress. This interval is given by the speed of the net and the distance between the sending node and its most distant neighbor. If a collision is detected, the net is "jammed" with noise for a period such that all devices know

(3) See Metcalfe, R. M. and Boggs, D. R., "Ethernet: Distributed Packet Switching for Local Computer Networks," Comm. ACM, Vol. 19, No. 7, July 1976.

a collision has occurred and then each sending device waits a random period of time to begin retransmission. This random delay is what sequences devices so that a deadlock of successive collisions is avoided (4).

More complex networks can be created with several Ethernets by having one of the nodes on the network be a "gateway" that knows how to communicate with another Ethernet or some other external network. These gateways can translate between packet conventions used in the Ethernet and those used in the ARPANET, TYMNET, TELENET, etc.

Xerox has implemented internally an extensive set of Ethernets with interconnections between them and with other external networks. These local networks operate at 5-10 Mbits/sec over distances of about 1 kilometer and perform well in terms of efficient use of the transmission medium and low latency between deciding to transmit and being able to get access to the medium (5). The Stanford Computer Science Department will be one of three recipients of grants from Xerox that will include Ethernet connection hardware. Since the Computer Science Department systems are integrally connected with a major user group on SUMEX (the Heuristic Programming Project) and since the Ethernet design is ideal for the integration of new satellite machines with the existing SUMEX facility, we have chosen it as the model for our planned facility changes. The proposed new topological design is shown in Figure 2 and will include creating new interfaces for each host machine, the TYMNET, the local teletype scanner, other peripheral devices, and a gateway to other local networks (e.g., the Computer Science Department machine and planned terminal clusters).

Communications Hardware Development

A final area of hardware development concerns communications. We have implemented line disconnect control hardware on local telephone lines similar to what exists logically for our network connections. Previously we were unable to detect when carrier dropped on phone connections, for example when a user hung up without logging out or was accidentally disconnected during a session. This left his job hanging so that the next person dialing up in that line would automatically be connected to the earlier job resulting in possible privacy or security loss. The system now receives a hardware interrupt when a line drops and if the job that was on that line is still active, the job is detached so it can be picked up and continued. Conversely, when a user logs out, we do an automatic disconnect on his phone line so that our incoming rotaries are not congested with unused, hoarded phone connections.

(4) A similar type of local network called CHAOSNET has been under development at MIT. It differs from Ethernet in that it uses delay counters to sequence colliding devices. The delay for each sender is determined by counting down at a prespecified rate the arithmetic difference in node address between the last successful transmission and the prospective sender. Thus by selecting node addresses corresponding roughly to the physical position of a node on the net, proper interleaving can be achieved to arbitrate collisions.

(5) See Shoch, J. F. and Hupp, J. A., "Performance of an Ethernet Local Network -- A Preliminary Report," Proceedings of the Local Area Communications Network Symposium, Boston, May 1979.

We are also developing a switch to allow more effective use of the 64 available teletype scanner ports. We typically have about 40-50 jobs on the system during peak loads (mid-afternoon) of which 10 are detached, 10 come from network or pseudo-teletype connections, 10 come from local dialup connections, and 15 come from leased or hard-line connections. With this mix the 64 scanner ports on the system are adequate. However, high speed displays or leased lines require dedicated ports whether or not they are in use and thus the scanner is overloaded with fixed line assignments, many of which are not in simultaneous use. We have looked at the economics of adding another scanner or of making it possible to switch available scanner ports to active lines and the switch is the more cost-effective. A microprocessor-based switch is now being installed and tested that will allow us to selectively connect 32 scanner ports to any of 64 dedicated lines.

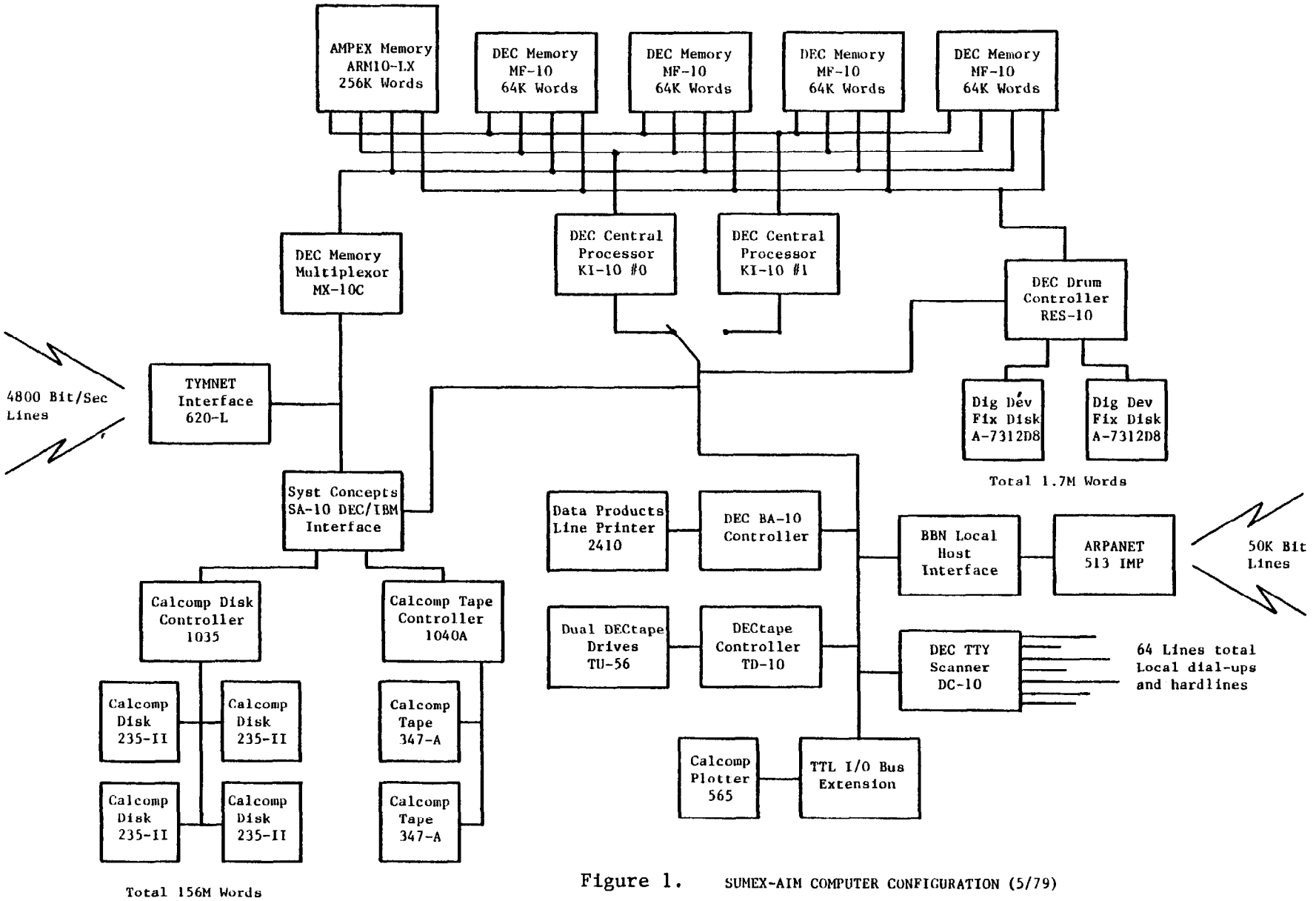


Figure 1. SUMEX-AIM COMPUTER CONFIGURATION (5/79)

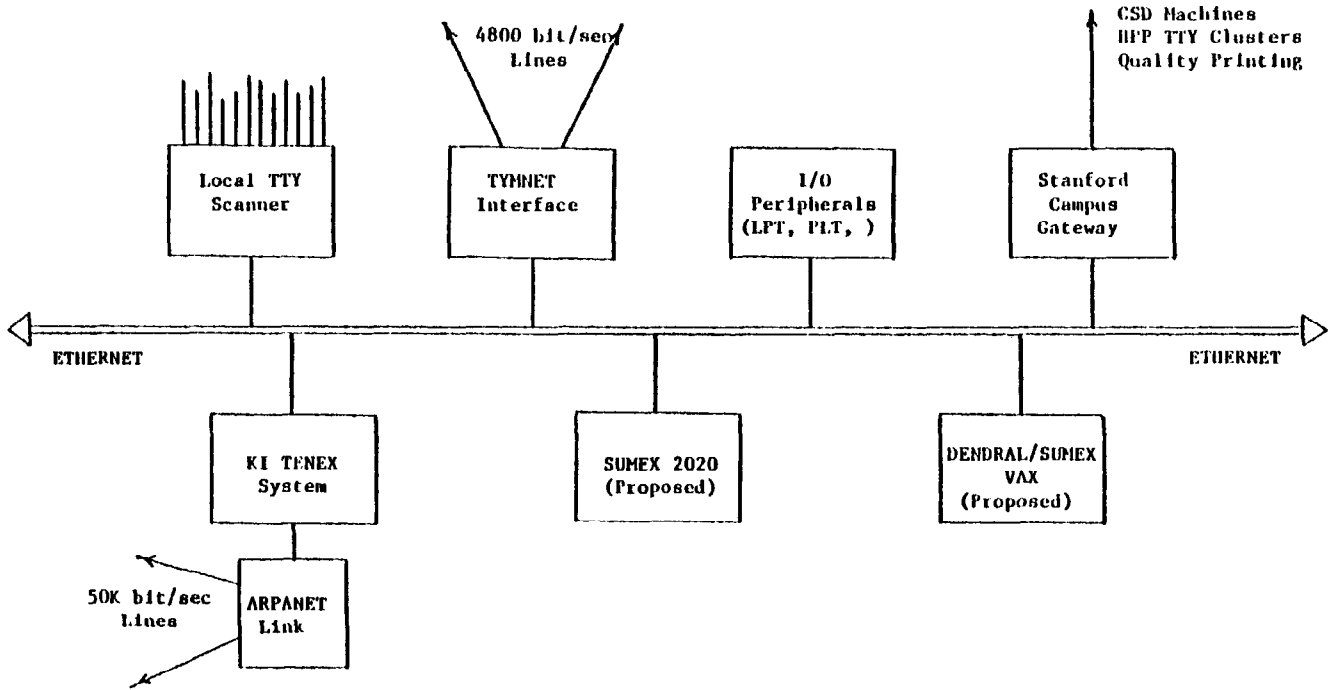


Figure 2. Planned Intermachine Connections via ETHERNET

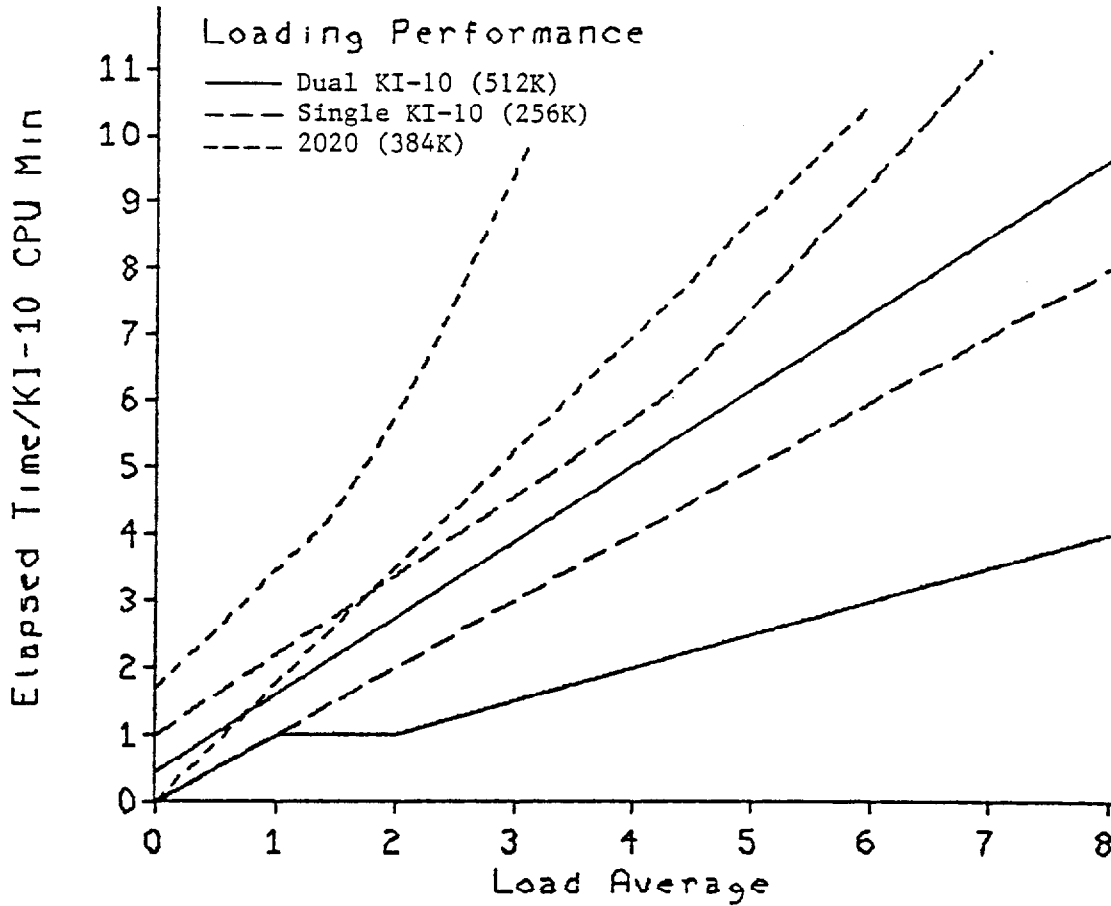


Figure 3. DEC KI-10 Versus 2020 Performance Under Load. For each of the three machine configurations, two graphs are given. The lower graph shows performance for small, CPU-intensive jobs and the upper graph shows performance for large, page-fault-intensive jobs. These curves bound the expected performance for typical user jobs. It is assumed that a KI-10 averages about 1.7 times the speed of a 2020.

2.1.2.2 System Software Development

Our system software work this past year has concentrated on several areas including system changes reflecting hardware development projects, correcting various system bugs, improved community loading controls, and implementing new features for better user community support.

Hardware Implementation

System work was required to enable the installation of the TELENET equipment (see Section 2.1.2.3) and the local communication line control hardware. We implemented "Xon/Xoff" facilities for the TELENET interface so that all terminals could run at an effective 1200 baud rate with output flow controlled by appropriate network "backpressure" commands when buffers fill for slower terminals. These changes were completed in the fall when the final evaluation of TELENET took place and significantly smoothed network output flow over what had been available before.

Servers were also implemented to handle the interrupt and I/O bus interfaces for the line disconnect control hardware and for the hardline switch interface. The switch interface is still in the process of being debugged.

Monitor Bug Fixes and Improvements

We found a number of subtle bugs in the system this past year that had been causing periodic problems in hung jobs or crashes. By now, all of the "obvious" bugs have been located and so those remaining are much more elusive, occurring infrequently or only after a long chain of rare events that is difficult to reconstruct. Examples of fixes include problems in DDMP, the program that periodically migrates altered file pages from core to refresh the disk image of these pages. Two bugs existed, one that caused infrequent error logging calls to mishandle the stack and one that overlooked certain pages under the assumption that future core garbage collections would take care of them. This latter bug caused relatively frequent file errors during crashes or when taking the system down because the overlooked pages were never refreshed on disk by core garbage collection since the system halted. We have had a significantly more reliable file system during crashes as a result of this fix.

Several bug fixes were made in the ARPANET code having to do with the handling of special control packets when aborting partially created connections and the release of connections after transmission errors had occurred.

We also found a bug in the fork manipulation code that caused jobs to hang occasionally when multiple fork manipulations were going on simultaneously. These resulted when two forks were attempting to examine the job fork structure data base, one got interrupted in progress, and the other made some changes that altered information in the tables that the first fork expected to remain as set up when it was interrupted.

A number of additional improvements were made to upgrade various monitor routines and JSYS's to conform with TENEX 1.34, to checksum monitor code as loaded to detect I/O errors or memory problems, to make the console teletype of the second processor available for use, and to improve operational procedures for taking crash dumps and reloading the system.

System Loading Controls

We previously reported on the system load controls we have implemented to allocate available system capacity effectively among projects and users according to Executive Committee guidelines. These include:

- 1) A "soft" CPU percentage control, assisted by a program which adjusts user percentages for the scheduler based on the dynamic loading of the system. This allocation control structure uses the scheduler's five queue system that ranks processes according to their degree of interactiveness (CPU time between requests for teletype inputs). Processes in the highly interactive queues (text editing, etc.) are scheduled at highest priority without consideration of allocation percentages. If no processes are runnable from these queues, more CPU-bound queues are scanned and processes are selected for running based on how much of their allocated time has been consumed during a given allocation control cycle time (currently 100 seconds). This system is not a reservation system in that it does not guarantee a given user some percentage of the system. It allocates cycles preferentially, trading off a priori allocations with actual demand but does not waste cycles.
- 2) an overload control mechanism that operates during peak loading periods to limit the number of active processes on the system to those that can be reasonably supported with acceptable response time. This avoids slaving all users to their terminals waiting inefficiently for the machine cycles they need to get useful work done when there are not enough to go around. Each project receives a pro rata share of the active slots the system can accommodate. Rather than allow many users to vie unproductively for each project's slots (as in a pie-slice system), we ask selected users within each group to restrict their use for periods of 20 minutes so that those remaining can work effectively within the project aliquot. Allocation of active slots is made on the basis of relative community and project percentage allocations (assigned by the AIM Executive committee). Within each project, slots are allocated either on a round-robin basis or taking into account optional project priorities among users. Under overload conditions, active jobs outside of the available slots are asked to slow down, thereby holding the load within tolerable limits. If such jobs do not voluntarily cooperate, they may be forced to comply.

This system has been in operation for the past year and has operated quite well. We continued to place no load limiting controls on the national AIM community projects, however, since they have historically consumed been below their allocated quota. Stanford users and staff have adapted their expectations of system response and find it more productive to coordinate their time on the machine with others in their project so as to work on a more lightly loaded system. Indeed, as can be seen from the loading data in Figure 10, the peak load average has been held to an average of 5.5 - 6.0 whereas total CPU time consumption, shown in Figure 8, has continued to rise.

Several problems were noted in the loading control system that required improvements in monitor functions this past year:

- 1) Users frequently wanted to designate a job as low priority or "background" so that it would run only when the system is lightly loaded and "go to sleep" otherwise.
- 2) Scheduled demonstration jobs were receiving no advantage in performance over other jobs, other than that due to holding the load average down. A scheme was needed to cause demo jobs always to be scheduled preferentially.
- 3) Forcible control of uncooperative jobs was initially implemented by detaching them or logging them out in extreme cases. This could cause loss of important work and a less destructive yet effective mechanism was needed.
- 4) A loophole for uncooperative jobs existed that would bypass controls with good probability. If more than one user were asked to slow down at a given time, one of those jobs could refuse to cooperate and continue intensive computing while the others slowed down. Frequently, the load reduction from cooperating jobs was enough to remove the overload condition during common, local bursts of usage. Thus, with the overload gone, the uncooperative user could continue without ever having slowed down.

To improve the control system, we implemented two new scheduler control functions. First, a job can be designated to run out of a given queue no matter how much CPU time it wants to consume. This allows demo jobs always to be scheduled out of the highest priority queue assuring a better service level. It also allows background jobs to be scheduled always from the low priority queues so they only run if nothing else is to be done.

Second, a job can be stopped for a specified period of time without ever being scheduled. This function allows uncooperative jobs to be slowed for a large percentage of time (max 97.5% currently) when their load must be reduced forcibly but does not do any other damage to the operation of such jobs that could result in lost work.

These new features have substantially improved the effectiveness of the overload control system. The loophole for uncooperative jobs was plugged by noting whether jobs requested to stop make any attempt to cooperate during the assigned grace period. If there is no change in their rate of CPU time consumption, the grace period is shortened so they will be forcibly stopped before more cooperative users stop and remove the overload.

Other Enhancements

We have made improvements in SUMEX system software in numerous other areas including the EXECutive program, the BSYS system for file archiving and retrieving, the printer spoolers, the CHECKDSK program for verifying file system integrity, system diagnostic programs, a monitor crash analysis program, and many smaller utility extensions and bug fixes. We have updated the EXEC to be compatible with the latest version running at other TENEX sites, incorporating the extensions we have made locally. The BSYS program has been updated to the

latest version available from BBN using their system for file restoration automation. Several bugs in the improved CHECKDSK program for verifying file system integrity have been made and improvements to give users a better idea of file names that might have been lost during a crash. Improved crash and system analysis programs have been developed to assist in sorting through the complex interlinked monitor tables when unraveling a core dump to determine the cause of a crash. These include several display programs to observe the dynamic operation of individual job structures or the ARPANET. These tools have been invaluable in tracking down the difficult bugs that remain in the system.

2.1.2.3 Network Communication Facilities

A highly important aspect of the SUMEX system is effective communication with remote users. In addition to the economic arguments for terminal access, networking offers other advantages for shared computing. These include improved inter-user communications, more effective software sharing, uniform user access to multiple machines and special purpose resources, convenient file transfers, more effective backup, and co-processing between remote machines.

Until this past year, we have based our remote communication services on two networks - TYMNET and ARPANET. These were the only networks existing at the start of the project which allowed foreign host access. A third commercial network system, TELENET, is now competitively operational and offers a growing selection of services. During this report period we established an experimental connection to TELENET to evaluate its technical and economic advantages relative of our existing connections. The results of this experiment are reported below.

Users asked to accept a remote computer as if it were next door will use a local telephone call to the computer as a standard of comparison. Current network terminal facilities do not quite accomplish the illusion of a local call. Data loss is not a problem in most network communications - in fact with the more extensive error checking schemes, data integrity is higher than for a long distance phone link. On the other hand, networking relies upon shared community use of telephone lines to procure widespread geographical coverage at substantially reduced cost. However, unless enough total line capacity is provided to meet peak loads, substantial queueing and traffic jams result in the loss of terminal responsiveness. Limited responsiveness for character-oriented TENEX interactions continues to be a problem for network users.

TYMNET:

TYMNET provides broad geographic coverage for terminal access to SUMEX, spanning the country and also increasingly accessible from foreign countries (see Figure 4 on page 21). Technical aspects of our connection to TYMNET have remained unchanged this past year and have continued to operate reliably. The total use of TYMNET dropped during the TELENET experimental connection (see Figure 14) but is now increasing again since the TELENET service was dropped.

TYMNET has made few technical changes to their network that affect us other than to broaden geographical coverage. The previous network delay problems are

still apparent although better cross-country trunks into New York and New England are available improving service there. TYMNET is still primarily a terminal network designed to route users to an appropriate host and more general services such as outbound connections originated from a host or interhost connections are only done on an experimental basis. This presumably reflects the lack of current economic justification for these services among the predominantly commercial users of the network. Whereas TYMNET is developing interfaces meeting X.25 protocol standards, the internal workings of the network will likely remain the same, namely, constructing fixed logical circuits for the duration of a connection and multiplexing characters in packets over each link between network nodes from any users sharing that link as part of their logical circuit.

We have continued to purchase TYMNET services through the NLM contract with TYMNET, Inc. Because of current tariff provisions, there is no longer an economic advantage to this based on usage volume. SUMEX charges are computed on its usage volume alone and not the aggregate volume with NLM's contribution to achieve a lower rate. A new tariff provision, based on "dedicated port" pricing, is advantageous to us though. This allows purchase of a number of logical network ports at the host for a fixed cost per month, independent of connect time or number of characters transmitted. Based on previous usage data, SUMEX could save approximately \$1,000 per month in service charges by taking advantage of this charging scheme. We will continue to work closely with NIH-BRP and NLM to achieve the most cost-effective purchase of these services.

ARPANET:

We continue our advantageous connection to the Department of Defense's ARPANET, now managed by the Defense Communications Agency (DCA). Current ARPANET geographical and logical maps are shown in Figure 5 and Figure 6 on page 22. Consistent with agreements with ARPA and DCA we are enforcing a policy that restricts the use of ARPANET to users who have affiliations with DoD-supported contractors and system/software interchange with cooperating network sites. We have maintained good working relationships with other sites on the ARPANET for system backup and software interchange. Such day-to-day working interactions with remote facilities would not be possible without the integrated file transfer, communication, and terminal handling capabilities unique to the ARPANET. The ARPANET is also key to maintaining on-going intellectual contacts between SUMEX projects such as the Stanford Heuristic Programming Project authorized to use the net and other active AI research groups in the ARPANET community.

TELENET

We recognize the importance of effective, economical communication facilities for SUMEX-AIM users and are continuously looking for ways to improve our existing facilities. During the past year, based on the approval of the AIM Executive Committee and the NIH-BRP, we established an experimental connection to the TELENET network to evaluate its performance for support of the SUMEX-AIM community (see Figure 7 on page 24 for an illustration of the current geographic coverage of TELENET). Our connection was via a TP-2200 interface with 12 asynchronous lines to the SUMEX host and one 4800 baud line connecting to the network proper. TELENET has many attractive features in terms of a symmetry analogous to that of the ARPANET for terminal traffic and file transfers and

being a commercial network, it does not have the access restrictions of the ARPANET. Its tariff schedule also affords lower costs than TYMNET for comparable service volume.

However, despite system changes we made to optimize TELENET performance (Xon/Xoff facilities to improve traffic flow), users felt a substantial degradation in service when using TELENET as opposed to TYMNET. We insisted that users use TELENET whenever possible between November 1978 and May 1979 to maximize user accommodation so that problems arising from differences in access conventions would not cloud judgements of services. Complaints included poor node reliability, intolerable delays in response, uneven flow of terminal output, and poor operational management of the network in keeping users informed of network and host status. From the system viewpoint at SUMEX, we detected similar problems. We received ineffective system engineering support in trying to tune network parameters to optimize performance for our user community and poor or erroneous feedback about network failures and problem resolution. In practice, TELENET offered no service advantages over TYMNET, since no file transfer connections above 1200 baud are currently allowed, no facilities to control local versus remote echoing exist, and no electronic mail system exists to facilitate communication between network operations staff and host nodes. Also company financial problems portend substantial delays in remedying these problems.

Because of grant budget limitations, we were forced to decide between the TYMNET and TELENET connections - only one could be afforded. Based on the distinct user preference expressed for TYMNET, we decided to terminate the TELENET connection as of May 1, 1979. We will continue to monitor TELENET developments (and those of other potential national network servers, e.g., AT&T, IBM, and Xerox) and may recommend a reevaluation of an alternative source for network services in the future.

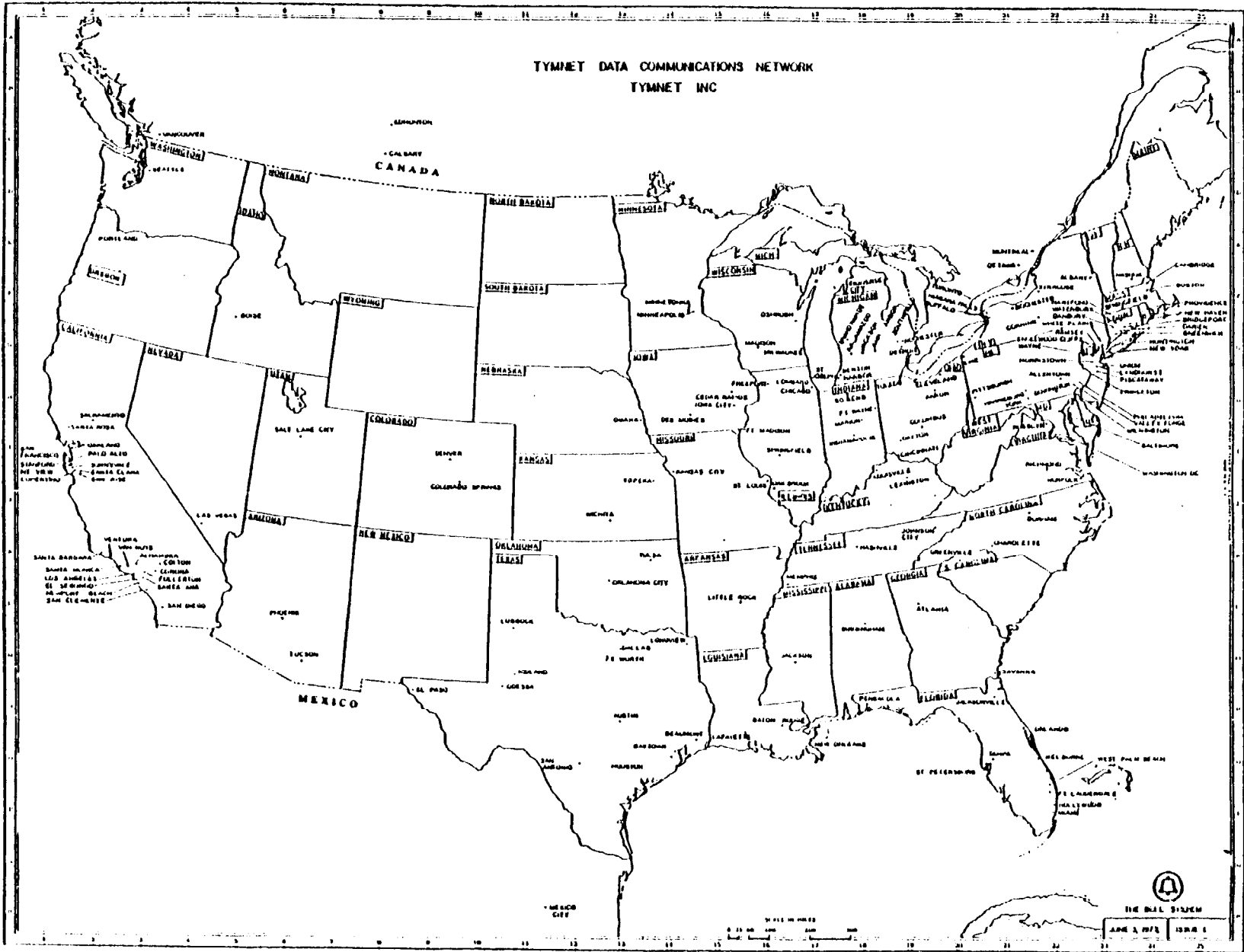


Figure 4. TYMNET Network Map

Figure 5. ARPANET GEOGRAPHIC MAP, MARCH 1979

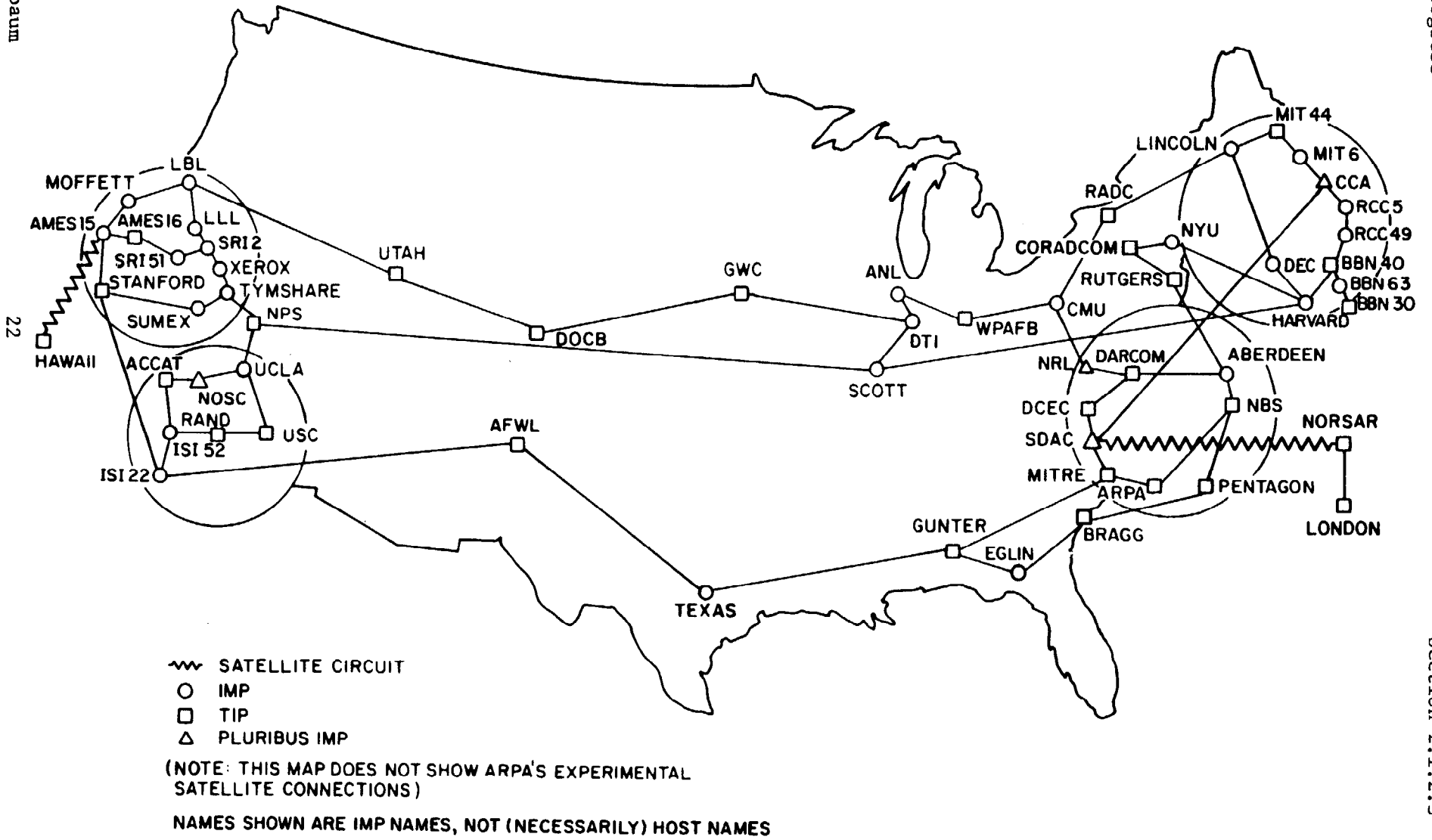


Figure 6. ARPANET LOGICAL MAP, MARCH 1979

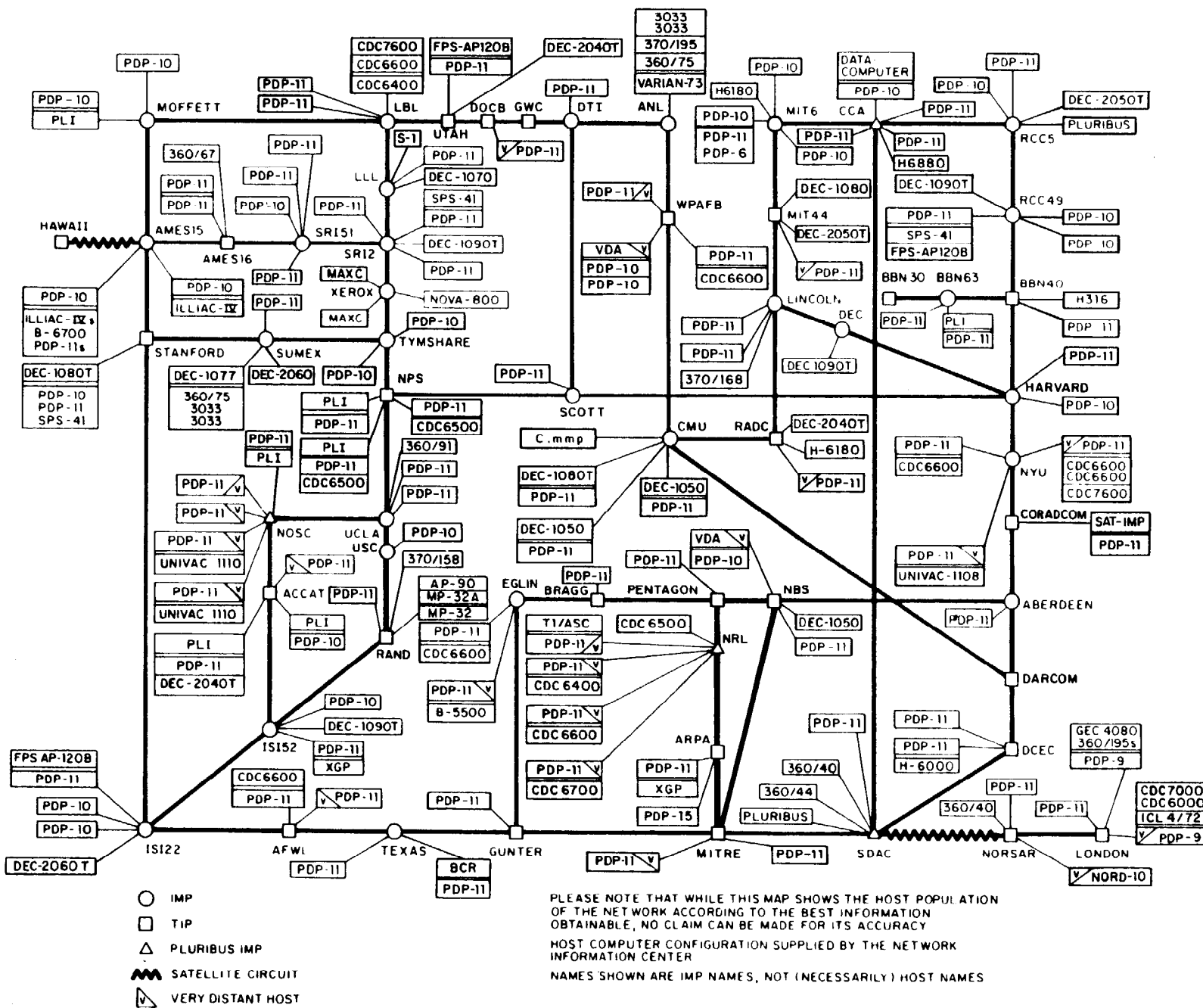
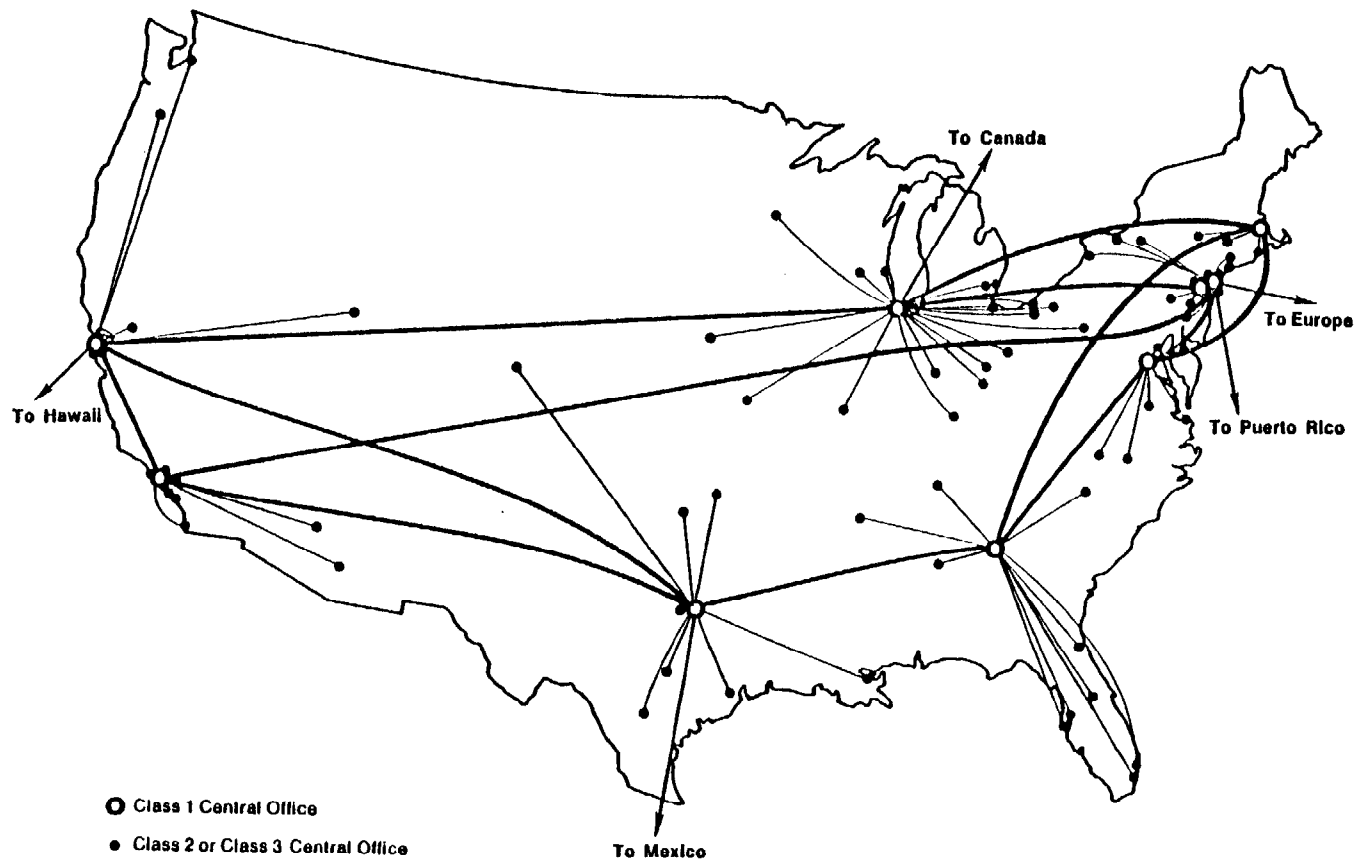
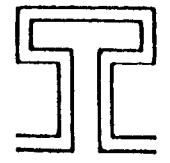


Figure 7

THE TELENET NETWORK



2.1.2.4 System Reliability and Backup

System reliability has been very good on average with several periods of particular hardware or software problems. The table below shows monthly system reloads and downtime for the past year. It should be noted that the number of system reloads is greater than the actual number of system crashes since two or more reloads may have to be done within minutes of each other after a crash to repair file damage or to diagnose the cause of failure.

	1978							1979				
	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR
<u>RELOADS</u>												
Hardware	6	8	5	6	8	10	1	4	2	2	6	4
Software	0	0	4	5	9	9	5	3	9	4	7	10
Environmental	3	0	1	0	1	0	0	0	1	0	1	0
Unknown Cause	7	4	1	4	5	5	1	1	0	0	1	1
	--	--	--	--	--	--	--	--	--	--	--	--
Totals	16	12	11	15	23	24	7	8	12	6	15	15
<u>DOWNTIME (Hrs)</u>												
Unscheduled	36	22	33	37	28	37	3	14	8	16	17	14
Scheduled	38	34	22	25	20	31	30	20	22	17	33	16
	--	--	--	--	--	--	--	--	--	--	--	--
Totals (Hrs)	74	56	55	62	48	68	33	34	30	33	50	30

TABLE 1. System Reliability by Month

During the year, we encountered several hardware problems that caused temporary increases in the number of crashes. These were very intermittent problems that were difficult to isolate and account for the increased number of reloads during September and October 1978 and again in March and April of 1979. Several problems resulted from oxidation of electrical contacts and we might expect an increase in such age-related failures as the system gets older.

Probably the most serious hardware failure was a head crash on one of the swapping disks. A rubber diaphragm burst forcing one set of heads to contact a platter. The debris from that crash then spread to the other surfaces and caused those heads to crash. We expect repairs to be complete by early July. This may forecast other problems caused by aging of rubber parts in the swapping disks and we will take steps to replace these if need be before another failure results.

We have had an on-going effort to increase software reliability and have fixed a number of bugs that have been perennial causes of crashes or file loss at system shut-down. Some of these fixes have required setting system stops to get appropriate dumps to analyze the problem causes and thereby also temporarily increased the number of crashes.

2.1.2.5 Core Research

Over the past year we have supported several core research activities aimed at developing information resources, basic AI research, and tools of general interest to the SUMEX-AIM community. Specific areas of current effort include:

- 1) The AI Handbook which is a compendium of knowledge about the field of Artificial Intelligence being compiled by students and investigators at several research facilities across the nation. The handbook is broad in scope, covering all of the important ideas, techniques, and systems developed during 20 years of research in AI in a series of articles. Each is about four pages long and is a description written for non-AI specialists and students of AI. The AI Handbook effort is described in more detail in Section 4.2.1 on page 130 and an outline of the current contents of the handbook can be found in Appendix I.
- 2) The AGE project which is an attempt to isolate inference, control, and representation techniques from previously developed knowledge-based programs; reprogram them for domain independence; write a rule-based interface that will help a user understand what the package offers and how to use the modules; and make the package available to other members of the AIM community. A more detailed description of progress on the AGE package can be found in Section 4.2.2 on page 133.
- 3) The MAINSAIL project which is an attempt to demonstrate the design of an ALGOL-like language system which facilitates software transportability between different machine/operating system environments. A final report on this effort is given below.

It should be noted that SUMEX is providing only partial support for the AI Handbook and the AGE projects with complementary support coming from an ARPA contract to the Heuristic Programming Project.

MAINSAIL System for Software Transportability

At the end of this grant year the MAINSAIL project will have successfully designed, demonstrated, and documented an ALGOL-like language system for machine-independent software design. This system includes the compiler, code generators, and run-time support for a range of target machine environments including TENEX, TOPS-20, TOPS-10, RT-11, RSX-11, and UNIX. The designs for other environments have been studied but resources have not allowed more extensive implementations. Within Council-approved funding and manpower limits and the AI charter of the SUMEX resource, we do not have access to the more extensive resources that would be required to continue effective development and export of this system beyond this initial research and demonstration phase. We are hopeful that the principal individuals involved (Messrs. Wilcox and Jirak and Ms. Dageforde) will be successful in forming a small private company to support and continue development of MAINSAIL with independent funding from a growing group of potential users. The following is a final summary on this demonstration phase of the MAINSAIL effort. A detailed final report is in preparation.

The primary effort during the past year has been directed at making MAINSAIL a stable, maintainable, complete system ready for distribution and

serious production programming. Implementations developed in prior years have been improved and new ones added. The number of evaluating users has increased, as well as the number of applications programs written in MAINSAIL. The project is now at the point where new implementations can be undertaken, and the groundwork for portability which has been laid over the previous years can now begin to really show its strength.

The compiler has undergone major examination, improvement, and reduction in size of data structures, and as a result is now able to run on machines with small address spaces (e.g., 32K words).

The language itself has remained stable. The runtime system has not undergone any major modifications since September.

Distribution of MAINSAIL beyond its initial test sites has begun. Due to the increasing size of the MAINSAIL user community the need for user support has also increased significantly. As part of our effort to evaluate MAINSAIL's effectiveness in actual applications we have provided user consultation within available resources but we have been limited in the amount of help we could actually provide while continuing active development efforts.

A research project based on MAINSAIL is underway, aimed at providing an efficient program execution and development environment on a high-level language "MAINSAIL machine" which directly executes a tailor-made MAINSAIL instruction set.

a) Implementations

The PDP-10 TENEX version of MAINSAIL has now been in use for about three years at two local sites. A version for a somewhat non-standard TOPS-10 has been used locally to a lesser extent for two years. Standard TOPS-10 was implemented about a year and a half ago and received a moderate amount of use at a remote site. This year standard TOPS-10 was sent to four new sites, including the NIH DCRT Computer Facility.

A TOPS-20 implementation was derived from the TENEX implementation during the past year. The TOPS-20 version is not yet complete in that it is simply a TENEX implementation with a few minor modifications. Utilization of features of the KL-processor instruction set and proper handling of structures in file names have not yet been implemented, but are relatively straightforward additions. This version of the TOPS-20 implementation is now undergoing evaluation at a number of sites, and is beginning to be the most requested version of MAINSAIL.

Due to the interest in using MAINSAIL on machines with small address spaces, substantial development work was done during this past year on PDP-11 implementations.

On many minicomputer configurations the limited address space can have an adverse effect on the performance of large programs. Whenever a working set of modules cannot be contained in primary memory the system begins to exhibit the classic thrashing condition. Since modules are normally swapped from disk the attendant I/O overhead seriously degrades the program's performance.

Some minicomputers have additional memory which is not directly addressable. Typically, this memory can be accessed only by changing a hardware relocation device. A portable caching algorithm has been developed to allow MAINSAIL to take advantage of such memory to reduce the effects of thrashing. The additional memory is used in a two-tier storage hierarchy with the disk. Since access to the additional memory is much faster than access to the disk, swapping from the additional memory takes less time than swapping from the disk. MAINSAIL modules are maintained in the memory cache in a most-recently-used fashion. When the cache fills up, the least recently used module is bumped from the memory cache. The modular design of MAINSAIL made this caching approach quite natural, and holds much promise for further utilization of memory hierarchies.

A PDP-11/40 running the RT-11 operating system has been running MAINSAIL programs for two years. The RSX-11M operating-system interface is complete. A PDP-11/34 running RSX-11M was used as our main testing site during the development of the compiler running in a small address space.

The operating-system interface for UNIX is also complete. A few MAINSAIL utility programs have been run on a PDP-11/34 using UNIX and there are no outstanding problems. This implementation requires further testing.

The runtime system has been run on a standard PDP-11/03 with DEC floppy disks. This was purely a demonstration effort for two main reasons: 1) the floppies are extremely slow, and 2) their storage capacity is insufficient for holding anything other than simple programs, since most of the storage is taken up by the operating system, its utilities, and the MAINSAIL runtimes.

The runtime system and the compiler have been used on a number of LSI-11 configurations. These configurations had either dual density non-DEC floppy disks or an RK equivalent hard disk pack. Some of these machines had an additional 32K words of video memory which MAINSAIL utilized as a module cache. Prior to the demonstration of the compiler under RSX-11M, the fastest PDP-11 compilation on record occurred on an LSI-11 with video memory and an RK type disk.

The operating system interfaces, once written, have caused few problems. There have been two major sources of difficulty in implementing for the PDP-11:

- 1) The porting of data between machines is often difficult. We are hampered by the availability of compatible peripherals. For instance, our primary RT-11 development machine has no magnetic tape nor floppy disks. It can communicate with other PDP-11's only by exchanging RK-type disk packs or with SUMEX over a 2400 baud terminal line.
- 2) PDP-11 code generation is non-trivial, and a number of bugs were discovered. This can be contrasted with the PDP-10 code generators, which have caused almost no problems because of the richness of the PDP-10 instruction set, and the ample word size.

The PDP-11 code generation problems have been decreasing in frequency. The demonstration of the compiler on the PDP-11 has increased confidence in the code generators though floating point code generation is only now beginning to undergo extensive testing.

The problems of data exchange have proven substantial. It is difficult to formulate a general strategy due to the diverse file systems which are encountered. These problems are often underestimated, resulting in unexpected delays in the development of portable systems.

A number of groups are interested in the development of other MAINSAIL implementations, including ones for the VAX, ECLIPSE and TI-990 computers. We hope to start work on these implementations this summer through the private company being formed.

b) Distribution and Use

The distribution beyond Stanford of PDP-10 versions of MAINSAIL was begun this year. MAINSAIL has been implemented at sites on the Arpanet, and ported via magnetic tape to other locations. All sites have been able to run MAINSAIL as soon as the files are taken off the tape. This is in contrast to the typical hardware manufacturer's software, which often takes days, or even weeks, to make executable.

There are currently three sites using the TENEX version, six using the TOPS-10 version, and five using the TOPS-20 version.

Extensive work was done this year on various PDP-11 configurations, and it is now beginning to be exported beyond the test sites here at Stanford.

One user has been writing MAINSAIL programs for two years and running them on his PDP-11/40. These include a 3-dimensional graphics package, a code optimizer for the DEC VT-11 display processor, a flow rate monitor for a cell-sorter connected to the PDP-11, and machine-independent arbitrary-precision arithmetic routines.

A geophysics group is writing MAINSAIL programs to extract data from ERTS tapes and to then perform a variety of image analyses on the extracted data. Another user is writing a machine-independent interprocessor communications facility.

A sampling of other MAINSAIL programs developed during the past year include a machine-independent tape transfer program; a program which compares two text files and prints out the differences on a per-line basis; a program which forms a new text file from selected pages of existing text files; a "conference" program enabling more than two people at once to carry out an on-line discussion; a "calculator" program; a record i/o package, which, given a pointer to a record, will print out the values of the fields of the record. Work has also begun on a portable text editor.

A number of sites are now evaluating MAINSAIL with the intent of using it for substantial product development. In most cases, the sites are primarily attracted by MAINSAIL's portability, since there has been no other language which previously played this role while at the same time providing a rich programming environment.

c) Compiler Design

A detailed analysis was made of the compiler, its algorithms and use of data structures. The goal was to reduce the size and number of data structures to allow the compiler to fit on machines with small address spaces, without sacrificing too much efficiency.

Once the compiler was able to fit, the next goal was to improve efficiency and reduce compilation time. First, an analysis of the compiler and of the runtime system uncovered some inefficiencies which were corrected.

Next, various compiler configurations were examined. By configuration is meant the various ways in which procedures can be combined into modules. On a machine with a large address space the compiler is most efficient if it consists of a few modules, since that reduces the number of intermodule calls. But on a machine with a small address space, module swapping is necessary, and compilation time is roughly proportional to the number of swaps. We wanted to determine whether a "better" configuration (one which required less swapping) than that of the existing compiler could be found.

A MAINSAIL program was written to simulate compilation on machines with various address spaces. The simulation was driven by exact data, obtained from traces of all procedure calls made during given compilations. A format was devised for easily specifying potential compiler configurations, and the simulator tested their efficiency. The resulting data showed that curves plotting amount of memory versus number of swaps are smoothly exponential. Examination of this data indicates that for 32K machines, another 10K would cut the number of module swaps in half, thus greatly increasing compilation speed.

As a result, two configurations are now in use: a "big" configuration to be run on machines with "large" address spaces, and a "small" configuration to be run on those with small address spaces. As predicted by the simulation, use of the "optimal" small configuration significantly increased the compilation speed on the PDP-11. Use of the "big" configuration, with just a few large modules, also improved the compiler speed on the PDP-10.

A new approach to code generation has been introduced over the past year. It utilizes tree structures for the intermediate representation, rather than the more primitive triples or quadruples. A tree structure is built for each procedure, and code is generated by walking the tree. This new approach will probably be used in all future code generators since it allows for procedure-wide optimization, and also supports the debugging version described later.

d) Language Design

The language itself has been very stable this past year, undergoing only a few simple additions. The fact that it has remained stable while supporting the past year of development is convincing evidence that the language has matured to the point of commercial viability.

The ability to access certain fields of the array descriptor for an array was added. These fields tell the name and bounds of the array. Similarly, the name of a file can be accessed via a pointer to the file descriptor.

MAINSAIL originally guaranteed ASCII character codes. Last year, for portability reasons, it was decided that MAINSAIL would no longer specify the exact character set used, but only that minimal assumptions would be made about the character set. A number of system procedures were added to complement the guaranteed character set assumptions.

e) Runtime Design

At the time of the last annual report, a new runtime system, oriented toward execution efficiency and less memory utilization, was under implementation. It has been very stable since its completion in September 1978.

Some examples of further improvements are: 1) the ability to have a map of memory printed, showing the number of pages used for control space, data space, and buffers, 2) tuning to the garbage collection facility, and 3) a new response that can be made to an error message will cause the printing of a table listing the procedure calls that led up to the call to the error message routine.

The concept of a "module library" has also been introduced. The output of each compilation (after assembly) is an executable file. When a program consists of a large number of modules, it quickly becomes inconvenient (if not impossible) to have a separate file for each executable module. "Module libraries", bulk repositories for modules, were designed to solve this problem. A utility module was written to provide the necessary management functions, as were procedures to insert and delete library files from a runtime list of libraries maintained by the MAINSAIL system. The MAINSAIL runtimes themselves, along with the compiler modules, now reside in module libraries.

f) Emulation Research

MAINSAIL is being used as the basis of research into a language-oriented approach to program representation and execution. Such an approach starts with language characteristics, which determine program representation (instruction set) and execution environment, which in turn determine the processor architecture. This is in contrast to the conventional machine-oriented approach in which the instruction set and processor architecture exist independently of the language, and hence dictate the representation and limit the execution environment. As technology provides increasing flexibility in machine design, high-level-language processors provide an alternative to general-purpose machine-language processors.

The MAINSAIL compiler, with its retargetable code generators and large body of machine-independent software, is an ideal basis for this study. A comprehensive study is being made of the static and dynamic characteristics of MAINSAIL programs. Based on this study, a number of language representations are obtained by varying two primary design criteria: the nature of an operand and the encoding of the instruction stream. The resulting representations range from a stream of bit-aligned fields which directly reflect the source language structure, to a sequence of simple instructions with highly-constrained operands.

Code generators, as well as instruction-set interpreters, have been developed for a number of such representations. Machine architectures which provide efficient implementations for these representations are also under

exploration. The goal is to provide an extremely efficient MAINSAIL processor from the standpoint of program execution time as well as program development time. Such a processor should be viewed as a "language processor" rather than a general-purpose processor since it is designed explicitly for the purpose of executing a single high-level language. A language processor can be used either as a stand-alone system which serves a single user, or as a component in a larger system consisting of many language processors (which need not all support the same language) that are assigned to appropriate user programs under control of an executive processor.

A MAINSAIL debugger based on this research is operational, though it has not been released for general use. This debugger involves an interpreter for a MAINSAIL instruction set (called "s-code", for structured code) which so closely captures the structure of MAINSAIL that it can be "decompiled" into what is essentially the source text, including the original variable names. The code generator for s-code utilizes the new tree-structured intermediate code, which is unbiased with regard to the form of the target code. The mode of operation on a conventional computer involves compilation of those modules which are to be debugged into s-code. These s-code modules may be freely mixed with native code modules (e.g., modules compiled into the PDP-10 instruction set). During execution, MAINSAIL automatically determines when an s-code module is to gain control, and at that point gives control to the interpreter.

The interpreter allows execution to progress in a manner which directly reflects the source program. The user can single step and place break points on the source-statement level, display and alter the values of variables, and display the decompiled text being executed. A screen-oriented debugger would involve the cursor moving along the displayed text as it was being executed in single-step mode, with the user moving the cursor to points at which break points are to be displayed, or under variables whose values are to be displayed. The current debugger has been designed to support such an approach, but does not yet support this mode of operation.

Program execution can be made to halt based on a variety of conditions such as entry to a particular module or procedure; execution of a particular statement; or upon execution of a specified number of statements since the start of the program. This latter type of break point allows the user to restart a program which encountered an error, and have it break a specified number of statement executions before the error. Single step operation then allows examination of the execution environment on a statement-by-statement basis up to the point of the error. Whenever the s-code interpreter detects an error (e.g., subscript out of range), it gives control to the debugger, which informs the user what module, procedure and statement caused the error, and displays decompiled text around the statement. The user can then use the full power of the debugger to determine the source of the error.

The entire runtime system and compiler can now be interpreted in this fashion. The "MAINSAIL machine" being designed as part of the research will directly execute the s-code representation, i.e., s-code is the (macro) instruction set of the machine. Due to the compactness of s-code (approximately one-third the size of equivalent PDP-10 code), and its transparency with respect to the MAINSAIL execution environment, the MAINSAIL machine will provide optimized program execution along with the debugging capabilities. Since s-code

is the instruction set of the MAINSAIL machine, all modules can be decompiled and debugged with no penalty in execution speed.

2.1.2.6 User Software and Intra-Community Communication

We have continued to assemble and maintain a broad range of utilities and user support software. These include operational aids, statistics packages, DEC-supplied programs, improvements to the TOPS-10 emulator, text editors, text search programs, file space management programs, graphics support, a batch program execution monitor, text formatting and justification assistance, and magnetic tape conversion aids. Over the past year we have undertaken several significant development efforts to provide needed new programs to the SUMEX-AIM community. These include:

- 1) TTYFTP - A number of users have had the need to move files between their local machines and SUMEX but were not connected to the ARPANET. These include for example the transfer of data between the PUFF project at Pacific Medical Center in San Francisco and SUMEX, distribution of MAINSAIL to various non-network sites, and movement of instrument data in support of the DENDRAL or Ultrasound Imaging (Ob-Gyn) projects. We have undertaken development of a file transfer program usable over any teletype line (hardline, dial-up, TYMNET, etc.) which incorporates appropriate control protocols and error checking. The design is based on the DIALNET protocols designed by Crispin at the Stanford AI Laboratory. Differences from DIALNET were necessary to achieve machine and data source independence. We also expanded the DIALNET packet opcodes to include a new packet (RCT) which prevents data overruns and augmented the DIALNET "request for connection" packet to contain additional needed parameters. TTYFTP is written in MAINSAIL so that we can take advantage of the machine independence inherent in the language. The program is written modularly, and has a scheduler module which can service up to eight FTP modules per line, one packet processor per line, and multiple lines. Because of this it can run as either a user process, or a server process. The latter can be either a listening server (handling in-coming lines) or a host server, started up by a user program and then logged off after all transfers are complete. We have preserved DIALNET compatibility so that we will be able to communicate to machines running DIALNET. After the TENEX implementation is completed, we will make the changes necessary to connect TENEX to a PDP-11 RT-11 system and follow that with an RSX-11M version. Since MAINSAIL is up and running under all three of these operating systems, this process is greatly simplified.
- 2) EMACS - We have continued to import and support the EMACS text editing system from MIT. This editor offers a broader range of services than TVEDIT but has lacked a smoothly human engineered interface. Substantial effort has gone into developing macro packages that improve the human engineering features of EMACS and providing introductory documentation for new users. This has been closely coordinated with similar efforts at SRI and MIT. A community of EMACS users is now developing at SUMEX.

- 3) ARCHED - In order to facilitate management of file archive directories, we have been developing a display-oriented editor to give improved interaction when posting retrieval requests and to allow records of previously archived files to have descriptive comments attached, be expunged (because they are outdated), or be moved into secondary archive directories. Facilities will exist to allow viewing files based on name template specifications or date constraints.

We have also made changes and updates to many of the existing programs. While many of these changes were maintenance bug fixes, major efforts were involved to bring up new versions of PASCAL, SAIL BACKUP, MACRO, LINK10, GLOB, PA1050, and a new set of utility routines used by many of the DEC CUSP's. Improvements were made in PUB (a text formatting program), MSG (a message reading program written by J. Vittal), and BBD (the bulletin board reading program developed at SUMEX). Several other new programs are in various stages of being brought up on the system including Knuth's text publication system, TEX; a program to periodically update a news summary file from the AP news service files kept at the Stanford AI Laboratory, APNEWS; a program to connect to the Stanford Center for Information Processing machines, GOTRAN; an improved program to locate users on the SUMEX system and on other ARPANET sites, FIND; and an improved mail facility for GUESTS.

2.1.2.7 Documentation and Education

We have spent considerable effort to develop, maintain, and facilitate access to our documentation so as to accurately reflect available software. The HELP and Bulletin Board subsystems have been important in this effort. As subsystems are updated, we generally publish a bulletin or small document describing the changes. As more and more changes occur, it becomes harder and harder for users to track down all of the change pointers. We are in the process of reviewing the existing documentation system again for compatibility with the programs now on line and to integrate changes into the main documents. This will also be done with a view toward developing better tools for maintaining up-to-date documentation.

2.1.2.8 Software Compatibility and Sharing

At SUMEX-AIM we firmly believe in importing rather than reinventing software where possible. As noted above, a number of the packages we have brought up are from outside groups. Many avenues exist for sharing between the system staff, various user projects, other facilities, and vendors. The advent of fast and convenient communication facilities coupling communities of computer facilities has made possible effective intergroup cooperation and decentralized maintenance of software packages. The TENEX sites on the ARPANET have been a good model for this kind of exchange based on a functional division of labor and expertise. The other major advantage is that as a by-product of the constant communication about particular software, personal connections between staff members of the various sites develop. These connections serve to pass general information about software tools and to encourage the exchange of ideas among the sites. Certain common problems are now regularly discussed on a multi-site level. We continue to draw significant amounts of system software from other

ARPANET sites, reciprocating with our own local developments. Interactions have included mutual backup support, experience with various hardware configurations, experience with new types of computers and operating systems, designs for local networks, operating system enhancements, utility or language software, and user project collaborations. We have been able to import many new pieces of software and improvements to existing ones in this way. Examples of imported software include the message manipulation program MSG, TENEX SAIL, PASCAL, TENEX SOS, INTERLISP, the RECORD program, ARPANET host tables, and many others. Reciprocally, we have exported our contributions such as the crash analysis program, drum page migration system, KI-10 page table efficiency improvements, GTJFN enhancements, PUB macro files, the bulletin board system, MAINSAIL, SPELL, SNDMSG enhancements, our BATCH monitor, and improved SA-10 software.

We have also assisted groups that have interacted with SUMEX user projects get access to software available in our community. For example, Prof. Dreiding's group in Switzerland became interested in some of the system software available here after attending the DENDRAL CONGEN workshops (see Section 4.2.3 on page 139). We have provided him with the non-licensed programs requested.

2.1.3 Resource Management

2.1.3.1 Organization

The SUMEX-AIM resource is administered between the Departments of Genetics and Computer Science of Stanford University. Its mission, locally and nationally, entails both the recruitment of appropriate research projects interested in medical AI applications and the catalysis of interactions among these groups and the broader medical community. User projects are separately funded and autonomous in their management. They are selected for access to SUMEX on the basis of their scientific and medical merits as well as their commitment to the community goals of SUMEX. Currently active projects span a broad range of application areas such as clinical diagnostic consultation, molecular biochemistry, belief systems modeling, mental function modeling, and instrument data interpretation (descriptions of the individual collaborative projects are in Section 4 beginning on page 64).

At the end of the last grant year, Professor Lederberg assumed his new role as president of Rockefeller University and Professor Feigenbaum, chairman of the Stanford Department of Computer Science, took over as principal investigator of the SUMEX project. This management transition took place without missing a beat and the SUMEX-AIM community continues to function with the same high level of vitality as before. This is due, in large part, to the depth of Professor Feigenbaum's prior involvement as co-principal investigator and Stanford's multi-disciplinary support of SUMEX-AIM. Professor Lederberg continues an active role in the SUMEX-AIM community as chairman of the AIM Executive Committee and on a more frequent basis through the system message facilities. Professor Stanley Cohen has continued his role on the Stanford SUMEX Advisory Committee and has assumed a new role on the national AIM Executive Committee. He provides biomedical ties and coordination with the Stanford Medical School and projects.

2.1.3.2 Management Committees

Since the SUMEX-AIM project is a multilateral undertaking by its very nature, we have created several management committees to assist in administering the various portions of the SUMEX resource. As defined in the SUMEX-AIM management plan adopted at the time the initial resource grant was awarded, the available facility capacity is allocated 40% to Stanford Medical School projects, 40% to national projects, and 20% to common system development and related functions. Within the Stanford aliquot, Prof. Feigenbaum and BRP have established an advisory committee to assist in selecting and allocating resources among projects appropriate to the SUMEX mission. The current membership of this committee is listed in Appendix III.

For the national community, two committees serve complementary functions. An Executive Committee oversees the operations of the resource as related to national users and makes the final decisions on authorizing admission for new projects and revalidating continued access for existing projects. It also establishes policies for resource allocation and approves plans for resource

development and augmentation within the national portion of SUMEX (e.g., hardware upgrades, significant new development projects, etc.). The Executive Committee oversees the planning and implementation of the AIM Workshop series currently implemented under Prof. S. Amarel of Rutgers University and assures coordination with other AIM activities as well. The committee will play a key role in assessing the possible need for additional future AIM community computing resources and in deciding the optimal placement and management of such facilities. The current membership of the Executive committee is listed in Appendix III.

Reporting to the Executive Committee, an Advisory Group represents the interests of medical and computer science research relevant to AIM goals. The Advisory Group serves several functions in advising the Executive Committee; 1) recruiting appropriate medical/computer science projects, 2) reviewing and recommending priorities for allocation of resource capacity to specific projects based on scientific quality and medical relevance, and 3) recommending policies and development goals for the resource. The current Advisory Group membership is given in Appendix III.

These committees have actively functioned in support of the resource. Except for the meetings held during the AIM workshops, the committees have "met" by messages, net-mail, and telephone conference owing to the size of the groups and to save the time and expense of personal travel to meet face to face. The telephone meetings, in conjunction with terminal access to related text materials, have served quite well in accomplishing the agenda business and facilitate greatly the arrangement of meetings. Other solicitations of advice requiring review of sizable written proposals are done by mail.

We will continue to work with the management committees to recruit the additional high quality projects which can be accommodated and to evolve resource allocation policies which appropriately reflect assigned priorities and project needs. We will continue to make information available about the various projects both inside and outside of the community and thereby promote the kinds of exchanges exemplified earlier and made possible by network facilities.

2.1.3.3 New Project Recruiting

The SUMEX-AIM resource has been announced through a variety of media as well as by correspondence, contacts of NIH-BRP with a variety of prospective grantees who use computers, and contacts by our own staff and committee members. The number of formal projects that have been admitted to SUMEX has more than trebled since the start of the project to a current total of 9 national AIM projects and 8 Stanford projects. Others are working tentatively as pilot projects or are under review.

We have prepared a variety of materials for the new user ranging from general information such as is contained in a SUMEX-AIM overview brochure to more detailed information and guidelines for determining whether a user project is appropriate for the SUMEX-AIM resource. Dr. E. Levinthal has prepared a questionnaire to assist users seriously considering applying for access to SUMEX-

AIM. Pilot project categories have been established both within the Stanford and national aliquots of the facility capacity to assist and encourage new projects in formulating possible AIM proposals and pending their application for funding support. Pilot projects are approved for access for limited periods of time after preliminary review by the Stanford or AIM Advisory Group as appropriate to the origin of the project.

These contacts have sometimes done much more than provide support for already formulated programs. For example, Prof. Feigenbaum's group at Stanford previously initiated a major collaborative effort with Dr. Osborn's group at the Institutes of Medical Sciences in San Francisco. This project in "Pulmonary Function Monitoring and Ventilator Management - PUFF/VM" (see Section 4.1.7 on page 98) originated as a pilot request to use MLAB in a small way for modeling. Subsequently the AI potentialities of this domain were recognized by Feigenbaum, Nii, and Osborn and a joint proposal was submitted to and funded by NIH. This past summer John Kunz from Dr. Osborn's laboratory spent approximately half time at Stanford to learn more about AI research and to participate more closely in the development of the PUFF/VM program.

Similarly, Prof. Feigenbaum and Ms. Nii recently spent two days with Profs. Kintsch and Polson at the University of Colorado, introducing them to the newly developed AGE package for use in formulating their program on modeling aspects of human cognition.

The following lists the fully authorized projects currently comprising the SUMEX-AIM community (see Section 4 for more detailed descriptions). The nucleus of five projects that were authorized at the initial funding of the resource in December 1973 are marked by "<i>" and the new projects admitted this past year by "<n>".

National Community -

- 1) Acquisition of Cognitive Procedures (ACT); Dr. J. Anderson (Carnegie-Mellon University)
- 2) Chemical Synthesis Project (SECS); Dr. T. Wipke (University of California at Santa Cruz)
- <n> 3) Hierarchical Models of Human Cognition; Drs. W. Kintsch and P. Polson (University of Colorado)
- <i> 4) Higher Mental Functions Project; K. Colby, M.D. (University of California at Los Angeles)
- 5) INTERNIST Project; J. Myers, M.D. and Dr. H. Pople (University of Pittsburgh)
- 6) Medical Information Systems Laboratory (MISL); M. Goldberg, M.D. and Dr. B. McCormick (University of Illinois at Chicago Circle)
- 7) Pulmonary Function Project (PUFF/VM); J. Osborn, M.D. (Institutes of Medical Sciences, San Francisco) and Dr. E. Feigenbaum (Stanford University)

- <i> 8) Rutgers Computers in Biomedicine; Dr. S. Amarel (Rutgers University)
- 9) Simulation of Comprehension Processes; Drs. J. Greeno and A. Lesgold (University of Pittsburgh)

Stanford Community -

- 1) AI Handbook Project; Dr. E. Feigenbaum
- <i> 2) DENDRAL Project; Drs. C. Djerassi and E. Feigenbaum
- 3) Generalization of AI Tools (AGE); Dr. E. Feigenbaum
- 4) Large Multi-processor Arrays (HYDROID); Dr. G. Wiederhold
- 5) Molecular Genetics Project (MOLGEN); Dr. E. Feigenbaum and L. Kedes, M.D.
- <i> 6) MYCIN Project; E. H. Shortliffe, M.D. and Dr. B. Buchanan
- <i> 7) Protein Structure Modeling; Drs. E. Feigenbaum and R. Engelmores
- <n> 8) RX Project; R. Blum, M.D.

As an additional aid to new projects or collaborators with existing projects, we provide a limited amount of funds for use to support terminals and communications needs of users without access to such equipment. We are currently providing support for 6 terminals and 4 modems for users as well as a leased line between Stanford and the University of California at Santa Cruz for the Chemical Synthesis project.

2.1.3.4 Stanford Community Building

The Stanford community has undertaken several internal efforts to encourage interactions and sharing between the projects centered here. Professor Feigenbaum organized a project with the goal of assembling a handbook of AI concepts, techniques, and current state-of-the-art. This project has had enthusiastic support from the students and substantial progress made in preparing many sections of the handbook (see Section 4.2.1 on page 130 for more details).

Weekly informal lunch meetings (SIGLUNCH) are also held between community members to discuss general AI topics, concerns and progress of individual projects, or system problems as appropriate. In addition, presentations from a substantial number of outside speakers are invited.

2.1.3.5 Existing Project Reviews

We have conducted a continuing careful review of on-going SUMEX-AIM projects to maintain a high scientific quality and relevance to our medical AI goals and to maximize the resources available for newly developing applications projects. At the last AIM workshop, meetings of the AIM Advisory Group and Executive Committee were held to review the national AIM projects. These groups recommended continued access for all formal projects then on the system. They also recommended phasing out the Organ Culture pilot project.

In the fall of 1978, meetings of the Stanford Advisory Group were held to review projects supported out of the Stanford aliquot. The recommendation of this group was to phase out support for the Hydroid Project, pending work more directly applicable to SUMEX-AIM goals. The group also recommended phasing out the Quantum Chemistry and Genetics Applications pilot projects unless stronger AI relevance were established immediately. The Quantum Chemistry project is attempting to develop ties to the DENDRAL stereochemistry effort. Since Prof. Loew will move to Rockefeller University this summer, her access to SUMEX would come under the jurisdiction of the AIM Executive Committee and we will ask them to review her application for continued support. The Genetics Application project has acquired their own machine for statistical calculations on genetic demographic data and has stopped using SUMEX.

2.1.3.6 AIM Workshop Support

The Rutgers Computers in Biomedicine resource (under Dr. Saul Amarel) has organized a series of workshops devoted to a range of topics related to artificial intelligence research, medical needs, and resource sharing policies within NIH. Meetings have been held for the past several summers at Rutgers.

In May 1979, a mini-AIM workshop devoted to clinical diagnosis programs was organized by MIT-Tufts and Rutgers and held in Vermont. This meeting was small (about 25 attendees) and emphasized detailed technical discussions about system designs and the strengths and weaknesses of various approaches. Many of the attendees were graduate students in order to maximize the benefit of personal contacts and discussions for on-going research projects. Topics covered in the discussions included state-of-the-art in explanation, causality in reasoning, strategies of focusing and dealing with multiple diagnostic problems, issues of representation and grain of description, creating and updating a knowledge base, planning strategies, issues of time representation, and inexact reasoning.

The SUMEX facility has served as a communications base for workshop planning and provided support for workshop demonstrations when requested. We expect to continue this support for future workshops. The AIM workshops provide much useful information about the strengths and weaknesses of the performance programs both in terms of criticisms from other AI projects and in terms of the needs of practicing medical people. We plan to continue to use this experience to guide the community building aspects of SUMEX-AIM.

2.1.3.7 Resource Allocation Policies

As the SUMEX facility has become increasingly loaded, a number of diverse and conflicting demands have arisen which require controlled allocation of critical facility resources (file space and central processor time). We have already spelled out a policy for file space management; an allocation of file storage is defined for each authorized project in conjunction with the management committees. This allocation is divided among project members in any way desired by the individual principal investigators. System allocation enforcement is implemented by project each week. As the weekly file dump is done, if the aggregate space in use by a project is over its allocation, files are archived from user directories over allocation until the project is within its allocation.

We have implemented effective system scheduling controls (see page 16) to attempt to maintain the 40:40:20 balance in terms of CPU utilization and to avoid system and user inefficiencies during overload conditions. The initial complement of user projects justifying the SUMEX resource was centered to a large extent at Stanford. Over the past five years of the SUMEX grant, a substantial growth in the number of national projects was realized. During the same time the Stanford group of projects has matured as well and in practice the 40:40 split between Stanford and non-Stanford projects is not ideally realized (see Figure 11 on page 49 and the tables of recent project usage on page 52). Our job scheduling controls bias the allocation of CPU time based on percent time consumed relative to the time allocated over the 40:40:20 community split. The controls are "soft" however in that they do not waste computer cycles if users below their allocated percentages are not on the system to consume the cycles. The operating disparity in CPU use to date reflects a substantial difference in demand between the Stanford community and the developing national projects, rather than inequity of access. For example, the Stanford utilization is spread over a large part of the 24-hour cycle, while national-AIM users tend to be more sensitive to local prime-time constraints. (The 3-hour time zone phase shift across the continent is of substantial help in load balancing.) During peak times under the new overload controls, the Stanford community still experiences mutual contentions and delays while the AIM group has relatively open access to the system. For the present, we propose to continue our policy of "soft" allocation enforcement for the fair split of resource capacity.

Our system also categorizes users in terms of access privileges. These comprise fully authorized users, pilot projects, guests, and network visitors in descending order of system capabilities. We want to encourage bona fide medical and health research people to experiment with the various programs available with a minimum of red tape while not allowing unauthenticated users to bypass the advisory group screening procedures by coming on as guests. So far we have had relatively little abuse compared to what other network sites have experienced, perhaps on account of the personal attention that senior staff gives to the logon records, and to other security measures. However, the experience of most other computer managers behooves us to be cautious about being as wide open as might be preferred for informal service to pilot efforts and demonstrations. We will continue developing this mechanism in conjunction with management committee policy decisions.

We have also encouraged mature projects to apply for their own machine resources in order to preserve the SUMEX-AIM resource for research and

development efforts and to support projects unable to justify their own machines. The DENDRAL project is currently applying for a VAX machine to support their planned development and program export work. This machine would be integrated with the SUMEX resource through the planned local network and would be dedicated to biomolecular structure elucidation problems. At the same time it would give SUMEX resource staff experience with the VAX architecture in anticipation of projected developments within the ARPANET AI community to move toward that machine for INTERLISP support. Other projects may make similar proposals in the near future.

2.1.4 Future Plans

Our plans for the next grant year are a continuation of the work in progress as discussed earlier. Specific goals are outlined below. Objectives for the individual collaborating projects are discussed in their respective reports (see Section 4 beginning on page 64).

1) RESOURCE OPERATIONS

We will continue to make available to the SUMEX-AIM communities an effective, state-of-the-art facility to support the development of medical AI programs and to facilitate collaborations between community members. Goals include:

- a) Continue development of the existing KI-TENEX facility to maximize effectiveness for community use. We expect to continue improving system reliability and efficiency, subsystem software, documentation and user help facilities, and communications facilities.
- b) Finish procurement of a satellite machine (DEC 2020) and integrate it into the existing SUMEX-AIM facility. This will include developing necessary hardware and software interfaces (Ethernet) and evolving management policies and tools with the AIM Executive Committee to allocate this resource most effectively to meet community needs. This system will also give us experience with the many issues of distributing computing resources among collaborating projects that we expect to face in future years.
- c) Recruit new applications and projects to broaden the range of high quality medical AI applications. Several potential user projects are currently pending review and we will explore others that might be suggested by advisory group members or other contacts. We will continue to review existing projects in relation to SUMEX AI goals and capacity and to encourage the development of independent resources to support mature projects.
- d) We plan to work closely with other AIM resource nodes, such as the one at Rutgers, to ensure effective community support between the facilities and to take further advantage of expertise in various user groups for system and user software development.
- e) We will submit an application for a follow-on renewal term to the current 3-year grant which terminates in July 1981. This application will focus on continued development of artificial intelligence tools and applications central to the needs of medical science and the development of effective computing resources within the SUMEX-AIM community to enable progress towards those goals.

2) TRAINING AND EDUCATION

Within our resources, we will continue to assist new and established user projects in gaining access to SUMEX-AIM facilities. Collaborating projects will provide their own manpower and expertise for the development and dissemination of their AI programs. Goals include:

- a) Continue to provide a high standard of system documentation and limited staff assistance for user problems.
- b) Allocate funds approved for "collaborative linkages" in cooperation with the AIM Executive Committee to assist collaborating projects to meet their needs for communication and access to the SUMEX-AIM resource.
- c) Provide continued support for the AIM workshop activities in the form of demonstration support, participation in workshop discussions, and assistance for potential pilot users in understanding the SUMEX-AIM community.

3) CORE RESEARCH

Next year, no further work is planned on the MAINSAIL project for which highly successful initial design and demonstration phases were completed this past year.

Our core research work will emphasize continued development of tools of general interest to the SUMEX-AIM community, AI information resources, and basic efforts to understand and build knowledge-based "intelligent agent" programs. This work will complement on-going collaborator project developments by providing links to make more general results available to the entire community. We will continue to provide partial funding for selected individuals in the Stanford Heuristic Programming Project for these core research goals with special relevance to SUMEX medical AI applications. This support is an appropriate share, complementing funding from other sources such as ARPA and NSF.

Attention will be focused on a number of areas of research:

- a) AI Handbook - complete publication of Volume I and concentrate on the research, draft, and external review process for Volume II.
- b) AGE - improve the user interface to the AGE "tool kit" including tutorial and design assistance subsystems. We will also extend the range of tools available including such mechanisms as backward-chained inference, heuristic search, portions of the MOLGEN "units" package, and semantic networks.
- c) Representation - design appropriate symbolic structures for modeling knowledge about a problem. Presently this phase is carried out entirely by system builders. Goals are to codify the knowledge used to make such decisions, both as an aid to the system builders and ultimately to enable programs themselves to choose appropriate representations.
- d) Reasoning - model the appropriate inference mechanisms for a problem and build systems that incorporate those models.
- e) Knowledge acquisition - design of systems that acquire knowledge by communication with human experts.

- f) Multiple uses of knowledge - design of systems that use the symbolic representation of the domain knowledge for additional purposes such as consensus building (accommodating conflicting advice from experts whose competence may be equal but whose "styles" vary), tutoring of human students by employing the knowledge base (both the information it contains and the way it is organized), and explanation (constructing a chain of rules which satisfactorily rationalize the system's behavior to an observer).

2.2 Summary of Resource Usage

The following data give an overview of SUMEX-AIM resource usage. There are four subsections containing data respectively for 1) overall system loading, 2) resource use by community, 3) resource use by project, and 4) network use.

2.2.1 Overall System Loading

The following plots display several different aspects of system loading over the life of the project. These include total CPU time delivered per month, the peak number of jobs logged in, and the peak load average. The monthly "peak" value of a given variable is the average of the daily peak values for that variable during the month. Thus, these "peak" values are representative of average monthly loading maxima and do not reflect the largest excursions seen on individual days.

These data show well the continued growth of SUMEX use and the self-limiting saturation effect of system load average, especially after installation of our overload controls early in 1978. Since late 1976, when the dual processor capacity became fully used, the peak daily load average has remained between about 5.5 and 6. This is a measure of the user capacity of our current hardware configuration and the mix of AI programs.

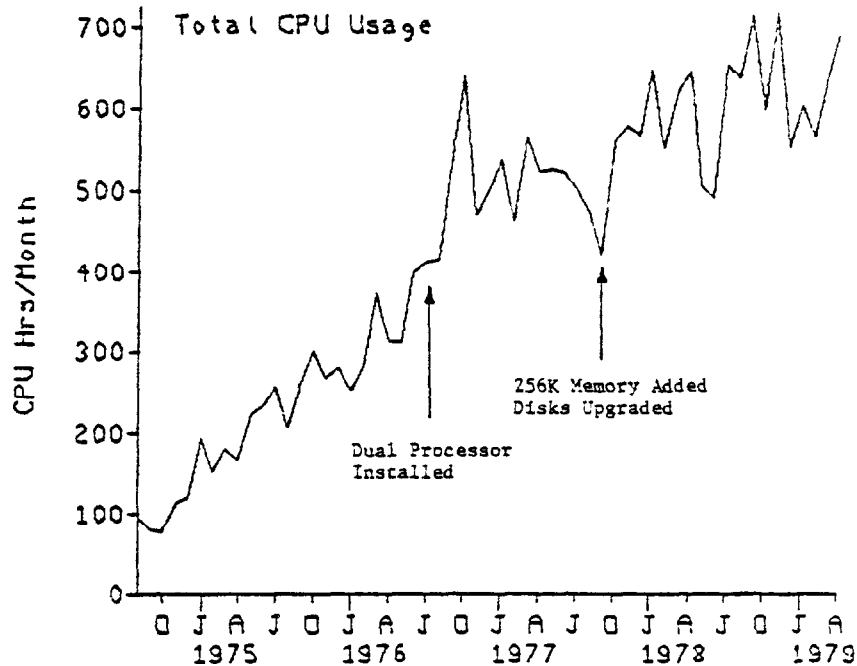


Figure 8. Total CPU Time Consumed by Month

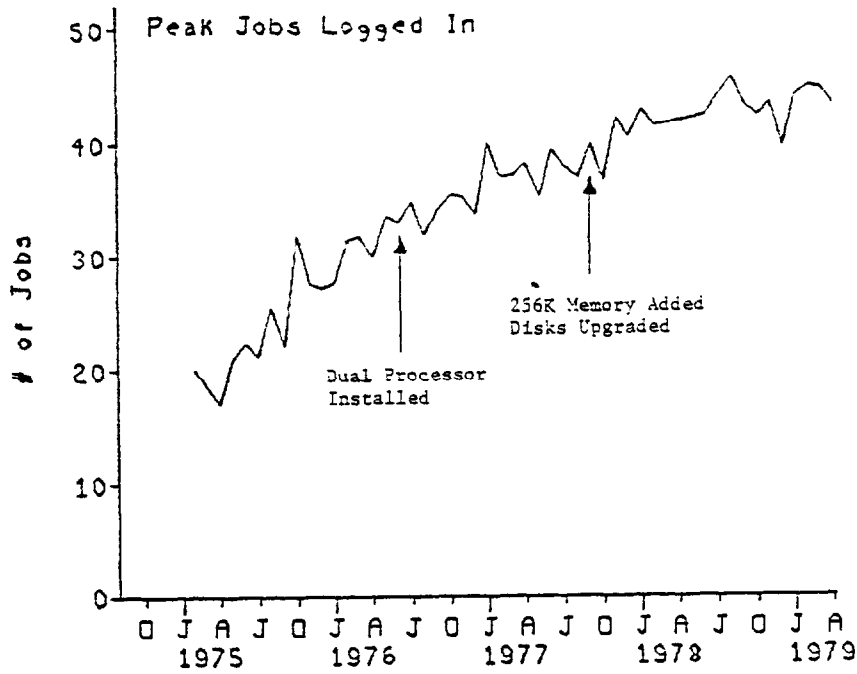


Figure 9. Peak Number of Jobs by Month

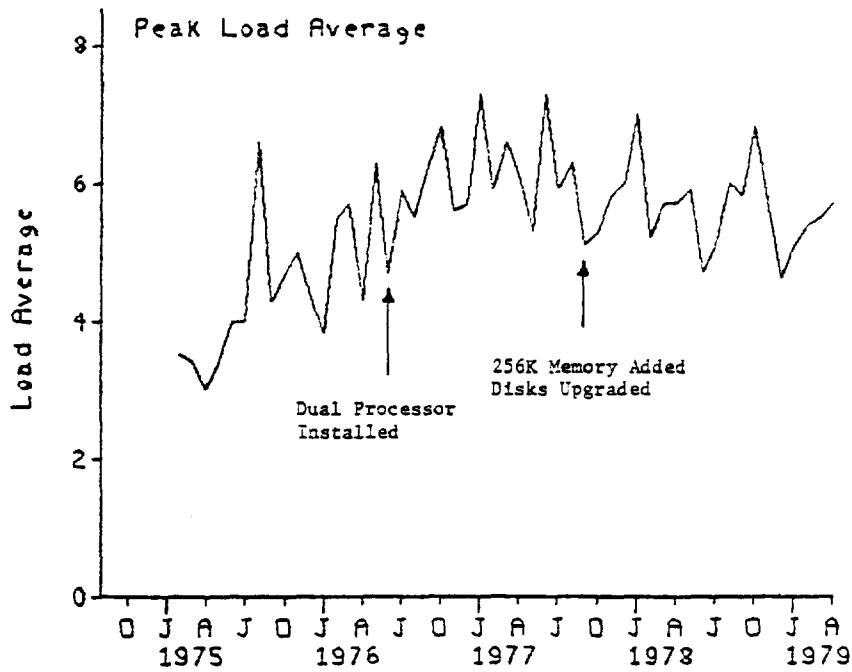


Figure 10. Peak Load Average by Month

2.2.2 Relative System Loading by Community

The SUMEX resource is divided, for administrative purposes, into 3 major communities: user projects based at the Stanford Medical School, user projects based outside of Stanford (national AIM projects), and common system development efforts. As defined in the resource management plan approved by BRP at the start of the project, the available system CPU capacity and file space resources are divided between these communities as follows:

Stanford	40%
AIM	40%
Staff	20%

The "available" resources to be divided up in this way are those remaining after various monitor and community-wide functions are accounted for. These include such things as job scheduling, overhead, network service, file space for subsystems, documentation, etc.

The monthly usage of CPU and file space resources for each of these three communities relative to their respective aliquots is shown in the plots in Figure 11 and Figure 12. Terminal connect time is shown in Figure 13. It is clear that the Stanford projects have held an edge in system usage despite our efforts at resource allocation and the substantial voluntary efforts by the Stanford community to utilize non-prime hours. This reflects the maturity of the Stanford group of projects relative to those getting started on the national side and has correspondingly accounted for much of the progress in AI program development to date.

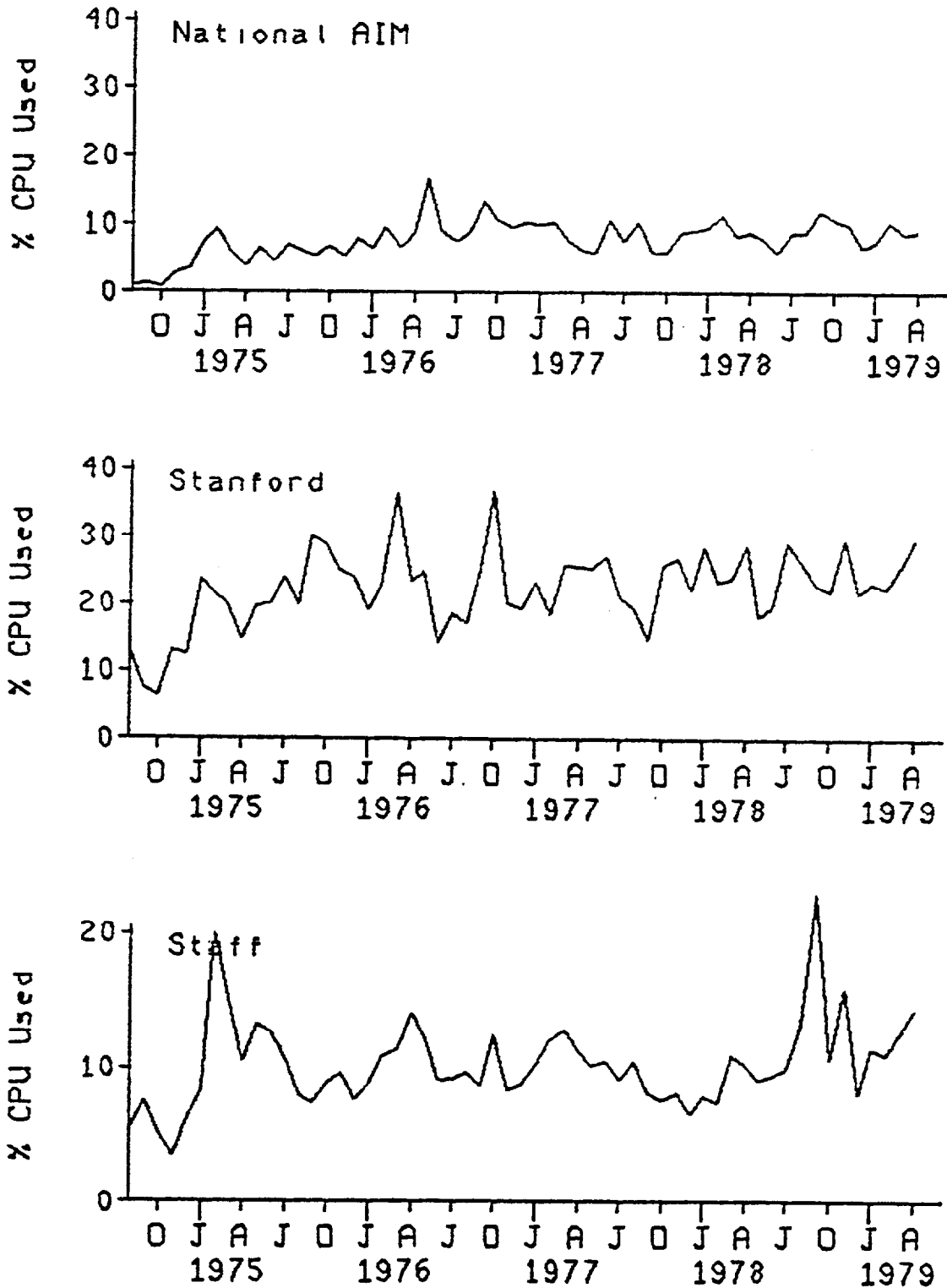


Figure 11. Monthly CPU Usage by Community

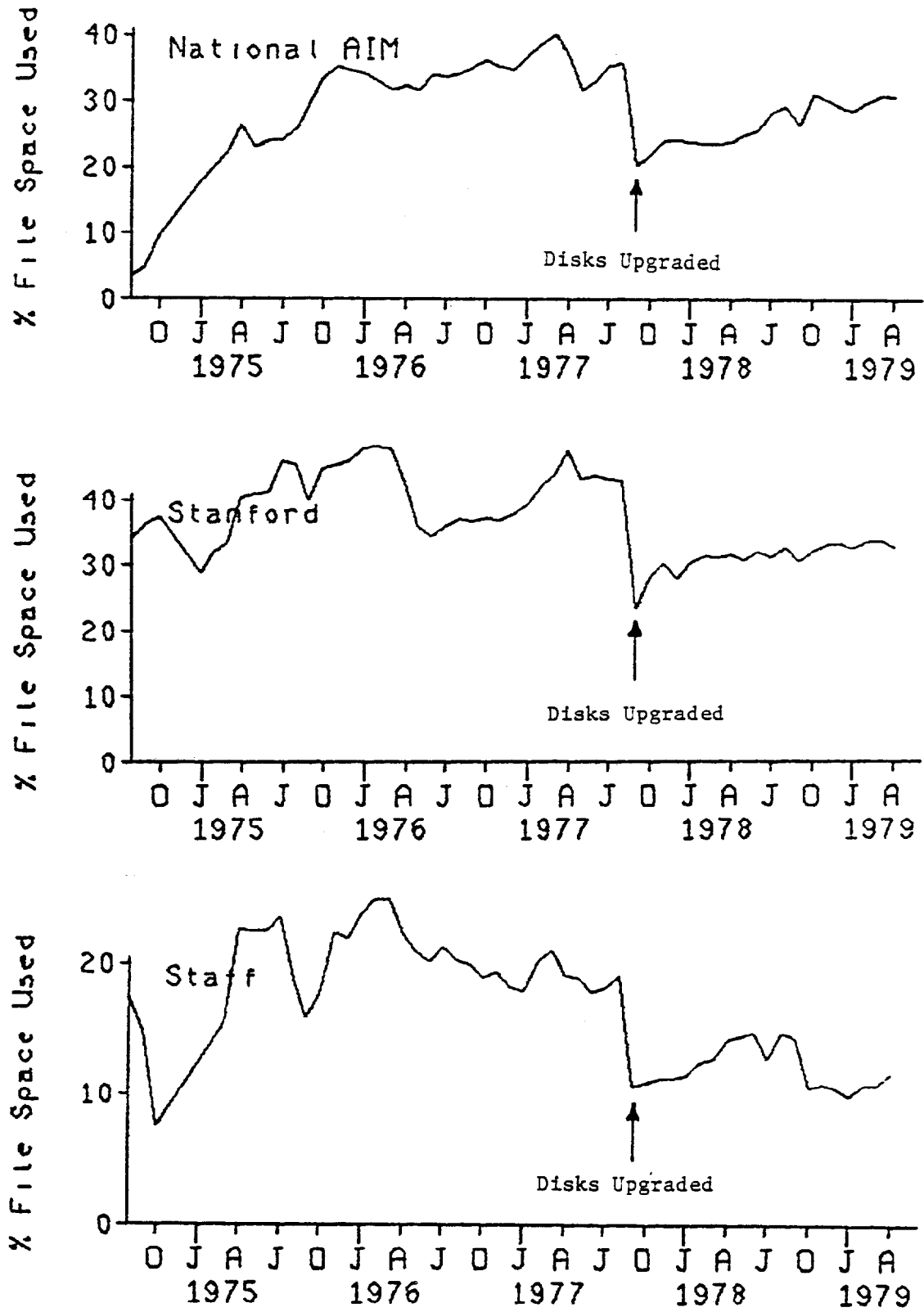


Figure 12. Monthly File Space Usage by Community

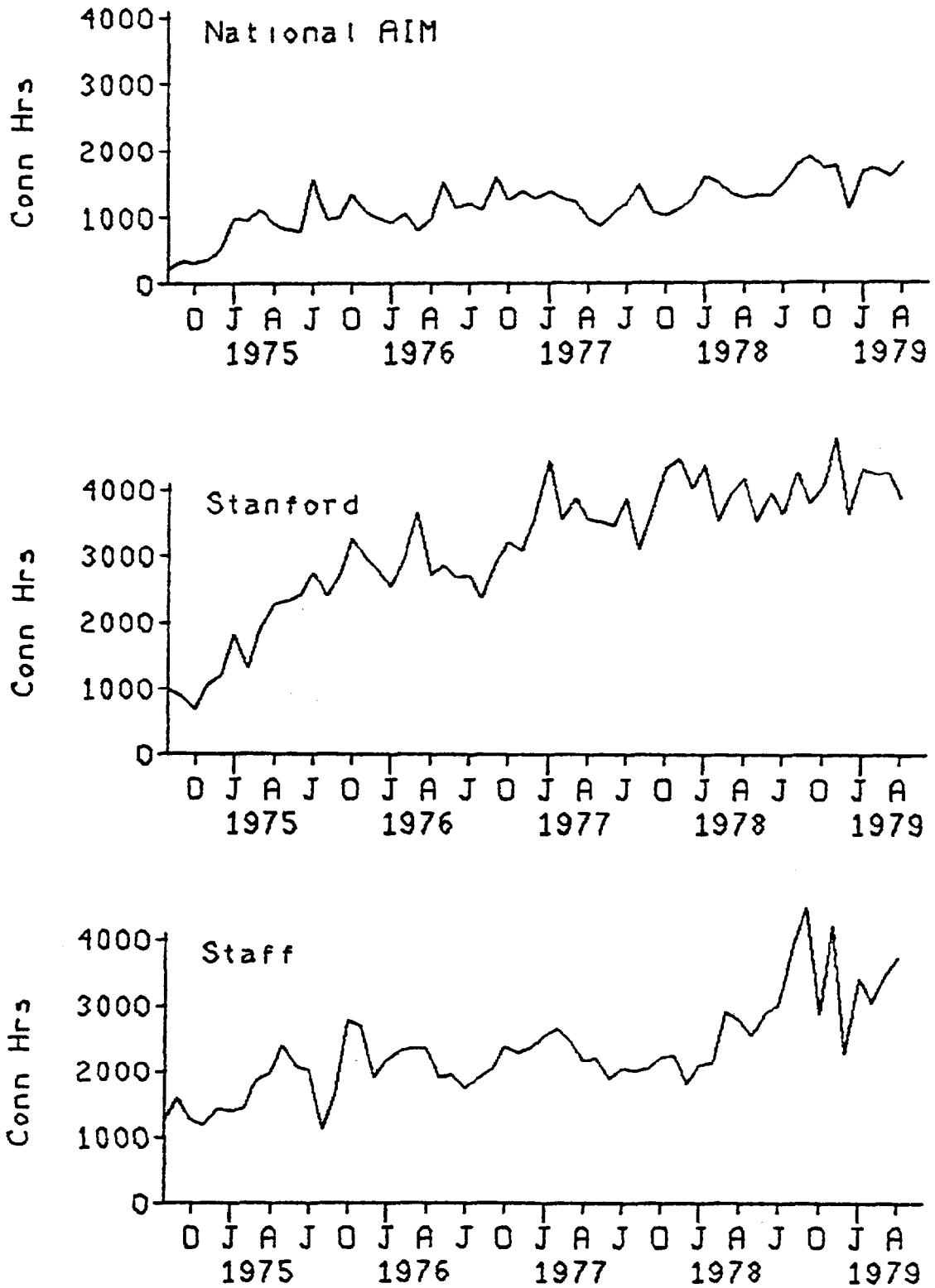


Figure 13. Monthly Terminal Connect Time by Community

2.2.3 Individual Project and Community Usage

The table following shows cumulative resource usage by project during the past grant year. The entries include a summary of the operational funding sources (outside of SUMEX-supplied computing resources) for currently active projects, total CPU consumption by project (Hours), total terminal connect time by project (Hours), and average file space in use by project (Pages, 1 page = 512 computer words). These data were accumulated for each project for the months between May 1978 and April 1979. Again the well developed use of the resource by the Stanford community can be seen. It should be noted that the Stanford projects have voluntarily shifted a substantial part of their development work to non-prime time hours which is not explicitly shown in these cumulative data. It should also be noted that a significant part of the DENDRAL and MYCIN efforts, here charged to the Stanford aliquot, support development efforts dedicated to national community access to these systems. The actual demonstration and use of these programs by extramural users is charged to the national community in the "AIM USERS" category, however.

RESOURCE USE BY INDIVIDUAL PROJECT - 5/78 THROUGH 4/79

<u>NATIONAL AIM COMMUNITY</u>	CPU (Hours)	CONNECT (Hours)	FILE SPACE (Pages)
1) ACT PROJECT "Acquisition of Cognitive Procedures" John Anderson, Ph.D. Carnegie-Mellon Univ.	111.39	1497.82	2555
2) CHEM SYNTHESIS PROJECT "Simulation & Evaluation of Chemical Synthesis" W. Todd Wipke, Ph.D. U. California, Santa Cruz	370.90	5730.58	8339
3) MOD HUMAN COGN PROJECT (since 12/78) "Hierarchical Models of Human Cognition" Peter Polson, Ph.D. Walter Kintsch, Ph.D. University of Colorado	38.26	654.28	223

4)	HIGHER MENTAL FUNCTIONS "Intelligent Speech Prosthesis" Kenneth Colby, M.D. UCLA	30.80	490.29	2687
5)	INTERNIST PROJECT "DIALOG: Computer Model of Diagnostic Logic" Jack Myers, M.D. Harry Pople, Ph.D. University of Pittsburgh	196.99	2658.47	7832
6)	MISL PROJECT "Medical Information Systems Laboratory" Morton Goldberg, M.D. Bruce McCormick, Ph.D. U. Illinois, Chicago Cir.	3.50	132.47	1120
7)	PUFF/VM PROJECT "Biomedical Knowledge Engineering in Clinical Medicine" John Osborn, M.D. Inst. Medical Sciences, San Francisco Edward Feigenbaum, Ph.D. Stanford University	97.48	3351.63	2222
8)	RUTGERS PROJECT "Computers in Biomedicine" Saul Amarel, D.Sc.	30.63	868.12	10093

9)	SCP PROJECT	18.30	436.90	275
	"Simulation of Cognitive Processes" James Greeno, Ph.D. Alan Lesgold, Ph.D. University of Pittsburgh			
10)	AIM PILOT PROJECTS			
	Psychopharm. Advisor	25.63	537.73	773
	Organ Culture	24.35	449.21	924
	Commun. Enhancement	1.83	121.71	329
	KRL Demonstrations	2.53	54.06	388
		-----	-----	-----
	AIM Pilot Totals	54.34	1162.71	2414
11)	AIM Administration	14.58	461.15	5808
12)	AIM Users on Stanford Projects			
	AGE	1.17	82.22	14
	DENDRAL	44.37	860.51	1092
	MOLGEN	.20	6.99	24
	MYCIN	5.12	137.33	295
	Guest (all projects)	47.01	812.21	189
	Other	.63	27.74	144
		-----	-----	-----
	AIM User Totals	98.50	1927.00	1762
		-----	-----	-----
	COMMUNITY TOTALS	1065.67	19371.42	45330

<u>STANFORD COMMUNITY</u>	CPU (Hours)	CONNECT (Hours)	FILE SPACE (Pages)
1) AI HANDBOOK PROJECT Edward Feigenbaum, Ph.D.	80.69	1935.01	2021
2) DENDRAL PROJECT "Resource Related Research Computers and Chemistry" Carl Djerassi, Ph.D.	1315.63	19639.31	21517
3) AGE PROJECT "Generalization of AI Tools" Edward Feigenbaum, Ph.D.	28.76	1022.46	1344
4) HYDROID PROJECT "Distributed Processing and Problem Solving" Gio Wiederhold, Ph.D.	39.65	1725.03	789
5) MOLGEN PROJECT "Experiment Planning System for Molecular Genetics" Edward Feigenbaum, Ph.D. Laurence Kedes, M.D. Douglas Lenat, Ph.D. Nancy Martin, Ph.D. U. New Mexico	384.31	6954.92	5730
6) MYCIN PROJECT "Computer-based Consult. in Clin. Therapeutics" Bruce Buchanan, Ph.D. Edward Shortliffe, M.D., Ph.D.	499.07	8384.56	8687

Section 2.2.3

Individual Project and Community Usage

7)	PROTEIN STRUCT MODELING "Heuristic Comp. Applied to Prot. Crystallog." Edward Feigenbaum, Ph.D.	206.48	2958.98	4392
8)	RX PROJECT (since 2/79) Robert Blum, M.D. Gio Wiederhold, Ph.D.	7.57	608.94	312
9)	STANFORD PILOT PROJECTS			
	Genetics Applic.	104.50	1874.51	482
	Quantum Chemistry	178.64	2004.44	810
	Ultrasonic Imaging	5.32	130.67	85
	Miscellaneous	.43	18.28	6
	Stanford Pilot Totals	288.89	4027.90	1384
10)	SU-ASSOCIATES	22.06	699.41	1557
	COMMUNITY TOTALS	2873.11	47956.52	47733

<u>SUMEX STAFF</u>	CPU (Hours)	CONNECT (Hours)	FILE SPACE (Pages)
1) Staff	953.68	28941.65	9028
2) MAINSAIL Development	446.39	9045.69	3804
3) Staff associates, misc.	65.62	2776.72	4503
COMMUNITY TOTALS	1465.69	40764.06	17335

<u>SYSTEM OPERATIONS</u>	CPU (Hours)	CONNECT (Hours)	FILE SPACE (Pages)
1) Operations	1949.22	78944.64	81114
	=====	=====	=====
RESOURCE TOTALS	7353.69	187036.64	191512

2.2.4 Network Usage

The following plots show total terminal connect time per month for TYMNET and ARPANET users since initial connection. No corresponding plot is presented for the experimental TELENET connection because of frequent line configuration changes during the connection period and the short period of active use.

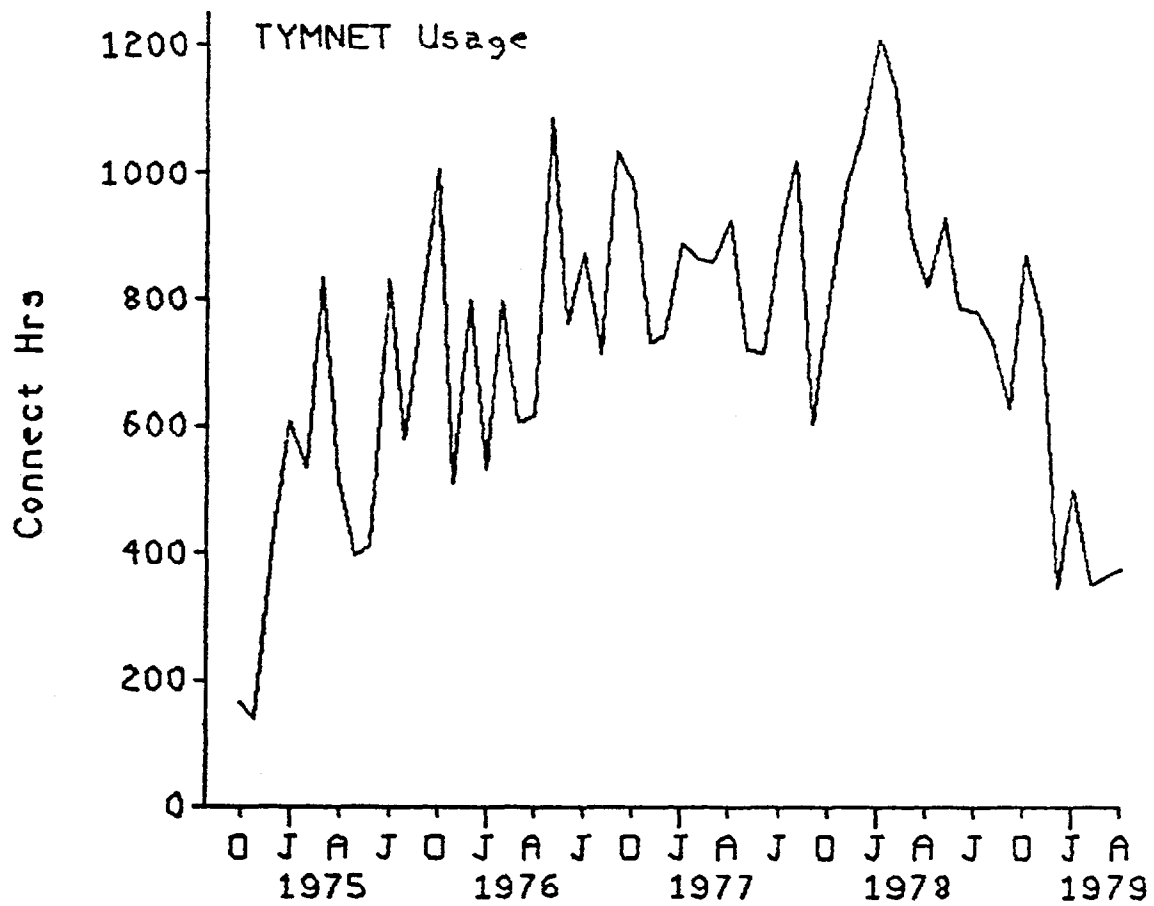


Figure 14. TYMNET Usage Data

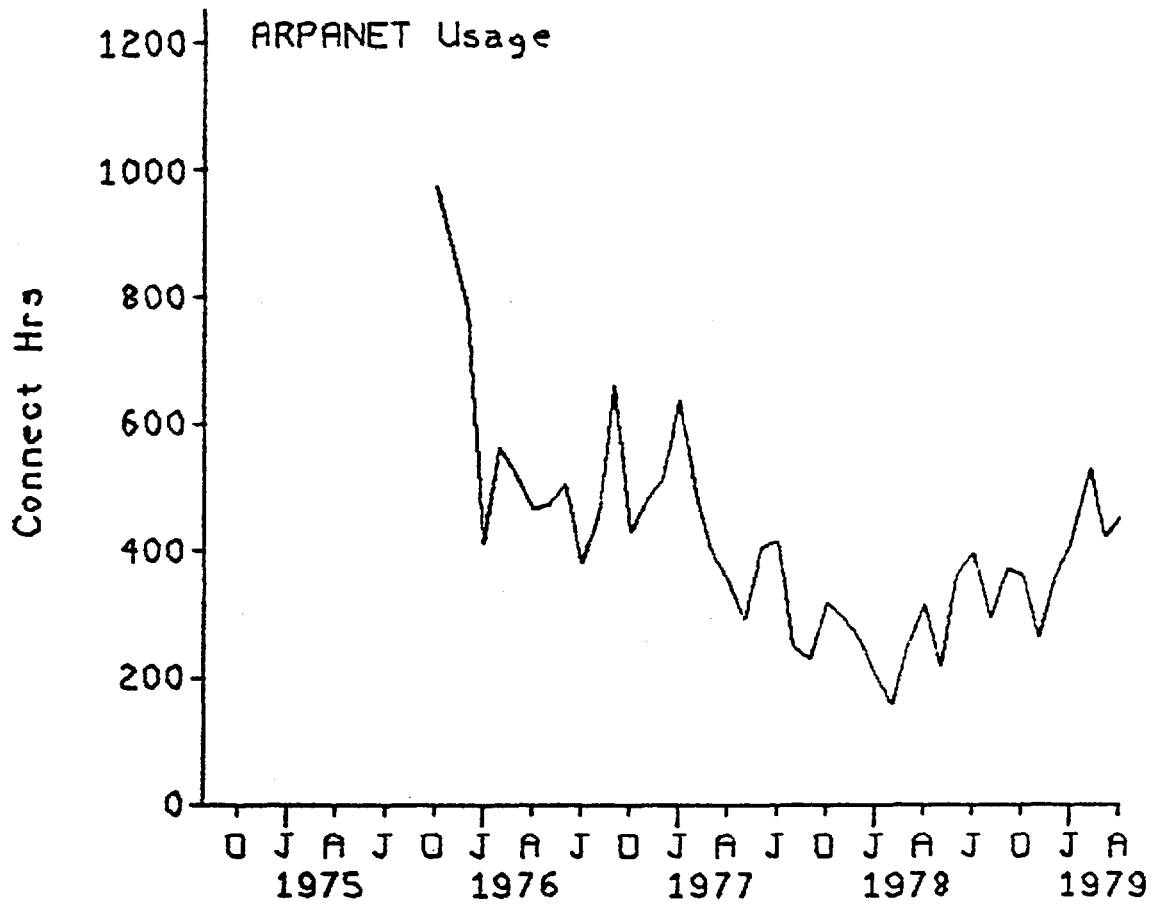


Figure 15. ARPANET Usage Data

2.3 Resource Equipment Summary

A complete inventory of resource equipment is being submitted separately along with the budget material.

2.4 Publications

The following are publications for the SUMEX staff and have included papers describing the SUMEX-AIM resource and on-going research as well as documentation of system and program developments. Publications for individual collaborating projects are detailed in their respective reports (see Section 4 on page 64).

- [1] Carhart, R.E., Johnson, S.M., Smith, D.H., Buchanan, B.G., Dromey, R.G., and Lederberg, J., Networking and a Collaborative Research Community: A Case Study Using the DENDRAL Programs, ACS Symposium Series, Number 19, Computer Networking and Chemistry, Peter Lykos (Editor), 1975.
- [2] Levinthal, E.C., Carhart, R.E., Johnson, S.M., and Lederberg, J., When Computers Talk to Computers, Industrial Research, November 1975
- [3] Wilcox, C. R., MAINSAIL - A Machine-Independent Programming System, Proceedings of the DEC Users Society, Vol. 2, No. 4, Spring 1976.
- [4] Wilcox, Clark R., The MAINSAIL Project: Developing Tools for Software Portability, Proceedings, Computer Application in Medical Care, October, 1977, pp. 76-83.
- [5] Lederberg, J. L., Digital Communications and the Conduct of Science: The New Literacy, Proc. IEEE, Vol. 66, No. 11, Nov 1978.
- [6] Wilcox, C. R., Jirak, G. A., and Dageforde, M. L., MAINSAIL - An Approach to Software Portability, in preparation.
- [7] Rindfleisch, T. C., Feigenbaum, E. A., and Lederberg, J., SUMEX-AIM - A Model for Resource Sharing and Scientific Collaboration, in preparation.

Mr. Clark Wilcox also chaired the session on "Languages for Portability" at the DECUS DECsystem10 Spring '76 Symposium.

In addition, a substantial continuing effort has gone into developing, upgrading, and extending documentation about the SUMEX-AIM resource, the SUMEX-TENEX system, the many subsystems available to users, and MAINSAIL. These efforts include a number of major documents (such as SOS, PUB, and TENEX-SAIL manuals) as well as a much larger number of document upgrades, user information and introductory notes, an ARPANET Resource Handbook entry, and policy guidelines.

3 Resource Finances

3.1 Budget Information

The budget for the SUMEX project detailing past actual costs, current year status, and estimates for the next grant year are submitted in a separate document to the NIH.

3.2 Resource Funding

The SUMEX-AIM resource is essentially wholly funded by the Biotechnology Resources Program (6). The various collaborator projects which use SUMEX are independently funded with respect to their manpower and operating expenses. They obtain from SUMEX, without charge, access to the computing and, in most cases, communications facilities in exchange for their participation in the scientific and community building goals of SUMEX.

(6) Except for participation by Stanford University in accordance with general cost-sharing and for assistance to SUMEX from other projects with overlapping aims and interests.

Collaborative Projects

4 Collaborative Project Reports

The following subsections report on the collaborative use of the SUMEX facility. Descriptions are included for the formally authorized projects within the national AIM and Stanford aliquots and the various "pilot" efforts currently under way. These project descriptions and comments are the result of a solicitation for contributions sent to each of the project Principal Investigators requesting the following information:

I. SUMMARY OF RESEARCH PROGRAM

- A. Technical goals
- B. Medical relevance and collaboration
- C. Progress summary
- D. List of relevant publications
- E. Funding support status (see below for details)

II. INTERACTIONS WITH THE SUMEX-AIM RESOURCE

- A. Collaborations and medical use of programs via SUMEX
- B. Sharing and interactions with other SUMEX-AIM projects
(via workshops, resource facilities, personal contacts, etc.)
- C. Critique of resource management
(community facilitation, computer services, capacity, etc.)

III. RESEARCH PLANS (8/79 - 7/81)

- A. Long range project goals and plans
- B. Justification and requirements for continued SUMEX use
[This section will be of special importance to the Advisory Committee and is your application for continued access.]
- C. Your needs and plans for other computational resources, beyond SUMEX/AIM
- D. Recommendations for future community and resource development

We believe that the reports of the individual projects speak for themselves as rationales for participation; in any case the reports are recorded as submitted and are the responsibility of the indicated project leaders.

4.1 National AIM Projects

The following group of projects is formally approved for access to the AIM aliquot of the SUMEX-AIM resource. Their access is based on review by the AIM Advisory Group and approval by the AIM Executive Committee.

4.1.1 Acquisition of Cognitive Procedures (ACT)

Acquisition of Cognitive Procedures (ACT)

Dr. John Anderson
Carnegie-Mellon University
Pittsburgh, Pennsylvania

I. Summary of Research Program

A. Technical goals:

To develop a production system that will serve as an interpreter of the active portion of an associative network. To model a range of cognitive tasks including memory tasks, inferential reasoning, language processing, and problem solving. To develop an induction system capable of acquiring cognitive procedures with a special emphasis on language acquisition.

B. Medical relevance and collaboration:

1. The ACT model is a general model of cognition. It provides a useful model of the development of and performance of the sorts of decision making that occur in medicine.
2. The ACT model also represents basic work in AI. It is in part an attempt to develop a self-organizing intelligent system. As such it is relevant to the goal of development of intelligent artificial aids in medicine.

We have been evolving a collaborative relationship with James Greeno and Allan Lesgold at the University of Pittsburgh. They are applying ACT to modeling the acquisition of reading and problem solving skills. We have made ACT a guest system within SUMEX. ACT is currently at the state where it can be shipped to other INTERLISP facilities. We have received a number of inquiries about the ACT system. ACT is a system in a continual state of development but we periodically freeze versions of ACT which we maintain and make available to the national AI community.

C. Progress and accomplishments:

ACT provides a uniform set of theoretical mechanisms to model such aspects of human cognition as memory, inferential processes, language processing, and problem solving. ACT's knowledge base consists of two components, a propositional component and a procedural component. The propositional component is provided by an associative network encoding a set of facts known about the world. This provides the system's semantic memory. The procedural component consists of a set of productions which operate on the associative network. ACT's production system is considerably different than many of the other currently available systems (e.g., Newell's PSG). These differences have been introduced in order to create a system that will operate on an associative network and in order to accurately model certain aspects of human cognition.

A small portion of the semantic network is active at any point in time. Productions can only inspect that portion of the network which is active at that time. This restriction to the active portion of the network provides a means to focus the ACT system in a large data base of facts. Activation can spread down network paths from active nodes to activate new nodes and links. To prevent activation from growing continuously there is a dampening process which periodically deactivates all but a select few nodes. The condition of a production specifies that certain features be true of the active portion of the network. The action of a production specifies that certain changes be made to the network. Each production can be conceived of as an independent "demon." Its purpose is to see if the network configuration specified in its condition is satisfied in the active portion of memory. If it is, the production will execute and cause changes to memory. In so doing it can allow or disallow other productions which are looking for their conditions to be satisfied. Both the spread of activation and the selection of productions are parallel processes whose rates are controlled by "strengths" of network links and individual productions. An important aspect of this parallelism is that it is possible for multiple productions to be applied in a cycle. Much of the early work on the ACT system was focused on developing computational devices to reflect the operation of parallel, strength-controlled processes and working out the logic for creating functioning systems in such a computational medium.

We have successfully implemented a number of small-scale systems that model various psychological tasks in the domain of memory, language processing, and inferential reasoning. There was a larger scale project to model the language processing mechanisms of a young child. This includes implementation of a production system to analyze linguistic input, make inferences, ask and answer questions, etc.

The current research is focused on developing mechanisms for the acquisition of skills. In the framework of the ACT system this maps into acquiring new productions and modifying old productions. We have developed learning devices to enable existing productions to create new productions, to adjust the strengths of existing productions, to produce more general variants of existing productions, to produce more discriminant variants of existing productions, and to combine a number of existing productions into a single compact production. We have developed the F version of the ACT system which has these learning facilities. We have so far tested out the system in a number of small learning examples. Current goals involve applying the system to the acquisition of language skills, development of mathematical problem solving skills, and acquisition of initial programming skills.

The basic insight in this research is to model skill acquisition as an interaction between deliberate learning and automatic induction. To the extent that the teacher or the learner is able to understand the skill to be acquired, it is possible for ACT to directly create the necessary productions. However, as a fallback for less structured situations, ACT has automatic induction mechanisms that try to develop the necessary mechanisms by an intelligent trial-and-error inductive process. Much of our research has gone to identifying the heuristics used by this inductive process. Traditionally, there has been a contrast in psychology between learning with understanding and learning by trial and error. It is now clear to us that most real learning situations involve a mixture and the key to understanding skill acquisition is to understand that mixture.

One major project is the investigation of the learning of skills in Geometry. We have written several versions of a program that provides reasons, i.e. postulate names, to worked-out proofs. A number of new mechanisms were developed for this program. For instance, we developed a semantic net representation of the goal tree for problem solving. We also developed ways for the program to automatically shift from a serial search to a parallel search for relevant postulates. There were also several applications of ACT's general learning mechanisms to learn and speed up the use of postulates.

D. Current list of project publications:

- [1] Anderson, J.R. Language, Memory, and Thought. Hillsdale, N.J.: L. Erlbaum, Assoc., 1976.
- [2] Kline, P.J. & Anderson, J.R. The ACTE User's Manual, 1976.
- [3] Anderson, J.R., Kline, P. & Lewis, C. Language processing by production systems. In P. Carpenter and M. Just (Eds.). Cognitive Processes in Comprehension. L. Erlbaum Assoc., 1977.
- [4] Anderson, J.R. Induction of augmented transition networks. Cognitive Science, 1977, 125-157.
- [5] Anderson, J.R. & Kline, P. Design of a production system. Paper presented at the Workshop on Pattern-Directed Inference Systems, Hawaii, May 23-27, 1977.
- [6] Anderson, J.R. Computer simulation of a language acquisition system: A second report. In D. LaBerge and S.J. Samuels (Eds.). Perception and Comprehension. Hillsdale, N.J.: L. Erlbaum Assoc., 1978.
- [7] Anderson, J.R., Kline, P.J., & Beasley, C.M. A theory of the acquisition of cognitive skills. In G.H. Bower (Ed.). Learning and Motivation, Vol. 13. New York: Academic Press, 1979.
- [8] Anderson, J.R., Kline, P.J., & Beasley, C.M. Complex Learning. In R. Snow, P.A. Frederico, & W. Montague (Eds.). Aptitude, Learning, an Instruction: Cognitive Processes Analyses. Hillsdale, N.J.: Lawrence Erlbaum Assoc., 1979.

II. Interaction With the SUMEX-AIM Resource

A. & B. Collaborations, interactions, and sharing of programs via SUMEX.

We have received and answered many inquiries about the ACT system over the ARPANET. This involves sending documentations, papers, and copies of programs.

The most extensive collaboration has been with Greeno and Lesgold who are also on SUMEX (see the report of the Simulation of Comprehension Processes project). There is an ongoing effort to assist them in their research. Feedback from their work is helping us with system design.

We find the SUMEX-AIM workshops ideal vehicles for updating ourselves on the field and for getting to talk to colleagues about aspects of their work of importance to us.

Due to memory space problems encountered by ACT (see section III.A.2) we expect that soon we will need to make use of the smaller version of INTERLISP developed at SUMEX for use in the CONGEN program.

C. Critique of resource management.

The SUMEX-AIM resource has been well suited for the needs of our project. We have made the most extensive use of the INTERLISP facilities and the facilities for communication on the ARPANET. We have found the SUMEX personnel extremely helpful both in terms of responding to our immediate emergencies and in providing advice helpful to the long-range progress of the project. Despite the fact that we are not located at Stanford, we have not encountered any serious difficulties in using the SUMEX system; in fact, there are real advantages in being in the Eastern time zone where we can take advantage of the low load on the system during the morning hours. We have been able to get a great deal of work done during these hours and try to save our computer-intensive work for this time.

Two location changes by the ACT project (from Michigan to Yale in the summer of 1976 and from Yale to Carnegie-Mellon in the summer of 1978) have demonstrated another advantage of working on SUMEX: In both cases we were back to work on SUMEX the day after our arrival.

III. Research Plans (8/79-7/81)

A. Long-range user project goals and plans:

Our long-range goals are: (1) Continued development of the ACT system; (2) Application of the system to modeling of various cognitive processes; (3) Dissemination of the ACT system to the national AI community.

1. System Development Efficiency problems are the most serious ones currently facing the ACT system. Even, the modest-size simulations of learning we have done (about 100 productions) run out of space in INTERLISP after 200 cycles and each cycle may take almost a minute of real-time during periods of moderate system load. We are developing the capability to represent productions as compiled LISP code which should significantly improve the speed of the system and, perhaps even more important, should alleviate space problems because of INTERLISP's ability to overlay compiled code. We also hope to implement ACT in the smaller versions of INTERLISP that have been developed at SUMEX.

2. Application to Modeling Cognitive Processes. We anticipate a gradual decrease in the amount of effort that will go into system development and an increase in the amount of effort that will go into application of the system for modeling. We mentioned above the modeling efforts that we are using to assess the suitability of the ACTF system. We have long-range commitments to apply the ACT learning model to the following three topics: Acquisition of language (both first and second language acquisition); acquisition of programming skills; acquisition of problem solving skills in the domain of geometry. We find each of these topics to be considerable interest in and of themselves, but they also will serve as strong tests of the learning model. We are hopeful that the systems that are acquired by ACT will satisfy computational standards of good artificial intelligence. Therefore, in future years we would also be interested in applying the ACT model to acquisition of cognitive skills in medically related domains such as diagnosis or scientific inference. SUMEX would be an ideal location for collaboration on such a project.

We are also designing a system that will learn to give reasons to proofs. It will have the ability to use existing knowledge about such things as iteration, to accept instructions from a textbook, and to automatically become more efficient as it works on proofs. One learning mechanism we are very interested in is composition, a more general version of the transitive rule of inference used to combine productions. It promises to be interesting in its ability to change goal trees while problem solving. We will investigate it further.

3. Dissemination of the ACT project Although a guest version of ACT has been implemented, a user manual will have to be completed for this version before it is truly accessible to guests. A manual for the E version of ACT has existed for some time, but a manual for the F(learning) version of ACT is currently in preparation.

B. Justification for continued use of SUMEX:

Our goal for the ACT system is that it should serve as a ready-made "programming language" available to members of the cognitive science community for assembling psychologically-accurate simulations of a wide range of cognitive processes. Our intention and ability to provide such a resource justifies our use of the SUMEX facility. This facility is designed expressly for the purpose of developing and supporting such national AI resources and is, in this regard, clearly superior to the (otherwise outstanding) facilities we have available locally from the Carnegie-Mellon computer science department. Among the most important SUMEX advantages are the availability of INTERLISP on a machine accessible by either the ARPANET or TYMNET and the existence of a GUEST login. It appears that, at least for the time being, ACT has no hope of being a national resource unless it resides at SUMEX and, given the local unavailability of a network-accessible INTERLISP, it would even be very difficult to shift any significant portion of our development work from SUMEX to CMU.

C. Needs and plans for other computational resources

Carnegie-Mellon's plans to begin upgrading its PDP-10 hardware to emerging state-of-the-art machines (VAX, LISP machines, etc.) promises to provide a

excellent resource eventually, and we hope to have access to that resource as it develops. However, given that a considerable amount of software development will be required, a sophisticated LISP system such as INTERLISP is not likely to be available on this hardware in the near future.

D. Comments and suggestions for future resource goals:

We would, of course, be delighted if the computational capacity of the SUMEX facility could be increased. The slowness of the system at peak hours is a limiting factor although it is not grievous. This problem is perhaps less grievous for us than Stanford-based users because of our ability to use morning hours. We do not feel any urgent need for development of new software.

4.1.2 Chemical Synthesis Project (SECS)

SECS - Simulation and Evaluation of Chemical Synthesis

Principal Investigator: W. Todd Wipke
Board of Studies in Chemistry
University of California at Santa Cruz

Coworkers: (Postdoctoral Fellows) S. Krishnan, C. Buse, and M. Huber
(Graduate Students) G. Ouchi and D. Dolata
(Programmers) T. Blume, M. Toy, and M. Case

I. SUMMARY OF RESEARCH PROGRAM

A. Technical Goals.

The long range goal of this project is to develop the logical principles of molecular construction and to use these in developing practical computer programs to assist investigators in designing stereospecific syntheses of complex bio-organic molecules. Our specific goals this past year focused on basic research into representation of strategies, incorporation of automatic processing of functional group interchange, and preparing a robust version of SECS for updating the ADP network copy and prerelease to NIH and other collaborators.

B. Medical Relevance and Collaboration.

The development of new drugs and the study of how drug structure is related to biological activity depends upon the chemist's ability to synthesize new molecules as well as his ability to modify existing structures, e.g., incorporating isotopic labels or other substituents into biomolecular substrates. The Simulation and Evaluation of Chemical Synthesis (SECS) project aims at assisting the synthetic chemist in designing stereospecific syntheses of biologically important molecules. The advantages of this computer approach over normal manual approaches are many: 1) greater speed in designing a synthesis; 2) freedom from bias of past experience and past solutions; 3) thorough consideration of all possible syntheses using a more extensive library of chemical reactions than any individual person can remember; 4) greater capability of the computer to deal with the many structures which result; and 6) capability of computer to see molecules in graph theoretical sense, free from bias of 2-D projection.

The objective of using SECS in metabolism is to predict the plausible metabolites of a given xenobiotic in order that they may be analyzed for possible carcinogenicity. Metabolism research may also find this useful in the identification of metabolites in that it suggests what to look for. Finally, it seems there may even be application of this technique in problem domains where one wishes to alter molecules so certain types of metabolism will be blocked.

C. Progress and Accomplishments.

Research Environment: At the University of California, Santa Cruz, we have a GT40 and a GT46 graphics terminal connected to the SUMEX-AIM resource by 1200 baud leased lines (one leased line supported by SUMEX). We also have a TI725, TI745, CDI-1030, DIABLO 1620, and an ADM-3A terminal used over leased lines to SUMEX. UCSC has only a small IBM 370/145, a PDP-11/45 and 11/70 (the latter are limited to small student time-sharing jobs of 12 K words per user), all of which are unsuitable for this research. The SECS laboratory is located in the same building as the synthetic chemists at Santa Cruz so there is very facile interaction.

THE SECS PROGRAM is a large interactive program. On SUMEX it occupies about 150K words if not overlaid and about 68K when overlaid. SECS is generally used from a GT4X terminal, but can with less convenience be used from a teletype. In the former case, the chemist draws in the target molecule to be synthesized using the light-pen. The basic sequence then is that the program analyzes the structure for rings, functional groups, stereochemistry, etc., builds a three-dimensional model, and if appropriate also a Huckel Molecular Orbital model of the pi-systems, and finally on the basis of this knowledge, selects from a library of chemical transforms those reactions which could be used in the last step of the synthesis of this target. First the program reviews the generated precursors to see that they do not violate simple chemical rules of valence and stability, then the chemist reviews the precursors to delete those that seem uninteresting, and to select one for further processing in the same way the original target structure was processed.

Bug Fixes, Additions and Modifications: In the past year considerable effort has been devoted to the elimination of bugs and improvement of human engineering features. All bugs which had been found by us or reported by other users have been corrected. By deliberately requesting SECS to perform contradictory or ambiguous tasks, several additional bugs were uncovered and fixed. The addition of some simple routines to handle input has made it virtually impossible for the user to crash the program by giving it incorrect input. The overall result is that SECS 2.7 is by far the most robust version of the program ever produced and is the pre-release version being made available to those who request it.

SECS Users Manual: The previous SECS Users Manual (version 2.0) has been completely rewritten to include the extensive additions and modifications which have been made since the release of version 2.0. The manual provides not only operating instructions, but background information and examples to show users how best to use SECS 2.7.

Hardcopy of the Synthesis Tree: A user can now specify structures in the synthesis tree to be plotted. This can be by individual structure, the lineage of a structure, or conditions such as all structures with a priority value greater than 60 or that have been rated "GOOD". A separate program then drives a local Zeta plotter to plot the synthesis tree with structures, transform names and priorities. The user specifies the format of the tree. Trees containing thousands of structures can be plotted--the plot is simply generated in strips that are later pasted together. This facilitates sending a chemist a permanent record of the synthesis tree that can be mounted on his wall and provide guidance to his ongoing experimental project.

Alchem Library: We received a number of transforms which had originally been written by the SECS group and subsequently modified by chemists at Merck. Most of these transforms are tremendous improvements. However, some transforms, particularly those involving bond migrations, had been modified in such a way that chemically reasonable transformations could be suppressed for what are purely strategic reasons. Our philosophy has always been to keep chemistry and strategic considerations separate. The Merck-modified transforms have been included in our chemistry library. Our current focus is on strategic control, but we are correcting ALCHEM transform errors when they appear. It is hoped that as SECS is used by more sites, we will receive additional input to our current library of approximately 400 transforms.

Strategic Control: In the early days of computer synthesis, the major problems were in representing reactions so the computer could carry them out correctly. The problem has now shifted to the question of how to properly guide the program efficiently toward pathways which are not only chemically plausible, but are also synthetically significant. We refer to this guiding as strategic control. Without strategic control, SECS applies all reactions that "fit" the target, which generates one level of the synthesis tree. Although in theory the chemist could select appropriate precursors and still find many good syntheses, in practice so many precursors are generated that it is difficult to pick out the "good" precursors, it is difficult to foresee where a given precursor might ultimately lead, and it is so tiring that one doesn't explore the synthesis tree as completely as one should. Feedback from users of SECS indicates they too recognize that strategic control is a major urgent need for this research.

The problem is to control the program without introducing unnecessary bias, since freedom from bias is the computer's advantage over manual analysis. We have developed a philosophy and an implementation which we feel may solve this problem. We define strategy as a general principle which helps guide one in generating a simple synthesis. Strategies are based on symmetry, mathematical considerations of yield, economy of operations, etc. We prevent strategies from being based on any particular reaction. When a strategy is applied to a particular synthetic target molecule, it generates goals. Goals are described only in terms of molecular structural changes or features, and may not, for example, refer to reactions. Thus, strategies create goals, and both are completely independent of the reaction library.

Our list structured language continues to evolve as need for new expressions occurs. We have generalized its structure to allow for any number of machine generated goals and improved the human interface to the goals, preventing accidental recursive goals, and providing extensive help and explanation of how to create and modify goals. Much of our effort has been directed toward creating goals to save the chemist time and to assure that good goals are not accidentally overlooked.

The following paragraphs describe some of the current strategy work.

Subgoals. When a chemical transform has a high priority and seems to be able to satisfy a goal on the goal list the transform is "relevant", but still may not be "applicable" owing to some mismatch between what the transform requires and what the operand structure has. This mismatch can spawn a SUBGOAL to change the structure until this transform is applicable. The first

utilization of subgoals in SECS is for automatic functional group interchange (FGI).

The new subgoals have been expanded to encompass enough information to allow the program to continue from the point where a structural mismatch forced the initial halt. After the subgoal has been satisfied, and the FGI intermediate has been created, SECS then returns to the originating transform and proceeds with the application of that transform. After this has been done for all subgoal created intermediates, SECS then presents the chemist with the multi-step tree that is produced.

On complex molecules with large number of functional groups many subgoals are created, even when duplicates are prevented. This caused problems due to storage limitations. This problem has been partially solved by enabling SECS to estimate the likelihood of success of the subgoal originating transform before generation or application of the subgoal. This not only saves space by preventing the creation of subgoals whose creating transform will predictably fail, but also saves CPU time by eliminating the need to try to satisfy these fruitless subgoals. In test cases, from 50% to 75% of the originating transforms could be shown to predictably fail, thus saving that much space and time.

Since this process involves looking at transforms in an uncertain environment, not all failures can be predicted. Approximately 10% of the subgoals created still lead to "useless" intermediates. However, none of the eliminated subgoals would have led to "fruitful" intermediates, so the process is quite acceptable.

A Functional Group Oriented Strategy. Another machine-generated strategy based on the functional groups present in the target molecule has been implemented in the SECS program. In its present form, those transforms which utilize functional groups regarded as sensitive are favored over those which do not. The effect is to focus the attention of the program on one part of the molecule until the sensitive functional group(s) are removed or altered or until that part of the molecule is removed completely. At present, three levels of functional group sensitivity have been defined for this purpose: very sensitive, sensitive and not sensitive. The classification of a particular functional group depends on its sensitivity toward a range of reaction conditions and its "protectability".

Similarity. We have previously reported the development of an algorithm for determining the degree of similarity between two chemical structures. Although that algorithm was mathematically satisfying in that $s=1.0$ only when the two structures were identical, it was time consuming to calculate. We have now developed a second algorithm, which is more empirical, but very rapidly computed. This second algorithm has been compared with the first on many examples and is found to be quite good for finding when two structures are synthetically similar. Both algorithms take into account atom types, bond types, stereochemistry, functional groups, rings, etc. Papers describing these functions are in draft form soon to be submitted for publication.

Currently the similarity module requires a special version of SECS. We plan in the next year to incorporate this module into the standard version of SECS so that the bonds that if broken could lead to identical or similar

fragments can be used to create a goal to guide SECS toward such efficient syntheses, even though there may not be a reaction capable of doing that rejoining step.

Synthetic Analysis of Methyl Homodaphniphyllate: Being primarily concerned with the development of the SECS program, seldom does the opportunity arise to perform an extensive synthetic analysis on a particular molecule. At the beginning of our program to develop a sophisticated planning and strategy module we wanted to enumerate those things which chemists think about when planning a synthesis. By talking to other chemists and analyzing total syntheses which had been published in the literature we obtained a list of strategies which tells the chemist what to do. Of equal importance is a list of strategies which tells the chemist what not to do. In order to find these strategies we performed an extensive synthetic analysis on methyl homodaphniphyllate. The hope was that we would find useful generalizations that could be later used to prevent SECS from creating useless precursors. The compound used in the analysis was chosen because it is the sort of molecule which SECS handles best in its present form, that is, a molecule having few functional groups and a multi-bridged ring system. In addition, none of the alkaloids in this family, of which the present molecule is the simplest, have been synthesized.

The analysis of this material was carried through to depths of up to 14 levels and over six thousand precursors were generated. Several reasonable synthetic sequences emerged and some results of the analysis were reported at the Natural Products Symposium, part of the Western Regional ACS Meeting held in San Francisco on September 29, 1978. This analysis demonstrated the current capability of SECS with respect to very large problems. It further pointed out the great savings in time and effort that will result from even simple strategic control. This example serves as a base case to be compared with a later analysis employing more sophisticated strategic control.

Strategy Knowledge Base Building: Over the past year we have collected strategies, written them down, and searched for a uniform, formal method for representing these principles. To our knowledge, this is the first such thorough analysis of synthesis from this point of view, and it requires an effort similar to that for building a medical diagnosis knowledge base. Given such a knowledge base, our approach is to analyze the target molecule for problem areas. Each area may trigger certain pieces of knowledge which trigger others until finally goals are put on the goal list to direct SECS with respect to this particular problem area. We have studied many planning programs reported in the literature and have discovered that these programs strive to find one plan, for example, to cause a robot to accomplish a particular command. But we want not one plan, but all good plans for the synthesis. And as we expand the synthesis tree, the number of plans to be remembered increases. Thus the question arises of how to represent multiple plans. Our goal list essentially does that. By stating constraints that must be satisfied it excludes large regions of the tree. Thus one can think of this as a representation of all plans consistent with those constraints.

The example below shows a piece of knowledge relating to the control of stereochemistry.

```
IF 1) ATOM X IS A STEREOCENTER &
   2) ATOM X IS THE ORIGIN OF FG Y, G
   3) STEREOGROUP Z IS WITHIN GAMMA OF ATOM X ALONG PATH W &
   4) STERIC DIFFERENTIATION OF STEREOGROUP Z IS
      MEDIUM OR HIGH, &
   5) IT IS NECESSARY TO INCREASE THE STERIC
      DIFFERENTIATION OF ATOM X, THEN
CONCLUDE: STEREOSPECIFICALLY MIGRATE FG Y ALPHA TO Z
          ALONG PATH W. (0.95)
```

A principle based on symmetry states "It is useful to search for fragmentations such that one or more of the fragments have equivalent sites of attachment." Corey's synthesis of caryophyllene alcohol made use of this principle, although the pathway was not exactly that suggested directly by this principle. In our plans for next year we describe how we intend to use these principles.

Stereoisomer Generator: Our work with the SEMA stereochemical naming algorithm and application of the symmetry group of a chemical graph has led to a stereoisomer generator that has been tested on all possible cyclic saturated hydrocarbons having up to 15 atoms and 5 rings. The algorithm non-redundantly generates each stereoisomer, reports the symmetry group for that isomer, the canonical stereodescriptors, and then determines if the stereoisomer is chiral or achiral. Another module reports whether the structure is likely to be stable or not based on symbolic analysis of the ring system and stereochemistry. One potential application of this, besides simply enumerating stereoisomers, is to make it possible for a chemist to enter complex ring systems without specifying stereochemistry at obvious centers. This algorithm can then look at which of the possible stereoisomers are reasonable, and ask the chemist which he/she intended. This would relax the specification of stereochemistry to more nearly match normal chemical convention.

Metabolism Prediction: Numerous structurally different chemical compounds have been found to induce neoplasia in man and animals. In many cases these chemical carcinogens are metabolically activated by mammalian enzyme systems to their ultimate reactive and toxic structure. Many of the mechanisms involved in this "bioactivation" process are known or are in the process of being discovered. Thus, it is now possible based on the structure of a compound and a thorough knowledge of biotransformations to make rational predictions of the plausible metabolites of a compound produced in a mammalian system. To study the metabolic activation of compounds we are creating a computer assistant which will generate the plausible metabolites of a compound utilizing the biotransformations known to occur in mammalian systems.

A new computer program called XENO for the metabolism of xenobiotic compounds has been developed based on technology from computer synthesis project. However, since metabolism is being simulated in the forward direction, whereas organic synthesis is simulated in the reverse direction, the XENO program is quite different in logic from SECS, although both use ALCHEM as a representation for reactions. The XENO data base of biotransforms was developed by careful survey of metabolism literature and consultation with a committee of metabolism

experts at NIH. We selected a mechanistic representation of metabolic processes which means a small data base suffices to represent most of the known processes. A critical evaluation of XENO by a panel of experts in Bethesda, Md. in February 1978 concluded that the data base of biotransforms must be considerably expanded, but even now it is able to raise some interesting questions of alternative metabolic pathways, etc. XENO is currently running on SUMEX-AIM.

D. List of Current Project Publications

- F. Choplin, R. Marc, G. Kaufmann, and W.T. Wipke, "Computer Design of Synthesis in Phosphorus Chemistry. Automatic Treatment of Stereochemistry," J. Chem. Info. and Computer Sci., 18, 110 (1978).
- F. Choplin, R. Dorschner, G. Kaufmann, and W. T. Wipke, "Computer Graphics Determination and Display of Stereoisomers in Coordination Compounds," J. Organometallic Chem., 152, 101 (1978).
- F. Choplin, C. Laurenceo, R. Marc, G. Kaufmann, and W.T. Wipke, "Synthese Assistee par Ordinateur en Chimie des Composes Organophosphores," Nouveau J. de Chimie, 2, (3) 285 (1978).
- W.T. Wipke, G. Ouchi, and S.Krishnan, "Simulation and Evaluation of Chemical Synthesis - SECS. An Application of Artificial Intelligence Techniques," Artificial Intelligence, 10, 999 (1978).
- M.L. Spann, K.C. Chu, W.T. Wipke, and G. Ouchi, "Use of Computerized Methods to Predict Metabolic Pathways and Metabolites," J. of Env. Pathology and Toxicology, 2, 123 (1978); also reprinted in "Hazards from Toxic Chemicals," ed. M.A. Mehlman, R.E. Shapiro, M.F. Cranmer and M.J. Norvell, Pathotox Publishers, Inc., Park Forest South, Ill., 1978, pp. 123-121.

In Press:

- S.A. Godleski, P.v.R. Schleyer, E. Osawa, and W.T. Wipke, "The Systematic Prediction of the Most Stable Neutral Hydrocarbon Isomer," Progress in Physical Organic Chemistry, in press.
- J.D. Andose, E.J.J. Grabowski, P. Gund, J.B. Rhodes, G.M. Smith, and W.T. Wipke, "Computer-Assisted Synthetic Analysis: The Merck Experience," in Computer-Assisted Drug Design, ACS Symposium Series, in press.
- W.T. Wipke, D. Dolata, M. Huber, and C. Buse, "Machine Reasoning About Synthesis," in Computer-Assisted Drug Design, ACS Symposium Series, in press.

II. INTERACTIONS WITH SUMEX-AIM RESOURCE

A. Collaborations and Medical Use of Programs via SUMEX.

SECS is available in the GUEST area of SUMEX for casual users, and in the SECS DEMO area for serious collaborators who plan to use a significant amount of time and need to save the synthesis tree generated. Much of the access by others has been through the terminal equipment at Santa Cruz because graphic terminals make it so much more convenient for structure input and output. We have assisted Professor J.E. McMurry of UCSC in his synthetic work towards aphidicolin and digitoxigenin (Total Synthesis of Cardiac Aglycones, HL-18118) using the model builder of SECS for evaluating plausible modes of ring closure. Numerous visitors to UC Santa Cruz have tried their own problems on the SECS program, generally taking away at least a couple of new ideas for research. Professor Ken Williamson of Mt. Holyoke College used SECS to build 3-D models of 50 compounds for C-13 nmr analysis, and his student provided us with a detailed report on their results and suggestions for improvements of our manual. Wilson Sallum of the University of Mass. Amherst working with Dr. E. McWhorter used SECS for the synthesis of various 3-naphthyl propionates. The synthesis suggested by SECS was successfully performed in the laboratory.

Synthetic chemists are beginning to come to us for a SECS analysis before beginning a laboratory synthesis. Dr. McMurry for example did a rather complete analysis of morphine before launching his recently successful synthesis. Plans for further new target analyses are underway between Dr. McMurry and Dr. Wipke.

Dr. Wipke has also used several SUMEX programs such as CONGEN in his course on Computers and Information Processing in Chemistry. Testing and collaboration on the XENO project with researchers at the NCI depend on having access through SUMEX and TYMNET.

B. Examples of Sharing, Contacts and Cross-fertilization with other SUMEX-AIM Projects:

We have had several discussions with the MYCIN group about our interest in an explanation capability for SECS. The AIM conference at Rutgers each year has been extremely valuable in generating ideas of new ways to apply current developments in AI to the problem of organic synthesis. Finally, it is impossible to count the daily exchanges that occur between researchers in the SECS group and other members of the AIM community on things related to languages, conferences, papers, seminars, and program sharing.

During the past year we have held weekly seminars on artificial intelligence related to the SECS project. These have been attended by Prof. Sharon Sickel (research area is theorem proving) and Prof. Michael Cunningham (research area: natural intelligence) of Information Sciences Dept. as well as

our group and other interested students and faculty. Visiting speakers include Peter Friedland (Stanford MOLGEN project), Dennis Smith and Ray Carhart (both of Stanford CONGEN project), Mark Stefik (Stanford MOLGEN), Jay Munyer (UCSC analogical reasoning), Ken Friedenbach (UCSC and TRW, Hierarchical planning for game of GO), and Stephan Unger (Syntex, drug design). This forum has been very stimulating to our current research in strategies.

John Kunz of the Pulmonary Function - Ventilator Management project developed at UCSF utilizing SUMEX has requested and received a copy of INTERC. This program was written to allow facile communication between the Santa Cruz 11/34 and SUMEX.

C. Critique of Resource Services:

We find the SUMEX-AIM network very well human engineered and the staff very friendly and helpful. The SECS project is probably one of the few on the AIM network which must depend exclusively on remote computers, and we have been able to work rather effectively via SUMEX. Basically we have found that SUMEX-AIM provides a productive and scientifically stimulating environment and we are thankful that we are able to access the resource and participate in its activities. SUMEX-AIM gives us at UCSC, a small university, the advantages of a larger group of colleagues, and interaction with people all over the country. We especially thank SUMEX for support of the leased line for our GT40.

D. Collaborations and Medical Use of Programs via Computers other than SUMEX.

Arrangements between the University of California, Santa Cruz and NIH have been begun to try to install a version of SECS on the NIH PDP-10 computer system, and possibly later on the NIH-CIS system. Under an arrangement approved in 1974 between First Data, Princeton University, and NIH, SECS has been available over TELENET so that the public could evaluate the state of the technology first hand, by simply contacting First Data. First Data was selected because that is the system the NIH PROPHET program is also on. As a result of that arrangement, anyone who wishes can use the SECS program without worrying about converting code for their machine, and a number of people in the private sector both in the US and abroad have done so. We are currently exploring updating the version of SECS on ADP (First Data) and have recently installed a version on the University of Penn. Medical School computer.

III. RESEARCH PLANS (7/79-7/81)

A. Long Range Project Goals and Plans.

The SECS project now consists of two major efforts, computer synthesis and metabolism, the latter being a very young project. Our plans for SECS for the next year include adding a high level reasoning module for proposing strategies and goals, and providing control which continues over several steps. This reasoning module also will be able to trace the derivation of goals and thus explain some of its reasoning. We also plan to focus on bringing the transform library up in sophistication to improve the performance and capabilities of SECS. Our library has been sufficient for previous testing, but now requires filling gaps in its knowledge.

Currently the similarity module requires a special version of SECS. We plan in the next year to incorporate this module into the standard version of SECS so that the bonds that if broken could lead to identical or similar fragments can be used to create a goal to guide SECS toward such efficient syntheses, even though there may not be a reaction capable of doing that rejoining step. We still have not had an opportunity to improve the teletype interface which we hope to attack soon. Our hash coding scheme allows very rapid retrieval of compounds from libraries of compounds. It now remains to create appropriate data bases of available starting materials complete with stereochemistry and other technical data to enable us to explore some starting-material oriented strategies. This will require an interactive data base builder/editor to be built first. Our users have brought to our attention ways to make SECS more machine independent, as well as suggestions for additions and improvements. We hope to assimilate these into our research goals wherever possible.

The XENO metabolism project will be expanding the data base to cover more metabolic transforms, including species differences, sequences of transforms, and stereochemical specificities of enzymatic systems. A second phase will apply our "similarity" function to determine when metabolites are similar to known carcinogens. We are also hoping to develop programs which will help maintain the growing data bases. It is not clear at this time how quantitative we can hope to be with XENO's predictions and that will be studied.

B. Justification and Requirements for Continued use of SUMEX.

The SECS and XENO projects require a large interactive time-sharing capability with high level languages and support programs. I am on the campus computing advisory committee and am the campus representative to the UC system-wide computing advisory committee and know that the UCSC campus is not likely in the future to be able to provide this kind of resource. Further there does not appear to be in the offing anywhere in the UC system a computer which would be able to offer the capabilities we need. Thus from a practical standpoint, the SECS and XENO projects still need access to SUMEX for survival. Scientifically, interaction with the SUMEX community is still extremely important to my research, and will continue to be so because of the direction and orientation of our projects. Collaborations on the metabolism project and the synthesis project need the networking capability of SUMEX-AIM, for we are and will continue to be interacting with synthetic chemists at distant sites and metabolism experts at the National Cancer Institute. Our requirements are for good support of FORTRAN. We now must run SECS overlaid, but the debugging tool DDT loses its symbol table during overlaying. This is a serious problem we hope can be fixed by SUMEX staff because without symbols, debugging is very difficult and time-consuming.

C. Needs beyond SUMEX-AIM.

Our needs are to develop local capabilities for printing, tape reading and writing. Our GT46 will be providing that this year. We also need some local production capability both to help offload SUMEX and to provide us needed computing when SUMEX is either not available or heavily loaded or load limited.

D. Recommendations for Community and Resource Development.

The AIM workshop is excellent, particularly if it is held on the WEST COAST once in a while. From a chemistry standpoint, the joint group meetings with the DENDRAL group plus ability to attend seminars at Stanford and have visitors participate in our seminar program really satisfy our needs for communication with people of similar interests. We have proposed a workshop for the benefit of the implementors rather than the principal investigators and administrators, for that would do wonders to develop the human resource. We feel the computer resource is rather efficiently used right now. The system does get sufficiently busy that guests simply get almost no time and consequently decide the programs they are using are poorly written and too slow. A system to handle guest production would help both guests and researchers. Even for programs that are still in research and development, some large scale testing is required which resembles production and could benefit from this production machine. A trivial suggestion but also important is that TV-EDIT be improved to not leave null characters in files which cause problems with compilers both at SUMEX and at other sites when the files are sent to another machine.

4.1.3 Hierarchical Models of Human Cognition

Hierarchical Models of Human Cognition (CLIPR Project)

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I. Summary of Research Program

The CLIPR project has only been on SUMEX since the first of the year, thus our work is in the earliest stages. However, one of our subgroups, the text comprehension group, has managed to accomplish a great deal during this time.

Technical Goals

The CLIPR project consists of two subprojects. The first, the text comprehension project, is headed by Walter Kintsch and is a continuation of work on understanding of connected discourse that has been underway in Kintsch's laboratory for over seven years. The second, the planning project, is headed by Peter Polson of the University of Colorado and Michael Atwood of Science Applications Incorporated, Denver, and is studying the processes of planning using software design tasks.

The goal of the text comprehension project is to show how the components of the prose processing model described by Kintsch (1974; Kintsch and van Dijk, 1978) might be implemented in a HEARSAY-like control structure. Previous theoretical work has been oriented towards the development and evaluation of individual components of a global model of human prose processing. This work, as well as other research in cognitive psychology and artificial intelligence, has described a number of components necessary for a successful system. The current goal of this research is to describe the interaction of these components in the understanding of a segment of prose. We expect that the AGE formalism, of multiple independent, but cooperating knowledge sources may be a useful system in which to model such interactions. Thus, the primary task of the text understanding project is to make use of the theoretical tools that are provided on SUMEX to integrate and further extend Kintsch's theoretical and empirical work on the understanding of prose.

Similarly, the process of planning in complex domains like the design of software is conceptualized as involving the interaction of different kinds of knowledge at varying levels of abstraction. Skilled designers have extensive knowledge about the design process, as well as diverse knowledge of various algorithms and the constraints imposed by particular computer systems and programming languages. These pieces of knowledge must interact in complex ways in order to produce a detailed design for a given piece of software. We have assumed that a HEARSAY-like model of these interactions can adequately describe the design process and the planning mechanisms that underlie the construction of software designs. We plan to use AGE in order to model the planning process in the software design task and to construct simulations of protocols collected from experts doing actual designs.

Medical Relevance and Collaboration

The text comprehension project impacts indirectly on medicine, as the medical profession is no stranger to the problems of the information glut. By adding to the research on how computer systems might understand and summarize texts, and determining ways by which the readability of texts can be improved, medicine can only be helped by research on how people understand prose. Development of a more thorough understanding of the various processes responsible for different types of learning problems in children and the corresponding development of a successful remediation strategy would also be facilitated by an explicit theory of the normal comprehension process.

The planning project is attempting to gain understanding of the cognitive mechanisms involved in design and planning tasks. The knowledge gained in such research should be directly relevant to a better understanding of the processes involved in medical policy making and in the design of complex experiments. We are currently using the task of software design to describe the processes underlying more general planning mechanisms that are also used in a large number of task oriented environments like policy making.

Both the text comprehension project and the planning project involve the development of explicit models of complex cognitive processes; cognitive modelling is a stated goal of both SUMEX and research supported by NIMH.

The primary focus of collaborative activities for both CLIPR projects has involved interactions with Penny Nii and Edward Feigenbaum concerning the software tools needed to carry out our modelling activities. In addition, the text comprehension group has initiated some collaborative research with Alan Lesgold of the SUMEX SCP Project. This research involves the sharing of software tools developed by James Miller of the CLIPR project. Finally, SUMEX'S ARPANET facilities have enabled the sharing of information and research plans with Barbara and Frederick Hayes-Roth of the Rand Corporation, with whom the planning group's modelling efforts are being carried out.

Progress Summary

The bulk of the programming that has been done so far has been by the text comprehension group. A LISP program has been written to analyze a set of twenty texts and produce reasonable predictions of both the recall of information from and the readability of these texts. The first stage of this system is nearly completed, and preliminary reports of this work have already been presented (Kintsch, 1979).

The initial activities of the planning group have focused on the preliminary development of a theoretical model for the planning processes of software design and on learning about the software available at SUMEX for modelling this task.

Both groups have been involved in learning AGE, and how it can be applied to their individual domains.

List of Relevant Publications

Kintsch, W. and van Dijk, T. A. Toward a model of text comprehension and production. *Psychological Review*, 1978, 85, 363-394.

Atwood, M. E., Polson, P. G., Jeffries, R., and Ramsey, H. R. Planning as a process of synthesis. Technical Report SAI-78-144-DEN, Science Applications, Incorporated, Denver, Co. December, 1978.

Kintsch, W. On modelling comprehension. Invited address at the American Educational Research Association convention. San Francisco, April 10, 1979.

II. Interactions with the SUMEX-AIM Resource

Sharing and Interactions with other SUMEX-AIM Projects

We have been working with Penny Nii and Edward Feigenbaum on the use of AGE as a modelling tool for both the prose comprehension project and the planning project. Feigenbaum and Nii have already made one 2-day visit to Colorado in which members of both projects were introduced to AGE. Access to theoretical tools like AGE are vital to the success of both projects.

The AGE super-structure will provide us a coherent framework within which to articulate our ideas and will greatly reduce the resources required to develop functioning models of comprehension and planning. In addition, by agreeing to serve as trial users of this developing system we hope to provide useful input to the AGE project staff. It is our hope that this collaboration will result in a system that is truly useable for the development of complex models of cognitive processes.

As noted above, the text comprehension project has discussed the possibility of collaborative research with other SUMEX users. Alan Lesgold of the Learning Research and Development Center at the University of Pittsburgh, a member of the SUMEX SCP project, has expressed interest in the use of the prose analysis program described above, as has James Voss of the Department of Psychology at the University of Pittsburgh. We are considering the possibility of making this program available to outside investigators via the guest facility of SUMEX.

Critique of Resource Management

The SUMEX-AIM resource is clearly suitable for the current and future needs of our project. We have found the staff of SUMEX to be cooperative and effective in dealing with special requirements and responding to our questions. The facilities for communication on the ARPANET have also facilitated collaborative work with investigators throughout the country.

III. Research Plans (8/79 - 7/81)

Long Range Projects Goals and Plans

The long range plans of both CLIPR projects require extensive use of the AGE facility as a basis for the development of the knowledge based systems that we have described in preceding sections. The needs of the text understanding project illustrate these requirements well. Although the prose program described above generates reasonable predictions of recall and readability, certain aspects of the predictions are clearly insufficient. These insufficiencies are caused by the lack of real world knowledge in the procedures that are used to generate the representation of the text. A more complete model of prose processing must be able to access information ranging from word definitions to frame structures, and we expect that AGE will be of use in the development of a model incorporating a more adequate knowledge base. We also expect to make use of the UNITS package as the basis for developing frame-like knowledge sources to be accessed by the AGE control structure. Thus, the understanding project is dependent upon SUMEX access in order to obtain both the necessary computing facilities and software tools for the continued development of this work.

The primary goal of the planning project is the development of a model, or a series of models, of human performance on the software design task. We intend to begin by modeling the protocols of experts on a particular task, eventually extending the model to other levels of experience and other tasks. To do this we will have to become more familiar with AGE and work on articulating our theory in a way that is compatible with the AGE framework. This will involve two parallel lines of effort. One is a deeper analysis of our protocol data, to increase our

knowledge of the detailed planning processes and knowledge structures experts are using to solve these problems. The second is the development of a model in AGE that can simulate these processes. We have to date been using SUMEX only for the latter activity, but we are beginning to discover that both objectives are so intertwined that it is counter-productive for us to be using separate computer systems. Thus we intend to transfer our protocol analysis activities to SUMEX. This will have the added advantage of making it easier for us to share this very rich data source with other investigators.

Justification and Requirements for Continued SUMEX Use

As noted in Section A, our research requires access to the AGE and UNITS systems, which are available only on SUMEX. In addition to any benefits we receive from access to SUMEX, AGE, and UNITS, the AGE and UNITS projects will also benefit from our testing of and experience with these experimental systems. Such interactions between the CLIPR and HPP projects have already been fruitful. We also expect that our interactions with Lesgold of the SCP project will continue by sharing both ideas and programs.

We anticipate that our CPU utilization may increase slightly due to the onset of our regular use of AGE. However, much of our programming efforts have been and will be isolated in non-peak early morning hours (due to the times in differences between Colorado and Stanford) and in overnight runs via the BATCH facility. Our CPU impact on everyday SUMEX use then will likely not increase.

In view of the additional files needed for AGE and UNITS, and the transfer of the planning group's protocols to SUMEX, our current disk allocation may become insufficient. We would thus appreciate an increase of 250 pages to a new total of 750 pages for our project. This increase, combined with use of the ARCHIVE facility for off-line storage of the majority of the planning group's protocols, should be sufficient for these needs.

Needs and Plans for Other Computational Resources

We currently use three other computing systems, two of which are local to the University of Colorado. One is the Department of Psychology's CLIPR system, which is a Xerox Sigma 3 used primarily for the real-time running of experiments to be modeled on SUMEX. The second is the University of Colorado's CDC 6400, which is used for various types of statistical analysis. Thirdly, the planning group has been using a PRIME computer located at Science Applications, Incorporated for the storage and analysis of protocols.

Being a remote site, we are clearly limited in our ability to get hard copy of SUMEX material, although the SUMEX staff has been most helpful in mailing whatever listings we need. We are now negotiating with the Boulder facility of the National Bureau of Standards for access to a PDP 11/40 that is connected to the ARPANET. This would provide us with hard copy in a way much more efficient for both ourselves and SUMEX. The tape drive on the 11/40 would also allow easier transfer of materials between SUMEX and our local computers.

Recommendations for Future Community and Resource Development

Our primary recommendation for future development within SUMEX involves (a)

the continued support of INTERLISP, which is needed for AGE and for other work we have underway on SUMEX and (b) the continued development of the AGE and UNITS projects. In particular we would like to see an extension of AGE to include a wider variety of control structures so that our psychological models would not be confined to one particular view of knowledge-based processing.

4.1.4 Higher Mental Functions Project

Higher Mental Functions Project

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Neuropsychiatric Institute
University of California at Los Angeles

I. Summary of Research Program

A. Technical goals

The goals of this project are to contribute new knowledge and invention to the fields of psychiatry and neurology using concepts, methods and instruments of artificial intelligence. To achieve these goals, the project is involved in simulation studies of paranoid conditions, psychiatric taxonomy, and intelligent speech prostheses for patients with communication disorders.

B. Medical relevance and collaboration

The research has obvious medical relevance. The project collaborates with psychiatrists, neurologists, speech pathologists and neurolinguists.

C. Progress summary

During the past year the project has designed and constructed two intelligent speech prostheses, ISP-I and ISP-II. These devices consist of portable microprocessors and voice synthesizers. Part of the software consists of an orthographic-to-phonetic translator of several thousand rules and special cases written in the form of a production system. An ISP-I provides the user with an infinite vocabulary, error-corrective feedback, an ability to sound spell and the capacity for the user to create his own mnemonics for his own unique expressions. An ISP-I is designed for users who have not suffered central brain damage to the language system. Such users are patients with cerebral palsy, Parkinsonism, laryngectomy, and patients with tracheostomies in intensive care units.

An ISP-II, in addition to all the features of ISP-I, contains a lexical-semantic memory which is used to aid the word-finding problems of patients who have suffered brain damage. Such patients include strokes, brain tumors, and head traumas. The programs for these devices are first worked out and debugged on a big machine, the SUMEX facility, and then transferred to the microprocessors. Of particular help is the large English dictionary at SUMEX which we use both for the solution of orthographic-to-phonetic problems and for the organization of lexical memories to aid word-finding.

A few improvements have been made to the simulation of paranoia, PARRY, which now serves as an example to other research projects of how to go about simulating psychopathology.

The psychiatric classification scheme is unreliable in many respects. Hence this project has undertaken the task of trying to characterize patients according to their cognitive structures, properties in addition to conventional signs and symptoms. An algorithm which runs at SUMEX analyzes patient self-report accounts to find the conceptual patterns and key ideas underlying surface structure sentences. A profile of the patient is formed from the key ideas and patients with similar profiles are clustered into groups. This work is still in the exploratory pilot-study stage.

D. List of relevant publications

Colby, K. M. Mind Models: An Overview of Current Work. MATHEMATICAL BIOSCIENCES, 39, 159-185, 1978.

Colby, K. M., Christinaz, D. and Graham, S. A Computer-Driven, Personal, Portable, and Intelligent Speech Prosthesis. COMPUTERS AND BIOMEDICAL RESEARCH, 11, 337-343, 1978.

Colby, K. M., Faught, W. S., and Parkison, R. C. Cognitive Therapy of Paranoid Conditions: Heuristic Suggestions Based on a Computer Simulation Model. COGNITIVE THERAPY AND RESEARCH, 3, 55-60, 1979.

II. Interactions with the SUMEX-AIM Resource

A. Collaborations

As described above, this project uses SUMEX (1) to run PARRY (2) to write software for intelligent speech prostheses and (3) to construct a psychiatric taxonomy based on patients' cognitive structures.

B. Interactions with Other SUMEX-AIM Projects

The project interacts with other SUMEX projects at the University of Texas at Galveston and at Michigan State University.

C. Critique of resource management

Incredible as it may sound, we have no criticism of SUMEX, only praise. The members of our project uniformly agree SUMEX represents the best system we have ever worked with. The system is up almost all of the time, the personnel are cooperative and congenial, and suggested improvements are listened to and effected.

III. Research Plans

A. Long range project goals and plans

We plan to continue for the next two years to work on the above-described projects. If funding can be obtained, the taxonomy effort will be expanded into a full-scale effort.

B. Justification for SUMEX use

This project uses SUMEX for each of its research sub-projects as already described. We need a large machine that can run large LISP programs efficiently. We also need the large English dictionary available at SUMEX. No comparable facilities exist at UCLA. Hence we are quite dependent on SUMEX for the continuation of this research in psychiatry and neurology.

C. Other computational resources

Our other computational needs involve microprocessors and improved speech synthesizers. These can be constructed and developed in our laboratory at UCLA.

D. Recommendations

About once a month, an obscure bug appears in the ARPA net which shuts everything down. We would recommend this bug be discovered and dealt with mercilessly.

4.1.5 INTERNIST Project

INTERNIST Project

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I. Summary of Research Program

A. Technical Goals

The major goal of the INTERNIST project is to produce a reliable and adequately complete diagnostic consultative program in the field of internal medicine. Although this consultative program is designed primarily to aid skilled internists in complicated medical problems, the program may have spin-off as a diagnostic and triage aid to physicians assistants, rural health clinics, military medicine and space travel.

To be effective, the program must be capable of multiple diagnoses (related or independent) in a given patient and it should deal effectively with the time axis in the development and course of disease states.

B. Medical Relevance and Collaboration

The program inherently has direct and substantial medical relevance.

The knowledge base should reach a critical stage of completeness within a year, at which point we shall invite collaboration in the field testing of the program in a number of medical institutions. Desires for such collaboration have been very positively indicated by more than an adequate number of sister academic health centers and community hospitals, etc.

The Department of Pediatrics at Pittsburgh has engaged in a collaboration with INTERNIST with the objective of a similar diagnostic program in the field of pediatrics.

C. Progress Summary

The original INTERNIST program described in previous progress reports and documented in Pople, Myers & Miller [3] continues to be the standard diagnostic program used to analyze clinical problems and to exercise newly developed portions of the knowledge base.

The structure of the medical knowledge base has remained comparatively constant during the past year. The knowledge base has been expanded by the addition of some sixty diseases plus twenty-nine in pediatrics. The existing knowledge base is under a process of continual editing which attempts to keep the data up to date by the addition new information about diseases as such becomes available, and which expands and corrects the old data base as omissions or errors are discovered. To our gratification, the progressive enlargement of the

knowledge base has in no significant adverse way affected the operation of the computer program.

The program and the knowledge base are continually being tested with challenging medical problems with good and reasonable success. The knowledge base remains too incomplete for any comprehensive or critical test on our hospital floors but the system is used on an ad hoc basis for clinical guidance.

Experience with this system has led to the identification of certain performance deficiencies that are being addressed in the design of a second generation diagnostic program (INTERNIST-II) the essential features of which are outlined in Pople [1]. A major objective in the design of the new program is to enable concurrent evaluation of the multiple components of a complex clinical problem, thereby enhancing the system's rate of convergence on the essential nature of the problem. A number of new concepts, not presently captured in the existing INTERNIST knowledge base, are required for this purpose; for example: the "constrictor" relation described in [1]; generalization of the INTERNIST disease hierarchy to a network permitting multiple categorization. For this purpose, a schema definition language has been devised, which enables the definition of disease categories such as "infectious disease," "collagen-vascular disease," "gastrointestinal hemorrhage," and others that cut across the basic INTERNIST hierarchy of organ system categories. Programs have been developed to map automatically onto these described nodes those terminal level disease entities which satisfy the node descriptions. By use of this expanded set of categories, the INTERNIST-II program is able to draw more precise boundaries around the sets of feasible hypotheses used to guide the acquisition of additional patient data. While still experimental, this new approach is expected to yield more efficient workup of complex clinical problems.

During 1978-79 two graduate students in computer science, one for the whole year and the other for six months, have made valuable contributions to INTERNIST both in the further development of the computer operating and analytical systems and in the organization and manipulation of the medical knowledge base.

One of our clinical fellows met an untimely death in November 1978 after contributing substantially to the medical knowledge base during his four months of activity. The other clinical fellow was diverted during the year from work in augmenting the medical knowledge base to the project of developing a CRT display and interface system for the clinical user of INTERNIST. This project became necessary because of the over 3,000 individual manifestations of disease in the system, which manifestations are necessarily arbitrarily worded at this point in development. The computer program utilized is ZOG, a very versatile menu selection system developed by Newell and colleagues at Carnegie-Mellon University. The project has been completed for our manifestations list as it exists today. It has proved to be very versatile and easy to use. A casual and new physician user can now learn in five minutes or so how to enter his data on a patient with a diagnostic problem and proceed to conclusions on the part of INTERNIST.

We underpredicted two matters involving time: (1) the many hours required to update and revise the existing medical knowledge base, and (2) the time required to program the necessary number of diseases required to bring the medical knowledge base to a "critical mass" for field testing. We are

approximately a year behind our original projected schedule. Nevertheless, real progress has been made, to wit, the addition of some sixty new diseases and the substantial revision of some previously programmed diseases. The continual analysis of actual diagnostic problems in internal medicine has pointed out many (in themselves) minor alterations needed in the knowledge base which, in the composite, have provided for much smoother and more "intelligent" operation.

As of July 1, 1979, Doctor Randolph Miller, a previous junior collaborator on INTERNIST, will have completed his formal graduate education in internal medicine and will be joining the INTERNIST project as a full-time junior faculty member (Assistant Professor of Medicine). Doctor Miller's presence and contribution should allow, in collaboration with others working on the program, the essential completing of the medical knowledge base in the academic year 1979-80.

D. Publications

1. Pople, H.E. "The Formation of Composite Hypotheses in Diagnostic Problem Solving: An Exercise in Synthetic Reasoning", Proceedings of the Fifth International Joint Conference on Artificial Intelligence, Boston, August 1977.
2. Pople, H.E. "On the Knowledge Acquisition Process in Applied A.I. Systems", Report of Panel on Applications of A.I., Proceedings of Fifth International Joint Conference on Artificial Intelligence, 1977.
3. Pople, H.E., Myers, J.D. & Miller, R.A. "The DIALOG Model of Diagnostic Logic and its Use in Internal Medicine, Proceedings of the Fourth International Joint Conference on Artificial Intelligence, Tbilisi, USSR, September 1975.
4. Pople, H.E. "Artificial Intelligence Approaches to Computer-based Medical Consultation, Proceeding IEEE Intercon, New York, 1975.

II. Interactions with SUMEX-AIM Resource

A, B. Collaborations and Medical Use of Program Via SUMEX

INTERNIST remains in a stage of research and development. As noted in the "Progress Summary" above, we are continuing to attempt to develop better computer programs to operate the diagnostic system, and the knowledge base cannot be used very effectively for collaborative purposes until it has reached a critical stage of completion. These factors have stifled collaboration via SUMEX up to this point and will continue to do so for the next year or two. In the meanwhile, through the SUMEX community there continues to be an exchange of information and states of progress. Such interactions particularly take place at the annual AIM Workshop.

Dr. Victor Yu, formerly associated with MYCIN, is now a faculty member at the University of Pittsburgh and has begun active participation in INTERNIST. Dr. Yu has been valuable in the programming of infectious diseases.

C. Critique of Resource Management

SUMEX has been an excellent resource for the development of INTERNIST. Our large program is handled efficiently, effectively and accurately. The staff at SUMEX have been uniformly supportive, cooperative, and innovative in connection with our project's needs.

III. Research Plans (8/78 to 7/81)

A. Long Range Project Goals and Plans

The primary goal of INTERNIST is to develop and complete an effective and reliable instrument for diagnostic consultation in internal medicine. To accomplish this a very extensive knowledge base must be developed, tested and continually updated. The initial stage of development is about 75% accomplished; a reasonable complete knowledge base, incorporating the new data structures identified in section I above, is a year in the future. With this development together with the improvement in the computer analytical program, INTERNIST will be suitable for a critical field trial, first in our own health center and, assuming success, in a half-dozen or so of additional health care institutions. Successful completion of the field test should make the program ready for practical clinical use.

B. Justification and Requirements for SUMEX Use

Neither the continued evaluation and development of INTERNIST's computer program nor the manipulation and further development of INTERNIST's knowledge base can be accomplished without a large computer resource such as SUMEX. SUMEX has thus far met our requirements admirably and those requirements for the research and development component of INTERNIST should remain relatively constant over the next three years. The SUMEX resource (or its equivalent) is absolutely essential to INTERNIST's progress.

C. Needs and Plans for Other Computational Resources

As predicted above, INTERNIST should be ready for field testing within two years. It is realized that it is not the purpose to SUMEX in its present form to support such extensive trials. Accordingly, a dedicated computer (or a dedicated portion of SUMEX) will be needed to carry out the trials. No specific plans have yet been made for this operation.

4.1.6 Medical Information Systems Laboratory

MISL - Medical Information Systems Laboratory

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I. Summary of Research Program

Funding for the Medical Information Systems Laboratory (MISL) under NIH grant 1-R01-MB-00114 was terminated in the spring of 1978. While the Laboratory continued its official existence for the last year, no active research was conducted. Consequently, the Laboratory has not used SUMEX-AIM services.

II. Interactions with the SUMEX-AIM resource

There has been no interaction to speak of between MISL and SUMEX-AIM.

III. Research Plans

Part of the work begun under MISL has been continued under other projects. Notably, continued development of a relational database system, RAIN, was funded by the Defense Advanced Research Projects Agency. That work is now virtually complete. It is expected that the Television Ophthalmoscopy (TVO) project, funded by the National Eye Institute, will make use of the RAIN database system. Now that RAIN is complete, TVO can proceed with its plans for an AI system called STARE (for structured analysis of the retina). Continued access to SUMEX-AIM would greatly benefit development of STARE, as it would facilitate communication and possible collaboration with other researchers in the AI in medicine community. It is hoped that the MISL account on SUMEX-AIM can be reassigned to the TVO project.

4.1.7 PUFF/VM Project

PUFF/VM: Biomedical Knowledge Engineering in Clinical Medicine

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and

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Stanford University

The immediate goal of this project is the development of knowledge-based programs to interpret physiological measurements made in clinical medicine. The interpretations are intended to be used to aid in diagnostic decision making and in therapeutic actions. The programs will operate within medical domains which have well developed measurement technologies and reasonably well understood procedures for interpretation of measured results. The programs are:

- (1) PUFF: the interpretation of standard pulmonary function laboratory data which include measured flows, lung volumes, pulmonary diffusion capacity and pulmonary mechanics, and
- (2) VM: management of respiratory insufficiency in the intensive care unit.

The second, but equally important, goal of this project is the dissemination of Artificial Intelligence techniques and methodologies to medical communities that are involved in computer aided medical diagnosis and interpretation of patient data.

I. Summary Of Research Program

PUFF

A. Technical Goals

The task of PUFF program is to interpret standard measures of pulmonary function. It is intended that PUFF produce a report for the patient record, explaining the clinical significance of measured test results. PUFF also must provide a diagnosis of the presence and severity of pulmonary disease in terms of measured data, referral diagnosis, and patient characteristics. The program must operate effectively over a wide range of pathological conditions with a broad clinical perspective about the possible complexity of the pathology.

B. Medical Relevance and Collaboration

Interpretation of standard pulmonary function tests involves attempting to identify the presence of obstructive airways disease (OAD: indicated by reduced flow rates during forced exhalation), restrictive lung disease (RLD: indicated by reduced lung volumes), and alveolar-capillary diffusion defect (DD: indicated by reduced diffusivity of inhaled CO into the blood). Obstruction and restriction may exist concurrently, and the presence of one mediates the severity of the other. Obstruction of several types can exist. In the laboratory at the Pacific Medical Center (PMC), about 50 parameters are calculated from measurement of lung volumes, flow rates, and diffusion capacity. In addition to these measurements, the physician may also consider patient history and referral diagnosis in interpreting the test results and diagnosing the presence and severity of pulmonary disease.

Currently PUFF contains a set of about 60 physiologically based interpretation "rules". Each rule is of the form "IF <condition> THEN <conclusion>". Each rule relates physiological measurements or states to a conclusion about the physiological significance of the measurement or state.

The interpretation system operates in a batch mode, accepting input data and printing a report for each patient. The report includes: (1) Interpretation of the physiological meaning of the test results, the limitation on the interpretation because of bad or missing data; the response to bronchodilators if used; and the consistency of the findings and referral diagnosis. (2) clinical findings, including the applicability of the use of bronchodilators, the consistency of multiple indications for airway obstruction, the relation between test results, patient characteristics and referral diagnosis. (3) Interpretation Summary, which consists of the diagnosis of presence and severity of abnormality of pulmonary function.

C. Progress Summary

Knowledge base:

PUFF is implemented on the PDP-10 in a version of the MYCIN system which is designed to accept rules from new task domains. Currently approximately 60 pulmonary physiology rules related to the interpretation of measurements mentioned above have been implemented. A typical rule is:

```
If (FVC(PP))>=80) and (FEV1/FVC<predicted-5) then PEAK FLOW RATES ARE
REDUCED, SUGGESTING AIRWAY OBSTRUCTION OF DEGREE
    if (predicted-15<= FEV1/FVC <predicted-5) MILD
    if (predicted-25<=FEV1/FVC <predicted-15) MODERATE
    if (predicted-35<=FEV1/FVC <predicted-25) MODERATE TO SEVERE
    if (FEV1/FVC <predicted-35) SEVERE
```

Results

The results of the PUFF system are reviewed in more detail in the 1978 SUMEX annual report. A version of the PUFF system is now in routine daily use at

Pacific Medical Center. Reports are reviewed by a physician pulmonary physiologist. Over one half of the reports are accepted by the physician without change; they are signed and entered into the patient record. Most of the remaining reports are modified with the addition of a small point in the test interpretation.

During the past year, substantial progress has been made toward each of the goals identified in 1978, specifically PUFF was changed to:

- (1) identify restrictive lung disease with greater accuracy.
- (2) modify some of the existing rules on OAD,
- (3) add rules to determine patient effort, or lack of effort, during the measurement acquisition,
- (4) add rules related to blood gas analysis, and
- (5) modify some parts of the PUFF program to increase the efficiency.

Table 1 summarizes agreement in severity of diagnoses made by two MD's and by PUFF rules. In 94% of 144 cases analyzed in a prospective study, the degree of severity (0=none; 1=mild; 2=moderate; 3=moderately-severe; 4=severe) of OAD diagnosed by the first MD was within a single degree of severity of OAD diagnosed by the second MD. In 96% of the 79 cases for which the first MD diagnosed OAD, the second MD diagnosed the severity of OAD within one level of the severity diagnosed by the first MD. Agreement within one degree of severity of the diagnoses by the first and second MD's was substantially lower in RLD and DD cases. These discrepancies occurred because the second MD consistently called RLD more severe than did the first MD, and he consistently did not diagnose diffusion defects when the first MD diagnosed DD of moderate or greater degree.

Diagnosis	Percent Agreement with 1st MD			
	All 144 cases		1st MD made Dx	
	Second M.D.	PUFF Rules	Second M.D.	PUFF Rules
Normal				
OAD	0.94	0.99	0.96	0.97
RLD	0.92	0.97	0.77	1.00
DD	0.87	0.87	0.60	0.80
Total	0.91	0.94	0.86	0.94

Table 1. Percent agreement within one degree of severity of diagnoses by two MD's and by the first MD and rules.

D. Relevant publications:

- [1] "A Physiological Rule-Based System for Interpreting Pulmonary Function Test Results", J.C. Kunz, R.J. Fallat, D.H. McClung, B.A. Votteri, J.S. Aikins, H.P. Nii, L.M. Fagan, E.A. Feigenbaum, HPP 78-154, Stanford Heuristic Programming Project, 1978.
- [2] "Prototypes: An Approach to Knowledge Representation for Hypothesis Formation", Aikins, J.S., HPP-79-10 (working paper), 1979.
- [3] "Use of Artificial Intelligence for Interpretation of Physiological Measurements: Pulmonary Function Diagnosis and ICU Ventilator Management", J.C. Kunz, L.M. Fagan, R.J. Fallat, D.H. McClung, Presented at the National Computer Conference by invitation, June 1978.
- [4] "Measurement, Modeling and Artificial Intelligence Using Respiratory Data", J.J. Osborn, Keynote Address to Computers in Critical Care and Pulmonary Medicine, May 1979, Proceedings Published by IEEE, 1979.
- [5] "Automated Interpretation of Respiratory Measurements in the ICU Using Techniques of Artificial Intelligence", J.C. Kunz, L.M. Fagan, E.A. Feigenbaum, J.J. Osborn, Proceedings of Computers in Critical Care and Pulmonary Medicine, IEEE Press, 1979.
- [6] "A Physiological Rule-Based System for Interpreting Pulmonary Function Test Results", J.C. Kunz, R.J. Fallat, D.H. McClung, B.A. Votteri, J.S. Aikins, H.P. Nii, L.M. Fagan, E.A. Feigenbaum, Proceedings of Computers in Critical Care and Pulmonary Medicine, IEEE Press, 1979.
- [7] "The Art of Artificial Intelligence: Themes and Case Studies of Knowledge Engineering", E.A. Feigenbaum, Proceedings of the IJCAI, (1977). (Also Stanford Computer Science Department Memo STAN-CS-77-612).

VM

A. Technical Goals

The Ventilator Manager program (VM) interprets the clinical significance of time varying quantitative physiological data from patients in the ICU. This data is used to manage patients receiving ventilatory assistance. An extension of a physiological monitoring system, VM (1) provides a summary of the patient's physiological status appropriate for the clinician; (2) recognizes untoward events in the patient/machine system and provides suggestions for corrective action; (3) suggests adjustments to ventilatory therapy based on a long-term assessment of the patient status and therapeutic goals; (4) detects possible measurement errors; and, (5) maintains a set of patient-specific expectations and goals for future evaluation. The program produces interpretations of the physiological measurements over time, using a model of the therapeutic procedures in the ICU and clinical knowledge about the diagnostic implications of the data. These therapeutic guidelines are represented by a knowledge base of rules created by clinicians with extensive ICU experience.

The PMC and SUMEX computers will be linked by telephone. The physiological measurements are generated every 2-10 minutes by the PMC computer system. This data now is taken to SUMEX on magnetic tape. It will be provided to VM in real time using the phone link. Information, suggestions to the clinicians, and/or requests for additional information will be sent back to the ICU for action.

B. Medical Relevance and Collaboration

To assist in the interpretation process, VM must be able to recognize unusual or unexpected clinical events (including machine malfunction) in a manner specifically tailored to the patient in question. The interpretation task is viewed as an ongoing process in the ICU, so that the physiological measurements must be continually reevaluated producing a current clinical picture.

This picture can then be compared with previous summary of patient status to recognize changes in patient condition upon which therapy selection and modifications can be made. The program must also determine when the measurements are most likely to be sensitive to error or when external measurements would be of diagnostic significance.

VM offers a new approach towards more accurate recognition of alarm conditions by utilizing the history and situation of the patient in the analysis. This is in contrast to the use of static limits applied to measurements generated to fit the "typical patient" under normal conditions. Our program uses a model of interpretation process, including the types and levels of conclusions drawn manually from the measurements to provide a summary of patient condition and trends. The program generated conclusions are stated at levels more abstract than the raw data; for example, the presence of hemodynamic stability/instability rather than in terms of heart rate and mean arterial pressure. When the data is not reliable enough to make these conclusions, additional tests may be suggested. The recognition of important conclusion for which external verification is sought, will also elicit the suggestion for confirming tests from the program.

C. Progress Summary

VM has been demonstrated using actual patient data recorded on magnetic tape. The input to VM is the values of 30 physiological measurements provided on a 2- or 10-minute bases by a automatic monitoring system. The output is in the form of suggestions to clinicians and periodic summaries (see example case below).

Example Case

The following case demonstrates the current state of development of the system. The data used in this example were obtained from a post-cardiac surgery patient from the ICU at Pacific Medical Center. The terms VOLUME, ASSIST, CONTROLLED MANDATORY VENTILATION (CMV), and T-PIECE refer to specific types of ventilatory assistance. The output format is:(a) ..time of day.., (b) generated comments for clinicians, starting with "***", and (c) commentary in {}.

```

..1350.. ..1351..
** SYSTEM ASSUMES PATIENT STARTING VOLUME VENTILATION.
                                     {monitoring started}
** HYPERVENTILATION                 {diagnostic conclusions
** TACHYCARDIA                       based on monitored data}
** PATIENT HYPERVENTILATING.         {suggested therapy based on
** SUGGEST REDUCING MINUTE VOLUME    diagnosis}
..1400..
. . .
..1450..
** HYPERVENTILATION
** TACHYCARDIA
** PATIENT HYPERVENTILATING.
** SUGGEST REDUCING MINUTE VOLUME
..1500..
** HYPERVENTILATION
** PATIENT HYPERVENTILATING.
** SUGGEST REDUCING MINUTE VOLUME
    
```

```

Current conclusions:                 {summary information}
HYPOTENSION PRESENT for 41 MINUTES
HYPERVENTILATION PRESENT for 33 MINUTES
SYSTOLIC B.P. LOW for 46 MINUTES
{etc.}
    
```

```

Conclusions:      {time of day} |.....|.....|.....|.
                  13      14      15      16
HEMODYNAMICS -- STABLE                =====
HYPERVENTILATION -- PRESENT           =      == == =====
HYPOTENSION -- PRESENT                 =====
TACHYCARDIA -- PRESENT                 =====

patient is on ASSIST                    ===== ==
patient is on CMV                       ===== ==
patient is on VOLUME                     ==
patient is on NOT-MONITORED             =====

Goal is CMV                             =====
Goal is VOLUME                           =====
                  |.....|.....|.....|.
                  13      14      15      16
    
```

The availability of new measurements requires updated interpretations based on the changing values and trends. As the patient setting changes--e.g., as a patient starts to breathe on his own during removal (weaning) from the ventilator--the same measurement values lead to different interpretations. In order to properly interpret data collected during changing therapeutic contexts, the knowledge base includes a model of the stages that a patient follows from admission to the unit through the end of the critical monitoring phase. Recognition of the appropriate patient context is an essential step in determining the meaning of most physiological measurements.

The majority of the knowledge of the VM program is concerned with the relations between the various concepts known by the program. These concepts include: measurement values, typical therapeutic decisions, diagnostic labels, and physiological states. The connections between concepts are represented by a form of production rules using the structure "IF premise THEN action."

The rules in VM are of the form:

```
IF    facts about measurements or previous conclusions are true

THEN

      1) Make a conclusion based on these facts;
```

A sample VM rule is shown below.

```
STATUS RULE: STABLE-HEMODYNAMICS
DEFINITION: Defines stable hemodynamics for most settings
APPLIES to patients on VOLUME, CMV, ASSIST, T-PIECE
COMMENT: Look at mean arterial pressure for changes in
         blood pressure and systolic blood pressure for maximum
         pressures.
IF
  HEART RATE is ACCEPTABLE
  PULSE RATE does NOT CHANGE by 20 beats/minute in 15 minutes
  MEAN ARTERIAL PRESSURE is ACCEPTABLE
  MEAN ARTERIAL PRESSURE does NOT CHANGE by 15 torr in 15 minutes
  SYSTOLIC BLOOD PRESSURE is ACCEPTABLE
THEN
  The HEMODYNAMICS are STABLE
```

Figure 2. Sample VM Interpretation Rule. The meaning of 'ACCEPTABLE' varies with the clinical context--i.e., whether the patient is receiving VOLUME or CMV ventilation, etc. This rule makes a conclusion for internal system use. Similar rules also make suggestions to the user.

II. Research Plans

A. Long Range goals and plans

PUFF

Consensus

Physician acceptance of assistance by knowledge-based programs is understandably inhibited by disagreements between physician diagnoses and those produced by the programs. This disagreement reflects a deeper underlying disagreement among the physicians themselves on the rules to be used for diagnosis. A more subtle problem arises when physicians agree on the diagnosis but cannot agree on the supporting evidence or the reasoning which led to the diagnosis.

We consider obtaining consensus among physicians an important problem for PUFF's acceptance. At the same time, the process of building consensus about a body of knowledge is an interesting area of research in artificial intelligence. The general question to be answered is: What components of the diagnostic process cause differences in the diagnosis? More specifically, in terms of the knowledge which the physicians bring to bear on the diagnostic process, are there differences in representation? (i.e. do physicians use different forms of knowledge?) Are there differences in the definition? (i.e. do physicians use different models or definitions of disease, manifestations, and diagnosis?) Are there differences in the process? (i.e. do physicians reason differently about the problem?)

A second set of questions is: When designing knowledge-based systems, should it be designed to be modifiable to conform to the user physician's diagnostic process? Or, should it be designed to act to identify and record areas of disagreement among the physicians? Should it warn the physicians, mediate the differences, or merely collect the information?

We would like to spend the next few years answering some of these questions in order to understand the problem of consensus building among physicians.

VM

The long range goal of the VM project is to develop and to evaluate an interpretation system which will improve patient care in the ICU.

To insure acceptance by physicians, a careful evaluation of the correctness of the advice of the program against a set of prospective cases will be carried out. A large amount of patient data has already been collected for this evaluation. An experimental period of use in the ICU by clinicians associated with our project is projected during 1979-81.

III. Interactions With The SUMEX-AIM Resource

A. Collaborations and medical use of programs via SUMEX

The PUFF/VM project requires very close collaboration between investigators at two institutions separated by fifty miles. This kind of collaboration, in which program development and testing proceeds concurrently on the same application system, requires a computer network facility for sharing of code, data and ideas. SUMEX has been used at PMC for running programs developed concurrently by Stanford and PMC staff, and data has been taken from the PMC computer system and transferred to SUMEX on magnetic tape for program development and testing.

B. Sharing and interactions with other SUMEX-AIM projects

We have participated in the AIM workshop and had very fruitful interaction with a number of other SUMEX users, directly influencing our perception of important problems and potentially appropriate solutions. Personal contacts at other conferences, at Stanford AI weekly meetings, and at PMC with visiting

members of the AIM community, have also been very helpful in keeping abreast of the current thinking of other members of the AI community and with members of the medical community interested in computer based physiological analysis and diagnosis. Specifically, within AIM, there is the closest possible collaboration with researchers on the MYCIN, MOLGEN and DENDRAL projects, who share common space, common techniques, and common attitudes.

C. Critique of resource management

The SUMEX community continues to be an extremely supportive environment in which to do research on uses of artificial intelligence in clinical medicine. The community has two equally vital resources -- the people with knowledge and interest in AI and the facility on which AI system development can proceed. They are equally excellent as resources, helping hands when faced with problems, and friendly support for continued productive research. The availability of INTERLISP; of a facility on which routine data processing functions (eg. manipulating magnetic tapes and making long listings) can take place; and of message-sending among remote users are all vital functions for our project. SUMEX provides them in an environment which is friendly and reliable.

D. Needs and plans for other computational resources

The computation facility at PMC is currently the source of all of the data being used by the PUFF/VM project, and it will continue in this capacity. We expect to link the two machines using a simple telephone dial-up link, but this represents the only system increment to the computational facility of the collaborative project. As the AI techniques developed under PUFF/VM enter routine clinical use at PMC, we have the requirement for system support on which these programs can execute.

VM will enter a period of very rapid development of its knowledge base during the summer of 1979. The basic form of the clinical knowledge has been developed and demonstrated; we expect to work rapidly to fill in a great deal of relevant detail. This knowledge base will require very careful validation as individual subsections near completion. The PUFF/VM grant has plans and resources for bringing large amounts of patient physiological data to SUMEX in real time, and these data will be available starting in the summer of 1979. The process of validation then will require running VM in real time so that PUFF/VM researchers can compare system interpretations of patient state with the actual state as determined by careful concurrent clinical evaluation. We believe that we can effectively use 3-4 hours per day of running VM in a real time test mode during the initial validation period. As the system operation becomes more predictable in 1980, longer running times will be required to identify system problems, and we predict the need to run the system for a full eight hour shift each day.

This test and validation process can be carried out with existing SUMEX resources. The current SUMEX load average is too high to support an effective interaction over a long period of time between clinical researchers and the system. In addition, the very large demand for computation for validating VM will place a great burden on the other SUMEX users. The proposed SUMEX PDP-10-compatible machine will be a potential vehicle for this validation effort if it is available and has easy loading of SUMEX PDP-10 INTERLISP programs onto the new machine.

E. Recommendations for future community and resource development

We perceive the evolution of our AI capability as moving from a highly speculative development state, for which the interactive development capabilities of SUMEX are vital, to a more stable but still changing validation-and-evaluation state. Ultimately we foresee rather stable specification of a program for routine clinical use. Thus, we see the need to transfer our AI techniques from the SUMEX PDP-10 to a local host. For this transfer, a principal long-range need is for software systems that will allow us to run AI systems on a mini-computer after they have been developed on the more powerful SUMEX facility. If the validation of PUFF/VM in the PMC clinical setting shows the programs to be effective in health care, then we hope and expect to be able to provide the capability on a routine basis.

4.1.8 Rutgers Computers in Biomedicine

Rutgers Research Resource - Computers in Biomedicine

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I. SUMMARY OF RESEARCH PROGRAM

A) Goals and Approach

The fundamental objective of the Rutgers Resource is to develop a computer based framework for significant research in the biomedical sciences and for the application of research results to the solution of important problems in health care. The focal concept is to introduce advanced methods of computer science - particularly in artificial intelligence - into specific areas of biomedical inquiry. The computer is used as an integral part of the inquiry process, both for the development and organization of knowledge in a domain and for its utilization in problem solving and in processes of experimentation and theory formation.

The Resource community includes 85 researchers and professionals - 37 members, 11 associates, 28 collaborators and 9 users. Members are mainly located at Rutgers. Collaborators are located in several distant sites and they interact, via the SUMEX-AIM and RUTGERS/LCSR facilities, with Resource members on a variety of projects, ranging from system design/improvement to clinical data gathering and testing of expert systems. Our collaborations are described further in section B. below. Resource users are located at Johns Hopkins University, University of Pittsburgh, Stanford University and the NIH campus.

Resource activities include research projects (collaborative research and core research), training/dissemination projects, and computing services in support of pilot user projects. The research projects are organized in three main AREAS OF STUDY. The areas of study and the senior investigators in each of these are:

- (1) Medical Modeling and Decision Making (C. Kulikowski).
- (2) Modeling Belief Systems and Commonsense Reasoning (C. F. Schmidt and N. S. Sridharan).
- (3) Artificial Intelligence: Representations, Reasoning, and System Development (S. Amarel).

The training/dissemination activities of the Rutgers Resource include sponsorship of the Annual AIM Workshop - whose main objective is to strengthen interactions between AIM investigators, to disseminate research methodologies and results, and to stimulate collaborations and imaginative resource sharing within the framework of AIM. The fourth AIM Workshop was held at Rutgers on June 25 to 28, 1978.

The RUTGERS/LCSR computer is being used not only for support of local research projects and AIM Workshop activities; but also for Pilot User Projects in the AIM community - within the general framework of the national AIM project. Computing activities in the Resource are coordinated by S. Levy. The RUTGERS/LCSR facility is directed by C. Hedrick.

B) Medical Relevance; Collaborations:

During 1978-79 we developed a versatile system for building consultation programs, called EXPERT. This system is being used extensively in the development and study of several medical consultation models - in collaboration with clinical investigators from several specialties.

In ophthalmology, the CASNET/Glaucoma knowledge base is being translated into the new EXPERT formalism. The development of the glaucoma knowledge base built in conjunction with the investigators of ONET (ophthalmological network) continues, and is being supplemented by knowledge of Japanese variants of the disease and the decision rules embodying the clinical judgement of a Japanese glaucoma expert: Dr. Y. Kitazawa. Preliminary contacts with British glaucoma specialists have also taken place, raising the prospect that in the near future we will be developing an international knowledge base for this disease. In addition, a model for neuro-ophthalmological consultation is being built in collaboration with Dr. William Hart of the Washington University School of Medicine. In this field we have continued the investigation of anatomical-physiological models for guiding reasoning.

In rheumatology, a vigorous new effort is taking place in developing a rheumatological consultant program using the EXPERT scheme. It has begun with a specialized model of diffuse connective tissue disorders in collaboration with Dr. Gordon Sharp of the University of Missouri at Columbia. Dr. Donald Lindberg, Director of the National Health Care Technology Center at the University of Missouri, initiated this activity and is actively participating and supporting the development of the consultation system. Collaboration with Japanese specialists in this area is also beginning. A knowledge base for generalized consultation in rheumatology to be used by primary care physicians is being developed in conjunction with Dr. William Pincus of the University of California at San Diego, and a similar program is being planned for use in Missouri. These studies are helping us understand better the problems of articulating medical knowledge needed at different levels of detail and specialization and have important implications for the future design of medical knowledge bases. Investigations on the use of a data base of cases for deriving decision-rules, and for updating an existing expert system are also proceeding using rheumatological case records. A rule learning scheme was developed and applied to a data base in allergy and immunology.

Other collaborations have been in the areas of endocrinology, where a thyroid consultation knowledge base was developed in conjunction with Dr. R. A. Nordyke of the Pacific Health Research Institute, and in clinical pathology, where a model for the interpretation of blood chemistry and blood gas analysis data is being developed by Drs. J. Smith and C. Speicher of Ohio State University at Columbus.

All the above applications have shown the versatility of the basic EXPERT representation scheme for rapidly developing medical knowledge bases. By continued testing and development of various domain models, the current boundaries of applicability of the EXPERT formalism are being explored, and new facilities added as required to improve the consultative performance of the programs developed.

In addition to the direct medical collaboration, we have continued investigating problems of modeling in enzyme kinetics with Dr. David Garfinkel of the University of Pennsylvania.

C) Progress Summary:

1. Areas of Study and Projects:

a) Medical Modeling and Decision-Making

Research activities during the past year have concentrated on the development of a new generalized consultative system scheme (knowledge representation and associated strategies of inference), called EXPERT, and its application to a number of different medical domains.

The structure of knowledge in EXPERT involves two data types: findings and hypotheses. The hypotheses (diagnostic, prognostic and treatment selection) are organized as a partially ordered network (PON) using hierarchical and causal relationships. The findings are organized according to observational constraints. Production rules are used to encode inferences among findings, between findings and hypotheses, and among hypotheses. Because of the PON organization of hypotheses, the knowledge base can be pre-compiled with attendant space and time efficiencies in the performance of the consultation programs that call on the knowledge base for decision-making advice.

As described in section B of this report, knowledge bases in ophthalmology, rheumatology, endocrinology and clinical pathology have served to test the versatility of the EXPERT formalism.

Another component of our research involves studies of explicit representations of anatomical and physiological knowledge, and the use of generalized heuristics for reasoning with such models. A preliminary model in neuro-ophthalmology has been developed using the AIMDS and other frame-based representations. In conjunction with the EXPERT investigation this work is yielding insights into the nature and applicability of compiled vs. interpreted medical knowledge. This work has important implications for the practical design of large-scale medical knowledge bases of the future.

Problems of updating a knowledge base and learning decision rules from a data base of case records are two other areas of investigation. A program for rule learning by five different fuzzy-logic heuristic methods was developed and tested using allergy case study data. Problems of the transferability of large-scale consultation programs to a minicomputer environment have also been investigated.

Clinical investigations in thyroid disease and hypertension (by investigators at Pacific Health Research Institute and Johns Hopkins School of Medicine) have been aided by Resource support and development of the BRIGHT system.

b) Modeling of Belief Systems and Commonsense Reasoning

The domain which we have been investigating is the understanding of human actions. A theory of action understanding is fundamental to theories of social psychology, communication and social interaction. Additionally, the understanding of human action involves the use of commonsense concepts of both physical and social causation. Commonsense concepts of causality represent one of the most articulated and complex knowledge bases that we use in understanding our everyday world. In developing a psychological theory of action understanding, we have provided an account of the deep semantic properties that underlie commonsense concepts such as action, plan, belief, and intention. This knowledge is represented in the frame-like AI system, AIMDS, which we developed in the Resource together with a process which exemplifies the use of what we term a hypothesize and revise search strategy. Our psychological theory is embodied in the BELIEVER system.

During this past year our efforts have focused on the investigation of the hypothesize and revise process and, in conjunction with this process, the development of a plan generator that can operate in the context of this process. The hypothesize and revise process is both predictive and responsive to the developing observations of actions and able to function robustly in the "open world" of everyday observations. Such a process is made possible because of the highly articulated nature of the commonsense model of social causality.

As a result of empirically testing the BELIEVER knowledge-based theory we have come to a deeper understanding of the methodology involved in testing such theories. The insights concerning problems of hypothesis formation and test can be seen as a generalization of certain central aspects of the theory of action understanding. This is not surprising since we view certain aspects of hypothesis formation and many aspects of theory testing as a type of interpretation task. As a result of this understanding, we have begun to design a system for the generation and test of hypotheses in our domain of social psychology which formalizes and generalizes upon our experience in testing the BELIEVER theory of action understanding.

c) Artificial Intelligence; Representations, Reasoning and Systems Development

A major part of our effort in this core area continued to be directed to collaborations with investigators in the other applications - oriented projects of the Resource. These collaborations are having an impact on the application areas of the Resource, and they are stimulating work on basic AI issues that are related to designs of knowledge-based systems.

During this period, work on AIMDS has provided a strong focus for studies in knowledge representation and in processes of interpretation and theory formation. This work is continuing in the context of an intensive collaboration towards the development of the BELIEVER theory of action interpretation. As part

of this work, considerable progress was made in representations of plan structures and in processes for generating and recognizing plans. Also, the AIMDS system has been extended considerably on basis of experience which has been accumulating from attempts to apply it in new tasks of interpretation, knowledge acquisition/learning and hypothesis formation.

Our efforts to develop unifying principles and conceptual frameworks for the design of AI systems were directed this period to three areas: the analysis of several major interpretation/diagnostic systems developed within the AIM community (MYCIN, CASNET/Glaucoma, BELIEVER and DENDRAL); the study of methods for automatic improvement of problem solving systems via shifts in problem representation obtained by the formation of macromoves from elementary moves; and continuing research on theory formation processes - both in the context of model-guided program formation, and in other rule-learning tasks.

Our research on natural language processing has continued with the objective to develop methods that facilitate communication between people (domain experts, users, designers) and computers. We have taken a fresh look at the problem of developing a convenient man machine interface for a glaucoma consultation system. Building on our previous work in this area, we have added several novel features to the design of our interface processor.

We are continuing to study problems of language acquisition/learning to gain insight into the general problem of knowledge acquisition in expert AI systems. However, we have shifted emphasis this year to an approach which assumes a more active teacher-learner dialogue in the language acquisition process. This led to the identification of rules that govern such a dialogue, and to the design of acquisition processes that embody these rules.

Our commitment to a strong AI programming environment resulted in improvements of the Rutgers/UCI LISP system, as well as in other systems programming developments. These efforts are strengthening the tools for design and experimentation that are available to Resource investigators on the RUTGERS/LCSR computer facility.

2) AIM Dissemination; Training

The Fourth Annual AIM Workshop was held at the Continuing Education Center at Rutgers University on June 25-28, 1978. There were approximately 90 invited participants who attended. This Workshop concentrated on several issues in the construction and validation of consultation programs in medicine, on certain aspects of AI in psychology, on current problems in AI research that are relevant to AIM applications, and on a number of management and funding issues concerning the SUMEX-AIM facility in particular and the AIM community in general.

For the first time in the Workshop series a sizable number of graduate students were invited to the Workshop. The inclusion of the graduate students was an important step in AIM community building, in that the people most actively involved in "systems building" were able to get together and discuss their work, with the invited talks and panels of the Workshop forming the context. Most of the project reports discussed in the evening sessions were presented by graduate students.

The program for the 1978 Workshop consisted of the following four classes of activities:

- (i) Invited talks on basic themes. The conference contained three invited talks on basic issues. Dr. C. Kulikowski spoke on AI and medicine, Dr. S. Amarel on current themes in AI research, and Dr. C. Schmidt spoke on the relation of AI and psychology. The complete texts of these talks are being included in the Proceedings that are now in preparation.
- (ii) Panel discussions on technical and management issues. The panel discussions were designed to give contrasting views on several issues of current concern. Dr. N. S. Sridharan and Dr. H. Pople chaired a panel on hypothesis formation and revision, a current issue in the construction of knowledge-based systems. Dr. R. Smith chaired a panel on issues in the design and transfer of knowledge-based systems, which spanned a wide range of hardware, software, and representation problems relating to transferring techniques and systems beyond the first stages of research. Dr. E. Feigenbaum chaired a panel on collaboration and AIM policy, which focused on management issues.
- (iii) Working groups (organized during the Workshop). There were six working groups, scheduled to run two in parallel for three periods of the Workshop. The working groups were: commentary on AIM systems, choice of representation for knowledge, issues of validation in building AIM systems, methods of plausible reasoning, handling multiple sources of knowledge, and technology options for the SUMEX resources.
- (iv) Informal reports on work in progress, mainly by graduate students. A total of sixteen informal reports were given in the evening sessions, two in parallel.

Prof. Herbert Simon of Carnegie-Mellon University gave the keynote address at the Workshop banquet. The banquet was attended by the Workshop participants, plus a number of guests from the Rutgers academic community.

The Proceedings (that are expected to be issued shortly) will give a detailed summary of the panels and working groups, as well as the text of the invited talks.

3) Pilot AIM Projects

The two pilot projects that started in the last period - BRIGHT (an NIH-sponsored clinical data base system) and MAINSAIL - continued this year. In addition, after the new KL-2050 computer was installed at Rutgers, two new pilot projects started: INTERNIST (extensive system development and testing) and CONGEN (mainly in support of demos).

4) Computing Facilities

Our plans to enhance the computing facilities at Rutgers - and to increase their availability to the AIM community - were implemented in the Fall of 1978. At present, the RUTGERS/LCSR facility includes a DEC KL-2050T configuration running under TOPS-20. This facility is accessible via TYMNET. [It was also

accessible via ARPANET until April 1979; we expect that our connection to the ARPANET will be restored soon.]

Computing in the Rutgers Resource continues to be distributed between the RUTGERS/LCSR facility and SUMEX-AIM, with the bulk of computing being done at Rutgers.

D) Up-to-Date List of Publications

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II. INTERACTIONS WITH SUMEX-AIM RESOURCE

The main use of the SUMEX-AIM facility by Rutgers Resource investigators is for system testing with collaborators around the country and for communications on collaborative projects - such as the AIM Workshop - with other scientists in the AIM community. Also, the level of interactions among systems people at the Stanford and Rutgers facilities has increased since the RUTGERS/LCSR system has become a 'server' node in the national AIM network. We continue to access SUMEX-AIM via TYMNET, and (until April-78) via ARPANET.

The ONET community works with the CASNET and EXPERT systems at both the Stanford and Rutgers sites; and up-to-date system copies are maintained at both sites. The research with the U. of Missouri on Rheumatic diseases (using EXPERT) is being done at both sites and each is being used to back up the other. Development of the INTERNIST system by the U. of Pittsburgh researchers has been going on on both the Stanford and Rutgers systems; each system backs up the other for use and demos. These network activities have been temporarily disrupted by the recent removal of the ARPANET link to the Rutgers system; we hope, however, to be reconnected to ARPANET in the near future, and these activities are expected then to go back to their previous levels.

SUMEX-AIM continues to provide the focus for our collaboration with Stanford on the AI Handbook project and for many of the activities surrounding the organization and running of the AIM Workshop. Stanford developments, such as the AGE system, are being explored by Rutgers investigators on the SUMEX-AIM facility. In general, SUMEX-AIM continues to play a vital role as a center for the exchange of ideas and systems with other scientists in the AIM community.

III. RESEARCH PLANS (8/79 - 7/81)

A) Long Range Project Goals and Plans

We are planning to continue along the main lines of research that we have established in the Resource to date with emphasis on broadening our activities in the medical systems area. We also plan to continue our participation in AIM dissemination and training activities as well as our contribution - via the RUTGERS/LCSR computer - to the shared computing facilities of the national AIM network.

B) Justification and Requirements for continued SUMEX use

The use of SUMEX-AIM by the Rutgers Resource will continue to be needed in support of our collaborative research projects, as well as joint AIM dissemination projects and for communications. We estimate a modest total annual level of usage at SUMEX-AIM of about 750 connect hours at an average compute to connect ratio of 1:25. Also, the participation of the RUTGERS/LCSR facility as a node in the AIM network of shared resources will continue to require close coupling and coordination with SUMEX-AIM at the systems level.

C) Plans for Computational Resources

The usage of the RUTGERS/LCSR computer is approaching the capacity limits of the current configuration. There is, however, considerable room to extend the system capacity by augmenting key components such as main memory. Also, considerable effort is still required to improve the system's environment and thus its reliability. These are directions of development that we foresee for the computational resources that are located at Rutgers. As far as more general planning for new resources is concerned, we believe that the emphasis should be on relatively small machines (DEC's 2020, VAX or equivalent) to be located in major user sites and to be configured as parts of a national network of AIM shared resources.

4.1.9 Simulation of Cognitive Processes (SCP)

Simulation of Cognitive Processes (SCP)

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I. SUMMARY OF RESEARCH PROGRAM

Technical Goals

The goals of this project remain the simulation of children's behavior in mathematics and reading tasks, done in such a way that various levels of proficiency, from moderate dysfunction and normal prereading skills to expertise, can be modeled. As this work continues, the investigators and several colleagues have also become involved in a more general study of the course of cognitive skill acquisition. The long-term (one to two years from now) effect of this additional work will be to force a more general level of theorizing about cognitive skills and about the course of learning. Such a general approach must, on the one hand, seek out the basic principles of cognitive learning and of how different levels of prior skill and aptitude interact with different types of training to produce learning. However, the work must be grounded in specific, detailed work on the learning and performance of specific skills.

Our work on SUMEX-AIM continues, therefore, to focus specifically on mathematics and reading. However, we have also begun a new activity, the development of a procedure and language acquisition system (PLAS). PLAS is part of an on-going project to investigate the utility of representing the skills of mathematics children demonstrate as well as the errors they make while learning mathematics in terms of a model of the acquisition of language and procedural knowledge. The system is a version of Anderson's Language Acquisition System, with a modified memory structure that incorporates structured programs as well as declarative knowledge. The system can understand sentences of arithmetic (construct memory structures which are executable as programs), speak (given a memory structure, a sentence in the language can be produced), and learn the meaning and syntax of new sentences (given a sentence-memory pair, the system constructs an augmented transition network to translate between them). Such a system, when given incorrect or incomplete knowledge, will produce behavior inappropriate for the task at hand. It is the purpose of our group to relate specific mathematical errors that people (children and adults) make to simulatable misconceptions and thereby to deduce techniques which will "debug" and enhance such knowledge.

In reading, as our work progresses on a longitudinal study of the course of acquisition for the subprocesses of reading, the task of simulating the interactions of various levels of the reading process is becoming much better defined. It is now clear that if these processes are to be simulated within ACT, as planned originally, it will be necessary for ACT to grow to include partial matching schemes for the testing of production conditions. Thus, we are testing

out pieces of a simulation while awaiting the development of the next generation of ACT. Our goals remain the characterization within ACT of the interactions of recognition and comprehension processes in children with different levels of automation of recognition processes, different levels of knowledge of the subject matter domain, and different basic cognitive aptitudes.

Medical Relevance and Collaboration

The range of ability levels we are dealing with in arithmetic and reading includes children who are below average and, in the case of reading, some children who are classified as learning disabled. By providing a framework within which the effects of differing levels of skill acquisition can be understood, we hope to eliminate the spurious use of vague medical categories such as minimal brain damage, etc., and thus more clearly delimit the cases in which there is a real medical problem from other cases in which a person is poor in basic cognitive skills.

Progress Summary

Progress this past year has been greatest in the area of arithmetic, though there has been some progress on reading, also. In arithmetic, work has progressed on children's ability to solve arithmetic word problems and on the PLAS system mentioned above. There has also been some work on geometry. Finally, there has been considerable empirical progress and clarification of our AI goals for the reading work. These will all be discussed in turn.

Arithmetic work

Three reports of work relevant to arithmetic learning have been written (Riley, 1979; Heller, 1979; Greeno, in press). Riley's and Heller's papers present further work investigating the processes that Heller modeled in the ACT system on SUMEX last year. Greeno's paper summarizes issues and results of that work, as well as Danforth's project on learning arithmetic syntax.

Procedure and Language Acquisition System - PLAS

Current status of PLAS. The system being developed is nearing the completion of its component modules. The memory building routines, the derivation tree to ATN grammar translator, and the ATN parser are all complete. There remains the derivation tree constructor (equivalent to BRACKET in LAS but simpler), the building of the module to merge ATNs, and the high level control structure of the system. This work has been aided by informal discussions with John R. Anderson and Patrick W. Langley at Carnegie-Mellon University and the ACT project. There follows a short summary of the most significant parts PLAS: memory, grammar, and syntax acquisition.

The memory of PLAS. All declarative and procedural knowledge of PLAS is stored in a uniform memory structure. There are nodes in the memory which are implemented in UCI LISP as atoms. Each node has a list of other nodes associated with it (has the property AS with a list as its value). The node is called the ASSOCIATION and its list of associated nodes its OFFSPRING (or ASSOCIATIVE). Each node also has a list of dominating nodes or PARENTS (also called the nodes AFFINITIVE) which provide a doubly linked structure for memory searching. There

is nothing more to the memory than that. Meaning is provided by linking some of the nodes (terminal nodes) to either executable primitive procedures or words of the language. Complex programs are constructed simply by creating associations of lower level programs. Declarative knowledge is incorporated through consistency of association of words with specific nodes in memory. In this way it is possible to combine declarative and procedural knowledge (not all such associations are useful or executable).

The augmented transition network grammar. The system contains an Augmented Transition Network (ATN) Grammar to parse input sentences and construct memory associations. The grammar is implemented as a finite labeled graph. The vertices of the graph are ATNs and the labels of the edges are actions to be performed (memory structures built) upon successful testing of a precondition. Each precondition is itself an ATN so that the graph representing an ATN is nothing more than a vertex (the graph) which has a set of triples (ATN ACTION ATN) representing the edges leading out of this vertex. Terminal ATNs test for the presence of a given word at the current position of the input string. They either succeed or fail.

Since it is not possible to determine whether a sentence has been successfully parsed until the last word has been examined, the actions on the links are pushed onto an action stack and executed sequentially when the parse succeeds. The actions are nothing more than the creation of associations. In fact the labels of the graph edges are associations in the memory. If a node of the memory is unbound then a new node is created and bound to it. The association thus formed is then available for the next action which may use it or some previously built association. In this way, the distinction bound vs. unbound controls the context of the discourse allowing associations from previous sentences to be incorporated into the meaning of the present sentence. Once the action stack has been processed, the last association is executed, in the sense that associations that contain primitive procedures are executed whereas declarative associations are skipped. Note that it is possible to "talk about" a procedure as well as "do" a procedure if the procedure is embedded in a declarative association.

The learning of syntax. The ATN grammar forces a hierarchical structuring of the parse of any sentence. When a sentence cannot be parsed by the grammar and the sentence is correct, then something else must be done to provide a derivation tree for the sentence. In PLAS the meaning of a new sentence is introduced directly into the system's memory. The only distinction between the associations for this sentence and those of any other sentence previously introduced is that of recency. This is expressed by the order of nodes in an association's AFFINITIVE (parents) list. Given the sentence and the updated memory, an exhaustive search is performed emanating from a specified node to each of the words in the sentence subject to the constraint that the linked structure so formed is a tree. The specified node can be any node of memory. To correspond with LAS, the node is the principal proposition of the meaning just introduced. Note that the node could also be the principal association of the last sentence parsed.

Given the derivation tree of a sentence, PLAS constructs an ATN grammar which will parse the sentence. This "mini-grammar" is then merged with the ATN grammar constructed from previous sentence-memory pairs. The merging process

entails the recognition of identical subgrammars and pattern matching between the memory associations (the actions) of the grammar.

Geometry

Two technical reports have been written (Greeno, Magone, and Chaiklin, in press; Greeno, in press) about the geometry work. They report an extension of an earlier model of geometry problem solving developed earlier in ACT (though not on SUMEX). The new development is a simulation of hierarchically organized planning knowledge of the kind analyzed by Sacerdoti. This way of organizing knowledge provides a natural interpretation of the occurrence of constructions. Plan schemata have the form of global actions, and knowledge includes the preconditions needed for each schema to apply. If none of the required preconditions is present in complete form, the system can identify partial matches to some patterns that would provide the needed preconditions and invoke procedures for pattern completion that involve constructing auxiliary lines. The structure also provides a natural interpretation of classical problem-solving set, since the top-down nature of planning can result in adoption of a plan that is then carried out without noticing the possibility of an alternative plan that might be easier.

Reading

The reading work has been mainly empirical this year. We have discovered that reasonable simulation of process interactions in reading will require extensions of ACT to allow partial matching schemes for production condition testing. We have had discussions with Anderson on this and have agreed to continue work on pieces of the simulation within ACTF, while awaiting ACTG, which will permit more natural simulation. Existing fragmentary simulations have allowed clarification of our models of reading dysfunction and permitted sensible redesign of later portions of a longitudinal study of reading acquisition (Lesgold, 1978; Lesgold, Resnick, & Beck, 1979). The next step is partial simulations of local-coherence resolving processes (Lesgold, Roth, & Curtis, in press).

List of Relevant Publications

- Greeno, J.G. Constructions in geometry problem solving. LRDC Technical Report, in press.
- Greeno, J.G. Preliminary steps toward a cognitive model of learning primary mathematics. In K. Fuson and W. Geeslin (Eds.), Models of children's mathematical learning, ERIC Information Center, in press.
- Greeno, J.G., Magone, M.E., & Chaiklin, S. Theory of constructions and set in problem solving. LRDC Technical Report, in press.
- Heller, J.I. Schemata in the solution of arithmetic word problems. Paper presented at the annual meeting of the American Educational Research Association, San Francisco, April, 1979.
- Lesgold, A.M. Word-memory access and reading: Toward more explanatory evidence. Paper presented at the annual meeting of the American Educational Research Association, Toronto, March, 1978.

Lesgold, A.M., Resnick, L.B., & Beck, I.L. Preliminary results of a longitudinal study of reading acquisition. Paper presented at the annual meeting of the Psychonomic Society, San Antonio, November, 1978.

Lesgold, A.M., Roth, S.F., & Curtis, M.E. Foreground effects in discourse comprehension. Journal of Verbal Learning and Verbal Behavior, in press.

Riley, M.S. The development of children's ability to solve arithmetic word problems. Paper presented at the annual meeting of the American Educational Research Association, San Francisco, 1979.

II. INTERACTIONS WITH THE SUMEX-AIM RESOURCE

Collaborations and medical use of programs via SUMEX
None.

Sharing and collaboration with other SUMEX-AIM projects

We have been in touch regularly with the ACT project members, and have agreed to test their new work with both simulations and by providing data in which both top-down-process-influencing variables and bottom-up-processing-influencing variables have been manipulated. Steven Roth has gathered such data. We have also been in touch with the group at Colorado [I don't know their project name], and are sharing information about possible future moves onto site-specific computer systems (see below) as well as the Kintsch discourse work, which relates to work we are doing (e.g., Lesgold, Roth, & Curtis, in press).

Critique of Resource Management

The system is getting crowded, but is certainly well managed. A critical issue for the future is the extent of decentralization and the proper role for a central resource. We see that role as one of communications among researchers and prototyping of work that does not yet merit a dedicated facility.

III. RESEARCH PLANS

Long range project goals and plans

Our plans are outlined in the above sections. We expect to have our own system at LRDC for INTERLISP use within the next year or so, depending upon progress within the lisp community in INTERLISP migration. Even then, it will be useful to have access to SUMEX to try out new ideas from other laboratories and to finish work that is hard to move (e.g., PLAS). However, in the long run, SUMEX will have been a major resource for a short period of time and a development tool for the next decade's work.

Justification and requirements for continued SUMEX use

As noted above, there is substantial work in progress that depends upon unique SUMEX resources, primarily the LISP systems. This, plus our interactions with Anderson, Kintsch, and Polson, make SUMEX the desirable place for our work. In terms of publication and influence on the field, the record is public. We are in the process of securing a new system (with ARPA support), and will be moving off of SUMEX as fast as we can. But, it will be at least a year before the lisp resources we need are available.

Needs and plans for other computer resources beyond SUMEX-AIM

Discussed above.

Recommendations for future community and resource development

SUMEX must continue to move from being primarily a computer-power resource to being the leadership node for a group of users who are increasingly able to get their own computer power pretty cheaply. For example, the long-term future requires continued thought about networking schemes that will allow all of our 1981 lisp machines to be as collaborative as we are now in a central resource. This is where forthcoming work should center. Also, such tasks as INTERLISP and other system migration development might sensibly concentrate in SUMEX.

4.2 Stanford Projects

The following group of projects is formally approved for access to the Stanford aliquot of the SUMEX-AIM resource. Their access is based on review by the Stanford Advisory Group and approval by Professor Feigenbaum as Principal Investigator. As noted previously, the DENDRAL project was the historical core application of SUMEX. Although this is described as a "Stanford project," a significant part of the development effort and of the computer usage is dedicated to national collaborator-users of the DENDRAL programs.

4.2.1 AI Handbook Project

Handbook of Artificial Intelligence

E. A. Feigenbaum and A. Barr
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I. SUMMARY OF RESEARCH PROGRAM

A. Technical Goals

The AI Handbook is a compendium of knowledge about the field of Artificial Intelligence. It is being compiled by students and investigators at several research facilities across the nation. The scope of the work is broad: Two hundred articles cover all of the important ideas, techniques, and systems developed during 20 years of research in AI. Each article, roughly four pages long, is a description written for non-AI specialists and students of AI. Additional articles serve as Overviews, which discuss the various approaches within a subfield, the issues, and the problems.

There is no comparable resource for AI researchers and other scientists who need access to descriptions of AI techniques like problem solving or parsing. The research literature in AI is not generally accessible to outsiders. And the elementary textbooks are not nearly broad enough in scope to be useful to a scientist working primarily in another discipline who wants to do something requiring knowledge of AI. Furthermore, we feel that some of the Overview articles are the best critical discussions available anywhere of activity in the field.

To indicate the scope of the Handbook, we have included an outline of the articles as an appendix to this report (see Appendix I on page 214).

B. Medical Relevance and Collaboration

The AI Handbook Project was undertaken as a core activity by SUMEX in the spirit of community building that is the fundamental concern of the facility. We feel that the organization and propagation of this kind of information to the AIM community, as well as to other fields where AI is being applied, is a valuable service that we are uniquely qualified to support.

C. Progress Summary

Because our objective is to develop a comprehensive and up-to-date survey of the field, our article-writing procedure is suitably involved. First drafts of Articles are reviewed by the staff and returned to the author (either an AI scientist or a student in the area). His final draft is then incorporated into a Chapter, which when completed is sent out for review to one or two experts in that particular area, to check for mistakes and omissions. After corrections and comments from our reviewers are incorporated by the staff, the manuscript is edited, and a final computer-prepared, photo-ready copy of the Chapter is generated.

We expect the Handbook to reach a size of approximately 1000 pages. Roughly half of this material will constitute Volume I of the Handbook, which will be going through the final stages of manuscript preparation in the Spring and Summer of 1979. The material in Volume I will cover AI research in Heuristic Search, Representation of Knowledge, AI Programming Languages, Natural Language Understanding, Speech Understanding, Applications-oriented AI Research, and Automatic Programming. Researchers at Stanford University, Rutgers University, SRI International, Xerox PARC, RAND Corporation, MIT, USC-ISI, Yale, and Carnegie-Mellon University have contributed material to the project.

D. List of Relevant Publications

The material in Volume I of the AI Handbook will appear in preliminary form as a Stanford Computer Science Technical Report in the Summer of 1979, and will be published shortly thereafter.

II. INTERACTIONS WITH SUMEX-AIM RESOURCE

A. Collaborations and medical use of programs via SUMEX

We have had a modest level of collaboration with a group of students and staff at the Rutgers resource, as well as occasional collaboration with individuals at other ARPA net sites.

B. Sharing and interactions with other SUMEX-AIM projects.

As described above, we have had moderate levels of interaction with other members of the SUMEX-AIM community, in the form of writing and reviewing Handbook material. During the development of this material, limited arrangements have been made for sharing the emerging text. As final manuscripts are produced, they will be made available to the SUMEX-AIM community both as on-line files and in the hardcopy, published edition.

C. Critique of Resource Management

Our requests of the SUMEX management and systems staff, requests for additional file space, directories, systems support, or program changes, have been answered promptly, courteously and competently, on every occasion.

III. RESEARCH PLANS (8/78 - 7/81)

A. Long Range Project Goals

The following is our tentative schedule for completion and publication of the AI Handbook:

Spring and Summer, 1979 - Volume I will go through final editing, computer typesetting, and printing.

Fall, 1979 through Spring, 1980 - Volume I will be published. Research for Volume II will be started and draft material will go through the external review process.

Summer, 1980 - Final editing, typesetting and publication of Volume II.

B. Justifications and requirements for continued SUMEX use

The AI Handbook Project is a good example of community collaboration using the SUMEX-AIM communication facilities to prepare, review, and disseminate this reference work on AI techniques. The Handbook articles currently exist as computer files at the SUMEX facility. All of our authors and reviewers have access to these files via the network facilities and use the document-editing and formatting programs available at SUMEX. This relatively small investment of resources will result in what we feel will be a seminal publication in the field of AI, of particular value to researchers, like those in the AIM community, who want quick access to AI ideas and techniques for application in other areas.

C. Your needs and plans for other computational resources

We use document preparation facilities (the XEROX Graphics Printer) at the Stanford AI Laboratory. We are also planning to use the new TEX typesetting system being developed by Prof. D. Knuth of the Stanford Computer Science Department.

D. Recommendations for future community and resource development

None.

4.2.2 AGE - Attempt to Generalize

AGE - Attempt to Generalize

H. Penny Nii and Edward A. Feigenbaum
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ABSTRACT: Isolate inference, control, and representation techniques from previous knowledge-based programs; reprogram them for domain independence; write a rule-based interface that will help a user understand what the package offers and how to use the modules; and make the package available to other members of the AIM community and labs doing knowledge-based systems development, and the general scientific community.

I. SUMMARY OF RESEARCH PLAN

Technical Goals

The general goal of the AGE project is to demystify and make explicit the art of knowledge engineering. It is an attempt to formulate the knowledge that knowledge engineers use in constructing knowledge-based programs and put it at the disposal of others in the form of a software laboratory.

The design and implementation of the AGE program is based primarily on the experience gained in building knowledge-based programs at the Stanford Heuristic Programming Project in the last decade. The programs that have been, or are being, built are: DENDRAL, meta-DENDRAL, MYCIN, HASP, AM, MOLGEN, CRYSLIS [Feigenbaum 1977], and SACON [Bennett 1978]. Initially, the AGE program will embody artificial intelligence methods used in these programs. However, the long-range aspiration is to integrate methods and techniques developed at other AI laboratories. The final product is to be a collection of building-block programs combined with an "intelligent front-end" that will assist the user in constructing knowledge-based programs. It is hoped that AGE will speed up the process of building knowledge-based programs and facilitate the dissemination of AI techniques by: (1) packaging common AI software tools so that they need not be reprogrammed for every problem; and (2) helping people who are not knowledge engineering specialists write knowledge-based programs.

Medical Relevance and Collaboration

AGE is relevant to the SUMEX-AIM Community in two ways: as a vehicle for disseminating cumulated knowledge about the methodologies of knowledge engineering and as a tool for reducing the amount of time needed to develop knowledge-based programs.

1. **Dissemination of Knowledge:** The primary strategy for conducting AI research at the Stanford Heuristic Programming Project is to build complex programs to solve carefully chosen problems and to allow the problems to condition the choice of scientific paths to be explored. The historical context in which this methodology arose and summaries of the programs that have been

built over the last decade at HPP are discussed in [Feigenbaum 1977]. While the programs serve as case studies in building a field of "knowledge engineering," they also contribute to a cumulation of theory in representation and control paradigms and of methods in the construction of knowledge-based programs.

The cumulation and concomitant dissemination of theory occur through scientific papers. Over the past decade we have also cumulated and disseminated methodological knowledge. In Computer Science, one effective method of disseminating knowledge is in the form of software packages. Statistical packages, though not related to AI, are one such example of software packages containing cumulated knowledge. AGE is an attempt to make yesterday's "experimental technique" into tomorrow's "tool" in the field of knowledge engineering.

2. Speeding up the Process of Building Knowledge-based Programs: Many of the programs built at HPP are intelligent agents to assist human problem solving in tasks of significance to medicine and biology (see separate sections for discussions of work and relevance). Without exception the programs were handcrafted. This process often takes many years, both for the AI scientists and for the experts in the field of collaboration.

AGE will reduce this time by providing a set of preprogrammed inference mechanisms that can be used for variety of tasks. Close collaboration is still necessary to provide the knowledge base, but the system design and programming time of the AI scientists can be significantly reduced. Since knowledge engineering is an empirical science, in which many programming experiments are conducted before programs suitable for a task are produced, reducing the programming and experimenting time would significantly reduce the time required to build knowledge-based systems.

Progress Summary

SUMMARY OF CURRENT USAGE

Currently AGE-1 is available to a limited number of groups on the PDP-10 at the SUMEX-AIM Computing Facility. In the process of building AGE, we have used it to write some programs: CRYPTO, a program that solves cryptogram problems [Aiello 1979]; two different versions of PUFF [Feigenbaum 1977; Kunz 1978]--one using the Event-driven control macro and another using the Expectation-driven control macro [Nii 1978]. Since the domain-specific knowledge for PUFF already existed and was being used in EMYCIN, the AGE version took about a week to bring up--time needed to reorganize the existing rules into KSs and to rewrite the rules in AGE rule syntax. Psychologists from the University of Colorado (see a separate description within the Pilot Projects Section) have begun to experiment with AGE in order to develop research programs in reading comprehension and design processes. It was also used by a person outside the AGE project to write a knowledge-based program for a part of the game of hearts [Quinlan 1979].

Profile Of The Current AGE System

To correspond to the two general technical goals described earlier, AGE is being developed along two separate fronts: the development of tools and the development of "intelligent" user interface.

Currently Implemented Tools

The current AGE system provides the user with a framework useful for incremental hypothesis formation, known as the Blackboard Model [Erman 1975; Lesser 1977]. The framework, with which the user builds his Blackboard-based program, has been implemented to allow flexibility in representation and in the application of other problem solving methods within the framework. It consists of three major components:

1. The Blackboard: The blackboard contains hypotheses in a hierarchical data structure; it represents the task domain in terms of a hierarchy of analysis levels of the task.
2. The Ks: The Ks contain the knowledge of the task domain (which the user must provide) that can perform the analysis. The Ks are represented as sets of production rules [Davis 1977].
3. The Control: The control component contains mechanisms that allow the user to (a) specify the conditions for the invocation of the Ks and (b) to select items on the blackboard for focus of attention.

A paper by Nii [1979] describes in somewhat more detail the current implementation of the Blackboard framework in AGE.

The "Intelligent" Front-end in AGE

Currently the "intelligence" in the front-end is limited to: (a) a tutorial subsystem that allows the user to browse through the textual knowledge base, and (b) a design subsystem that guides the user through each step of program specification.

Tutor Subsystem: The textual knowledge base contains (a) a general description of the building-block components at the conceptual level, (b) a description of the implementation of these concepts within AGE, (c) a description of how these components are to be used within the user's program, (d) how they can be constructed by the user, and (e) various examples. The information is organized in a network to represent the conceptual hierarchy of the components and to represent the functional relationship among them.

Design Subsystem: The knowledge necessary for AGE to guide the user in design and construction is represented in a data structure in the form of an AND/OR tree that. It represents, on one hand, all the possible structures available in the current AGE system; and, on the other hand, represents the decisions the user must make in order to design his program. Using this schema, the design subsystem guides the user from one design decision point to another. At each decision point, the user has access to the textual knowledge base, to advice on the decisions to be made at that point, and to acquisition functions that aid the user in specifying the appropriate component.

A paper by Aiello [1979] contains an extensive example of the various interactions currently possible in AGE.

II. RESEARCH PLAN

Research Topics

The task of building a software laboratory for knowledge engineers is divided into two main sub-tasks:

1. The isolation of techniques used in knowledge-based systems. It has always been difficult to determine if a particular problem solving method used in a knowledge-based program is "special" to a particular domain or whether it generalizes easily to other domains. In existing knowledge-based programs, the domain specific knowledge and the manipulation of such knowledge using AI techniques are often so closely coupled that it is difficult to make use of the programs for other domains. One of our goals is to isolate the AI techniques that are general and determine precisely the conditions for their use.

2. Guiding the user in the initial application of these techniques. Once the various techniques are isolated and programmed for use, an intelligent agent is needed to guide the user in the application of these techniques. Initially, we assume that the user understands AI techniques, knows what she wants to do, but does not understand how to use the AGE program to accomplish her task. A longer range interest involves helping the user determine what techniques are applicable to her task, i.e. we will assume that the user does not understand the necessary techniques of writing knowledge-based programs. Some immediate questions to be posed are: Is there a "best way" to represent knowledge that would apply to many task domains? Is there a flexible data representation that could describe many types of objects? What is the best way to handle differences in the ability of the users of the AGE program?

Research Plan

Version 1 of the AGE program is now complete. Next step in the research and development plan includes the following:

1. Improving the Front-end

Tutor Subsystem: Although the current textual knowledge base is organized to provide explanation in various forms, the program is not intelligent enough to know what the user does not understand. The problems involved in providing an intelligent tutorials are similar to those in Intelligent CAI. AGE will track the research in this area and improve the Tutor subsystem.

Design Subsystem: Although the current Design subsystem provides acquisition functions that allow the user to interactively specify the knowledge of the domain and control structure, it does not (aside from simple advice) provide the user any help in the designing process. For example, AGE should be able to provide some heuristics on what kinds of inference mechanisms and representation are appropriate for different kinds of problems. We have begun collecting knowledge-engineering heuristics, but much more work is needed in building a design-aid system that will be useful to the user.

2. Adding More Tools

Our concept of a software laboratory is a facility by which the users are provided with a variety of preprogrammed problem-solving frameworks--similar in spirit to designs of prefabricated houses. The user augments and modifies a framework to develop his own programs. At the same time, we need to provide the user with diverse tools. We currently have a framework for developing user programs that use the Blackboard framework. We are currently adding a framework for backward-chained inference mechanisms. Another inference mechanism, the heuristic search paradigm, will be added. We will also integrate parts of Unit Package and add the capability for representing knowledge as a semantic network.

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4.2.3 DENDRAL ProjectResource-Related Research - Computers In Chemistry
The DENDRAL ProjectProf. Carl Djerassi
Department of Chemistry
Stanford UniversityI. SUMMARY OF RESEARCH PROGRAMI.A. Technical Goals

In the second year of our current grant we have continued to address the problems of computer-assisted structure elucidation and the applications of the resulting programs to biomedical structure elucidation. We have focussed our attention on development of interactive computer programs which are designed to act as chemists' assistants in exploration of the potential structures for unknown compounds. These programs take into account structural information derived from a variety of sources including both physical and chemical methods. We are extending the interpretative power of these programs to enable them to draw meaningful structural conclusions from chemical data. To meet these objectives we are developing a series of computer programs, described in more detail below, which emulate several important aspects of manual approaches to structure elucidation.

I.B. Medical Relevance and Collaboration

Chemical structure elucidation is a problem common to many efforts throughout the biomedical community. Knowledge of chemical structure is a necessary first step to further study of properties relevant to biomedicine, such as those involved in pharmacology or toxicology. Our instrumentation and computer programs have been directed specifically both to development of new techniques to assist in biomolecular structure elucidation and to applications to a number of structural problems in our own group and the research groups of our collaborators. As our research has matured, we have been able to move toward computer representation and manipulation of three-dimensional representations (specifically, configurational stereoisomerism at this time) of molecular structure. Recent and proposed developments will provide computer assistance in a wide range of problems which require this level of structural description, for example, relationships of structure to observed properties such as biological activities. We have paid particular attention during the past year to the dissemination and availability of our programs to large segments of the biomedical community. These collaborative efforts are described in detail in Section II.

II.C. Progress Summary

Reprogramming CONGEN

We previously discussed a preliminary effort to reprogram the structure generator algorithm of CONGEN into the BCPL language. This early experience showed BCPL to be a compact and efficient language containing all of the basic features needed for the full reprogramming effort. Continued development has produced a version of CONGEN in BCPL which contains nearly all of the features of the INTERLISP/SAIL/FORTRAN version. The primary exception is the perception of aromaticity, and this feature is currently being implemented. The BCPL version has the following advantages over the previous one;

- a) It requires less than 10% as much computer memory, due partly to the more compact coding and partly to the use of an overlay structure;
- b) It uses about 2-5 times less computer time on typical cases than the most highly-tuned (block compiled) previous version of CONGEN;
- c) The redesigned front-end provides significantly more error checking, a simpler and more flexible input format, and a more thorough "help" facility;
- d) It can easily deal with problems an order of magnitude larger.
- e) It is exportable to a variety of different computers.

Overlay Structure

As portions of CONGEN were developed in BCPL, estimates of its eventual size could be made and it became obvious that the entire program would occupy a somewhat larger amount of memory (about 150 K words as compared to the roughly 450 K words for the earlier version) than is usually available to individual users at many installations (on the order of 50-60 K words at TOPS-10 sites). Because the processing in CONGEN falls naturally into several independent activities (generating intermediate structures, imbedding, defining substructures, etc.), the program can easily be broken into separate overlay segments which need to communicate only relatively small amounts of information. In the interest of transportability, though, it was decided not to rely upon the overlay mechanism provided by any particular operating system or language. The safest approach seemed to be to divide the overall program into completely independent, separately runnable modules capable of starting one another and communicating with one another via disk files. The drawback of this approach is that there may be a significant overhead in creating and reading files, and in switching from one module to another. But because all information needed to describe a CONGEN session is maintained on file, the program is unusually robust; even if an error causes the program to crash, CONGEN can simply be restarted and it will restore the complete environment which existed before the erroneous command was issued. Also, a particular operating system may offer some means of accomplishing overlays efficiently, and by interfacing the modules through a small control program, it should be possible to take advantage of such facilities. Under TENEX on the PDP-10, for example, a program may control a large number of forks (independent virtual address spaces) each containing a

separate program. We have successfully interfaced the CONGEN modules through a small fork-manipulating program so that the overhead of starting a particular module is paid only once for each CONGEN session.

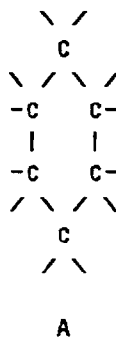
The current CONGEN is composed of eight modules, the largest of which occupies about 46 K words of memory and the rest of which fall in the range 15-36 K words. We are exploring ways of reducing the size of this largest module (SURVEY - see below) to bring it into this range also. The modules and their functions are as follows:

- a) CONGEN (35 K) - Main control module, user interaction, error checking;
- b) EDITS (19 K) - User interaction for defining substructures;
- c) GENERA (26 K) - Generation of intermediate structures;
- d) PRUNE (15 K) - Elimination of structures based on structural features;
- e) IMBED (36 K) - Expansion of superatoms in intermediate structures;
- f) DRAW (26 K) - Output of structural drawings to the user's terminal;
- g) SURVEY (46 K) - Examination of large structure lists for frequency of occurrence of standard structural features; and
- h) STEREO (24 K) - Generation of stereoisomers.

CONGEN Developments

The reprogramming effort has been far from a transliteration of existing algorithms into BCPL. In many portions, the basic algorithmic approach taken in the previous version was reformulated to allow for a more effective representation and solution of the problem. The major milestones in CONGEN development which have paralleled the reprogramming are as follows:

1) Imbedder. The mathematical technique for expanding superatoms in intermediate structures developed by Brown was reexamined and reformulated to allow for a more compact representation. The primary difference in our new approach is that the topological symmetry group of the atoms, rather than the free valences, is used in the computation. For example, the superatom A below, with twelve free valences, has twelve topological symmetry operations



interchanging its atoms, but because of the pairwise interchanges between free valences on each atom, the free-valence group has $64 \times 12 = 768$ symmetry elements. The BCPL version of the imbedder carries the symmetry information as 11 permutations of 6 objects (the identity permutation is not explicitly represented) requiring 66 words of memory, rather than as 768 permutations of 12 objects requiring 9216 words of memory. By implicitly representing interchange symmetry among free valences, among the termini of internal bonds being allocated to the superatom and among monovalent atoms being attached to the superatom, the new version is able to use a drastically smaller amount of space for the storage of symmetry information.

Neither of these approaches to imbedding can perceive all possible sources of duplicate structures, so it was necessary also to develop a final filter package to canonicalize the imbedded structures and compare them for duplicates. However, the new version stores the structure representations on an external random-access file rather than in the computer's memory as was done before, and only a list of pointers to these filed structures is stored internally. As a result, the new imbedder can deal with thousands rather than hundreds of imbedded structures using only a modest amount of memory.

2) Constraints. The basic structure generation and imbedding algorithms are of little practical use without the ability to constrain their output based on the presence or absence of structural features. The graph matcher and cycle finder, which accomplish constraint testing, were translated with little change from their INTERLISP counterparts. Inclusion of constraints in the imbedder, where they serve only as a filter on the final output structures, was straightforward. In the structure generator, however, the constraint-testing mechanism was merged much more intimately with the generation process. The main aspects of this merging are as follows:

- a) As soon as hydrogen atoms are distributed among the non-hydrogen atoms (the first activity of the generator), the distributions are checked against the constraint substructures to determine which distributions can be ruled out a priori. If a substructure is required to be present and contains three methine carbons (CH), for example, the generator will immediately discard hydrogen distributions which do not contain at least three such carbons. Many constraints supplied to the generator place restrictions on the possible distributions of hydrogen atoms, and by this mechanism such constraints are tested most efficiently.
- b) The order in which the generator assembles its atoms is influenced by which atoms appear in the constraints. If a substructure forbidding the construction of peroxides (O-O) is present, the generator will be encouraged to consider possible interconnections among oxygen atoms first so that the presence of peroxides can be avoided early in the computation. Because different constraints may encourage different starting atoms, a scoring scheme has been developed which is used to establish the overall order of atom assembly, taking all constraints into account.

3) Interactive aids. Much effort has been directed toward the development of a robust and helpful interactive system to allow a user easily to define a CONGEN problem and to make use of the basic algorithmic tools. The primary accomplishments in this direction have been as follows:

- a) The development of LINSTR, a package of BCPL functions for interactive input from the user, accessed by all of the interactive CONGEN modules. The line-input and prompting functions in LINSTR provide for three levels of help information which can easily be passed from the main program. The first level consists of prompts which are typed to the user when information is required by the program. The novice may step through the prompting sequences supplying one piece of information at a time in response to these prompts, while the expert user may anticipate the prompts and type ahead his responses on the line to avoid the prompts. This, together with the ability of the LINSTR functions to accept unambiguous abbreviations for keywords, allows a great deal of flexibility in the form of the input. For example, the following two sequences accomplish the same effect in the program (user's responses underlined):

Step-by-step input;

```

DEFINE
DEFINITION TYPE: SUBSTRUCTURE
NAME: R6
(NEW SUBSTRUCTURE)
>RING 6
>DONE
R6 DEFINED

```

Condensed input;

```

DE S R6;R 6;DO
(NEW SUBSTRUCTURE)
R6 DEFINED

```

A second level of help is provided by the '?' facility which can be evoked at any prompt in the program. At these points, the '?' input will cause helpful information passed by the main program to LINSTR to be typed to the user. The third level of help is provided by a similar '??' facility, which will cause the program to refer to a much more extensive on-line help document to give a full description of the expected information, and the context in which it will be used. This third level is still under development; the basic mechanism has been developed but we have not yet constructed the on-line documentation.

- b) The simplification and extension of the basic commands. The number of basic CONGEN commands has been reduced from 29 to 14 by the consolidation of commands with similar function (e.g., SHOW is now a general purpose method of obtaining information about the session and replaces six previous commands) and eliminating little-used options (e.g., TREEGEN). The number of EDITSTRUC commands has likewise been reduced from 23 to 17. Also, previous concepts which were somewhat artificial have been removed. For example, a user does not now need to distinguish between superatoms and patterns when he defines a substructure. The representations for these two types of substructure have been consolidated and a defined substructure can be used in either

context. As another example, the user does not need to place substructures on BADLIST any more - the new input sequence allows him to express the presence or absence of substructural features in a natural statement such as 'exactly 3' or 'at most 1' or 'none'. The new command structure seems easier for users to remember and work with. Our experience in the workshops held at Stanford (see below), which were attended by many persons totally unfamiliar with computers and interactive systems, indicated that the new interface between scientist and the machine was much simpler to use and represented a major improvement over the old version of CONGEN to which some of the persons had been exposed previously.

Stereochemistry

The first version of the stereoisomer generator program was written in SAIL and has been improved in several ways. The program has been modified to process lists of structures to count and/or generate the possible stereoisomers. Thus with the existing CONGEN structure generator it is now possible for the first time to generate all the possible stereoisomers for a given empirical formula completely and irredundantly. These stereoisomers are represented in a compact canonical form and are written onto a disk file by the program along with other information about the structure. Three additional features which were proposed in the last annual report have been added to this program. First, at the user's discretion, the program will compute cis and trans double bond designations for the stereoisomers and write these on the file. Second R and S designations for tetravalent stereocenters based on the Cahn-Ingold-Prelog conventions are computed for stereocenters which are not fixed by any nontrivial symmetry element. These designations were thought to be the most useful and most stable with respect to future changes of the R/S nomenclature system. Third, the ability to handle stereochemistry of common heteroatoms with valence less than 5 has been added. A small interactive package has been added for deciding whether trivalent nitrogen atoms are free to invert. The user is given a choice for each such nitrogen atom.

This program has been included with the current LISP version of CONGEN (it runs as a separate fork) and is available to all users who can access SUMEX. It has been extensively tested on well over 1000 structures.

Since the CONGEN program has been recently reprogrammed into BCPL to create an exportable version, it was decided to also reprogram the STEREO program into BCPL and carry on further developments in that language to ensure compatibility and exportability. With the exception of the parts of the program which compute R/S symbols and handle heteroatoms interactively, this reprogramming has been accomplished. Further developments on this program include a fairly extensive interactive package which allows the user to obtain information about the generated stereoisomers. The user may obtain drawings of projected stereocenters showing absolute configurations of stereocenters (e.g., Fischer projections, Newman projections, double bonds) or obtain drawings of linear segments of structures showing all the configurations of the included stereocenters. The user may also obtain information about the symmetry and equivalent atoms in any stereoisomer. This program is currently running with the BCPL version of CONGEN and was available and tested during the recent series of workshops. This program has been exported with this version of CONGEN.

The experimental version of the BCPL program has been modified to allow for some constrained generation of stereoisomers. The algorithm and program for exhaustive generation were written with this eventuality in mind. An additional interactive session has been added to the stereoisomer generator which allows the user to add constraints before generating the stereoisomers. At present, the user may input constraints on the absolute or relative stereochemistry of any stereocenters. Thus if part of the stereochemistry of a structure is known, it is possible to constrain the stereoisomer generator to produce just those isomers consistent with the known stereochemistry. This parallels the procedure in the structure generator of CONGEN.

Structure checking functions for CONGEN

A program, "STRUCC", has been developed to provide functions for checking sets of structures for desired substructural features or for compatibility with recorded mass-spectral or nmr data. While primarily devised for processing sets of structural isomers produced by means of CONGEN, STRUCC can also take as input sets of structures created through the REACT program or defined through an extension of CONGEN's EDITSTRUC function.

The main structure checking functions currently available through STRUCC are:

- 1) EXAMINE: This EXAMINE function is an extended version of that available in standard CONGEN. Amongst other extensions are facilities for checking for specified ring-fusions or spiro-junctions within structures.
- 2) MSA: The MSA ("Mass Spectral Analysis") functions provide a means for using mass spectral data to rank candidate structures. The MSA functions can employ either ordinary "half-order theory", or a model of fragmentation in which bond break plausibilities are related to specified substructural features.
- 3) LOOK: The LOOK functions are intended to assist a user in investigating the utility of proposed experiments for differentiating between candidate structures. LOOK provides a mechanism for determining the various different ways in which particular superatom parts are incorporated into candidate structures.
- 4) TSYM: The TSYM function allows some simple forms of symmetry constraint to be defined. These constraints use only topological symmetry.
- 5) RESONANCECHECK: The RESONANCECHECK function is intended for checking that all constraints have been given to the structure generator. The function can identify differences in candidate structures that would be associated with features in the ¹Hnmr or ¹³Cnmr that one might reasonably expect to be fairly obvious (e.g. different numbers of hydroxy protons, different numbers of carbonyl carbons etc). Generally, such differences are found in cases where the user has forgotten to specify substructural features incompatible with the observed data, or has misapplied the constraints so that not all instances of unwanted features are eliminated.

- 6) NMRFLT: The NMRFLT functions represent a first attempt at developing a system for predicting proton resonance spectra of candidate structures, and for using differences between predicted and observed spectra as a basis for pruning the structure list.

The STRUCC system is also used as a test-bed for new structure evaluation functions. When functions are considered to be sufficiently developed to be of use, top-level calls to those functions are added to STRUCC's repertoire of commands.

STRUCC has a user-interface similar to that of CONGEN and incorporates many of the same subsystems (e.g. EDITSTRUC and DRAW).

Meta-DENDRAL

INTSUM - The INTSUM program for the analysis of spectra has been improved by using confidence factors in the place of many of the original program constraints. This feature allows association of likelihoods with fragmentations. It thus allows consideration of a much wider range of possible processes while limiting the final explanations for spectrum peaks to the most plausible explanations.

Additional improvement of the program allows logical separation of the concepts of H-transfers and neutral composition transfers. This provides a better correlation between the explanations provided by the program and those expected by the chemist.

RULEGEN - A significant problem in generalizing the INTSUM explanations has always been reducing the size of the search space so as to be able to produce interesting rules in a reasonable amount of time. In addition to the constraints already provided, the RULEGEN program now allows use of existing rules to filter the peak explanations to be considered. This is an important step in allowing the program to focus on rules which account for peak explanations not yet encompassed by existing rules. As an aid in better understanding the process of rule formation, the program is now capable of generating additional information about the search space. This information serves as data for other programs which can then analyze and present to the user compact descriptions of the rule search done by RULEGEN.

EDITSTRUC INTERFACE - The latest versions of the structure editor, EDITSTRUC, and the structure drawing programs have been interfaced to allow their use in all appropriate places in INTSUM and RULEGEN. The newest programs for conversion of EDITSTRUC structures recognize a larger subset of the structural features which may be specified within EDITSTRUC. This allows the user greater flexibility in the specification of substructures in user-created rules.

PREDICTION and RANKING - The programs allowing the entry and use of user-defined rules have been extended to allow prediction of the molecular ion and inclusion of confidence factors in the rules.

The process of spectrum prediction from Meta-DENDRAL rules has previously involved the matching of rules against only those sites in the molecules considered as possible breaks. With the use of user-entered rules, and program

developed rules containing greater structural detail, the program was generalized to allow prediction based on graph matching alone, without the prior generation of possible break sites.

HUMAN ENGINEERING - Many minor improvements have been made in the program's interaction with the user. In general, these improvements have been designed according to the following criteria: 1. Messages should be informative yet not excessively long or wordy; 2. User typing should be kept to a minimum; 3. Programs should behave in ways which people find understandable; 4. During execution, programs should provide occasional information concerning their progress.

RESULTS - The practical value and capability of new programs are best evaluated by applying them to real, non-trivial problems. In our case, we have chosen the biologically important marine sterol compounds. Their mass spectra are predominant in the structure elucidation of new compounds in spite of the fact that relatively few of the fragmentation mechanisms are known. Often very similar spectra are recorded due to the great similarity of common skeletons.

Our study involves the comparison of predicted spectra of known structures with the observed spectra of unknown compounds. We want to compare the usefulness of different methods of forming the rules used for spectrum prediction. We distinguish 3 methods:

- 1) Half-order theory (can be supplemented by functional group rules);
- 2) Class-specific rules (selected by the chemist);
- 3) Computer-generated rules.

Our results were obtained using nine selected 4-demethylsterols (six isomers of composition C₂₉H₄₈O, two C₂₈H₄₆O and one C₂₇H₄₄O). Each spectrum of the nine selected marine sterols was considered to be the observed spectrum and ranked against 23 candidate structures (the 23 candidates contained 17 different C₇ - C₁₁ sidechains and three 4-demethylsterol skeletons). For the half-order theory an overall average performance of (2.4 0.9) was obtained. The first number gives the number of candidates ranked better than the correct one, the second represents the number of candidates ranked equally with the correct one. In this case the average value is not very representative, as its value is strongly reduced by a compound which was ranked in 17th place. This compound, the 23-demethylgorgosterol, contains a cyclopropane in the sidechain for which no special fragmentation processes are considered in the simple half-order theory. The ranking can be greatly improved by providing fragmentation rules for cyclopropane rings.

The results of the second method (class specific rules), depends on the quality and number of selected rules. For this study we selected about 17 skeleton breaks (observed in more than 70 percent of the structures) from the INTSUM results of 23 marine sterols to which we added 13 known fragmentation processes. These processes (associated with neutral transfers, intensity range, and a confidence factor) were entered using the new rule editor program. The overall performance of these rules was (0.3 0) which means that, with the exception of three compounds, which were ranked in the second position, the

correct structure was always ranked first. A further improvement is seen when the distribution of the scoring values is considered. For these rules, much better separations were observed than with the half-order theory. Also, the quality of the predicted spectra are sufficient to consider the creation of a library which could be visually compared without the need of a computer. For the third method no results can be summarized here, as the computer generated rules are still being developed. The improvement of this last step will be a main goal of the next year.

MAXSUB Program - The function of the MAXSUB program is to detect common structural features in a potentially diverse but related set of compounds. This problem is one faced by chemists engaged in structure/activity studies, particularly in design of new, biologically active compounds based on known compounds with known activities. However, any problem involving an "activity" related to structure, including spectral signatures, is in principle amenable to analysis by MAXSUB. MAXSUB, by determining common features of structures displaying common activities, is presumably focussing on those aspect of the structures which are related to the activity. However, in its current state, the program is only experimental. Many types of activity are intimately connected with stereochemical aspects of structure and MAXSUB does not include any stereochemistry. It does represent a foundation for further study of the problem because the algorithms can in principle deal with three-dimensional descriptors of atoms and bonds. Some work may be done on this program in the next grant period.

GENOA Program - The GENOA program (for GENERation with Overlapping Atoms) has been developed from a preliminary INTERLISP version to overcome one of the most serious deficiencies of the current CONGEN program. This deficiency is that substructures and atoms input to CONGEN's structure generator must not overlap. This condition is probably the most serious stumbling block to the chemist's interpretation of partial structural information for the CONGEN program. The GENOA program overcomes this problem by allowing structures to overlap in all possible ways. This program removes the need for the chemist to interpret his data in terms of nonoverlapping substructures and enhances the "intelligence" of the program as a chemist's assistant.

Briefly, GENOA obtains the molecular formula for an unknown compound, and the number (may be an integer, a range or zero) and name of inferred substructures, one at a time. For each new substructure, GENOA builds the requested number and ensures that the required number of all previous substructures is met. Utility functions allow definition of substructures, and visualizing and saving all intermediate results. Substructural statements are simply made to GENOA. The program determines not only how the required substructures can be built, but also makes structural inferences concerning the implications of each statement.

After the last known substructure is specified, a simplified structure generator, not the one utilized in CONGEN, is used currently to build complete structures (alternatively the problem could be saved at this stage and additional substructural information supplied at a later time, continuing the problem where it was left off). The generator is quite inefficient and creates many duplicate structures which must be removed (automatically). Control is then passed directly to the CONGEN program where all the currently available utilities for

further processing, e.g., STEREO, MSANALYZE, may be used to prune or explore further the structural candidates.

II.D. List of Relevant Publications

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II. Interactions with the SUMEX-AIM Resource

II.A Use of programs via SUMEX

CONGEN Workshops

In early December, 1978, we held at Stanford a series of mini-workshops on the use of an exportable version of the CONGEN program. Invitees included members of the chemical and biochemical community who are actively engaged in solving the structures of unknown chemical compounds encountered in research in industrial, academic and government research laboratories. The primary purpose of these workshops was to introduce experts in the field of structure elucidation to the first version of the exportable program. These persons were chosen for their chemical and biochemical expertise; few had significant experience with computers previously. Thus, they represented what we think is a good cross-section of the community of potential users of CONGEN. We held three three-day sessions of the workshop so that we could offer access to a computer terminal for all the persons at one session and so that we could provide close supervision and assistance as they began to learn and use CONGEN. We also implemented a recording scheme so that an interactive session at the terminal could be recorded as a text file and available after the problem was completed for close scrutiny for the chemist and for ourselves. Such scrutiny reveals, for example, common difficulties in certain portions of the user interaction thereby pointing out areas for improving the interaction.

To help alleviate the impact on SUMEX, the CONGEN program was brought up on the Rutgers-AIM (RUAIM) system and half the participants used it there via TYMNET. There were three users (average) on SUMEX and three on RUAIM during our terminal sessions. Nevertheless, our impact on SUMEX was very large and control on other users had to be applied during our terminal sessions.

Although the version of CONGEN used in the workshops was not complete, enough of the program existed in close to final form to allow us to fulfill our other purposes. We wanted to ensure that any remaining program errors could be detected and fixed prior to making the program more widely available. The best way we have found to do this once a program is essentially debugged is to confront the program with a wide variety of problems from many different users. We also wanted to determine if there were major deficiencies in any part of the program which made it difficult to understand or use. Eliminating such deficiencies would ensure that an exported version would meet the needs of the persons attending the workshop, i.e., that some minimum standards of acceptability could be determined and met. Finally, we needed to determine the computing facilities available to this group and in detailed discussions to explore opportunities for export to their own laboratories. This allows us to set some priorities on developing versions for various makes of computers.

Conclusions from the Workshop

There are several conclusions which can be drawn from the workshop experience. The reaction of all persons attending the workshop was very positive, not only concerning organization and intellectual stimulation, but also with the problem-solving capabilities of the program. The following are major positive aspects of the workshop experience:

- a) we were able to meet our goal of demonstration of exportability by utilizing CONGEN on two different computers during the workshop;
- b) every participant found the program of sufficient utility to express an interest in obtaining a version in some way for his or her own laboratory;
- c) the interface to CONGEN, extensively modified based on experience with the old version of the program, proved much simpler to use, much more chemically logical and consistent and much more helpful to the user in providing guidance and error checking;
- d) several new problems were analyzed successfully at the workshops, either by verification of the unambiguous nature of the structural assignment or by obtaining a list of candidate solutions to guide further experimentation;
- e) installation of the exportable version has been completed successfully at two different sites, Lilly Research and Smith, Kline and French Research, and several more will follow in the next two months.

There are some common criticisms expressed by the persons attending the workshop which, in our opinion, represent points of focus for the remainder of the grant period and for a renewal application. Briefly, the major deficiencies were as follows:

- a) The requirement of specifying non-overlapping structural units is non-intuitive and thus unnatural. Other programs, like CONGEN, share this difficulty, but we are in a position to remedy it based on recent research so that future versions may be easier to use;
- b) The program is very complex and lacks sufficient documentation or internal 'help' facilities. We recognize this and to some extent it is a reflection of the lack of maturity of the new version. We plan to provide better on-line help facilities accessible from within the program and a much more comprehensive program guide with examples.
- c) The teletype oriented drawing program produces some drawings which are difficult (if not impossible) to interpret. Providing the chemist with a connection table of such drawings, as we can do currently, is no long-term solution. Here we face the problem of diminishing the exportability of the program if we restrict its use to certain types of graphics terminals (there are many types, each requiring different programs to operate). Currently there is no graphics terminal which is competitive in price to character-oriented terminals. One way to solve this problem is to encourage collaborators to provide their own graphics packages which we can then in turn offer to others.

CONGEN Workshop attendees, affiliation, and interests

- 1) Dr. Henry Stoklosa, E.I. DuPont de Nemours. Dr. Stoklosa has been affiliated with a group at DuPont involved with computer applications to chemical problems, including computer-aided organic synthesis.

- 2) Dr. G.W.A. Milne, National Institutes of Health. Dr. Milne is currently in charge of the National Institutes of Health contribution to the NIH/EPA Chemical Information System. His interests included not only evaluation of the utility of the program but also exploration of ways in which CONGEN might be interfaced to the Chemical Information System.
- 3) Dr. William Brugger, International Flavors and Fragrances. Dr. Brugger represents the key person at IFF Research responsible for computer applications in their laboratories. Structure elucidation is a major activity of this company not only in analysis of natural and synthetic products but also in assessing the relationships between chemical structure and toxic properties affecting human health.
- 4) Dr. Douglas Dorman is head of the NMR laboratory at Lilly Research Laboratories and works closely with mass spectroscopists and other chemists in solving structures of a variety of compounds related to existing or new products. Dr. Dorman has been familiar with the "old" (non-exportable) version of CONGEN and thus was able to critique the new program not only on its merits but also on comparison with the old version.
- 5) Dr. Jon Clardy, Cornell University. Dr. Clardy is a recognized leader in development and applications of the technique of X-ray crystallography in structure elucidation. His attendance of the workshop was based on an interest in learning about alternative, computer-based approaches to the problem. As his letter points out, the ability to use CONGEN to help solve structures before expenditure of time and effort in X-ray analysis would be an important benefit.
- 6) Mr. In Ki Mun, Cornell University. Mr. Mun attended the workshop representing Prof. Fred McLafferty at Cornell. Prof. McLafferty's group has had for many years an interest in use of computer techniques to help solve structures, based primarily on mass spectral data. His research in this area has led to programs which suggest the presence of functionalities in an unknown molecule. CONGEN can, in principle, complete such a schema for analysis by piecing together the inferred functionalities.
- 7) Dr. Reimar Breuning, Munich. Dr. Breuning learned of the existence of the workshops from discussions with Prof. Djerassi at the IUPAC meeting on natural products. He is actively involved in natural products structure elucidation at Munich.
- 8) Dr. David Lynn, Columbia University. Dr. Lynn attended the workshop representing Prof. Koji Nakanishi, the latter a recognized expert in the area of structure elucidation of a number of classes of natural products of relevance to human health. Dr. Lynn is to act as the focal point for introduction of the computer methods to that research group.
- 9) Dr. Y. Gopichand, University of Oklahoma. Dr. Gopichand attended the workshop representing the marine natural products group of Prof. Francis Schmitz. This group specializes in structure elucidation of halogenated terpenoid molecules possessing a variety of biological activities and marine sterols representing intermediates or end products in steroid biosynthesis.

- 10) Ms. Wendy Harrison, University of Hawaii. Ms. Harrison attended the workshop representing the marine natural products group of Prof. Paul Scheuer at Hawaii. This group is engaged in structure elucidation problems similar to those encountered in Prof. Schmitz's laboratory, although focus is on different classes of organisms.
- 11) Dr. Laszlo Tokes and Dr. Michael Maddox, Syntex Research. Drs. Tokes and Maddox are, respectively, in charge of the mass spectrometry and NMR laboratories at Syntex Research. They are responsible for the majority of structure elucidation problems which rely on physical methods. Their interest in CONGEN is that it might help them solve certain problems in less time than required by manual methods.
- 12) Dr. John Figueras, Kodak Research Laboratory. Dr. Figueras attended representing the Analytical Sciences Division of Kodak's Research Laboratory. This division is responsible for data collection and analysis in support of the structure elucidation activities of the Laboratory including not only new developments in the photographic process but also the new technology of thin-film bound enzymes systems for clinical analyses.
- 13) Dr. Charles Snelling, University of Illinois. Dr. Snelling attended the workshop representing Prof. Kenneth Rinehart in the Chemistry Dept. at Illinois. Prof. Rinehart is also an acknowledged expert in structure elucidation with emphasis on macrolide antibiotics, halogenated terpenoids and other classes of natural and synthetic products of relevance to human health problems.
- 14) Dr. Gilles Moreau, Roussel UCLAF. Dr. Moreau attended the workshop representing the French pharmaceutical concern Roussel UCLAF. This company maintains an active group in computer applications in chemistry and wished to evaluate CONGEN for its use in their structural problems.
- 15) Prof. Andre Dreiding, Zurich. Dr. Dreiding has been interested in both the problem-solving and the pedagogical aspects of CONGEN for some time. He had previously used the old version and was gratified to see the improvements in the new version.
- 16) Dr. James Shoolery and Dr. Michael Gross, Varian Associates. Dr. Shoolery is in charge of Varian's NMR application laboratory and Dr. Gross is in charge of computer software for Varian's NMR/computer systems. Their respective interests match their responsibilities.
- 17) Dr. Daniel F. Chodosh, Smith, Kline and French. Dr. Chodosh was not actually invited to the workshop, but happened to visit our group during one of the sessions. He was sufficiently impressed that he procured a tape to carry away a copy of the program with him. He has now been supplied with a version of CONGEN for the PDP-10 and has it running at the SKF research laboratories in Philadelphia.

Recent GUEST access

In addition, the following persons during the past year have asked for information about and access to CONGEN. For the most part we have granted access

through the GUEST directory, setting up an account only for those users with more than occasional log-ins.

Dr. David Cowburn
Physical Biochemistry
The Rockefeller University
New York City

Prof. Cowburn now has an account on SUMEX in the EXODENDRAL account and is interested in extensions of CONGEN relevant to his work on peptide conformational analysis.

Douglas Henry
School of Pharmacy
Oregon State University
Corvallis, Oregon

He has been sent our programs for structure drawing for use on his own computer.

The following have asked for and received information on access to CONGEN at SUMEX via the GUEST facility.

Dr. H. Kating
Institut für Pharmazeutische Biologie
Der Universitaet
Bonn, Germany

Dr. Adalbert Kerber
Lehrstuhl D für Mathematik
Aachen, Germany

Dr. Brenda J. Kimble
Radiobiology Laboratory
University of California
Davis, California

Dr. J. Neubuser
Lehrstuhl D für Mathematik
Aachen, Germany

Dr. George Padilla
Dept. of Physiology
Duke University Medical Center
Durham, N.C.

Dr. W. Sieber
Sandoz Ltd.
Basel, Switzerland

Dr. Babu Venkataraghavan [We also helped him bring up the Fortran draw
Lederle Laboratories program on the DEC-10 system at Lederle]
Pearl River, New York

Dr. Stephen Wilson
Dept. of Chemistry
Indiana University
Bloomington, Indiana

Prof. Glenn D. Prestwich
Dept. of Chemistry
State University of New York at Stony Brook
Stony Brook, New York 11794

Dr. Andrew Stuper
RCG Group
Rohm and Haas
Norrilstown and McKean Roads
Springhouse, Pa. 19477

Prof. E. F. Domino
Department of Pharmacology
M6322 Medical Sciences Building
Ann Arbor, Michigan 48109

Prof. John D. Roberts
Div. of Chem. and Chem. Engr.
Calif. Inst. of Tech.
Pasadena, Calif. 91125

In addition there has been further use of CONGEN by several of the workshop participants who are only able to access the program by remote connection to SUMEX.

II.B. Interaction with other SUMEX-AIM projects

We continue to have interaction with other SUMEX projects as well as other resources funded by NIH. For example, we have continual contact with the SECS project headed by W. T. Wipke at Santa Cruz. Prof. Wipke and several of his co-workers spend time with us here at Stanford. Dr. Martin Huber of this group was an informal participant at one of our Workshops held last December. Drs. Smith and Wipke have collaborated in organizing a symposium on computer handling of structural information at the American Chemical Society meeting in Hawaii in April, 1979. The proximity of our groups, both geographically and especially through SUMEX, encourage this sharing of ideas on related areas and we expect the cooperation to continue as long as SUMEX exists to facilitate it.

We also interact with the MOLGEN project at Stanford, primarily in the area of experiment planning as it relates to structure determination. Although the structures which MOLGEN is trying to determine are in many ways more complex, requiring different representations in the computer, our methods for structure generation have provided some insights for them and we have been guided in our initial attempts toward experiment planning by their much more intensive effort.

We have interacted with the Rutgers-AIM resource during our workshops in order to distribute the heavy computing load and to locate our newly exportable CONGEN program on another machine. As indicated in the previous section, this

experiment was completely successful and demonstrates one way in which the two resources can work together.

II.C. Critique of Resource Management

Our major problem continues to be one of insufficient SUMEX capacity for production use of our applications programs, particularly during prime time. This reflects itself in our inability to guarantee high-quality, interactive access to our collaborators, who have structures of important biomolecules to solve and who can use the current version of CONGEN or a related program to help solve them. It is also reflected in our own inability to carry out detailed (and frequently time-consuming) tests of experimental versions of new programs within our own group. Thus, not only do applications suffer, but new developments as well. The gradual increase in difficulty in answering the demands of both development and applications, in a period of steadily increasing load on the existing SUMEX facility, has prompted us to propose a dedicated machine for our own project, described in more detail in Section III, closely interdigitated with the SUMEX resource. In this way we hope to divert all applications use of our programs to the dedicated machine, thus decreasing our load on SUMEX.

Other than this issue, we have no complaints. The system and its support staff continue to be extremely cooperative in aiding us in our collaborative efforts, in providing assistance on problems related to languages, editors and other system-supported facilities and in advising us when we consider new directions in our own work.

We do have one request. There is currently no mechanism for keeping statistics on GUEST use of our programs. Because we have been asking most of our collaborators to access SUMEX via the GUEST directory, it is important for us to know who has been logged on, what programs they have been running and how much time they have consumed. Although we do have a recording mechanism to keep track of some use, a general capability for monitoring use of GUEST would be very helpful to us.

III. RESEARCH PLANS (8/79 - 7/81)

III.A. Long Range Goals

We will continue to develop our programs for computer-assisted structure elucidation and pursue the dissemination of these programs to the biomedical community. Specifically, we will further develop the ability of our programs to take account of the three-dimensional nature of chemical structures. Nearly all properties of compounds relevant to biomedicine require this information. We will further develop our GENOA program for interpretation of constraints which may involve overlapping substructures. This will represent a significant advance to the intelligence of our programs by allowing the program to take information from the chemist in a much more intuitive manner. We will also further develop programs to aid in spectral interpretation and prediction and experiment planning.

Our current grant period ends on April 30, 1980. We have submitted a renewal proposal for the June 1 deadline, for funding for a five-year period

5/1/1980 - 4/30/1985. An important aspect of this renewal proposal is our relationship to SUMEX. This new proposal is again for Resource Related Research, but now related to the SUMEX resource rather than the mass spectrometry laboratory as it is now. We have proposed purchase of a dedicated computer system as part of the proposal, to be interfaced with SUMEX in order to shift production use of our applications program to the new machine. Our relationship with SUMEX involves this computer as an experiment in resource sharing for programs which have matured to the point where outside collaborators can make fruitful use of the programs in their own biomedical research.

III.B. Justification and Requirements for Continued SUMEX Use

Our continued funding from NIH attests to the biomedical relevance of our effort and the importance of our research. We foresee an increased relevance to biomedicine because of our further emphasis on three-dimensional chemical structures and increased efforts at dissemination of working programs to the biomedical community. Important aspects of our research involve ongoing and planned, future collaborative efforts involving applications of our newly developed techniques to structure/property relationships of several classes of biologically important molecules, including peptides, sterols and other marine natural products, and opiate agonists and antagonists. SUMEX is our means of carrying out this research.

The SUMEX resource provides an excellent and reliable "critical mass" of services, software, and programs for further development of our programs. SUMEX has been, and will continue to be, our only source of source of computational support for our own work and that of our collaborators, at least until action is taken on our renewal proposal. Even should our renewal be funded in total, we plan on continued utilization of SUMEX for our development efforts. The system we propose to purchase is insufficient to meet all our computational needs and is heavily dependent on SUMEX to provide needed peripheral equipment, access to a variety of languages, text editors, etc., and a support staff to aid us in our development efforts when SUMEX-related problems arise.

III.C. Other Computational Resources

As mentioned in previous sections, we have, in a renewal proposal submitted to the NIH, requested additional computational resources as part of our new relationship to the SUMEX resource. The proposal is to purchase a stripped-down (in terms of peripheral equipment) Digital Equipment Corp. VAX-11/780 computer for the specific purpose of providing a highly-responsive, interactive environment for production use of our applications programs such as CONGEN and GENOA. This will ease significantly our demands on the already overburdened SUMEX machine. Our plans, however, are dependent on SUMEX for continued development, so that both computational resources are important for the conduct of the research as proposed.

III.D. Recommendations for the Future

Now that we have developed a plan for resource sharing involving purchase of hardware for our own group as an augmentation to the SUMEX facility, we are hoping that this effort alone will help ease the load average on the SUMEX machines. If there were some way to facilitate the same approach for other

research projects using SUMEX, given that they have matured to the point where outside collaborators desire access, then the entire community would benefit. We are hoping that, if our efforts are successful, we will act as a model to guide others in the same direction. A great deal of development work can be done on SUMEX even at high load averages. It is when the programs which result from this development begin to be applied to real-world biomedical problems that SUMEX response begins to deteriorate, and then everyone suffers from an overloaded machine.

4.2.4 HYDROID Project

HYDROID - Studies in Distributed Processing and Problem Solving

Prof. Gio Wiederhold
Depts. of Computer Science and Electrical Engineering
Stanford University

The potential of multi-processor networks is nearly universally appreciated and many research groups are working either on theoretical related issues or on actual implementations. Several medically related groups are expending effort on multi-processor developments (e.g., U. of Wisc., U. of Texas at Austin, etc), but we believe that a number of basic system design issues should be resolved first. These groups have aggregate resources much greater than we currently have. The demands of the required simulations are such that usage of SUMEX is not feasible. As noted in the previous year's report we have in fact used SUMEX mainly as a means of communication and not as a computational resource. One outcome of our demonstrated interest is the initiation of a joint project with IBM on distributed computing at Stanford, although here we are talking about a dozen, rather than hundreds or thousands of processors. A proposal to develop intelligently communicating databases for chronic disease management will use these facilities, as well as DEC equipment at Stanford's CS dept. and microprocessor based systems.

Two Ph.D. theses were produced under the aegis of this project. Reid Smith's "Contract Net" provides a powerful framework for the study of interacting parallel processes. Hector Garcia-Molina's work on the "Performance of Update Algorithms in a Distributed Database" has lead to efficient algorithms for the maintenance of consistency in the databases in multiprocesses or network.

1. Garcia-Molina, Hector: "Performance Comparison of Update Algorithms for Distributed Databases," Technical Note 143, CSL, Stanford University, Sept. 1978.
2. Garcia-Molina, Hector: "Performance Comparison of Update Algorithms for Distributed Databases, Part II" ; CSL Tech Note 146, Dec. 1978.
3. H. Garcia-Molina, "Crash Recovery in the Centralized Locking Algorithm"; November 1978, to appear as a Tech Note.
4. H. Garcia-Molina, "Restricted Update Transactions and Read Only Transactions"; January 1979, to appear as a CSL Tech Note.
5. H. Garcia-Molina, "Partitioned Data, Multiple Controllers, and Transactions with an Initially Unspecified Base Set"; February 1979, to appear as a CSL Tech Note.
6. H. Garcia-Molina, "A Concurrency Control Mechanism for Distributed Databases Which Uses Centralized Locking Controllers"; submitted to the Fourth Berkeley Conference on Distributed Data Management and Computer Networks, August 1979.

7. H. Garcia-Molina, "Centralized Control Update Algorithms for Distributed Databases"; submitted to the First International Conference on Distributed Processing Systems, October 1979.

We will continue to track progress in this area, and when new results or systems appear assess their usefulness to a SUMEX-AIM like environment. We believe it remains important to look for more efficient ways to carry out the highly demanding computations in the area of artificial intelligence, and whereas improved heuristics and algorithms play a primary role in that search the exploitation of new hardware will complement such efforts.

4.2.5 MOLGEN Project

MOLGEN - An Experiment Planning System for Molecular Genetics

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Department of Computer Science
Stanford University

I. SUMMARY OF RESEARCH PROGRAM

A. Technical Goals

The MOLGEN project has constructed--and is extending--a computer system capable of generating the experiment-planning sequences needed to solve given structural problems in molecular genetics. In particular we have developed a system which is capable of acquiring and representing information about genetic objects, transformations, and strategies. The knowledge base presently includes information on DNA structures, restriction enzymes, laboratory techniques, and a growing collection of genetic strategies for discovering information about various aspects of DNA molecules. Several specific subproblems such as simulating Ligase enzymes, determining safe restriction enzymes for gene excision, and inferring DNA structures from segmentation data have been explored. We have designed our effort to facilitate generalization to other domains beyond genetics in future research and applications.

The MOLGEN project has both an applications and a computer science dimension. Along the latter dimension, we seek to deepen our knowledge of the art and science of creating programs that reason with symbolic knowledge at several levels (in this case, biological, genetic, topological, and chemical) to aid human problem solvers. To facilitate this, we have developed a knowledge representation system with a knowledge acquisition package. The system, known as the Units Package, may be used to build a knowledge base in any suitable domain. It provides an object-centered approach for storage of both declarative and procedural information concerning all entities in the domain. The task domain, molecular genetics, serves as a rich intellectual and scientific environment in which to develop and test our ideas.

The major computer science issues we are addressing during the current grant period are:

- (1) Extending the UNITS package to efficiently represent a larger variety of knowledge; including four distinct notations for dealing with instances, schemata, descriptions, and variables; more meta-level information, nodes with multiple parents; explicit facts about the representation itself; and more efficient updating strategies for maintaining a very large knowledge base of units on disk.
- (2) Creation of program schemata and instances for general problem solving steps. Domain-independent knowledge about general problem solving methods also fits into the knowledge representation structure we have devised.

- (3) Domain Specific Critics. Mechanisms for the activation of various domain specific strategies when certain predefined situations occur during the course of experiment design.
- (4) Development of a specific planning strategy designed to provide high-performance for the class of genetic experiments known as discrimination experiments. The idea is based on indexing abstracted experimental designs to the types of structural features for which they have proven useful.
- (5) Constraint posting and Orthogonal planning. It has been observed that efficient planning proceeds hierarchically -- first making general decisions and later tending to the details. This research considers some planning problems with open-ended goals; part of the task of planning is to make the goals specific. A technique called "constraint posting" is presented for guiding the process of hierarchical planning by utilizing the interactions between parts of a plan. With this technique, a planning program can add details to a plan after recognizing and analyzing situations where more details are needed. The planner can skip around between different parts of the plan, suspending work on one section and moving to another rather than making uninformed decisions. The planner can accumulate constraints, which tie together decisions in separate parts of the plan. Other ideas include (1) a layered control structure termed "orthogonal spaces" which organizes the "plan-making" operations into explicit spaces separate from the domain knowledge and (2) some representations for hierarchical constants and variables which facilitate reasoning about abstract and undetermined objects during planning.

Along the applications dimension, we are attempting to develop tools that can benefit molecular geneticists. We believe there is substantial benefit to be derived from programs that act as "intelligent assistants" to scientists. First of all, the sheer amount of detailed knowledge a scientist is expected to know makes it likely that good experiments are being missed. Second, we believe that an intelligent planning assistant can offer some help in reasoning about the consequences of combining experimental facts in many possible ways.

A third motivation for applying artificial intelligence techniques to an experimental science like molecular genetics is to help us better understand the scientific method. The rigorous detail required for creating computer programs that assist in the performance of scientific tasks forces us to explicate concepts and procedures much more carefully than practicing scientists usually do.

B. Medical relevance and collaboration

Molecular genetics has at least two major connections to medical research. Learning about the basic mechanisms which control the operation and transmission of genetic information is necessary to understand and treat the wide range of diseases and health conditions that are genetically controlled. Also, recent developments in molecular genetics offer the promise of using genetic mechanisms to produce essentially limitless amounts of drugs and other biomedical substances.

The MOLGEN project is a joint effort of the Computer Science Departments of Stanford and the University of New Mexico and the Genetics Department of Stanford. Major participants are Professor Nancy Martin and Gary Klimowicz of the University of New Mexico; Professor Edward Feigenbaum, Professor Douglas Lenat, Professor Bruce Buchanan, Peter Friedland, and Mark Stefik of the Stanford Computer Science Department, Jerry Feitelson of the Stanford Genetics Department, Professor Laurence Kedes of the Stanford Medical School. Assistant Professor Douglas Brutlag of Stanford's Biochemical Department, Professor Joshua Lederberg, president of Rockefeller University and consulting professor of Computer Science at Stanford, and Dr. John Sninsky, a molecular biologist working in Professor Stanley Cohen's laboratory, are also collaborating in the MOLGEN project.

C. Progress summary

The major effort in MOLGEN has been the creation of a knowledge management system. In addition, several specific problems which arise in genetics have been examined in sufficient detail to result in reports and/or special purpose programs. We report briefly on two such programs, SAFE written by Peter Friedland, and GA-1 written by Mark Stefik.

Knowledge management system

The success of MOLGEN as an experiment planner will depend on the quality of its knowledge base. Therefore, much of the research effort to date has been in the design and implementation of a knowledge representation and acquisition system. All of the information relevant to the planning process will be an explicit part of the knowledge base. The motivation for this aspect of the design is the necessity to expand the program capabilities in a modular fashion and to explain the rationale behind the program's planning behavior. We need to represent concepts (e.g. enzyme), instances (e.g. EcoRI), relationships among concepts, and relationships among instances. In addition, we need to represent processes. We have purposely limited the expressive power of our representations to enable us to clearly define their semantics.

The result of this work is the Unit Package. Although this package has been designed in the context of our genetics application, the package does not contain any genetics knowledge.

One important aspect of the design of the system is that the knowledge base contains knowledge about its own data representations. We have provided what we term a "bootstrap knowledge base." It contains domain independent knowledge about commonly used data types. When using our knowledge base in a new domain, an artificial intelligence researcher would probably start with the bootstrap knowledge base and then proceed to create units for the specific knowledge of his task area. Both the AGE and genetics knowledge bases have been started in this manner. The bootstrap knowledge base serves to illustrate our approach to extensibility. Most of the bootstrap knowledge base is made up of primitive datatypes. To add a new datatype to our system, one needs to provide the knowledge base with procedures for some basic operations -- such as editing and printing. Actually, the same approach is used in the unit package for defining a new datatype as is used for defining a new enzyme. The process of defining new datatypes requires, however, an understanding of Interlisp because the primitive processes in the system are grounded in that language. New datatypes must be defined together with their basic operations and entered into the knowledge base.

Knowledge base contents

The genetics knowledge base is growing rapidly. Approximately 60% of the commonly used enzymes have been characterized. A beginning has been made on the characterization of organisms such as bacteria and phages, plasmids and other vectors, and genes. Our knowledge base also contains a growing collection of genetic strategies for discovering information about various aspects of DNA molecules, as well as a hierarchy of laboratory techniques which are used to instantiate the strategies. The hierarchy of techniques includes modification, separation, visualization, sequence analysis, and bacteriological techniques at many levels of abstraction.

Safe program

The geneticist needs to predict what restriction enzymes can safely be used to excise a gene, i.e. which ones can be guaranteed not to cut the functional part of the gene. We would also like to know the approximate location of the possible cutting sites of other restriction enzymes. This would all be very easy if the complete DNA sequence of the gene was known. Sequence information is becoming more and more prevalent, but it is still uncommon to know the complete sequence of a gene. However, it is not unusual to know what protein the gene codes for and to know the amino acid sequence of a protein.

Knowing the amino acid sequence does not provide full information because of the degeneracy in the genetic code. One codon (a triplet of nucleotides) specifies only one amino acid, but up to six different codons may specify the same amino acid. The problem therefore, is combinatorically difficult. Typical proteins are up to 300 amino acids long (900 nucleotides), and all possible nucleotide sequences which would produce the protein in the three possible phases have to be considered.

The SAFE program lists the restriction enzymes that are currently stored in the knowledge base and allows the user to add new ones. Besides determining which enzymes are safe to use for gene excision in a particular DNA molecule, the program also gives the position in the amino acid sequence where the possible cutting site would be located.

GA-1 program

A common task in molecular genetics laboratories is the analysis of DNA structure from restriction enzyme segmentation data. This task is one of the simplest, although time-consuming, analysis tasks in molecular genetics. Two standard approaches to solving this problem were examined: a data-driven strategy and a model-driven strategy. These approaches are discussed and compared in terms of sensitivity to missing data, efficiency in the use of data, and other measures of performance in [Stefik, 78]. A program was designed and implemented which is superior to human performance on smaller problems, both in speed and reliability. However, on large problems human problem solvers can use extra structural constraints to out perform the program. The current program uses only constraints derived from segmentation data itself. Geneticists usually know additional information -- eg. that a given segment is on the end or that certain segments must be adjacent.

A further benefit of this work was the suggestion of two new lab techniques: combining multiple enzyme digests and incomplete digests. These ideas arose from a systematic examination of evidence and inference rules that went into building the program.

D. Publications

Challenger J., A Program for Printing DNA Structures, CIS Report 78-3 (April 1978)

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Friedland P., Knowledge-Based Experiment Design in Molecular Genetics, submitted to Sixth International Joint Conference on Artificial Intelligence (August 1979)

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Stefik M., Friedland P., Machine Inference for Molecular Genetics: Methods and Applications, Proceedings of the National Computer Conference, (June 1978)

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Stefik M., Inferring DNA Structures From Segmentation Data: A Case Study, Heuristic Programming Project Report HPP-78-3 (January 1978) Stefik, M., An Examination of a Frame-structured Representation System, HPP-78-13 (Working Paper) (August 1978)

II. INTERACTIONS WITH THE SUMEX-AIM RESOURCE

All system development has taken place on the SUMEX-AIM facility. The facility has not only provided excellent support for our programming efforts but has served as a major communication link among members of the project. Through the SUMEX-AIM facility, program development has taken place concurrently at Stanford and New Mexico. Systems available on SUMEX-AIM such as INTERLISP, TV-EDIT, and BULLETIN BOARD have made possible the project's programming, documentation and communication efforts. The interactive environment of the facility is especially important in this type of project development.

We have taken advantage of the collective expertise on medically-oriented knowledge-based systems of the other SUMEX-AIM projects. In addition to especially close ties with other projects at Stanford, we have greatly benefitted by interaction with other projects at yearly meetings and through exchange of working papers and ideas over the system.

The combination of the excellent computing facilities and the instant communication with a large number of experts in this field has been a determining factor in the success of the MOLGEN project.

III. RESEARCH PLANS

A. Project goals and plans

In exploring the three major motivations mentioned in section I.A. for creating the MOLGEN project, there are many specific subproblems. We have identified five for concentrated effort in the next two year period.

- (1) Creating a more comprehensive genetics knowledge base. Expanding the knowledge base within the area of DNA structural manipulation problems.
- (2) Making use of the process of hypothesis formation to help debug MOLGEN-produced experiment designs. This process is especially important in a domain like molecular genetics where incomplete knowledge about objects and processes is the rule rather than the exception.
- (3) Experiment planning by analogy. MOLGEN provides an excellent environment for exploring various types of analogical reasoning. We integrate problem-solving by analogy into the experiment design system as one of the possible tools for solving subproblems.

Each time the Heuristic Programming Project at Stanford has built another large AI program, we have learned more about how to do it better and faster next time. For example, the production rule interpreter in Heuristic Dendral (for special-purpose rules) became the general rule interpreter of MYCIN. One of the significant products of MOLGEN research will be the sets of ideas and programs for encoding and manipulating large amounts of knowledge about a scientific discipline. We have transferred some parts of the MOLGEN Units package to another project interested in building a knowledge base about AI methods and techniques. Making the tools used here available for use in new programs is an important aspect of our work and is generally important for cumulation of knowledge in the AI field. In order to do this we must reformulate the methods so they are more generally applicable and more readily combined in diverse ways.

B. Justification and requirements for continued SUMEX use.

The MOLGEN project is dependent on the SUMEX facility. While we have solved many of the original problems facing us in a manner useful to working geneticists, we are just in the middle phase of building a planning system. Without support from SUMEX to complete this system, many of the results of the last two years will be ineffective. In the past six months our interactions with geneticists outside of Professor Lederberg's laboratory have increased greatly. The geneticists are excited about helping us with our knowledge base. Also, with our help, they are finding useful ways to use the computing facility in their current research. Thus the serendipity of supporting MOLGEN is the creation of many useful computer research programs.

We are asked to state our requirements for continued SUMEX use. We project that our usage of processor cycles and file storage will grow to twice the current levels in the coming year.

4.2.6 MYCIN/EMYCIN Project

MYCIN/EMYCIN Project

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I. Summary of Research

A. Technical goals

MYCIN is an interactive consultation program which gives physicians antimicrobial therapy recommendations for patients with infectious diseases. The system must often decide whether and how to treat a patient before definitive laboratory results are available. It must recommend a therapeutic regimen which minimizes the risk of toxic side-effects while covering for all organisms which are likely to be causing the infection. The system currently has knowledge about treating three major infections - bacteremias (blood infections), cystitis and meningitis. The primary goal of the project has been to develop a program which would provide the same quality advice that a physician would get from a human infectious disease consult. Formal evaluations of the program's recommendations for patients with bacteremia and with meningitis have shown that this goal has been achieved.

Another important goal has been that the system should be easy to use and acceptable to a physician. To accomplish this, numerous human engineering features have been incorporated into the consultation, and an extensive explanation facility has been developed which enables the system to explain its reasoning and to justify its recommendations.

MYCIN's knowledge about infectious diseases is represented in production rules which are invoked by goal-directed backward chaining starting from the top-level goal of determining the appropriate therapeutic regimen.

The success of the MYCIN program in the area of infectious diseases led researchers to try to generalize and expand the methods employed in that program to a number of ends:

- to develop consultation systems for other domains,
- to explore other uses of the knowledge base,
- to further facilitate interaction both for the developer of a knowledge-based system, and for the user of such a system, and
- to experiment with using other knowledge representations in conjunction with the production rules used in MYCIN.

B. Medical Relevance

The MYCIN program was designed to help alleviate the problem of antimicrobial misuse documented in Shortliffe, 1976. We felt that MYCIN would be clinically useful when it was able to handle all major infections that are likely to be encountered in a hospital. It has not been possible to produce a clinically useful program in a few years due to the very large investment in time and human resources which are required of to develop, test and formally evaluate a rule set for each major infection area.

Through our collaboration on building the PUFF program, however, we learned that it is possible in a short period of time to develop a clinically useful consultation system using the domain-independent parts of the MYCIN program. Our effort to extract the "Essential" parts of MYCIN has been named EMYCIN; the development of EMYCIN can facilitate the creation of rule-based consultation systems for dealing with a number of medical problems.

C. Progress Summary

EMYCIN

Much of the work in the past year has been devoted to improving EMYCIN's facilities for allowing a system builder to construct and debug a knowledge base for a consultation system. This has included extensive documentation of the concepts used in EMYCIN consultation systems, the support programs for developing the knowledge base, and features of a working consultation system.

A knowledge-base debugging package was developed to assist the system builder in the task of testing, refining, and validating the knowledge base. This package includes: 1) the EMYCIN explanation facility; 2) a program that automatically explains how the system arrived at the results of a consultation; 3) a program that reviews each result of a consultation, allowing the user to judge whether the result is correct, and assisting the user in refining the knowledge base in order to correct any errors noted in the result or in intermediate conclusions; and 4) a program that automatically compares the results of a consultation to stored "correct" results for the same case, and explains any errors in the conclusions.

SACON

A new EMYCIN application called SACON was developed; this provided the EMYCIN developers with numerous ideas for improving EMYCIN facilities. A SACON consultation is meant to provide advice to a structural engineer regarding the use of a structural analysis program called MARC. The MARC program uses finite-element analysis techniques to simulate the mechanical behavior of objects. The engineer typically knows what he wants the MARC program to do--e.g., examine the behavior of a specific structure under expected loading conditions--but does not know how the simulation program should be set up to do it. The MARC program offers a large (and, to the novice, bewildering) choice of analysis methods, material properties, and geometries that may be used to model the structure of interest. From these options the user must learn to select an appropriate subset that will simulate the correct physical behavior, preserve the desired accuracy, and minimize the (typically large) computational cost. A year of experience with

the program is the typical time required to learn how to use all of MARC's options proficiently. The goal of the automated consultant is to bridge the "What-to-How" gap, by recommending an analysis strategy. This advice can then be used to direct the MARC user in the choice of specific input data--e.g., numerical methods and material properties. Typical structures that can be analyzed by both SACON and MARC include aircraft wings, reactor pressure vessels, rocket motor casings, bridges, and buildings.

The development of SACON represents a major test of the domain-independence of the EMYCIN system. Previous applications using EMYCIN have been primarily medical with the consultations focusing on the diagnosis and prescription of therapy for a patient. Structural analysis, with its emphasis on structures and loadings, allowed us to detect the small number of places where this medical bias had unduly influenced the system design, notably text strings used for prompting and giving advice.

The expert who provided the knowledge for the SACON program found that his knowledge was easily cast into the rule-based formalism and that the existing predicate functions and context-tree mechanism provided sufficient expressive power to capture the task of recommending an analysis strategy. The existing interactive facilities for performing explanation, question-answering, and consultation were found to be well developed and were used directly by our application. None of these features required any significant reprogramming and, for the most part, worked without modification.

GUIDON

Recent work has included the development of a tutoring system which uses the knowledge base of an EMYCIN consultation system as a manual of principles about the domain which can be taught to students. The tutorial program is domain-independent and can present whatever material is represented in the manual. The manual can be interpreted in two ways: (1) as a "runnable model" capable of performing the task to be learned by the student, and (2) as a set of principles to be discussed with the student.

The first version of GUIDON is being developed using the MYCIN manual of rules for diagnosing infections and prescribing antibiotic therapy. Other MYCIN-like manuals that are available include PUFF and SACON.

An important distinction between GUIDON and traditional computer-aided instructional programs is the independence of the tutor from the domain knowledge. As long as a manual is represented as a set of conditional rules (with the relevant objects identified and explicitly related), the tutor will be able to present the material. One area of investigation is the teaching of explicit problem-solving strategies that constitute approaches for applying the conditional rules to particular problems. Thus, this project represents a significant twist in knowledge-based AI research: we are taking knowledge that has been formalized in AI programs (the "manual") and TRANSFERRING IT BACK to humans, to students who want to learn the methods and strategies used by the experts in their field.

In separating teaching strategies from problem-solving strategies, we have explicitly stated the instructional methods we wish to test. Tutorial dialogue

knowledge is represented as procedures built from sequences of conditional rules. Thus, the teaching strategies for planning and directing the mixed-initiative dialogue can be readily displayed and changed. This will enable experimentation with alternate strategies, as well as making it easy to show them to other researchers.

Finally, GUIDON's mixed-initiative dialogue capabilities are more complex than in previous "intelligent computer aided instruction." The tutor engages the student in a dialogue while the student is working on a specific, complex task. A model of the student's knowledge in terms of the manual of rules guides teaching strategies for quizzing the student and presenting new information. The combination of a flexible environment for solving the problem (provided by the options we give the student for gaining more information and for keeping track of what remains to be done) and an active tutor that endeavors to convey problem-solving expertise, makes this a unique tutorial system.

D. Publications

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II. Interaction With the SUMEX-AIM Resource

A great deal of interest in MYCIN has been shown by the medical and academic communities. Among the people who have visited the project or asked for GUEST access to the MYCIN program are Dr. Solveig Pflüeger of the University of Texas at San Antonio Medical School, Dr. Robert H. Rosenberg of Seattle Radiologists, Inc., and Dr. Jeffrey P Krischer, Chief of Health Services Research and Development at the University of Florida. Dr. Peter Szolovitz of MIT and Dr. Steven Zucker of McGill University in Montreal have demonstrated the MYCIN program in their university classes. Dr. Harold Goldberger of MIT made extensive use of the MYCIN program last last summer in his study of medical AI programs. Dr. Ves Morinov of the Norwegian Computing Center has used the MYCIN program to demonstrate the benefits of using a rule-based representation for consultation systems. The MYCIN program was demonstrated at the Third Rheumatology - Information Science Meeting in March 1978, at the Annual meeting of the American College of Physicians in San Francisco in March 1979, and at a monthly meeting of the Stanford Computers in Medicine Group in May 1979.

EMYCIN has generated a great deal of interest in the academic and business communities. We have been in frequent contact with Bud Frawley and Philippe Lacour-Gayet of Schlumberger, Milt Waxman of the Hughes Aircraft Corporation, and Harry Reinstein from IBM Scientific Research Center. of EMYCIN. Two students at the Naval Postgraduate School in Monterey, California working under the direction of Colonel Ronald J Roland are developing an EMYCIN system in the domain of selecting decision aids for solving problems in business organizations. Dr. Don Walter of UCLA is currently seeking funding for developing an EMYCIN system in the domain of diagnosis and management of epilepsy.

During the past year the MYCIN program was used in a study of debugging techniques for Artificial Intelligence systems. This work was a SUMEX Pilot project undertaken by Mitch Model as part of the work on his PhD thesis, "Understanding System Behavior in a Complex Computational Environment." Using the display LISP at Xerox PARC, Model developed a general approach and some specific tools to be used in debugging AI systems in which, for various reasons, traditional debugging tools are inadequate. The primary object of the work was the KRL-1 system; however, to test the generality of the approach, it was important to apply it to other AI systems. A mechanism was developed for communicating between two LISP jobs over the ARPANET. After minor experimentation, it was possible add this mechanism to the MYCIN program at SUMEX. Model was then able to test the generality of his approach by having MYCIN (running on SUMEX) send monitoring information over the ARPANET to his system running on MAXC computer at Xerox PARC.

We have continued collaboration with the EMYCIN-based projects RX, HEADMED and PUFF. Our development of a domain-independent system is facilitated by having a number of very different working systems on which to test our additions and modifications to EMYCIN. All the projects have provided us with useful comments and suggestions.

We have also interacted with members of the SECS project on SUMEX who are interested in developing a question answering system for SECS similar to the one in MYCIN.

C. Critique of Resource Management

The SUMEX facility has maintained the high standards that we have praised in the past. The staff members are always helpful and friendly, and work as hard to please the Sumex community as to please themselves. As a result, the computer is as accessible and easy to use as they can make it. More importantly, the machine is a reliable and convenient research tool. Special thanks to T.Rindfleisch for maintaining high professional standards for all aspects of the facility.

We continue to feel the need for more computing power. Most of our research and development takes place in the hours from 7 p.m. to 10 a.m., but it is unreasonable to expect all our collaborators to adjust their own schedules around a computer.

4.2.7 Protein Structure Project

Protein Structure Modeling Project

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I. Summary of Research Program

A. Technical goals

The goals of the protein structure modeling project are to 1) identify critical tasks in protein structure elucidation which may benefit by the application of AI problem-solving techniques, and 2) design and implement programs to perform those tasks. We have identified two principal areas which have both practical and theoretical interest to both protein crystallographers and computer scientists working in AI. The first is the problem of interpreting a three-dimensional electron density map. The second is the problem of determining a plausible structure in the absence of phase information normally inferred from experimental isomorphous replacement data. Current emphasis is on the implementation of a program for interpreting electron density maps (EDM's).

B. Medical relevance and collaboration

The biomedical relevance of protein crystallography has been well stated in an excellent textbook on the subject (Blundell & Johnson, Protein Crystallography, Academic Press, 1976):

"Protein Crystallography is the application of the techniques of X-ray diffraction ... to crystals of one of the most important classes of biological molecules, the proteins. ... It is known that the diverse biological functions of these complex molecules are determined by and are dependent upon their three-dimensional structure and upon the ability of these structures to respond to other molecules by changes in shape. At the present time X-ray analysis of protein crystals forms the only method by which detailed structural information (in terms of the spatial coordinates of the atoms) may be obtained. The results of these analyses have provided firm structural evidence which, together with biochemical and chemical studies, immediately suggests proposals concerning the molecular basis of biological activity."

The project is a collaboration of computer scientists at Stanford University and crystallographers at the University of California at San Diego (under the direction of Prof. Joseph Kraut) and at Oak Ridge National Laboratories (Dr. Carroll Johnson). Our principal collaborator at UCSD is Dr. Stephan Freer.

C. Progress summary

We have completed a major cycle of design review and program reorganization, resulting in the system described in publication number three below. The system now has a completely rule-based control structure proceeding from strategy rules, to a set of task rules, ending with individual knowledge sources. This new design seems powerful and flexible enough to provide the basis of a useful EDM interpretation system for protein structure determination. We have also continued our efforts to improve the power of our data representations. To this end we have implemented a new preprocessor to assign functional labels to segments. This program consists of heuristics that attempt to capture the knowledge a human uses when he visually examines a skeletonized EDM. We find the use of labeled segments greatly aids the main CRYVALIS program by allowing rules to be written in terms much closer to what humans use rather than the language in which the EDM skeleton is defined.

Finally, we are compiling documentation on the system and the knowledge it embodies. These documents should be complete enough that we, or another group, will have little difficulty picking up where we leave off. We also feel that explicit documentation of our model-building heuristics will be useful to the crystallographic community as they provide a new viewpoint, complementary to their traditional methods.

D. List of Publications

- 1) Robert S. Engelmores and H. Penny Nii, "A Knowledge-Based System for the Interpretation of Protein X-Ray Crystallographic Data," Heuristic Programming Project Memo HPP-77-2, January, 1977. (Alternate identification: STAN-CS-77-589)
- 2) E.A. Feigenbaum, R.S. Engelmores, C.K. Johnson, "A Correlation Between Crystallographic Computing and Artificial Intelligence," in Acta Crystallographica, A33:13, (1977). (Alternate identification: HPP-77-25)
- 3) Robert Engelmores and Allan Terry, "Structure and Function of the CRYVALIS System," paper accepted for presentation at IJCAI-79.

II. Interaction with the SUMEX-AIM resource

A. Collaborations

The protein structure modeling project has been a collaborative effort since its inception, involving co-workers at Stanford and UCSD (and, more recently, at Oak Ridge). The SUMEX facility has provided a focus for the communication of knowledge, programs and data. Without the special facilities provided by SUMEX the research would be seriously impeded. Computer networking has been especially effective in facilitating the transfer of information. For example, the more traditional computational analyses of the UCSD crystallographic data are made at the CDC 7600 facility at Berkeley. As the processed data, specifically the EDM's and their Fourier transforms, become available, they are transferred to SUMEX via the FTP facility of the ARPA net, with a minimum of fuss. (Unfortunately, other methods of data transfer are often necessary as well -- see below.) Programs developed at SUMEX, or transferred to SUMEX from other laboratories, are shared directly among the collaborators. Indeed, with some of the programs which have originated at UCSD and elsewhere, our off-campus collaborators frequently find it easier to use the SUMEX versions because of the interactive computing environment and ease of access. Advice, progress reports, new ideas, general information, etc. are communicated via the message and/or bulletin board facilities.

B. Interaction with other SUMEX-AIM projects

Our interactions with other SUMEX-AIM projects have been mostly in the form of personal contacts. We have strong ties to the DENDRAL, Meta-DENDRAL and MOLGEN projects and keep abreast of research in those areas on a regular basis through informal discussions. The SUMEX-AIM workshops provide an excellent opportunity to survey all the projects in the community. Common research themes, e.g. knowledge-based systems, as well as alternate problem-solving methodologies were particularly valuable to share.

C. Critique of Resource Services

The SUMEX facility provides a wide spectrum of computing services which are genuinely useful to our project -- message handling, file management, Interlisp, Fortran and text editors come immediately to mind. Moreover, the staff, particularly the operators, are to be commended for their willingness to help solve special problems (e.g., reading tapes) or providing extra service (e.g. immediate retrieval of an archived file). Such cooperative behavior is rare in computer centers.

It has become increasingly evident, however, that as CRYNALIS expands, the facility cannot provide enough machine cycles during prime time to support the implementation and debugging of new features. For example, our segment-labeling preprocessor requires about an hour of machine time per 100 residues of protein (this is typically five to eight hours of terminal time during working hours) even when the Lisp code is compiled.

A continuing deficiency is the lack of even a rudimentary file transfer facility between SUMEX and the computing system in the UCSD Chemistry Department. Our day-to-day collaboration with Dr. Freer at UCSD would be greatly enhanced by a DIALNET or similar low-cost facility.

III. Use of SUMEX during the remaining grant period (8/79 - 7/81)

A. Long-range goals

Our current research grant ended on April 30, 1979, with a six-month finishing-up period. Due to the transfer of Dr. Engelman to the Defense Advanced Research Projects Agency for a two year term, it was decided by the principal investigator to withdraw the pending renewal application. However, the expected utility of the CRYSTALIS system is well recognized, and has generated many requests, from both the AI and protein-crystallographic communities, to preserve the research for future resumption. As stated earlier, a documentation effort is in progress to effect that preservation. It is hoped that the work will be resumed after a two year hiatus.

The long range goals continue to be to exploit the rule-based control structure for investigating alternative problem-solving strategies, to investigate modes of explanation of the program's reasoning steps, and to expand and generalize the system to cover a wider range of input data.

B. Justification for continued use of SUMEX

During the next few months, efforts will continue to complete an extensive documentation of the CRYSTALIS system, support programs, and data file structures. This documentation will be transferred to UCSD, ORNL and Carnegie-Mellon University, who have requested it, and other interested institutions. Also, some small use of SUMEX will be made for occasional file transfers to other computing facilities.

4.2.8 RX Project

The RX Project: Inferring Knowledge from Clinical Data Banks
Utilizing Techniques from Artificial Intelligence

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I. Summary of Research Program

A. Technical goals:

Introduction:

The RX Project is a new member of the SUMEX community, having been accorded its current status as an autonomous project only as of February, 1979. Since RX is a new research project, we shall focus on the goals and medical relevance of the Project, only touching lightly on the other topics of the outline.

I. SUMMARY OF RESEARCH PROGRAM

Medical and Computer Science Goals

The objective of the RX Project is to develop a prototype computer-based system for reliably extracting knowledge pertaining to the evolution and treatment of chronic diseases from data in patient records stored in the form of computerized clinical data banks.

Computerized clinical data banks and automated medical records keeping have been major research concerns in many parts of the United States for at least a couple of decades. Among the earliest data banking endeavors was the ARAMIS Project, which has been under development at Stanford by Dr. James Fries and his colleagues since 1967. A prototype ambulatory records system was generalized in the early 1970's by Prof. Gio Wiederhold and Stephen Weyl in the form of a Time-Oriented Database (TOD) System. The TOD System, run on the IBM 370/168 at the Stanford Center for Information Processing (SCIP), now supports the ARAMIS Data Bank (American Rheumatism Association Medical Information System) as well as a host of other chronic disease data banks which store patient data gathered at many institutions nation-wide. At the present time ARAMIS contains records of over 10,000 patients with a variety of rheumatologic diagnoses. Over 30,000 patient visits have been recorded, accounting for 20,000 patient-years of observation.

The fundamental objective of ARAMIS, the other TOD research groups, and all other clinical data bank researchers is to use the raw data which has been gathered by clinical observation in order to study the evolution and medical management of chronic diseases. Unfortunately, the process of reliably extracting knowledge from raw data has proved to be refractory to existing techniques because of problems stemming from the complexity of disease, therapy, and outcome definitions; the complexity of time relationships; potential biases in compared subsets; and problems of missing and outlying data.

A major objective of the RX Project is to explore the utility of symbolic computational methods and knowledge-based techniques at solving this problem of accurate knowledge inference from non-randomized, non-protocol patient records. The methodology employed by the RX Project involves the use of a frame-based medical knowledge base conceptually similar to that developed by the KRL and MOLGEN research groups of the Heuristic Programming Project. The frame-based organization, in which disease states corresponding to individual conceptual units will be hierarchically organized, provides a major tool for increasing the homogeneity of patient subsets. Embedded within the knowledge base will be production rules containing time-dependent predicates for use in transforming the set of raw data into a collection of meaningful clinical events. This process of conceptual abstraction will make subsequent statistical analysis far less sensitive to missing or outlying data.

A second objective of the RX Project is to use its knowledge base to mediate interactive consultation with a clinician. In other words, the knowledge base is called upon both to extract and store new knowledge from a clinical data bank and to use that knowledge to facilitate interactive consultation. From the start this objective has guided selection of appropriate methods for knowledge representation and choice of control structures.

As a test bed for system development we intend to focus attention on the 270 records of patients with systemic lupus erythematosus (SLE) contained in the Stanford portion of the ARAMIS Data Bank. SLE is a major multi-system chronic rheumatologic disease with a broad spectrum of manifestations and can lead to death in the third decade of life. With many perplexing diagnostic and therapeutic dilemmas, it is a disease of considerable medical interest.

In the future we anticipate the development of collaborative arrangements with other project users of the TOD System such as the National Stroke Data Bank, the Northern California Oncology Group, and the Stanford Divisions of Oncology and of Radiation Therapy.

The RX Project is a new research effort only in existence for less than a year, and, hence the project is very much in a developmental stage. The primary issues being addressed at this stage are those concerned with the specifics of knowledge representation and flow of control, rather than with the testing of specific hypotheses in chronic disease management.

We believe that this research project is broadly applicable to the entire gamut of chronic diseases which constitute the bulk of morbidity and mortality in the United States. Consider five major diagnostic categories which are responsible for approximately two thirds of the two million deaths per year in the United States: myocardial infarction, stroke, cancer, hypertension, and

diabetes. Therapy for each of these diagnoses is fraught with controversy concerning the balance of benefits versus costs.

- 1) Myocardial Infarction: Indications for and efficacy of coronary artery bypass graft vs. medical management alone. Indications for long-term antiarrhythmics ... long-term anticoagulants. Benefits of cholesterol-lowering diets, exercise, etc.
- 2) Stroke: Efficacy of long-term anti-platelet agents, long-term anticoagulation. Indications for revascularization.
- 3) Cancer: Relative efficacy of radiation therapy, chemotherapy, surgical excision - singly or in combination. Optimal frequency of screening procedures. Prophylactic therapy.
- 4) Hypertension: Indications for therapy. Efficacy versus adverse effects of chronic antihypertensive drugs. Role of various diagnostic tests such as renal arteriography in work-up.
- 5) Diabetes: Influence of insulin administration on microvascular complications. Role of oral hypoglycemics.

Despite the expenditure of billions of dollars over recent years for randomized controlled trials (RCT's) designed to answer these and other questions, answers have been slow in coming. RCT's are expensive of funds and personnel. The therapeutic questions in clinical medicine are too numerous for each to be addressed by its own series of RCT's.

On the other hand, the data regularly gathered in patient records in the course of the normal performance of health care delivery is a rich and largely underutilized resource. The ease of accessibility and manipulation of these data afforded by computerized clinical data banks holds out the possibility of a major new resource for acquiring knowledge on the evolution and therapy of chronic diseases.

The goal of the research which we are pursuing on SUMEX is to increase the reliability of knowledge derived from clinical data banks with the hope of providing a new tool for augmenting knowledge of diseases and therapies as a supplement to knowledge derived from formal prospective clinical trials. Furthermore, the incorporation of knowledge from both clinical data banks and other sources into a uniform knowledge base should increase the ease of access by individual clinicians to this knowledge and thereby facilitate both the practice of medicine as well as the investigation of human disease processes.

Progress Summary

The initial testbed for the RX Project will be a subset of the clinical records stored in the ARAMIS Data Bank. These data are available to us on the Stanford Center for Information Processing (SCIP) IBM 370/168 on which ARAMIS is resident. Mr. Ron Code of the SCIP Staff has written a program for formatting this data into a form suitable for transfer to SUMEX. Transfer of patient records from SCIP to SUMEX is currently implemented via the "TRAN" line, a 2400 baud local hardline.

A record package has been implemented at SUMEX to transform the time-oriented data from ARAMIS into a form suitable for further transformation - the conceptual abstraction, which we have described previously. The algorithms for conceptual abstraction have been developed, and the data structures for storing medical knowledge and abstracted records have been worked out in detail. Programs implementing these algorithms are underway.

Algorithms for statistical manipulation of the abstracted patient records have been developed in collaboration with Mr. Guy Kraines, biostatistician for ARAMIS, and Prof. Byron Brown, Chairman of Biostatistics at the Stanford Medical Center. Methods will include multivariate, logistic regression and Cox model regression for time-dependent parameters.

Publications

Blum, Robert L.; Wiederhold, Gio: Inferring Knowledge from Clinical Data Banks Utilizing Techniques from Artificial Intelligence. Proc. of The 2nd Annual Symp. on Computer Applications in Medical Care, pp. 303 to 307, IEEE, Washington, D.C., November 5-9, 1978.

II. INTERACTIONS WITH THE SUMEX-AIM RESOURCE

Collaborations

Since our project is new, we have not yet developed programs which may be used by others. There is, however, a tremendous sphere of collaboration which we expect in the future. Once the RX program is developed, we would anticipate

collaboration with all of the ARAMIS project sites in the further development of a knowledge base pertaining to the chronic arthritides. The ARAMIS Project at SCIP is used by a number of institutions around the country via commercial leased lines to store and process their data. These institutions include the University of California School of Medicine, San Francisco and Los Angeles; The Phoenix Arthritis Center, Phoenix; The University of Cincinnati School of Medicine; The University of Pittsburgh School of Medicine; Kansas University; and The University of Saskatchewan. All of the rheumatologists at these sites have closely collaborated with the development of ARAMIS, and their interest in and use of the RX project is anticipated. We hasten to mention that we do not expect SUMEX to support the active use of RX as an on-going service to this extensive network of arthritis centers, but we would like to be able to allow the national centers to participate in the development of the arthritis knowledge base and to test that knowledge base on their own clinical data banks.

III. RESEARCH PLANS

Project Plans (August 79 to July 81)

During the next year we will continue to develop the basic software needed to implement the "conceptual abstraction" algorithms and programs need for manipulation of the time-oriented records. We will elaborate a preliminary frame-structured knowledge base pertaining to systemic lupus erythematosus (SLE).

During the following year - August, 80 to July, 81 - we expect to populate the knowledge base using probabilities derived from the time-oriented records of the 270 patients with SLE. We will begin to investigate specific disease questions pertaining to SLE using records from the other ARAMIS institutions. Among these dilemmas are

- 1) the role of immunosuppressive therapy as adjunctive therapy for aggressive lupus nephritis,
- 2) the role of renal biopsy in the management of lupus nephritis,
- 3) the indications for and optimal administration of steroid therapy,
- 4) the usefulness of serologic indices as a guide to therapy.

Justification for Continued Use of SUMEX

Although we have just stated the following justifications in our recent application for autonomous project status to the SUMEX Advisory Board, we shall repeat them here for emphasis.

Computerized clinical data banks possess enormous potential as tools for assessing the efficacy of new diagnostic and therapeutic modalities, for monitoring the quality of health care delivery, and for support of basic medical research. Because of this potential, many clinical data banks have recently been developed throughout the United States. However, once the initial problems of data acquisition, storage, and retrieval have been dealt with, there remains a set of complex problems inherent in the task of accurately inferring medical

knowledge from a collection of observations in patient records. These problems concern the complexity of disease and outcome definitions, the complexity of time relationships, potential biases in compared subsets, and missing and outlying data. Concisely stated, the major problem of medical data banking is in the reliable inference of medical knowledge from primary observational data.

We see in the RX Project a method of solution to this problem through the utilization of knowledge engineering techniques from artificial intelligence. The RX Project, in providing this solution, will provide an important conceptual and technologic link to a large community of medical research groups involved in the treatment and study of the chronic arthritides throughout the United States and Canada, who are presently using the ARAMIS Data Bank through the SCIP facility via TELENET.

Beyond the arthritis centers which we have mentioned in this report, the TOD (Time-Oriented Data Base) User Group involves a broad range of university and community medical institutions involved in the treatment of cancer, stroke, cardiovascular disease, nephrologic disease, and others. Through the RX Project, the opportunity will be provided to foster national collaborations with these research groups and to provide a major arena in which to demonstrate the utility of artificial intelligence to clinical medicine.

SUMEX as a Resource

To discuss SUMEX as a resource for program development, one need only compare it to the environment provided by our other resource, the IBM 370/168 installation at SCIP - the major computing resource at Stanford. Of the programs which we use daily on SUMEX - INTERLISP, MSG, TVEDIT, BBD, LINK- there is nothing even approaching equivalence on the 370, despite its huge user community. These programs greatly facilitate communication with other researchers in the SUMEX community, documentation of our programs, and the rapid interactive development of the programs themselves. The development of a program involving extensive symbolic processing and as large and complex as RX at the SCIP facility, would require a staff many times as large as ours. The SUMEX environment greatly increases the productive potential of a research group such as ours to the point where a large project like RX becomes feasible.

Other Computational Resources

It is clear that the scope of potential application of the RX Project is vast. Even within the term of the current SUMEX-AIM grant period through July, 1981, we anticipate the involvement of several of the national ARAMIS collaborating institutions in developing and testing arthritis knowledge bases which reflect their own patient populations and therapeutic biases. The current SUMEX machine configuration will not be able to support this national interaction because the central processors of the KI-10 are already taxed to the limit. Ours is among the SUMEX groups which would greatly benefit by the addition of one or more PDP-10 compatible machines, which could provide dedicated support to our anticipated national user community. Another resource which we will need shortly is a faster and more reliable means for transferring data interactively between SUMEX and the SCIP IBM 370. Our current method utilizes a 2400 baud line with transmission from SCIP to SUMEX only, and is fraught with a high error rate. This is adequate for the current period of software development, when data can be

checked by hand; but will be useless for bulk transfer of patient data, as will be needed when other data banks need to be rapidly processed.

4.3 Pilot AIM Projects

The following are descriptions of the informal pilot projects currently using the AIM portion of the SUMEX-AIM resource pending funding, and full review and authorization.

4.3.1 Communication Enhancement Project

Communication Enhancement Project

John B. Eulenberg and Carl V. Page
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I) Summary of Research Program.

A) Technical goals.

The major goal of this research is the design of intelligent speech prostheses for persons who experience severe communication handicaps. Essential subgoals are:

- (1) Design of input devices which can be used by persons whose movement is greatly restricted.
- (2) Development of software for text-to-speech production.
- (3) Research in knowledge representations for syntax and semantics of spoken English in restricted real world domains.
- (4) Development of micro-computer based portable speech prostheses.

B) Medical Relevance and Collaboration.

Members of our group are in touch with Dr. Kenneth Colby and his group at UCLA who have been working on similar problems for people who have aphasia.

The need for such technology in the medical area is very great. Millions of people around the world lead isolated existences unable to communicate because of stroke, traumatic brain injury, cerebral palsy or other causes. The availability of inexpensive micro-processors and voice synthesizers allows development of complex experimental systems to study human communication. The knowledge gained from these experimental systems should lead in a few years to prototypes of very low cost which will permit many people to engage in the vital acts of communication required for a "normal" life in human society.

Despite the importance of the problems in this area, it has been difficult to coordinate the many professions which are involved. We believe that both research and the support of research in this area suffers from the lack of an identifiable community of workers. To alleviate this problem, we have joined with the Trace Center of the U. of Wisconsin to publish the first newsletter for dissemination in this area called "Communication Outlook", the first issue was published in April, 1978. There are now over 1100 paid subscribers. Subscribers and contributors to the Newsletter come from a wide variety of disciplines and from many countries. John B. Eulenberg helped to organize the first Federal workshop for governmental agencies who have some interest in funding work in these areas. Represented were the Bureau of Education for the Handicapped, The Veterans Administration, The Civil Service Commission, NIH, NSF, and others. We

have also been in touch with United Cerebral Palsy associations at the state and national levels. Much of our effort has been in educating those medical, educational, and governmental communities with an interest in this area on the available technology since most of them are not accustomed to funding the development of high-technology systems.

C) Progress summary.

Although some facets of the research have been underway at MSU for several years, we have been using SUMEX-AIM for two years, having received our password in March, 1977.

During the last past two years, we have:

1) Organized a research team of 4 students possessing background in artificial intelligence lead by Dr. Carl V. Page to start a semantics-speech generator. This group had a very primitive prototype (written in Sail) running in June, 1977. The system uses statistical, grammatical and semantic information to generate sentences by anticipation. A similar group was organized in 1978 but it produced well documented but not fully debugged programs. One of the students from the original group expects to work on the project this summer. 2) Converted a large program (Orthophone) for English text to speech synthesizer codes to SAIL from Algol.

3) Obtained local support for terminals and space to use the SUMEX-AIM facility. At present, the lack of a dedicated tie-line from East Lansing to Tymshare in Ann Arbor or Detroit is a problem for us during 0600 to 0900 PST.

4) Last year, Dr. Reid of our project designed and built a wheel-chair portable personal communication system for a 10 year old boy who has cerebral palsy. It is micro-computer based and can accept inputs via an adaptive switch from a series of menus displayed on a TV screen, via Morse code, or by a keyboard. Its outputs can be TV display, hard copy, spoken English, Morse code, or musical sounds. As the memory available for small systems will soon be substantial, we will need to specify the content and connection of the choice menus using the knowledge gained in our SUMEX-AIM project. Although our prototype for semantic generation has not run satisfactorily, it has influenced the design of the next system, the "SAL" board for wheel-chairs described below. 5) This year a communication aid using knowledge sources has been built into a lap board. Called the "SAL" prosthesis (Semantically accessible language), it uses a magnetic input to translate Bliss symbols into spoken language. Some ideas from the grammatical portions of our SUMEX-AIM project have found their way into the SAL system. The SAL system consists of an aluminum encased lap tray with an array of 252 reed switches arranged in a 12 row by 21 column matrix. Spacing between switches is one inch. They are activated by a small magnet held by the user on a mitt or a finger splint. The keyboard is interfaced to a Southwest Technical Products 6800 computer possessing 8K of EPROM and 8K of RAM. Voice output is from a Votrax VS-6 sound synthesizer while visual output is provided by a LED array. The current system allows 512 lexical items. Frame cells provide a choice of syntactic frame, which the user may specify at the inception of the formation of a sentence to supply structural information. Each syntactic frame is a skeletal syntactic phrase marker representing a class of sentence structures. After choosing a given syntactic frame, the user goes on to choose the lexical items. The generation of appropriate pronouns depends on

their role in the sentence. Thus the Bliss symbol for the speaker will come out "I" or "me" depending on the role. The system uses syntactic, phonetic, and orthographic features of previous inputs in order to generate its outputs. We expect to gain experience from our SUMEX-AIM prototype to guide the choice of semantics for the successors of this system. 6) Dr. John Eulenberg will be taking his Sabbatical leave in Palo Alto beginning in September, 1979. He will be associated with the Childrens' Hospital at Stanford and Telesensory Systems Inc. We have found in the past that SUMEX-AIM has provided us with a means to communicate with other members of our project when they were California. It is very important for the many ongoing projects which we have to be able keep Dr. Eulenberg in close communication with the rest of our project during his leave.

7) We have built and tested a myoelectric interface and used it (together with a miniature FM transmitter) for input of changing muscle potentials into a computer. There is reason to believe that this means of input may provide a higher bit rate than other known means for those people who possess severe cerebral palsy.

8) We continue to develop basic educational software for severely impaired persons. For example we have developed a "talking" system for drilling students in Bliss symbolics. Another system we have developed teaches spelling using a voice synthesizer and TV screen. A classroom in a Northville, Michigan public school now contains a Nova 2/10 for the evaluation of our systems.

D) Up-to-date list of publications. (1976 to date)
By John B. Eulenberg

"Technical Systems Development, Headin", Interim Report, April, 1976,
Experimental Applications of Two-Way Cable Delivery, NSF Grant No. APR 75-14286.

"Interactive New Hired Information Access System with Both Voice and Hard Copy Output: User's Guide to NHQUERRY", April 11, 1976 (With Steven Kludt and Jerome Jackson (Artificial Language Laboratory Report AEB 041176))

"Language Individualization in a Computer-Based Speech Prosthesis System",
National Computer Conference, New York, June 9, 1976.

"Individualization in a Speech Prosthesis System", Proceedings of 1976 Conference
on Systems and Devices for the Disabled, June 10, 1976.

"The LEAF Language", Interim Report, September, 1976, NSF Grant No. APR 75-14286.

"Microprocessor-Based Artificial Language for Communication Prostheses", with M. R. Rahimi, Proc. of the National Electronics Conference, Vol. XXXI, October, 1977.

"A programmable Multi-Channel Modem Output Switch", September 22, 1976, with Joseph C. Gehman and Juha Koljonen (Artificial Language Laboratory Report AEB 092276)

"SMPTE Time Code Interface and Computer-Controlled Video Switcher", with Michael Gorbitt and Dennis Phillips, Interim Report, March, 1977 NSF Grant APR 75-14286.

"Representation of Language Space in Speech Prostheses", with R. Reid and M. Rahimi, Proc. of Fourth Annual Conference on Systems and Devices for the Disabled, June, 1977.

"Administration and Management of a Computer-Based Communication Enhancement Program", with M. R. Rahimi and L. Neiswander, Proc. of Amer. Acad. for Cerebral Palsy and Developmental Medicine, October, 1977. "When [-VOICE] becomes [+VOICE]- The Phonological Competence of People Who Cannot Speak", with Carol Myers Scotton, Proceedings of the Annual Confer. of the Linguistic Soc. of America, December, 1977.

"Toward a Semantically Accessible Communication Aid", (With M. A Rahimi) Proceedings of the National Electronics Conference, Vol. xxxii, Chicago, Illinois, October, 1978.

By Carl V. Page:

"Heuristics for Signature Table Analysis as a Pattern Recognition Technique", IEEE Transactions on Systems, Man and Cybernetics, Vol. SMC-7, No. 2, February 1977.

"Discriminant Grammars, an Alternative to Parsing". with Alan Filipski, Proceedings of the IEEE Workshop on Picture Processing, Computer Graphics, and Pattern Recognition, April 22, 1977. "Pattern Recognition and Data structures". Chapter in "Data Structures in Computer Graphics and Pattern Recognition" Edited by Allen Klinger, Academic Press, 1977. "A Survey of Artificial Intelligence in Computer-Aided Instruction", with Alice Gable (To appear in the International Journal of Man-Machine Systems, 1979) "Economic Consequences of Robots Possessing Computer Vision Systems", Proceedings of the Upper-Midwest Small College Computer Conference, St. Cloud State University, St. Cloud, Minn. April, 1979.

II. INTERACTION WITH SUMEX-AIM RESOURCE

A. Collaborations and medical use of programs via SUMEX.

We have shown Mycin and Puff to physicians and clinical staff and discussions continue with them concerning possible research. During a visit to our campus in October, Dr. Bruce Buchanan lectured on Mycin and stimulated some of our Medical School faculty to explore research opportunities with us. As a consequence, Dr. Carl V. Page has participated in a proposal to NSF with Dr. Su-Wah Chan (principal investigator) titled "A Structural Analysis of Problem Complexity in Information Processing Behaviors as Related to Human Problem Solving". We hope that some other research possibilities derive from this effort.

B. Sharing and interactions with other SUMEX-AIM projects.

During the past year we have had personal contact with the SUMEX-AIM staff. Dr. Eulenberg attended the 1978 Workshop in the Summer. Dr. Page used the facility while working in California as a means keep in touch with the project in East Lansing. The communication aspect of the project has been useful for us in the past and will continue to be so in the future inasmuch as Dr. Eulenberg will be spending his Sabbatical in Palo Alto.

C. Critique of resource management.

We have found the staff to be professional and helpful. We have not used the system enough to comment on the management of the facility except to say that we have become somewhat disillusioned with the SAIL compiler.

III. RESEARCH PLANS (8/79-7/81)

A. Long Range project goals and plans.

We will continue to explore the interactions of different knowledge sources in the problem of generation of language. Such information as is learned will be scaled down so that it can be used in the design of portable, intelligent, speech prostheses.

B. Justification and requirements for continued SUMEX use.

We do not require any more resources than we have had in the past. Unfortunately our SUMEX research has not had the priority with us that it deserves. In one sense, our SUMEX research represents to us the future of work in this area, but we are involved with commitments for systems for communication enhancement that must be delivered soon. We expect to change the pattern of our funding to

emphasize the kinds of problems we have addressed to SUMEX, beginning the process next year. Our prototype system on SUMEX has been built by volunteer student effort rather than our financial support. We hope to change this policy when pressing needs are satisfied. Our prototype has already had some influence on the design of a wheel-chair portable system, the SAL prosthesis mentioned above. We have planned to incorporate at least one Ph. D. thesis into this research area. One of our former employees, Mr. Douglas Appelt has been doing his thesis in this area at Stanford and we believe that it is a good area. However, before we can advise a student to start a thesis dependent on the system, we need assurance that we will have access to SUMEX for at least two years at some reasonable level comparable to what we have now.

C. Other Computational needs.

We use minicomputers and the central computers at MSU in addition to SUMEX. We have no plans to secure any additional equipment.

D. Recommendations for future community and resource development.

1. We have not heard much lately about the KRL language. If it is available or can be made available, we would be interested in considering it for our project.
2. We would be interested programs to help scale down a system developed on SUMEX-AIM to smaller machines.
3. We are interested in programs to facilitate the hardware design process for microcomputer based systems.

4.3.2 Computerized Psychopharmacology Advisor

A Computerized Psychopharmacology Advisor

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I. Summary Research Program

A. Technical Goals.

We are developing a computer-based automated system for education and consultation in clinical psychopharmacology. Our technical goals are envisioned in three phases:

- . To develop a theory of expert teaching, consulting and decision-making in clinical psychopharmacology.
- . To model this theory on a computer system which responds in real time and communicates in natural language.
- . To evaluate this theory and model as a representation of psychiatric knowledge by analyzing both the performance of the system and the effort required for the system's development.

B. Medical Relevance and Collaboration.

1. Medical Relevance.

For many years, it has been recognized that potent psychopharmacological agents are frequently used in an unsystematic manner. There are at least 50 discrete syndromes currently identified in clinical psychiatry which have unique hierarchies of plausible pharmacological treatments. Each therapeutic regimen in each hierarchy may involve several classes of drugs which can often be preferentially ranked. A particular member of a class of drugs may be recommended on the basis of a patient's medical history, family history, response to previous treatments, current physical status, or current mental status. In addition, each treatment program has its own set of potential side effects, adverse reactions and drug-drug, drug-host, drug-age, drug-gender, drug-state of health, and drug-other treatment interactions.

Conventional sources of information for education or verification (books, journals, lectures, and seminars) are seldom quickly accessible or specifically pertinent. A traditional alternative is to consult a specialist. In addition to availability, reliability and validity, a good consultant has the ability to understand questions in their proper context and sequence, to give advice which can be explained or documented as needed, and to provide follow-up consultations which incorporate new information from clinical developments or additional expertise.

Our research on the Clinical Psychopharmacology Advisor is directed towards implementing all of the characteristics of a good consultant, which have only been outlined above, in a functional computer program. To our knowledge, no other computer program currently available, or under development, is pursuing all of these goals in clinical psychopharmacology.

2. Collaboration.

2.1 Principal Investigator: Jon F. Heiser, M.D., Associate Professor,
Department of Psychiatry and Behavioral Sciences

2.2 Co-principal Investigator: Ruven E. Brooks, Ph.D., Assistant Professor,
Department of Psychiatry and Behavioral Sciences

2.3 Pharmacist, University of Texas Medical Branch: Carla Maria Brandt,
B.S. (January 1979-present)

2.4 Resident Physician, Department of Psychiatry and Behavioral Sciences:
Rao Chalasani, M.D. (April-June, 1979)

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C. Progress Summary.

After carefully reviewing alternative contexts in which to generate the Psychopharmacology Advisor, we selected the EMYCIN software. MYCIN is a computer program which functions as a consultant in the diagnosis and treatment of infectious diseases. EMYCIN is a version of the MYCIN system with all the knowledge and references to infectious disease removed but with all the features for diagnosis, treatment recommendation, explanation and knowledge acquisition retained. Our choice of EMYCIN was determined by the availability of the EMYCIN software (including a significant amount of professional consultation, collaboration and system maintenance supplied by the MYCIN staff), the suitability of EMYCIN to most of our initial design considerations, and the desire of the MYCIN staff to test the EMYCIN software in a different clinical domain. EMYCIN has thus become our working theory and model of expert teaching, consulting and decision-making in clinical psychopharmacology.

Our initial goal was to develop a small, but fully functioning, Clinical Psychopharmacology Advisor. Approximately 250 rules, utilizing about 120 clinical parameters, were developed and used to diagnose and recommend therapy. The system, affectionately called HEADMED, had sound knowledge about the differential diagnosis of the major affective disorders and schizophrenia. The Psychopharmacology Advisor had perfunctory information concerning paranoid disorders and personality disorders. HEADMED also had skeletal knowledge about neuroses, behavior disorders, substance abuse, organic brain disorders, including both the type of brain disorder (e.g. delirium or dementia), and the cause of brain disorders (e.g. intoxication or trauma). The program has never known anything about child psychiatry, sexual disorders and other psychiatric conditions.

The HEADMED software had the capability of recommending a drug treatment, if indicated, and of cautioning about potentially harmful interactions with a compromised host and with other chemical substances. The system also could print out advice concerning dose and duration of therapy, pharmacokinetics, warnings about common side effects and possible adverse reactions.

Having been satisfied with the feasibility of using EMYCIN as a language for performing consultations in clinical psychopharmacology, our interest shifted to critically evaluating this application of EMYCIN and to modifying data structures and control mechanisms so that a a consultation process which is more natural, complete, and accurate occurs. We have also begun concentrating our attention on psychiatric disorders whose management might include prescription of a tricyclic antidepressant, one of the major classes of psychotherapeutic medications, and on outputting individual case-oriented advice and precautions concerning management and monitoring of a patient receiving a tricyclic antidepressant medication (see reference I.D.5 below). Thus we have begun to develop knowledge structures which can utilize this information to compute diagnostic formulations and therapeutic plans which are highly specific to the unique properties and circumstances of a particular patient.

We have discovered what we believe is an essential design problem for medical expert systems, that of controlling the amount and the type of information which the system requests from the user. This problem is inherent in medical expert systems because of the nature of the distribution of clinical states, and the nature of the training and the background of physicians. The problem also exists for human consultants, and a complete and general solution for computer systems is probably not achievable. However, several techniques show promise for reducing the magnitude of the problem in various clinical domains. These include system use of dynamic and static domain models, user control over sophistication level, and user access to the rationales behind information requests.

D. List of Relevant Publications.

1. Heiser, J.F., Brooks, R.E., and Ballard, J.P. Artificial Intelligence in Psychopharmacology. Abstracts - VI World Congress of Psychiatry, Honolulu, Hawaii, 28 August - 03 September 1977, page 135.
2. Heiser, J.F., Brooks, R.E., and Ballard, J.P. A Computerized Psychopharmacology Advisor. Continuing Medical Education Syllabus and Scientific Proceedings in Summary Form, The 131st Annual Meeting of the American Psychiatric Association, Atlanta, Georgia, 8-12 May 1978, American Psychiatric Association, Washington D.C., 1978, page 216.
3. Heiser, J.F., Brooks, R.E., and Ballard, J.P. A Computerized Psychopharmacology Advisor. The 11th C.I.N.P. Congress, Collegium Internationale Neuro-Psychopharmacologicum, 9-14 July 1978, Vienna, Austria, Book of Abstracts, page 233, c/o INTERCONVENTION, Kinderspitalgasse 5, A-1095, Vienna, Austria.
4. Heiser, J.F. and Brooks, R.E. Design Considerations for a Clinical Psychopharmacology Advisor. In Orthner, F.H. (ed.), Proceedings, The Second Annual Symposium on Computer Applications in Medical Care, 5-9 November 1978, Washington, D.C., Institute of Electrical and Electronics Engineers, Inc., New York, 1978, pages 278-286.
5. Cutler, N.R. and Heiser, J.F. The Tricyclic Antidepressants. Journal of the American Medical Association, vol. 240, pages 2264-2266 (Editorial comment on page 2287. Error retraction: "Corrections", vol.241, page 566. Letters to the Editor and replies, in press.)

6. Heiser, J.F., Colby, K.M., Faught, W.S., and Parkison, R.C. Can Psychiatrists Distinguish a Computer Simulation of Paranoia from the Real Thing? Tentatively accepted for publication in the Journal of Psychiatric Research.
7. Brooks, R.E. and Heiser, J.F. Letter to the Editor, American Journal of Psychiatry (in press: vol. 136, page 857, June 1979), regarding the article Roberts, B.: A Look at Psychiatric Decision Making, American Journal of Psychiatry, volume 135, pages 1384-1387, 1978.
8. Heiser, J.F. Observations on Computerizing Clinical Psychopharmacology. Continuing Medical Education Syllabus and Scientific Proceedings in Summary Form, The 132nd Annual Meeting of the American Psychiatric Association, Chicago, Illinois, 14-18 May 1979 (in press).
9. Brooks, R.E. and Heiser, J.F. Controlling Question Asking in a Medical Expert System. Proceedings of the 6th International Joint Conference on Artificial Intelligence, 20-23 1979, Tokyo, Japan (in press).

II. Interactions with the SUMEX-AIM Resource.

A. Collaborations and Medical Use of Programs via SUMEX.

The MYCIN group has collaborated with our group since work on the Psychopharmacology Advisor began. The MYCIN group supplies invaluable software support to the EMYCIN program. Our group has participated in writing documentation of the EMYCIN software which presumably is useful to all EMYCIN users.

B. Sharing and Interactions with Other SUMEX-AIM Projects.

Collaboration with Kenneth Mark Colby, M.D. and members of the Higher Mental Functions Project, begun two years ago, has continued in the form of writing and having (tentatively) accepted for publication a paper reporting a "Turing Test" which was performed on-line on SUMEX, with the psychiatrist-judges located at the University of California, Irvine, the patient-person at the University of California, Los Angeles (UCLA) and PARRY at SUMEX. Prepublication copies of this paper (see I.D.6. above: Heiser et al. Can Psychiatrists Distinguish a Computer Simulation of Paranoia from the Real Thing?) are available upon request. In addition, demonstrations of the PARRY and DOCTOR programs have been given on-line, using SUMEX, to various groups of mental health professionals, computer scientists and other qualified and interested individuals.

C. Critique of Resource Management.

We continue to find the SUMEX resource a hospitable environment. We feel that the choice of operating system and associated utilities was an unusually good one, and it has become a standard against which we judge other systems.

We strongly support the decision to continue with the Tymshare network service; the negative effects on our work of the unpredictable patterns of response delay in the Telenet service seemed disproportionate to the small cost savings. (We suspect that the difference in performance levels raises some fundamental issues about the suitability of packet switched networks for terminal-remote host communications.)

The situation we criticized last year, in regard to the documentation of the EMYCIN software, has improved substantially with the availability of document files on the system. This has had an extremely positive impact on our work in informing us of useful software features which we otherwise had no idea existed.

We hope that this level of documentation will continue to be maintained in the future.

We are increasingly concerned with the level of system loading. We find ourselves increasingly restricting our work sessions to the 8am-10am period, as only during this time is a moderate level of load guaranteed.

III. Research Plans (August 1979 - July 1981)

A. Long Range Project Goals and Plans.

1. Evaluation of the Psychopharmacology Advisor.

When the performance of the Psychopharmacology Advisor approaches an optimal level in the judgment of the Principal Investigators and the Advisory Panels, a formal evaluation will be performed. Elaborate plans have been made for three types of evaluation: as a simulation of the Principal Investigator; as a national expert; and as an actual psychopharmacology advisor. In each evaluation the system will be tested on two sets of cases: one which represents the population of patients likely to be encountered in practice, thereby measuring whether HEADMED can do well what it must do most often; and one which represents unusual or exceedingly complicated cases, thereby measuring whether the program can do well in situations where usual practices may not suffice. Details of the evaluation plans are available upon request.

In order to evaluate the EMYCIN formalism regarding both its inherent properties as a consulting algorithm and its appropriateness for the domain of clinical psychopharmacology, we are seeking the answers to five questions:

- 1) Is it beneficial to capture knowledge and control structure in the same formalism
- 2) Are certainty factors a useful way in which to encode uncertain information
- 3) Can the needed input be captured through the parameter/value system
- 4) Are the rules really modular
- 5) Is the backward chaining rule structure appropriate

B. Justification and Requirements for Continued SUMEX Use.

As mentioned in the preceding section, we consider the use of the EMYCIN software as integral to our project, at least for the next two years, or until we have learned enough about the domain of clinical psychopharmacology to know how to supersede the EMYCIN formalism.

C. Our Needs and Plans for Other Computational Resources, beyond SUMEX/AIM.

Our only immediate need for other computational resources beyond SUMEX/AIM continues to be for local, high-speed printing, preferably combined with local file storage. Our current slow-speed printing is unsuitable for listings of large rule sets or of system code. The planned acquisition of a 1200 baud printing terminal may substantially reduce the problem.

Our future plans will depend greatly on the outcome of our current effort. If the EMYCIN formalism proves suitable for our domain, we may find the conversion effort sufficiently worthwhile to transport EMYCIN to our local environment. If we discover that a major redesign is needed, we will make our future computing plans in light of that design.

D. Recommendations for Future Community and Resource Development.

We recommend the acquisition of additional computing power for the SUMEX resource.

Alternatively, consideration should be given to developing portable versions of major systems so that users can run them at their own sites on a variety of host machines.

4.4 Pilot Stanford Projects

The following are descriptions of the informal pilot projects currently using the Stanford portion of the SUMEX-AIM resource pending funding, and full review and authorization.

4.4.1 Quantum Chemical Investigations

Theoretical Investigations of Biomolecular Structures

Dr. Gilda Loew
Molecular Theory Laboratory
Department of Genetics
Stanford University Medical School

I. Summary of Research Program

The focus of the molecular theory laboratory is the application and development of computer-based techniques for characterizing molecular conformation, electronic structures, molecular interactions, and chemical and biochemical reactivity. A variety of biomedical problems is under investigation using interactive computational tools that guide biochemists and pharmacologists in modeling metabolic processes and drug-receptor interactions, and in screening chemicals for carcinogenicity.

A brief summary of our major research interests is given below.

A. Chemical Carcinogenesis

We are developing screening algorithms for twelve classes of known and suspected carcinogens under a three-year contract with the National Cancer Institute. The goal of this project is to determine mechanistically meaningful molecular parameters which correlate with known mutagenic and carcinogenic potencies, and to incorporate these parameters into heuristic screening procedures for untested compounds. A particular emphasis is on understanding alternative models for metabolic activation and ultimate interaction with DNA (references 1-6).

B. Mechanisms of Opiate Action

We have continued our studies to identify and calculate the molecular properties that regulate the ratio of agonism to antagonism in morphine-like, flexible, and peptide opiates. We are also studying the interaction of opiates with model anionic receptor sites such as methyl sulfate and methyl phosphate. This work is in its sixth year of support from the National Institute of Drug Abuse.

The results of these studies can serve as a guide to medicinal chemists and pharmacologists interested in the design of non-addictive analgesics and their mode of action. We are currently collaborating with two such groups: one at SRI and one at UCSF Medical Center, Department of Pharmacology (Ref 7-10).

C. Mixed-Function Oxygenase Metabolism

The cytochrome P-450 family of enzymes plays an important role in activating and detoxifying a wide range of drugs and chemicals in mammalian organ systems. Under grants from NSF, NIH, and NCI, we are using computer programs to

characterize models of the biologically active states of the P-450 family, and to calculate electromagnetic properties of states leading to enzyme activation.

In complementary activity, we are developing chemical reactivity criteria for different classes of substrates such as aromatic carcinogens and general anesthetics. The goal of this work is to provide programs which will predict major metabolites of different drug classes and potential carcinogens, and thus serve as a guide in estimating their toxicity. To test the predictors developed, drug toxicity and chemical mutagenicity data generated by Professor Bruce Ames at U.C. Berkeley and other laboratories are being used (references 1,4,11,12).

D. Structure, Function, and Electromagnetic Properties of Heme Proteins

The procedure for the characterization of heme proteins initially requires a determination of a model for the active site. The model has to be large enough to realistically describe interactions at the active site, but not so large that it becomes economically infeasible to perform a calculation on the molecule. Once a general model is chosen, the specific geometry for the molecule must be determined. With the aid of experimental crystal structures of related compounds, we use the SUMEX-AIM facility to interactively determine an approximate model geometry. The atomic coordinates are transmitted over the ARPANET to the CDC-7600 computer at LBL, where large scale molecular orbital programs are used to calculate the electronic structure and conformation, as well as the mode of binding of a number of biologically relevant ligands such as CO, O₂, and CN⁻. The calculated electronic structures and conformations are then transmitted back to SUMEX where a set of auxiliary programs is used interactively to determine if the model yields values in agreement with experiment. These programs calculate measurable electromagnetic properties such as quadrupole splitting observed in Mossbauer resonance spectra, g-values and hyperfine splittings in electron spin resonance spectra, and magnetic moments. This correspondence between observables and basic molecular structure enhances the usefulness of experimental data in inferring such fundamental molecular properties as the nature of metal-ligand binding and how small changes in conformation at the active site affect biological function. This work has had continual support from NSF for the past twelve years (references 12,13).

E. Studies of Peptide Conformation

The specific link between amino acid sequence and three dimensional protein structure has been difficult to establish. Thus far X-ray crystallographic studies have provided the main source of information on protein structure. Statistical analyses of frequency of occurrence of individual amino acids and short peptide sequences in different protein conformations (e.g., helical and beta-turn regions) have recently been performed by Chou and Fasman at Brandeis University. With the tabulated frequencies they have transmitted to us as a data base, we have begun a program at SUMEX to determine the feasibility of using energy-conformation studies to link amino acid sequence to conformation. A pilot study of eight tetrapeptides (ref 14) has yielded favorable results.

A related interest is conformers of peptides with specific pharmacological or biological activity. In particular, conformational studies of endogenous peptide opiates and their analogs have been made to determine likely candidate structures for interactions at the opiate receptor. Results of such studies can serve as a guide to design of clinically useful peptide opiates.

II. Interactions with SUMEX-AIM Resource

A. Opiate Narcotics: Two groups, one at SRI and one at Beckman Corporation, are using our computer-generated results as a guide in the synthesis and testing of clinically useful alkaloid and peptide opiates. A group under Professor Horace Loh at the UCSF Pharmacology Department is using our results to study the mode of action of opiates with model receptors which are nerve-cell membrane components.

B. Dr. George Pack, now at the Illinois School of Medicine in Rockford, is using our programs via the TYMNET facility to study mechanisms of DNA denaturation.

C. Collaboration with NASA-Ames Life Science Division: SUMEX-AIM is used to communicate with a complex computer graphics system at NASA-Ames, which in turn is coupled to programs that search for low-energy molecular conformations. This combination of facilities is a powerful tool for investigating the interactions in drug-receptor and enzyme-inhibitor complexes. Using these programs, structure-activity profiles and energetically permissible conformational subspaces may be determined for different classes of compounds.

D. The National Resource for Computation in Chemistry recently became a part of the Lawrence Berkeley Laboratory computer center. We are utilizing SUMEX to exchange programs and expertise with NRCC staff.

E. The community of AIM scientists is a valuable resource in itself, and we have exchanged a great deal of information about hardware, software, and chemistry with other SUMEX users and staff. We are currently pursuing a new collaboration with Jim Nourse and Dennis Smith of the CONGEN and DENDRAL projects, linking their structure-generating capabilities with our programs to determine energetically feasible conformations. Such a set of conformations is necessary to aid in the interpretation and enhance the utility of NMR spectral data.

III. Research Plans

We plan to continue research in the same general areas as our current projects: systematic studies of iron-containing proteins; structure-activity studies of opiates and other drugs; drug metabolism and activation of chemical carcinogens; structure-activity studies of classes of chemical carcinogens; structure of adducts of small drugs and carcinogens to DNA components; and studies of peptide conformation.

A. Long Range Goals and Plans

1. We plan to continue developing programs that will aid in screening large numbers of compounds for carcinogenic/mutagenic activity. Such programs would provide a much needed cost- and time-effective alternative to current animal testing procedures.

2. We plan to continue studies of drug metabolism by cytochrome P-450. Our study will be broadened by consideration of many classes of drugs where

oxidative metabolism would contribute to toxicity or significantly alter efficacy or duration of action. These programs could aid the clinician in choice of drugs, and pharmacologists and medicinal chemists in design of safer and more effective analogs.

3. We plan to continue studies of opiate narcotics to understand the basis for agonist vs. antagonist behavior, and the mode in which diverse classes of opiates can bind to analgesic receptors.

4. We plan to continue studies linking structure, spectra, and biological function of heme proteins in their role as oxygen transport and electron transfer agents.

B. Justification for Continued SUMEX Use

Because of its unique interactive capability, SUMEX-AIM has become essential to our research efforts. The SUMEX system is an excellent environment for creating, debugging, and distributing programs and results. In addition, the communications facilities, such as software for handling messages and distributing bulletins of general interest, are unique to SUMEX and essential to keeping in touch with colleagues in computer science as well as in medicinal chemistry.

SUMEX will continue to play a central role in our research efforts, and we are looking at auxiliary equipment to optimize our use of the facility. We have recently enhanced our ability to communicate with SUMEX by acquiring a hard-copy terminal capable of transmitting and receiving at speeds up to 9600 baud. This unit is the first component of an intelligent preprocessing capability that we are developing. The system will be based on microcomputer technology and will provide virtually unlimited flexibility in distributing our processing load across several host computers.

In the short term, however, we envision a need for a modest (20%) increase in our file space allocation.

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4.4.2 Ultrasonic Imaging Project

Ultrasonic Imaging Project

James F. Brinkley, M.D. (Depts. Computer Science, Obstetrics and Gynecology)
W. D. McCallum, M.D. (Dept. Obstetrics and Gynecology)
Stanford University

I. Summary of Research Program

A. Technical Goals

The long range goal of this project is the development of an ultrasonic imaging and display system for three-dimensional modeling of body organs. The models will be used for non-invasive study of anatomic structure and shape as well as for calculation of accurate organ volumes for use in clinical diagnosis. Initially, the system will be used to determine fetal volume as an indicator of fetal weight; later it might be adapted to measure left ventricular volume, or liver and kidney volume.

The general method we plan to use is the reconstruction of an organ from a series of ultrasonic cross-sections taken in an arbitrary fashion. In this technique a real-time ultrasonic scanner is coupled to a three-dimensional acoustic position locating system so that the three-dimensional orientation of the scan plane is known at all times. A series of scans is recorded over the organ whose volume is being determined; at a later time a light pen is used to outline the borders of the organ for input to SUMEX. The computer then combines the position and light pen information into the reconstruction which may be displayed or used to find volume.

We plan to develop this system in phases, starting with an earlier version developed at the University of Washington. During the first phase the previous system will be adapted and extended to run in the SUMEX environment. A clinical study will then be carried out to determine its effectiveness in predicting fetal weight. At the same time computer vision techniques will be used to develop the system further in the direction of increased applicability and ease of use. We thus hope to develop a limited system in order to demonstrate the feasibility of the technique, and then to gradually extend it with more complex computer processing techniques, to the point where it becomes a useful clinical tool.

B. Medical relevance

This project is being developed in collaboration with the Ultrasound Division of the Department of Obstetrics at Stanford, of which W.D. McCallum is the head.

Fetal weight is known to be a strong indicator of fetal well-being: small babies generally do more poorly than larger ones. In addition, the rate of growth is an important indicator: fetuses which are "small-for-dates" tend to have higher morbidity and mortality. It is thought that these small-for-dates fetuses may be suffering from placental insufficiency, so that if the diagnosis could be

made soon enough early delivery might prevent some of the complications. In addition such growth curves would aid in understanding the normal physiology of the fetus. Several attempts have been made to use ultrasound for predicting fetal weight since ultrasound is painless, noninvasive, and apparently risk-free. These techniques generally use one or two measurements such as abdominal circumference or biparietal diameter in a multiple regression against weight. We recently studied several of these methods and concluded that the most accurate were about ± 200 gms/kg, which is not accurate enough for adequate growth curves (the fetus grows about 200 gms/week). The method we are proposing is based on the assumption that fetal weight is directly related to volume since the density of fetal tissue is nearly constant. We are hoping that by utilizing three dimensional information more accurate volumes and hence weights can be obtained.

In addition to its use in predicting fetal weight, this system could be used to determine other organ volumes such as that of the left ventricle. Left ventricular volumes are routinely obtained by means of cardiac catheterization in order to help characterize left ventricular function. Attempts to determine ventricular volume using one or two dimensional information from ultrasound has not as yet demonstrated the accuracy of angiography. Therefore, three-dimensional information should provide a more accurate means of non-invasively assessing the state of the left ventricle.

C. Progress Summary

During the four months since this project was approved we have concentrated on setting up the initial system to determine volume. The main projects have been to adapt the previous software to SUMEX, and to develop the data acquisition system necessary for obtaining the ultrasound scans and associated position information. The following tasks have been accomplished:

1. A three-dimensional line drawing package has been adapted to run with the OMNIGRAPH graphics system at SUMEX.
2. Most of the previously written data analysis programs have been extended and adapted to run at SUMEX.
3. Most of the data acquisition hardware has been obtained and is now ready to be integrated into a complete system. The hardware includes:
 - a) A Toshiba real-time ultrasonic phased array scanner, in routine clinical use at the Dept. of Obstetrics.
 - b) A Sony video tape recorder and Hitachi monitor, for use in recording the scans prior to their being outlined with the light pen.
 - c) A custom built acoustic position locating system for determining the position of the scan plane in space, supplied to us by W.E. Moritz at the University of Washington.
 - d) A Datamedia computer terminal for communicating with SUMEX and controlling the procedure.

- e) A microprocessor-based video graphics system supplied to us by Varian Corporation. This system includes a light pen, dual floppy disks and video display memory. During the data acquisition phase of a volume determination it will be used to outline the borders of the organ being imaged from scans recorded on video tape. The outline and position information will be stored on floppy disk prior to being transferred to SUMEX for analysis. During the analysis phase the system will act as a low resolution graphics terminal for confirming that the computer has developed an accurate model of the organ. (Higher resolution graphics will be displayed on the GT-40 terminal associated with SUMEX).

D. Publications

Brinkley, J.F., Moritz, W.E., Baker, D.W., "Ultrasonic Three-Dimensional Imaging and Volume From a Series of Arbitrary Sector Scans", to be published in *Ultrasound in Medicine and Biology*.

McCallum, W.D., Brinkley, J.F., "Estimation of Fetal Weight from Ultrasonic Measurements", *American Journal of Obstetrics and Gynecology*, 133:2, pp.195-200, Jan. 1979.

II. Interactions with SUMEX-AIM resource

A. Collaborations

None at present, although we hope to work with some of the many people in this community who have expertise in image processing.

B. Sharing and Interactions

Mostly personal contacts with the Heuristic Programming Project and MYCIN project at Stanford. The message facilities of SUMEX have been especially useful for maintaining these contacts.

C. Resource management

Generally acceptable at present since we are still developing programs. However we may have problems later if we try to do the clinical study in the afternoon since we often get bumped off the system.

III. Research Plans

A. Long Range project goals and plans

As mentioned in Part I we plan to implement this system in phases, each phase requiring use of more sophisticated artificial intelligence techniques. The major phases are as follows:

1) Set up prototype system and test its ability to predict fetal weight.

We are currently in the process of doing this. Most of the hardware has been acquired, and most of the programs for SUMEX have been written. At present we are programming the video graphics system and starting to integrate the components into a complete system for determining fetal volume. We will then have to calibrate the system on test objects before starting the clinical study. The clinical study is expected to take about two years, during which time we will be continuing to develop the prototype system.

2) Improve volume calculations

The method presently used to find volume is very cumbersome and works only for very regular objects. (For this reason we are not including the limbs in our initial fetal volume studies). The present method takes about 15 minutes of operator interaction with the computer (beyond the time taken to outline the scans with the light pen). The time required is due to the fact the the program uses a very simple algorithm to interpolate the points necessary for finding volume, and it often makes mistakes. By utilizing artificial intelligence techniques of heuristic search we hope to decrease this time.

3) Extend the technique to more irregular objects

Since fetal limbs clearly contribute to volume, and since we ultimately would like to develop accurate three-dimensional models of organs, we would like to extend this technique to handle more irregular objects. For this step we plan to utilize some of the results of the computer vision groups, particularly Tom Binford's group at the Stanford Artificial Intelligence Lab, to develop an internal model of an organ which can guide the program in its attempt to fit the outline information to a three-dimensional model. The most likely representation for this model would be some modification of the generalized cones developed by Binford for computer vision.

4) Automatic border recognition

In addition to the time taken to compute volume, a significant amount of time is required to outline the ultrasonic cross-sections with a light pen since about 20 scans are required for each volume. This fact alone may make the system too difficult to use except in a research setting. Therefore we would ultimately like the computer to do the outlining. Although ultrasonic image quality is still fairly poor, there is much work being devoted to improving the images, so in a few years we should see images which are more amenable to direct computer border recognition. In our proposed system the scans would be directly digitized and the model developed in phase 3 used to guide the program in its search for borders.

B. Justification for continued use of SUMEX

The goals of this project seem to be compatible with the general goals of SUMEX, ie to develop the uses of artificial intelligence in medicine. By concentrating on simple objectives at first we hope to demonstrate the utility of this method and therefore of the artificial intelligence techniques which will increasingly become a part of it.

In addition, our ability to use a general purpose system will greatly speed up our ability to develop new programs and to collaborate with others. We expect the SUMEX network connections to be especially useful for interacting with other groups working on image processing problems.

C. Needs for resources

For the first phase of our project the present system should be adequate unless we get bumped too often. The only additional resource we will need is a dedicated hardwired line to allow us to transfer data to SUMEX at a reasonable rate. (At present we operate at 150 baud). Once we get to the point of directly digitizing the ultrasound scans our needs will increase dramatically, and we will have to rethink them at that point.

Appendix IAI Handbook Outline

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This is a list of the Chapters in the Handbook. Articles in the first eight Chapters are expected to appear in Volume I. A tentative list of the all of articles in each Chapter follows.

- I. Introduction
- II. Search
- III. AI Programming Languages
- IV. Representation of Knowledge
- V. Natural Language Understanding
- VI. Speech Understanding
- VII. Applications-oriented AI Research
- VIII. Automatic Programming
- IX. Theorem Proving
- X. Vision
- XI. Robotics
- XII. Information Processing Psychology
- XIII. Learning and Inductive Inference
- XIV. Planning, Reasoning, and Problem Solving

I. INTRODUCTION

- A. The AI Handbook (intent, audience, style, use, outline)
- B. Overview of AI
- C. History of AI
- D. An Introduction to the AI Literature

II. Heuristic Search

- A. Overview
- B. Problem representation
 - 1. State-space representation
 - 2. Problem-reduction representation
 - 3. Game trees

- C. Search Methods
 - 1. Blind state-space search
 - 2. Blind AND/OR graph search
 - 3. Heuristic search in problem-solving
 - a. Basic concepts in Heuristic Search
 - b. A*: optimal search for an optimal solution
 - c. Relaxing the optimality requirement
 - d. Bidirectional search
 - 4. Heuristic search of an AND/OR graph
 - 5. Game tree search
 - a. Minimax
 - b. Alpha-beta
 - c. Heuristic Search of Game Trees
 - D. Example Search Programs
 - 1. Logic Theorist
 - 2. General Problem Solver
 - 3. Gelernter's geometry theorem-proving machine
 - 4. Symbolic Integration Programs
 - 5. STRIPS
 - 6. ABSTRIPS
- III. AI Programming Languages
- A. Historical Overview of AI Languages
 - B. Comparison of AI Language Features
 - C. LISP
- IV. Representation of Knowledge
- A. Issues and problems in representation theory
 - B. Survey of representation techniques
 - C. Representation Schemes
 - 1. Logic
 - 2. Semantic nets
 - 3. Production systems
 - 4. Procedural representations
 - 5. Semantic primitives
 - 6. Direct (Analogical) representations
 - 7. Higher Level Knowledge Structures
- V. Natural Language Understanding
- A. Overview - History & Issues
 - B. Grammars
 - 1. Review of formal grammars
 - 2. Transformational grammars
 - 3. Systemic grammars
 - 4. Case Grammars

- C. Parsing techniques
 - 1. Overview of parsing techniques
 - 2. Augmented transition nets, Woods
 - 3. CHARTS - GSP
- D. Text Generating systems
- E. Machine Translation
 - 1. Overview & history
 - 2. Wilks' machine translation work
- F. Natural Language Processing Systems
 - 1. Early NL systems
 - 2. PARRY
 - 3. MARGIE
 - 4. LUNAR
 - 5. SHRDLU
 - 6. SAM

VI. Speech Understanding Systems

- A. Overview
- B. Some early ARPA speech systems
 - 1. DRAGON
 - 2. HEARSAY I
 - 3. SPEECHLIS
- C. Recent Speech Systems
 - 1. HARPY
 - 2. HEARSAY II
 - 3. HWIM
 - 4. SRI-SDC System

VII. Applications-oriented AI Research

- A. Overview of AOAIR
- B. TEIRESIAS - Issues in Expert Systems Design
- C. Medicine
 - 1. Overview of Medical Applications Research
 - 2. MYCIN
 - 3. CASNET
 - 4. INTERNIST
 - 5. Present Illness Program (PIP)
 - 6. Digitalis Advisor
 - 7. IRIS
- D. Chemistry
 - 1. Overview of Applications in Chemistry
 - 2. Applications in Chemical Analysis
 - 3. The DENDRAL Programs
 - a. DENDRAL
 - b. CONGEN and its extensions
 - c. Meta-DENDRAL
 - 4. CRYVALIS
 - 5. Applications in Organic Synthesis

E. Mathematics

1. REDUCE
2. MACSYMA
3. AM

F. Education

1. Overviews
 - a. Historical Overview of AI Research in Educational Applications
 - b. Issues and Components of Intelligent CAI Systems
 2. SCHOLAR
 3. SOPHIE
 4. WEST
 5. BUGGY
 6. WUMPUS
 7. EXCHECK
 8. WHY
- G. Miscellaneous Applications Research
1. SRI Comp. Based Consultant
 2. PROSPECTOR
 3. RITA (Rand)
 4. AI applications to Information Retrieval

VIII. Automatic Programming

- A. Automatic Programming Overview
- B. Techniques for Program Specification
- C. Approaches to AP
- D. AP Systems
 1. PSI
 2. SAFE
 3. Programmer's Apprentice
 4. PECOS
 5. DAEDALUS
 6. PROSYSTEM-1
 7. Heidorn's IBM System
 8. LIBRA - Program Optimization

IX. THEOREM PROVING

- A. Overview
- B. Logic
- C. Resolution Theorem Proving
 1. Basic resolution method
 2. Syntactic ordering strategies
 3. Semantic & syntactic refinement
- D. Non-resolution theorem proving
 0. Overview
 1. Natural deduction
 2. Boyer-Moore
 3. LCF

- E. Uses of theorem proving
 - 1. Use in question answering
 - 2. Use in problem solving
 - 3. Theorem Proving languages
 - 4. Man-machine theorem proving
 - 5. In Automatic Programming
- F. Proof checkers

X. VISION

- A. Overview
- B. Image-level processing
 - 1. Overview
 - 2. Edge Detection
 - 3. Texture
 - 4. Region growing
 - 5. Overview of Pattern Recognition
- C. Spatial-level processing
 - 1. Overview
 - 2. Stereo information
 - 3. Shading
 - 4. Motion
- D. Object-level Processing
 - 1. Overview
 - 2. Generalized cones and cylinders
- E. Scene level processing
- F. Vision systems
 - 1. Polyhedral or Blocks World Vision
 - a. Overview
 - b. COPYDEMO
 - b. Guzman
 - c. Falk
 - d. Waltz
 - e. Navatya
 - 2. Robot vision systems
 - 3. Perceptrons

XI. ROBOTICS

- A. Overview
- B. Robot Planning and Problem Solving
- C. Arms
- D. Present Day Industrial Robots
- E. Robotics Programming Languages

XII. Information Processing Psychology

- A. Overview
- B. Memory Models
 - 1. Overview
 - 2. EPAM
 - 3. Semantic Net Models
 - a. Quillian & Collins
 - b. HAM-ACT (Anderson & Bower)
 - c. LNR ASNs
 - 4. Production Systems a Memory Models (Newell, Moran, ACT)
 - 5. Higher level structures (Schemas, scripts & Frames)
- C. Human Problem Solving
- D. Behavioral Modeling
 - 1. Belief Systems
 - 2. PARRY
 - 3. Conversational Postulates (Grice, TW)
 - 4. Abelson, J. Carbonell, Jr.,

XIII. Learning and Inductive Inference

- A. Overview
- B. Simple Inductive Tasks
 - 1. Sequence Extrapolation
 - 2. Grammatical Inference
- C. Pattern Recognition
 - 1. Character Recognition (Selfridge, etc.)
 - 2. Other (e.g. Speech)
- D. Learning Rules and Strategies of Games
 - 1. Formal Analysis
 - 2. Individual Examples of Games-learning programs
- E. Single Concept Formation
- F. Multiple Concept Formation: Structuring a Domain (AM, Meta-DENDRAL)
- G. Interactive Cumulation of Knowledge (TEIRESIAS)

XIV. Problem Solving, Planning & Reasoning by Analogy

- A. Overview of Problems Solving
- B. Planning
 - 1. Overview (pointers to discussions in Search, Robotics, AI Langs)
 - 2. STRIPS (see IID5)
 - 3. ABSTRIPS (see IID6)
 - 4. NOAH
 - 5. HACKER
 - 6. INTERPLAN (Tate)
 - 7. Rieger's inference engine ?
 - 8. Rutgers work (Schmidt, Sridharan) ?
 - 7. QA3 (see IXE1)

C. Reasoning by Analogy

1. Overview
2. Evans's ANALOGY Program
3. ZORBA
4. Winston (see Learning)

D. Constraint relaxation

1. Waltz (see Vision)
2. REF-ARF

E. Game playing

(This overview must point to work in search and discuss
GP programs of various misc. sorts)

Appendix IISatellite Machine Evaluation

In the Council award for our present three-year grant term, funds were approved to purchase an additional computer that would meet two pressing needs of the SUMEX-AIM community. First, it would serve as a dedicatable machine for more operational evaluation of mature programs such as INTERNIST, PUFF/VM, MYCIN, and DENDRAL. Second, it would augment the existing SUMEX capacity to help alleviate the chronically heavy load for program development. The following provides more detailed background information about future computing trends relevant to SUMEX-AIM community needs and evaluation summaries for the two candidate systems available to meet current SUMEX augmentation requirements.

Computing Trends:

As we projected in our application, this past year has indeed been a time of rapid change in the computing scene. Recently, however, the direction of future DEC and ARPANET community development efforts has clarified to the extent that a preferred course for near term SUMEX computer planning is clear.

- 1) DEC'S LONG-TERM PLANS - Over the past few months there has been increasing confirmation (although certainly no formal announcement) that DEC may be moving their development efforts from the PDP-10/20 series of machines to the VAX series. This decision is apparently based on the limited address space of the PDP-10 and the difficulty of changing this aspect of its architecture. We will likely not see a tangible effect of this decision for 2-3 years on TOPS-20 support. We also will not see the previously expected, more cost-effective version of the 2020 that could have extended our current design options.

This trend toward VAX raises many additional questions for long-term planning including when large capacity VAX systems will be available; what time-sharing monitor will be able to provide comparable services to TENEX/TOPS-20; and when languages and software functionally equivalent to TENEX/TOPS-20 systems will be available on VAX. A usable VAX for AI work will probably take more than 2 years to mature.

- 2) INTERLISP STATUS - Also over the past year, Xerox has withdrawn its support for INTERLISP development and maintenance. INTERLISP, of course, forms the basis of many of our AI programs and its continued support is critical to SUMEX projects. A number of approaches to solve this problem have been under discussion in the ARPANET AI community. In view of DEC's apparent plans to concentrate its future work on VAX, ARPA has tentatively decided to support moving INTERLISP to VAX as the best long-term solution. This effort will also likely take 1-2 years for completion.

Based on this forecast, 2-3 years appears to be the time frame over which today's decision about how best to meet current SUMEX community needs must be assessed. It is clear that the optimum strategy is to purchase a relatively inexpensive PDP-10-compatible system as soon as possible. The technological

transition getting under way will take some time to become established and this will tend to preserve the value of such an investment even beyond the next 2-3 year period.

Evaluation of Currently Available Machines

There are only two candidate machines that are available, meet our requirements for software compatibility, and are priced within our budget; the DEC 2020 and the Foonly F2. Promises of additional alternatives have not materialized to date and we do not expect this situation to change. Following is a comparison of the strong and weak points of each of these candidates.

- 1) DEC 2020 - This machine was first announced near the end of 1977 and has a good field reliability record. It is fully supported by DEC and runs under the TOPS-20 operating system. Versions of INTERNIST, MYCIN, CONGEN, etc. already exist compatible with TOPS-20 INTERLISP so software compatibility is not an issue. LISP benchmarks done at SRI indicate the 2020 averages 5-10% faster than a KA-10 (a single KI-10 averages 70% faster than a KA-10). However, the 2020 is considerably slower than this average for floating point arithmetic since it has no floating point hardware. Also, the 2020 can be expected to support no more than 3 large LISP users simultaneously since its swapping performance is poor under load because of limited I/O capacity. Figure 3 gives a comparison of the performance of a 384K 2020 against single- and dual-processor KI-10's under increasing load. Curves for CPU-intensive and page-swapping-intensive loads are shown in the figure. It will be seen that the elapsed time needed to accumulate 1 KI-10-equivalent CPU minute on the 2020 is larger not only because of the intrinsically slower speed of the 2020 but also because of the poorer swapping performance of the disk paging used in TOPS-20 systems. The SUMEX KI-10 system uses a a fixed head swapping device to significant advantage.

With these load limitations and a list price of about \$250,000, the price/performance index of the 2020 would not be very impressive. However, we have recently been offered a used machine at a substantial discount that would be available almost immediately. This discount improves the price/performance index substantially and makes the 2020 a very attractive choice to meet current community needs.

There is also some hope that the list price of 2020's will drop over the next year so that other groups may be able to acquire more cost-effective versions if desired.

- 2) FOONLY F2 - This machine has been under development for the past year by a small company (Foonly, Inc.) that is an offshoot of the Stanford AI Laboratory. The first machine (a proprietary version) has recently been installed at TYMSHARE. It is not working yet to an extent to evaluate performance. Another F2 is to be delivered to Systems Control, Inc. in Palo Alto about the end of May. Based on design specifications, this machine will likely perform comparably to the DEC 2020 or slightly faster. It has the advantage of lower cost (\$122,500 for a configuration comparable to the 2020 above). The major disadvantages of the F2 are that Foonly is a very small company and few machines have been ordered or produced to date. In addition to raising questions about future support for the machine, these factors show

up in delays for integrated circuit deliveries and hence slow production of new machines. The SCI machine has slipped more than a month already and future deliveries are quoted to take at least 120 days "depending on semiconductor availability". The F2 would run a version of TENEX so software compatibility should be no problem. However, hardware and software maintenance would likely have to be done in-house with no long-term assurance of the availability of vendor assistance or parts. Another machine, the F4, has been discussed by Foonly and may have a factor of 1.5-2 increase of speed and would be priced comparably to the 2020. No orders for the F4 have been placed yet, however, and none has been built.

Based on this background, we feel the discounted DEC 2020 is the better solution. It is deliverable immediately, meets our needs for software compatibility, will be supported and maintainable by DEC for a long time, and will likely retain better future resale value. Given the unpredictable delivery schedule for Foonly machines, the smallness of the company, and the investment we would have to make in a "one of a kind" machine, we feel that the F2 does not have a sufficient price advantage to override the other attendant risks.

Appendix IIIAIM Management Committee Membership

The following are the membership lists of the various SUMEX-AIM management committees at the present time:

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