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Appendix E

Scientific Subproject Abstracts

The following are brief abstracts of our collaborative research projects.

National AIM Project: ATTENDING Project:
A Critiquing Approach to
Expert Computer Advice

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Our project is exploring the "critiquing" approach to bringing computer-based advice to the practicing physician.

Critiquing is a different approach to the design of artificial intelligence based expert systems. Most medical expert systems attempt to simulate a physician's decision-making process. As a result, they have the clinical effect of trying to tell a physician what to do: how to practice medicine. In contrast, a critiquing system first asks the physician how he contemplates approaching his patient's care, and then critiques that plan. In the critique, the system discusses any risks or benefits of the proposed approach, and of any other approaches which might be preferred. It is anticipated that the critiquing approach may be particularly well suited for domains, like medicine, where decisions involve a great deal of *subjective* judgment.

To date, several prototype critiquing systems have been developed in different medical domains:

1. ATTENDING, the first system to implement the critiquing approach, critiques anesthetic management.

2. HT-ATTENDING critiques the pharmacologic management of essential hypertension.

3. VQ-ATTENDING critiques aspects of ventilator management.

4. PHEO-ATTENDING critiques the laboratory and radiologic workup of a patient for a suspected pheochromocytoma.

In addition, a domain-independent system, ESSENTIAL-ATTENDING, has been developed to facilitate the implementation of critiquing systems in other domains.

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Stanford Project: BBICU -- BLACKBOARD APPLICATIONS IN THE INTENSIVE CARE UNIT

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We are designing a data-interpretation and therapy-planning system for the intensive care unit (ICU). Fundamental research issues in temporal reasoning are associated with the ICU application area including assimilation of incoming data, representation of time-oriented intervals, and description of ongoing physiological processes [Fagan 84]. In addition, in ICUs of the 1990s, many more physiological measurements will need to be collected at frequent intervals, and increased access to the current medical record in coded format will be possible. Processing of incoming data will have to be opportunistic, selecting from a number of models that have different computational requirements and accuracy. We will use a blackboard architecture, known as BB1, that has evolved from earlier work on protein-structure elucidation and construction layout [Hayes-Roth 85]. BB1 is particularly well suited for the ICU project because it maintains separate blackboards for domain and control knowledge.

Although we have selected the blackboard structure as the organizing principle, many knowledge representation issues remain. First, we must represent the structure and function (anatomy and physiology) of the respiratory system. By characterizing the pathophysiology in terms of generic faults, we will create a more flexible means to diagnose problems in unusual situations -- in contrast to the phenomenological rules used in earlier systems.

Second, we must coalesce quantitative and qualitative models. The physiology of the respiratory and cardiac systems have been modeled in detail, but it is impractical to base the entire reasoning process on complex mathematical equations. Instead, we are developing methods to transform quantitative models into simpler formulations. We must make explicit the simplifying assumptions and associate them with their corresponding models, so that we can select an applicable model for situations of varying complexity.

Using the approach of our project for planning treatments for cancer patients [Langlotz 87], we will use strategic knowledge to create patient-specific specializations of standard treatment plans. We will use decision analytic methods to evaluate and explain the various treatment options available at any point in time. The long-term goal of this project is to embed the decision-making components within the data management tasks of the ICU.

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National AIM Project: DECISION SUPPORT FOR TIME-VARYING CLINICAL PROBLEMS

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Time-varying systems, which include many areas of medicine, science, economics, and business, can be described mathematically by differential equations. They are distinct from the pattern-matching and logic-based domains dealt with so successfully by existing expert system methods, because they can include feedback relationships. It is generally felt that they are best approached by enhancement of existing methods for deep model-based reasoning.

The goal of this project is to develop AI methods for capturing and using knowledge about time-varying systems. The strategy is to address general problems in model-based knowledge representation and reasoning. The intermediate objective is to develop methods which are powerful enough to work in selected realistic situations yet are general enough to be transportable to other, unrelated knowledge domains.

The tactical approach is to work on well-defined yet complex and interesting problems in the medical domain. We have, therefore, selected the human cardiovascular system as our prototype of a time-varying system, and are developing methods for representing and reasoning about its mechanical and electrical activities in the normal and diseased states.

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Stanford Project: GUIDON/NEOMYCIN --
KNOWLEDGE ENGINEERING
FOR TEACHING MEDICAL DIAGNOSIS

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The GUIDON/NEOMYCIN Project is a research program devoted to the development of a knowledge-based tutoring system for application to medicine. The key issue for the GUIDON/NEOMYCIN project is to develop a program that can provide advice similar in quality to that given by human experts, modeling how they structure their knowledge as well as their problem-solving procedures. The consultation program using this knowledge is called NEOMYCIN. NEOMYCIN's knowledge base, designed for use in a teaching application, is the subject material used by a family of instructional programs referred to collectively as GUIDON2. The problem-solving procedures are developed by running test cases through NEOMYCIN and comparing them to expert behavior. Also, we use NEOMYCIN as a test bed for the explanation capabilities incorporated in our instructional programs.

The goal of current work is to construct a knowledge-based tutoring system that teaches diagnostic strategies explicitly. By strategy, we mean plans for establishing a set of possible diagnoses, focusing on and confirming individual diagnoses, gathering data, and processing new data. The tutorial program has capabilities to recognize these plans, as well as to articulate strategies in explanations about how to do diagnosis. The strategies represented in the program, modeling techniques, and explanation techniques are wholly separate from the knowledge base, so that they can be used with many medical (and non-medical) domains. That is, the target program will be able to be tested with other knowledge bases, using system-building tools that we provide.

SOFTWARE AVAILABLE ON SUMEX

GUIDON--A system developed for intelligent computer-aided instruction. Although it was developed in the context of MYCIN's infectious disease knowledge base, the tutorial rules will operate upon any EMYCIN knowledge base.

NEOMYCIN--A consultation system derived from MYCIN, with the knowledge base greatly extended and reconfigured for use in teaching. In contrast with MYCIN, diagnostic procedures, common sense facts, and disease hierarchies are factored out of the basic finding/disease associations. The diagnostic procedures are abstract (not specific to any problem domain) and model human reasoning, unlike the exhaustive, top-down approach implicit in MYCIN's medical rules. This knowledge base is used in the GUIDON2 family of instructional programs, being developed on D-machines.

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National AIM Project: INTERNIST-I/QMR (Quick Medical Reference)

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The major goal of the INTERNIST-I/QMR Project is to produce a reliable and adequately complete diagnostic consultative program in the field of internal medicine. Although this program is intended primarily to aid skilled internists in complicated medical problems, the program may have spin-offs as a diagnostic and triage aid to physicians' assistants, rural health clinics, military medicine and space travel. In the design of INTERNIST-I and QMR, we have attempted to model the creative, problem-formulation aspect of the clinical reasoning process, and to design program components that can help physicians at key points in this process. The program can compose differential diagnoses, dynamically, on the basis of clinical evidence. During the course of an INTERNIST-I consultation, it is not uncommon for a number of such conjectured problem foci to be proposed and investigated. With the QMR program, the physician is given more control over the direction of the problem-solving activities than was possible with INTERNIST-I. QMR is broader in scope than INTERNIST-I in that it provides quick and efficient access to the INTERNIST-I/QMR knowledge base to provide low and intermediate level informational support for physicians' decision-making, in addition to providing consultative advice.

SOFTWARE AVAILABLE ON SUMEX

Versions of the INTERNIST-I KB are available for experimental use, with permission from the developers. In the past year, copies have been shared with Drs. Gregory Cooper and Homer Chin of Dr. Shortliffe's group at Stanford. The INTERNIST-I and QMR knowledge bases are Copyright 1986-88 by the University of Pittsburgh. Quick Medical Reference and QMR are registered trademarks of the University of Pittsburgh. The project continues to be oriented primarily towards research and development; hence, a stable production version of the system is not yet available for general use. QMR has been shared on a restricted basis with a limited number of academic colleagues, who have agreed to give the QMR development team feedback on the program's strengths and weaknesses.

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National AIM Project: MENTOR -- MEDICAL EVALUATION OF THERAPEUTIC ORDERS

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The goal of the MENTOR project is to implement and begin evaluation of a computer-based methodology for reducing therapeutic misadventures. The project uses an on-line expert system to continuously monitor the drug therapy of individual patients and generate specific warnings of potential and/or actual unintended effects of therapy. The appropriate patient information is automatically acquired through interfaces to a hospital information system. This data is monitored by a system that is capable of employing complex chains of reasoning to evaluate therapeutic decisions and arrive at valid conclusions in the context of all information available on the patient. The results reached by the system are fed back to the responsible physicians to assist future decision making.

Specific objectives of this project include:

1. Implement a prototype computer-based expert system to continuously monitor in-patient drug therapy that uses a modular medical knowledge base and a separate inference engine to apply the knowledge to specific situations.

2. Select a small number of important and frequently occurring drug therapy problems that can lead to therapeutic misadventures and construct a comprehensive knowledge base necessary to detect these situations.

3. Evaluate the prototype MENTOR system with respect to its impact on the on the physicians' therapeutic decision making as well as its effects on the patient in terms of specific mortality and morbidity measures.

The work in this project builds on the extensive previous work in drug monitoring done by these investigators in the Division of Clinical Pharmacology at Stanford and the University of Maryland School of Pharmacy.

Stanford Project: MOLGEN -- AN EXPERIMENT PLANNING SYSTEM FOR MOLECULAR GENETICS

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The MOLGEN project has focused on research into the applications of symbolic computation and inference to the field of molecular biology. This has taken the specific form of systems which provide assistance to the experimental scientist in various tasks, the most important of which have been the design of complex experiment plans and the analysis of nucleic acid sequences. Our current research concentrates on scientific discovery within the subdomain of regulatory genetics. We desire to explore the methodologies scientists use to modify, extend, and test theories of genetic regulation, and then emulate that process within a computational system.

Theory or model formation is a fundamental part of scientific research. Scientists both use and form such models dynamically. They are used to predict results (and therefore to suggest experiments tc test the model) and also to explain experimental results. Models are extended and revised both as a result of logical conclusions from existing premises and as a result of new experimental evidence.

Theory formation is a difficult cognitive task, and one in which there is substantial scope for intelligent computational assistance. Our research is toward building a system which can form theories to explain experimental evidence, can interact with a scientist to help to suggest experiments to discriminate among competing hypotheses, and can then revise and extend the growing model based upon the results of the experiments.

The MOLGEN project has continuing computer science goals of exploring issues of knowledge representation, problem-solving, discovery, and planning within a real and complex domain. The project operates in a framework of collaboration between the Heuristic Programming Project (HPP) in the Computer Science Department and various domain experts in the departments of Biochemistry, Medicine, and Biology. It draws from the experience of several other projects in the HPP which deal with applications of artificial intelligence to medicine, organic chemistry, and engineering.

SOFTWARE AVAILABLE ON SUMEX

SPEX system for experiment design.

UNITS system for knowledge representation and acquisition.

SEQ system for nucleotide sequence analysis.

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Stanford Project: ONCOCIN -- KNOWLEDGE ENGINEERING FOR ONCOLOGY CHEMOTHERAPY CONSULTATION

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The ONCOCIN Project is overseen by a collaborative group of physicians and computer scientists who are developing an intelligent system that uses the techniques of knowledge engineering to advise oncologists in the management of patients receiving cancer chemotherapy. The general research foci of the group members include knowledge acquisition, inexact reasoning, explanation, and the representation of time and of expert thinking patterns. Much of the work developed from research in the 1970's on the MYCIN and EMYCIN programs, early efforts that helped define the group's research directions for the coming decade. MYCIN and EMYCIN are still available on SUMEX for demonstration purposes.

The prototype ONCOCIN system is in limited experimental use by oncologists in the Stanford Oncology Clinic. Thus, much of the emphasis of this research has been on human engineering so that the physicians will accept the program as a useful adjunct to their patient care activities. ONCOCIN has generally been well-accepted since its introduction, and we are now testing a version of the program which runs on professional workstations (rather than the central SUMEX computer) so that it can be implemented and evaluated at sites away from the University.

Significant extensions to the basic ONCOCIN project have included the OPAL oncology knowledge acquisition system, the PROTEGE system for description of knowledge acquisition tools for clinical trial application areas, and the ONYX system for strategic therapy planning.

SOFTWARE AVAILABLE ON SUMEX

MYCIN-- A consultation system designed to assist physicians with the selection of antimicrobial therapy for severe infections. It has achieved expert level performance in formal evaluations of its ability to select therapy for bacteremia and meningitis. Although MYCIN is no longer the subject of an active research program, the system continues to be available on SUMEX for demonstration purposes and as a testing environment for other research projects.

EMYCIN-- The "essential MYCIN" system is a generalization of the MYCIN knowledge representation and control structure. It is designed to facilitate the development of new expert consultation systems for both clinical and non-medical domains.

ONCOCIN-- This system is in clinical use but requires Lisp machines to be run. Much of the knowledge in the domain of cancer chemotherapy is already well-specified in protocol documents, but expert judgments also need to be understood and modeled.

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National AIM Project: Computer-Aided Diagnosis of Lymph Node Pathology (PATHFINDER)

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The Pathfinder Project is centered on the construction of an expert system for assisting pathologists with the diagnosis of tissue pathology. Pathfinder research is focused on the domain of lymph node pathology. The project is based at the University of Southern California in collaboration with the Stanford University Medical Computer Science Group. Ongoing AIM research has been addressing fundamental problems of knowledge representation, reasoning strategies, user modeling, explanation, and user acceptance. The central focus of research has been on developing tractable knowledge acquisition and reasoning methods for probabilistic reasoning. In addition to the ongoing theoretical research, the team have implemented an expert system program and a tool for knowledge acquisition. The Pathfinder expert system provides diagnostic advice on eighty common benign and malignant diseases of the lymph nodes based on 150 histologic features. Currently a more sophisticated knowledge base that represents probabilistic dependencies is being developed. A probabilistic knowledge acquisition tool has been implemented on the Macintosh that enables a user to assess probabilistic relationships by graphically noting similarities and differences between diseases hypotheses.

SOFTWARE AVAILABLE ON SUMEX

Pathfinder -- A pilot version of the Pathfinder program is available for experimentation on the DEC 2060 computer. This version is an early version of the program that has not been completely tested.

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Stanford Project: PROTEAN Project

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The goals of this project are related both to biochemistry and artificial intelligence: (a) use existing AI methods to aid in the determination of the 3-dimensional structure of proteins in solution (not from x-ray crystallography proteins), and (b) use protein structure determination as a test problem for experiments with the AI problem-solving structure known as the Blackboard Model. Empirical data from nuclear magnetic resonance (NMR) and other sources may provide enough constraints on structural descriptions to allow protein chemists to bypass the laborious methods of crystallizing a protein and using X-ray crystallography to determine its structure. This problem exhibits considerable complexity, yet there is reason to believe that AI programs can be written that reason much as experts do to resolve these difficulties. A prototype knowledge-based system assembles major secondary structures of a protein into families of structures compatible with a given set of distance constraints under the control of an explicit assembly strategy. Structures can also be refined at the atomic level of detail using constraints within secondary structures and between amino acid side chains to further restrict the 3-dimensional structure found. By generalizing this approach to the assembly of arrangements of objects subject to constraints, we have developed a language for specifying actions and control for problem solving in similar problem domains.

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National AIM Project: KNOWLEDGE ENGINEERING FOR RADIATION THERAPY

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We are developing an expert system for planning of radiation therapy for head and neck cancers. The project will ultimately combine knowledge-based planning with numerical simulation of the radiation treatments. The numerical simulation is needed in order to determine if the proposed treatment will conform to the goals of the plan (required tumor dose, limiting dose to critical organs). The space of possible radiation treatments is numerically very large, making traditional search techniques impractical. Yet, with modern radiation therapy equipment, the design of treatment plans might be significantly aided by automatically generating plans that meet the treatment constraints. The project will result in systematization of knowledge about radiation treatment design, and will also provide an example of how to represent and solve design problems with a knowledge based system.

This project has some relevance to computer science as well, in that our approach, if successful, may contribute to a better understanding of design problem solving with knowledge-based systems.

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Stanford Project: RADIX -- DERIVING KNOWLEDGE FROM TIME-ORIENTED CLINICAL DATABASES

PENGUIN -- Applying Database and Knowledge base Technology to Medical Instrumentation

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The RADIX research has been phased out during this year. RADIX had two main goals: (1) to explore the usefulness of knowledge-based techniques to derive medical knowledge from clinical database (DB) systems containing non-randomized, non-protocol patient observations and (2) to develop a program and set of techniques for automated summarization of patient records. The process of reliably deriving causal relationships has proven to be quite difficult because of the complexity of disease states and time relationships, strong sources of bias, and problems of missing and outlying data. However, the experience gained in the RADIX project and its predecessor project, RX, continues to influence basic research directions. The problem of automated knowledge acquisition remains an important area of research, and we expect that the foundations laid here will influence work of others as well.

PENGUIN is a project aimed at developing methods for bringing together expert system and database technologies in an integrated advice system. Databases and expert systems share a common goal -- generating useful information for action -- but accomplish their tasks separately, using different principles. It is clear, however, that future information systems will require both the problem-solving capabilities of expert systems (ESs) and the data-handling capabilities of database management systems (DBMSs). Indeed, combining database and expert system technologies into expert database systems (EDSs) is an emerging research area. One can define an EDS as "a system for developing applications requiring knowledge-directed processing of shared information". From a perspective of developing advanced biomedical information systems, this definition conveys two goals: (1) enhancing DBMSs with structuring and manipulation tools that take more semantics into account; (2) allowing ESs to access and to handle efficiently information stored in database(s). In this research project, we investigate the hypothesis that the object-oriented approach to knowledge and information representation can serve as a unifying scheme for developing EDSs.

We explore this hypothesis in a practical biomedical environment, Fluorescence Activated Cell Sorting (FACS). FACS is emerging as a major source of information for biomedical research and clinical practice. Currently, achieving good FACS performance requires analyzing and integrating various complex data and knowledge sources in order to fulfill the information needs of FACS investigators. This work

involves a close collaboration between researchers in the Medical Information Sciences Program and the Departments of Computer Science and Genetics.

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Stanford Project: REFEREE Project

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The goals of this project are related both to medical science and artificial intelligence: (a) use AI methods to allow the informed but non-expert reader of the medical literature to evaluate a randomized clinical trial, and (b) use the interpretation of the medical literature as a test problem for studies of knowledge acquisition and fusion of information from disparate sources. REFEREE and REVIEWER, a planned extension, will be used to evaluate the medical literature of clinical trials to determine the quality of a clinical trial, make judgments on the efficacy of the treatment proposed, and synthesize rules of clinical practice. The research is an initial step toward a more general goal - building computer systems to help the clinician and medical scientist read the medical literature more critically and more rapidly for use in making clinical decisions.

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