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APPENDIX H

AIM MANAGEMENT COMMITTEE MEMBERSHIP

The following are the membership lists of the various SUMEX-AIM management committees at the present time:

AIM EXECUTIVE COMMITTEE:

=====================

LEDERBERG, Dr. Joshua (LEDERBERG) (Chairman)
Department of Genetics, S331
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Stanford, California 94305
(415) 497-5801

AMAREL, Dr. Saul (AMAREL)
Department of Computer Science
Rutgers University
New Brunswick, New Jersey 08903
(201) 932-3546

BAKER, Dr. William R., Jr. (BAKER) (Executive Secretary)
Biotechnology Resources Program
National Institutes of Health
Building 31, Room 5B25
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LINDBERG, Dr. Donald (LINDBERG) (Adv Grp Member)
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AIM ADVISORY GROUP:
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REDDY, Dr. D. R. (REDDY)

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APPENDIX I

USER INFORMATION - GENERAL BROCHURE

Revised May 1976

The Stanford University Medical Experimental Computer (SUMEX) was established in January, 1974, to constitute the first national shared computing resource for medical research. An innovative effort to help biomedical scientists meet today's research requirements and to explore computer applications in many health fields ranging from basic research to bedside care, SUMEX is directed by Professor Joshua Lederberg, Chairman of Stanford's Department of Genetics. The project has been funded by a grant from the Division of Research Resources of the National Institutes of Health (Biotechnology Resources Program) for an initial term that expires in July, 1978.

At present, SUMEX consists of a powerful time-shared dual processor DEC-10 computer system. It is available to approved users throughout the United States over computer communications networks. The project's goals for its present 5-year term are: 1) the encouragement of applications of artificial intelligence in medicine (AIM), and 2) the managerial, administrative and technical demonstration of a nationally-shared technological resource for health research.

Such a resource offers scientists both a significant economic advantage in sharing expensive instrumentation and a greater opportunity to share ideas about their research. This is especially timely in computer science, a field whose intellectual and technological complexity tends to nurture relatively isolated research groups. Each group may then tend to pursue its own line of investigation with limited convergence on working programs available from others. In this respect, computer applications have demonstrated less mutual incremental progress from diverse sources than is typical of other sciences. The SUMEX-AIM project seeks to reduce these barriers to scientific cooperation in the field of artificial intelligence applied to health research.

ARTIFICIAL INTELLIGENCE

The term "artificial intelligence" (AI) refers to research efforts aimed at studying and mechanizing information-processing tasks that have required the application of some degree of human intelligence. Controversial speculations on how far this eventually may lead only distract from pragmatically useful applications of currently feasible art. The current emphasis in the field is to understand the underlying principles of a) efficient acquisition and utilization of material knowledge, and b) the programmed representation of conceptual abstractions in reasoning, deductive, and problem-solving activities. At present, these are far more specialized and inflexible than human intellectual functions; 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.

AI systems are characterized by complex computational processes that are primarily non-numeric, e.g., graph-searching and symbolic pattern analysis. They involve procedures whose execution is controlled by diverse types and forms of knowledge about a given task domain, such as models, fragments of "advice", and systems of constraints or heuristic rules. Unlike conventional algorithms commonly based on a well-tailored method for a given task, AI procedures typically use a multiplicity of methods in a highly conditional manner--depending on the specific data in the task and a variety of sources of relevant information. The tangible objective of this approach is the practical development of computer programs which, using formal and informal knowledge together with mechanized hypothesis formation and problem-solving procedures, will offer more general and effective consultative tools for the clinician and medical scientist. Contexts in which experimental data already are acquired by machine may offer even richer opportunities.

Each authorized project in the SUMEX-AIM community is concerned in some way with the application of these principles to medical and health research problems. This type of "intelligent" assistance by computer program is perhaps best illustrated by the following brief descriptions of a selected sample of SUMEX-AIM projects.

DENDRAL

The DENDRAL project at Stanford, under the direction of Professor Lederberg, Genetics; Professor Edward Feigenbaum, Computer Science; and Professor Carl Djerassi, Chemistry, is aimed at assisting the biochemist in interpreting molecular structures from spectroscopic, physical and chemical information. In cases where the characteristic spectra of a compound are not catalogued in libraries, the DENDRAL programs carry out the rather laborious processes a chemist must go through to interpret the spectrum from "first principles". One of the DENDRAL programs, CONGEN (for CONstrained structure GENeration), is an interactive program designed to assist the chemist in the enumeration of structural isomers, based on inferences about structural features of an unknown compound. These inferences, whether obtained from physical, chemical or spectroscopic data, are supplied to CONGEN as structural fragments and related information, using a standard computer terminal connected to SUMEX-AIM. The program uses atoms and superatoms (non-overlapping structural fragments known to be present in the molecule) to construct structures; the procedure is restricted by a variety of constraints on desired and undesired substructures and ring systems. There is no direct algorithmic path available to determine such a molecular structure from the spectral data--only the inferential process of hypothesis generation and testing within the domain of reasonable solutions defined by a knowledge of organic and physical chemistry.

This process, as implemented in the computer, is a simplified example of the cycle of inductive hypothesis--deductive verification that is often taught as a model of the scientific method. (Whether this is a faithful description of contemporary science is arguable, and how it may be implemented in the human brain is unknown. Regardless, these are useful leads rather than absolute preconditions for the pragmatic improvement of mechanized intelligence for more efficient problem-solving.) The elaboration of these approaches with existing hardware and software technologies is the most promising approach to enhancing the application of computers to the vaguely structured problems that dominate our task domains.

A new pilot project, MOLGEN, has been motivated by the success of the DENDRAL effort. MOLGEN uses similar paradigms in an effort to mechanize experiment-planning in molecular genetics, particularly work on DNA structure and inter-species transfer being conducted in Professor Lederberg's laboratory. Whereas the DENDRAL goal was a hypothesis (i.e., a chemical structure) to explain a set of experimental data, MOLGEN begins with a stipulated DNA structure and seeks suggested experiment plans that could either falsify or validate the asserted structure. At present, this entails a substantial effort in representing existing knowledge of experimental techniques (i.e., enzyme specificities, electron-microscopy, electrophoresis) and the physical biochemistry of DNA.

THE RUTGERS PROJECT
COMPUTERS IN BIOMEDICINE

Professor Saul Amarel, a Rutgers University computer scientist, directs several research efforts designed to introduce advanced methods in computer science--particularly in artificial intelligence and interactive data base systems--into specific areas of biomedical research.

For example, a group led by Professor Casimir Kulikowski is developing computer-based consultation systems for diseases of the eye in collaboration with Dr. Aran Safir, an ophthalmologist from the Mount Sinai School of Medicine. An important development in this area is the establishment of a national network of collaborators (called the ONET) for computer diagnosis and treatment of glaucoma. The computer system, which includes an elaborate pathophysiologic model of the disease, is being tested through the SUMEX-AIM network at five eye centers: Mount Sinai Hospital and Medical Center, New York; Washington University, St. Louis; The Johns Hopkins University, Baltimore; the University of Illinois at Chicago Circle; and the University of Miami. Glaucoma, in one form or another, affects 2% of all people over 40 years of age. It is a disease in which increased pressure within the eye may lead to irreparable optic nerve damage and blindness. The computer-based program has great potential for assisting clinicians and researchers in understanding the disease, diagnosing it more accurately and improving its treatment.

In another project, Professor Charles Schmidt, a social psychologist, is developing a theory of how people arrive at interpretations of the social actions of others in collaboration with Professor N.S. Sridharan, a computer scientist. The theory will be tested in situations such as the psychiatric interview and the legal trial. The computer system which currently represents the theory is called "Believer". It includes a large body of statements about people's motivations and actions.

The Rutgers project includes, in addition, several fundamental studies in artificial intelligence and system design. These provide much of the support needed for the development of complex systems such as the glaucoma consultation and the "Believer" programs.

SIMULATION AND EVALUATION OF CHEMICAL SYNTHESIS

The development of new drugs and the study of how drug structure is related to biological activity depends on the chemist's ability to synthesize new molecules and modify existing structures, e.g., incorporating isotopic labels into biomolecular substrates. The Simulation and Evaluation of Chemical Synthesis (SECS) project, directed by Dr. Todd Wipke, Associate Professor of Chemistry at the University of California, Santa Cruz, is aimed at assisting the synthetic chemist in designing stereospecific syntheses of complex bio-organic molecules.

The molecule to be synthesized is presented to SECS using interactive computer graphics. The program studies the chemical graph and also 3-dimensional and electronic models of the molecule which it knows how to construct; then, using fundamental chemical principles, and various heuristics, it works backwards from the target to predict possible precursors which are one synthetic step away from the target. The chemist selects the precursors to be considered by the program for further analysis. Thus, SECS acts as a consultant, working with the chemist to form a chemist-computer team. The chemist helps guide the search and decides when to stop the analysis. Knowledge about chemical transformations is expressed directly by chemists in ALCHEM, an English-like language interpreted by SECS. Goals for further development of the project include generation of constraining strategies based on symmetry, steric and electronic considerations, and expansion of the chemical transform data base.

In addition to its on-going development on the SUMEX-TYMNET system, an experimental version of SECS is available over TELENET from First Data Corporation in Waltham, Massachusetts. SECS also runs on a Univac system at the University of Strasbourg, France, and on PDP-10's at the Universities of Darmstadt and Heidelberg, Germany. Feedback from this outside use of SECS spotlights areas for needed work and provides positive evidence of the usefulness of SECS as a tool in synthetic design.

MYCIN
Computer-based Consultation in Clinical Therapeutics

Dr. Stanley Cohen, Professor and Head of the Division of Clinical Pharmacology at Stanford, directs this research in collaboration with Dr. Stanton Axline and with computer scientists interested in artificial intelligence and medical computing. The MYCIN system models the decision processes of medical experts, utilizing both clinical data and the judgmental knowledge of experts to provide physician nonspecialists with consultative advice regarding clinical therapeutics. Although initial research concerns the use of antimicrobial agents in the treatment of bacteremias, the system is being expanded to deal with the treatment of other infections.

The primary component of the system is the Consultation program which uses the physician's response to computer-generated questions about a patient to make deductions about the case. It then advises the physician on the infectious disease diagnosis and the recommended treatment for the patient. The utility and flexibility of this program are increased by three adjunct programs: 1) a Question-Answering program which answers questions about the system's knowledge base and about a specific consultation, 2) an Explanation program which justifies the consultative advice and explains the system's deduction process, and 3) a Knowledge Acquisition program which extends the knowledge base of the system through dialogue with an expert.

Goals for further development of the system include implementation and evaluation of the system in the clinical setting at the Stanford University and Palo Alto Veterans Administration Hospitals.

ACT
A Model of Human Cognition

The ACT Project is directed by Dr. John Anderson, Associate Professor of Psychology at Yale University. The ACT program provides a uniform set of theoretical mechanisms to model such aspects of human cognition as memory, inferential processes, language processing, and problem-solving. The knowledge base consists of two components. The propositional component is provided by an associative network encoding a set of known facts which provide the system's semantic memory. The procedural component consists of a set of productions which operate on the associative network. The production system used is considerably different than those in other currently available systems, e.g., Newell's PSG, and allows the system to operate on an associative network and to more accurately model certain aspects of human cognition.

ARTIFICIAL INTELLIGENCE METHODOLOGY APPLIED TO PROTEIN CRYSTALLOGRAPHY

Members of the artificial intelligence project at Stanford also are collaborating with Professor Joseph Kraut, Dr. Stephan Freer and other protein crystallographers at the University of California, San Diego. They are using the SUMEX-AIM facility as the central repository for programs, data and other information of common interest. The general objectives of the project are: 1) to identify critical tasks in protein structure elucidation which may benefit by the application of AI problem-solving techniques, and 2) to design and implement programs to perform those tasks.

Two principal task areas have been identified where collaboration is of practical and theoretical interest to both protein crystallographers and computer scientists working in AI: 1) interpreting a 3-dimensional electron density map, and 2) determining a plausible structure in the absence of phase information normally inferred from experimental isomorphous replacement data.

INTERNIST

The INTERNIST project, under the direction of Dr. Harry Pople and Dr. Jack Myers at the University of Pittsburgh, is a large-scale, computerized medical diagnostic system utilizing the methods and structures of artificial intelligence. Unlike most computer diagnostic programs, which are oriented to differential diagnosis in a rather limited area, the INTERNIST system deals with the general problem of diagnosis in internal medicine and currently accesses a medical data base encompassing approximately 50% of the major diseases in internal medicine.

MEDICAL INFORMATION SYSTEMS LABORATORY

The Medical Information Systems Laboratory (MISL) at the University of Illinois, Chicago Circle Campus, has been established under the direction of Dr. Bruce McCormick of the Department of Information Engineering, in collaboration with Dr. Morton Goldberg of the Department of Ophthalmology at the University of Illinois Medical Center.

The foremost goal of the resource is the exploration of artificial intelligence techniques in automated clinical decision-making in ophthalmology. Investigations into the construction of a data base in ophthalmology, and into distributed data base design, are ancillary goals. Incorporating reliable clinical information into the ophthalmology data base is a critical prerequisite to adequate clinical decision support. Core research concerns the exploration of inferential relationships between analytic data and the natural history of selected eye diseases, both in treated and untreated form.

MISL utilizes the computer facilities of the University of Illinois and the SUMEX-AIM network, providing the administrative structure for assembling the expertise of the collaborating departments. Serving as a bridge between diverse academic worlds, MISL promotes close involvement between engineering and medical faculty. The Illinois Eye and Ear Infirmary at the Medical Center, with a throughput of 50,000 patients per year, provides an ideal setting for the direct application of computer technology to real problems in clinical medicine.

SUMEX-AIM Management

A significant part of the SUMEX-AIM experiment has been the development of a management structure to maximize the utility of the computer capability for a national community.

Users of the SUMEX facility are divided for administrative purposes into two groups: 1) local, at Stanford University School of Medicine, and 2) national, elsewhere in the United States. As Principal Investigator for the SUMEX grant, Dr. Lederberg reviews Stanford medical school projects with the assistance of a local advisory committee. National users may gain access to the facility through an advisory panel for a national program in Artificial Intelligence in Medicine (AIM). The AIM Advisory Group consists of members-at-large of the AI and medical communities, facility users and the Principal Investigator of SUMEX as an ex-officio member. A representative of the National Institutes of Health-Biotechnology Resources Program (NIH-BRP) serves as Executive Secretary.

The SUMEX-AIM computing resource is allocated initially to qualified users without fee. This, of course, entails a careful review of the merits and priorities of proposed applications. At the direction of the Advisory Group, expenses related to communications and transportation to allow specific users to visit the facility also may be covered.

SUMEX-AIM is aware of the necessity of making the central facility available for trial use by potential users and collaborators. A GUEST mechanism has been established for those who have an indicated requirement for brief access to certain programs. Those who have been given an appropriate telephone number and login procedure can dial up SUMEX-AIM to exercise these programs on a trial basis. A specific objective of many user projects is the demonstration of their programs for the benefit of a highly dispersed national community.

USER QUALIFICATIONS

The SUMEX-AIM facility is a community effort, not merely a machine service. Applications for membership are judged on the basis of the following criteria:

1) The scientific interest and merit of the proposed research and its relevance to the health research missions of the NIH.

2) The congruence of research needs and goals to the AI functions of SUMEX-AIM as opposed to other computing alternatives.

3) The user's prospective contributions and role in the community, with respect to computer science, e.g., developing and sharing new systems or applications programs, sharing use of special hardware, etc.

4) The user's potential for substantive scientific cooperation with the community, e.g., to share expert knowledge in relevant scientific specialties.

5) The quantitative demands for specific elements of the SUMEX-AIM resource, taking account of both mean and ceiling requirements.

FACILITY INFORMATION

The computer facility, consists of dual DEC Model KI-10 CPU's running under a locally-developed dual processor TENEX operating system. It has 256K words (36-bit) of high-speed memory, 1.6M words of swapping storage, 70M words of disk storage, two 9-track 800 bpi industry-compatible tape units, a dual DEC-tape unit, a line printer, and communications-network interfaces providing user terminal access. SUMEX may be accessed by local telephone lines, through the TYMNET and as a host over the ARPANET communications network.

Program (software) support will evolve from the basic system as dictated by the research goals and needs of the user. Initially, available programs include a variety of TENEX user, utility and text editor programs. Major user languages include INTERLISP, SNOBOL, SAIL, FORTRAN-10, BLISS-10, BASIC, Macro-10, OMNIGRAPH and MLAB.

POTENTIAL USERS

Potential users seeking further information are invited to write:

Elliott Levinthal, Ph.D.
AIM User Liaison
SUMEX-AIM Computer Project
c/o Department of Genetics, S047
Stanford University Medical Center
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Telephone: (415) 497-5813

Procedures for access to SUMEX-AIM are governed by the:

Biotechnology Resources Program
Division of Research Resources
National Institutes of Health
Building 31, Room 5B19
Bethesda, Maryland 20014

APPENDIX J

GUIDELINES FOR PROSPECTIVE USERS

SUMEX-AIM RESOURCE
INFORMATION FOR POTENTIAL USERS

National users may gain access to the facility resources through an advisory panel for a national program in Artificial Intelligence in Medicine (AIM). The AIM Advisory Group consists of members-at-large of the AI and medical communities, facility users and the Principal Investigator of SUMEX as an ex-officio member. A representative of the National Institutes of Health-Biotechnology Resources Program (NIH-BRP) serves as Executive Secretary.

Under its enabling 5-year grant, the SUMEX-AIM computing resource is allocated to qualified users without fee. This, of course, entails a careful review of the merits and priorities of proposed applications. At the direction of the Advisory Group, expenses related to communications and transportation to allow specific users to visit the facility also may be covered.

USER QUALIFICATIONS

The SUMEX-AIM facility is a community effort, not merely a machine service. Applications for membership are judged on the basis of the following criteria:

1) The scientific interest and merit of the proposed research and its relevance to the health research missions of the NIH.

2) The congruence of research needs and goals to the AI functions of SUMEX-AIM as opposed to other computing alternatives.

3) The user's prospective contributions and role in the community, with respect to computer science, e.g., developing and sharing new systems or applications programs, sharing use of special hardware, etc.

4) The user's potential for substantive scientific cooperation with the community, e.g., to share expert knowledge in relevant scientific specialties.

5) The quantitative demands for specific elements of the SUMEX-AIM resource, taking account of both mean and ceiling requirements.

In many respects, this requires a different kind of information for judgment of proposals than that required for routine grant applications seeking monetary funding support. Information furnished by users also is indispensible to the SUMEX staff in conducting their planning, reporting and operational functions.

The following questionnaire encompasses the main issues concerning the Advisory Group. However, this should neither obstruct clear and imaginative presentation nor restrict format of the application. The potential user should prepare a statement in his own words using previously published material or other documents where applicable. In this respect, the questionnaire may be most useful as a checklist and reference for finding in other documentation the most cogent replies to the questions raised.

For users mounting complex and especially non-standard systems, the decision to affiliate with SUMEX may entail a heavy investment that would be at risk if the arrangement were suddenly terminated. The Advisory Group endeavors to follow a responsible and sensitive policy along these lines--one reason for cautious deliberation; and even in the harshest contingencies, it will make every effort to facilitate graceful entry and departure of qualified users. Conversely, it must have credible information about thoughtful plans for long-term requirements including eventual alternatives to SUMEX-AIM. SUMEX-AIM is a research resource, not an operational vehicle for health care. Many programs are expected to be investigated, developed and demonstrated on SUMEX-AIM with spinoffs for practical implementation on other systems. In some cases, the size, scope and probable validation of clinical trials would preclude their being undertaken on SUMEX-AIM as now constituted. Please be as explicit as possible in your plans for such outcomes.

Applicants, therefore, should submit:

1) One to two-page outline of the proposal.

2) Response to questionnaire, cross-referenced to supporting documents where applicable.

3) Supporting documents.

4) List of submitted materials, cross-referenced.

We would welcome a draft (2 copies) of your submission for informal comment if you so desire. However, for formal consideration by the SUMEX-AIM Advisory Group, please submit 13 copies of the material requested above in final form.

Elliott Levinthal, Ph.D.
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Stanford University Medical Center
Stanford, California 94305
Telephone: (415) 497-5813

May, 1976

SUMEX-AIM RESOURCE

QUESTIONNAIRE FOR POTENTIAL USERS

Please provide either a brief reply to the following or cite supporting documents.

A) MEDICAL AND COMPUTER SCIENCE GOALS

1) Describe the proposed research to be undertaken on the SUMEX-AIM resource.

2) How is this research presently supported? Please identify application and award statements in which the contingency of SUMEX-AIM availability is indicated. What is the current status of any application for grant support of related research by any federal agency? Please note if you have received notification of any disapproval or approval, pending funding, within the past three years. Budgetary information should be furnished where it concerns operating costs and personnel for computing support. Please furnish any contextual information concerning previous evaluation of your research plans by other scientific review groups.

3) What is the relevance of your research to the AI approach of SUMEX-AIM as opposed to other computing alternatives?

B) COLLABORATIVE COMMUNITY BUILDING

1) Will the programs designed in your research efforts have some possible general application to problems analogous to that research?

2) What application programs already publically available can you use in your research? Are these available on SUMEX-AIM or elsewhere?

3) What opportunities or difficulties do you anticipate with regard to making available your programs to other collaborators within a reasonable interval of publication of your work?

4) Are you interested in discussing with the SUMEX staff possible ways in which other artificial-intelligence research capabilities might interrelate with your work?

5) If approved as a user, would you advise us regarding collaborative opportunities similar to yours with other investigators in your field?

C) HARDWARE AND SOFTWARE REQUIREMENTS

1) What computer facilities are you now using in connection with your research or do you have available at your institution? In what respect do these not meet your research requirements?

2) What languages do you either use or wish to use? Will your research require the addition of major system programs or languages to the system? Will you maintain them? If you are committed to systems not now maintained at SUMEX, what effort would be required for conversion to and maintenance on the PDP-10 - TENEX system? What are the merits of the alternative plan of converting your application programs to one of the already available standards? Would the latter facilitate the objectives of Part B), Collaborative Community Building?

3) Can you estimate your requirements for CPU utilization and disk space? What time of day will your CPU utilization occur? Would it be convenient or possible for you to use the system during off-peak periods? Please indicate (as best you can) the basis for these estimates and the consequences of various levels of restriction or relaxation of access to different resources. SUMEX-AIM's tangible resources can be measured in terms of:

   a) CPU cycles.

   b) Connect time and communications.

   c) User terminals (In special cases these may be supported by SUMEX-AIM.).

   d) Disk space.

   e) Off-line media-printer outputs, tapes (At most, limited quantities to be mailed.).

   Can you estimate your requirements? With respect to a) and b), there are loading problems during the daily cycle.--Can you indicate the relative utility of prime-time (0900-1600 PST) vs. off-peak access?

4) What are your communication plans (TYMNET, ARPANET, other)? How will your communication and terminal costs be met? See following note concerning network connections to SUMEX-AIM.

5) If this is a development project, please indicate your long-term plans for software implementation in an applied context keeping in mind the research mission of SUMEX-AIM.

Our procedures are still evolving, and we welcome your suggestions about this framework for exchanging information. Needless to say, each question should be qualified a) "insofar as relevant to your proposal", and b) "to the extent of available information".

Please do not force a reply to a question that seems inappropriate. We prefer that you label it as such so that it can be dealt with properly in future dialogue.

Above all, we are eager to work with potential users in any way that would help minimize bureaucratic burdens and still permit a responsible regard for our accountability both to the NIH and the public. Please do not hesitate to address the substance of these requirements in the format most applicable to you.

NETWORK CONNECTIONS TO SUMEX-AIM

TYMNET

Attached is a list of available TYMNET nodes and associated telephone numbers. The cost to users of using TYMNET is the telephone charge from user location to the nearest TYMNET node. This is available only for communication to SUMEX-AIM and not for other facilities that may be connected to TYMNET. In some cases, there are "foreign exchanges" set up by users. These may offer less expensive communication. Details of these possibilities can best be learned by calling the nearest TYMNET node. The telephone company can provide information on comparative costs of leased lines, toll charges, etc. The initial capital investment for TYMNET installation as well as login and hourly charges is provided by SUMEX-AIM. Standard usage charges on TYMNET are approximately $3/connect-hour.

ARPANET

SUMEX-AIM is connected to the ARPANET. Our name is SUMEX-AIM; our nickname is AIM. We support the new TELNET protocol. Our network address is decimal 56, octal 70. This provides convenient access for ARPANET Hosts and Associates and those who have accounts with ARPANET.