A Hybrid Systems Approach to Integration of Medical Models

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Abstract

We discuss a fundamental problem in the provision of quality care at acceptable, society-wide costs: the integration of what is now a dichotomy in medical models. The dichotomy is one between phenomenological models of high-level decisions and evolution models of low-level dynamics. The dominant modeling concepts are based traditionally on a) “Homeostatis” and b) “physical dynamics” – such as those encountered in pharmacology, quantitative pathophysiology, and more recently in immunology. We introduce a novel idea of the hybrid system state which is used to provide a basis for integration of medical models.

Example: A Medical Emergency[1]

Having taken ill, a traveler is hospitalized and undergoes tests, including X-rays, CAT scans, and MRI. At the same time, the attending medical professionals quickly retrieve test results from the traveler’s last physical examination. The images are compared, diagnosis made, and treatments prescribed. This scenario is difficult if not impossible today, in part because diagnostic images are commonly not in computer-readable form and network speeds are generally too slow to transmit large three-dimensional

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[1] High Performance Computing and Communications (HPCC) Program, Page 48

image data sets.

Truly remote medical care will depend on services, standards, tools, and user interfaces to store, find, transmit, manipulate, display (and superimpose), compare and analyze three-dimensional image data from several sources. Diagnostic test results and large image data sets from the physical examination must be available on computers that can be accessed from the hospital's computers over a communications network; they must be retrieved quickly; the scientific data used in guidng the diagnosis and treatment must also be available from electronic libraries and must be quickly retrieved; and the privacy of these patient records must be protected. All of this supposes completion of rather extensive and complex inter-professional medical arrangements. In addition, it must be done using a user interface customized for the practice of "distance medicine," including collaborations among different sources of expertise.

Use of the NII to integrate existing information systems to meet this kind of medical emergency requires consideration (and we propose expansion) of the foundation of computable models.

1 Introduction

We live in a world which is continuous in many aspects such as time, space and energy. Many models used in medical information systems rely on accurate models of continuous variables. Application of digital computers requires the use of computational models which can assist in understanding and modifying the world in some manner. But there is a problem: while we have remarkably accurate models of many aspects of the physical universe and can use these models to predict the change (evolution) of variables over time, computing each of an infinite number of values for even a single continuous variable is *not possible*. In order to build useful computer programs we are thus left with the need to determine how many computations are sufficient to obtain a valid ("close enough") approximation of a physical object's evolution over time in accordance with spatial, temporal and energy constraints. This is an old observation and is, in fact, the fundamental motivation for scientific studies of computer simulation and control.

Statement of the medical system integration problem

Consider the challenge of intelligent integration of medical information systems posed by the medical emergency discussed above. Even at the lowest level (treating a single patient), the setting for medical decision-making is very complex. Clinicians consider data from patient interviews, previous interventions, physical examination, laboratory tests, and various models to perform assessment diagnosis, evaluate patient prognosis, and prepare therapeutic plans. Information system support for clinical activities requires acquisition and efficient processing of data from many sources and depends heavily on the use of models. The dominant modeling concepts are based traditionally on a) "homeostatis" and b) "physical dynamics" – such as those encountered in pharmacology, quantitative pathophysiology, and more recently in immunology [1] (see Table 1).

The qualitative reasoning of homeostasis accommodates clinical intuition and empirical associations, which is of great importance among humans, but very difficult to systematize or automate for representation as computable models. Modeling of homeostasis information has often been captured as discrete changes or decisions (events) described by rules. Selection, verification and validation of sets of rules and their use in medical decision making has been a long-standing issue [1, 3, 7].

On the other hand, the quantitative reasoning of analytical models of physical dynamics accommodates well-defined conceptual representations of continuous change in spatial and temporal attributes of: patient variables (e.g. response of the immune system to an infectious organism, amount of oxygen in the blood, or concentration of a particular chemical), medical equipment variables (e.g. flow rate of oxygen in a respirator, rate of administration of a particular medicine, data transfer rate for a temporary communications link), and support structure variables (e.g. light intensity, room temperature, background noise, cost of treatmen, profit, loss). Also analytical representations of information can be captured as differ-

Representation Class	Qualitative Characteristics	Mathematical Basis	Areas of Applicability
Dynamic Systems models	• Quantitative reasoning • Continuous change • Clinical analysis of dynamical change (e.g. pharmacology, immunology, and quantitative pathophysiology) • Analytical associations	Differential Operators	• Prediction of: disease growth, immune system reactions, pharmacological variations, chemical reactions, . . . • Continuous monitoring • Analysis of radiological morphological variables
Phenomenological models	• Qualitative reasoning • Homeostasis • Clinical intuition • Empirical associations	Algebraic Topologies (T-Zero)	• Diagnosis • Patient management • Therapeutic interventions • Epidemiology • Safety • Starting and stopping • Data exchange protocols

Table 1: Dichotomy of Models Used in Medical Information Systems Development

ential equations, stochastic processes and numerical input-output tables which can be used for efficient processing of computable models. However presentation of results from analytical models creates substantial practical difficulties compared to the more intuitive qualitative reasoning of homeostasis.

Information systems based on both approaches have existed for many years. These systems operate at different levels, from local (e.g. monitoring of patient status in an intensive care unit) to more comprehensive (e.g. clinical, hospital, or area support). As the availability of patient data becomes more widespread and stored in different forms, an opportunity occurs for increased functionality when heterogeneous sources of information can be integrated [1]. The benefits of systems-based integration to medical research and education is documented in [8, 9].

An earlier solution for integration of a few systems at the local level was developed by the Maryland Institute for Emergency Medical Services Systems (MIEMSS). A comprehensive solution to large-scale trauma care (approximately 200 persons) was sought when the Maryland Shock-Trauma Center was created several years ago [5, 6]. A central feature of the Center is the availability of a detailed set of treatment protocols for response to different trauma situations. Another feature is transmission of patient data to an emergency care facility while a patient is enroute. The MIEMSS solution for small-scale integration of medical information systems support for clinical activities was developed based on a comparison to those used in the military to coordinate complex activities. These information systems support activities are collectively referred to as command, control and communications (C^3). The central role of clinical C^3 is represented diagrammatically in Figure 1 [1].

Various activities in Figure 1 are modeled by *two different classes of models* (see Table 1). The *class of logical (phenomenological) models* is key to the intuitive representation of medical activities. These activities include human interactions between patients and clinicians, capture of treatment protocols, description of measurement sequences, portrayal of disease diagnosis, evaluation of alternative conclusions of prognosis, development of therapeutic plans, and display of medical information to clinical staff. Logical models have been used extensively in constructing diagnostic expert systems. Logical models are the basis of entity-relationship and object-oriented models of medical events. An area of application of logical

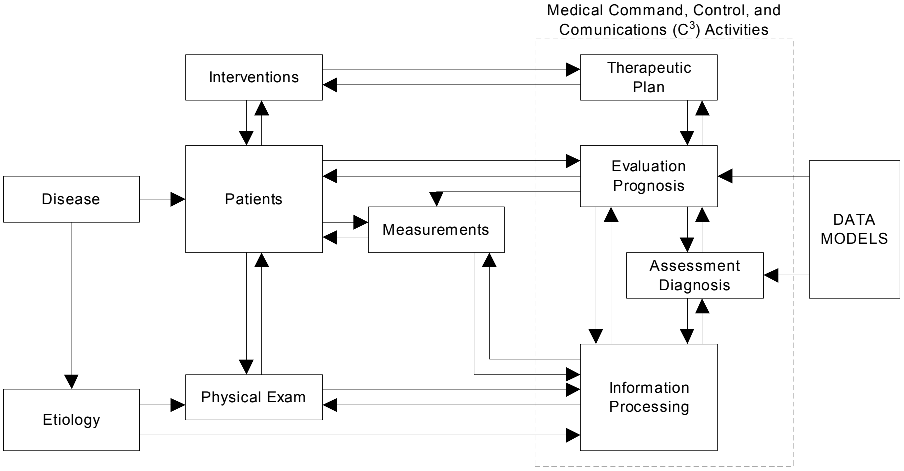

Figure 1: Medical Decision-Making Architecture

models receiving growing attention is the area of radiological models of skeletal and visceral portions of the body. In this regard, there is a tremendous amount of ongoing work in abstraction of visual representations to obtain logical assertions. This area is a potential source of dual-use of military technology since image-understanding has been a thrust of military research for many years. Two current scene interpretation projects are the ARPA Image Understanding Architecture project and the ARPA Image Understanding Environment project which are respectively focusing on the hardware and software aspects of image processing. The *class of evolution (dynamical system) models* is key to the quantitative representation of medical activities. These activities include quantitative changes in disease, capture of immunological variability, description of allergic dynamics, portrayal of pharmacokinetics, evaluation of observations and measurements, development of real-time control programs (e.g. machine-assisted breathing), and display of real-time information at different time scales. The image understanding activities of radiological models is based on two-dimensional representations of three-dimensional models.

The coupling of qualitative abstractions with quantitative dynamics has been previously recognized as a crucial challenge for construction of intelligent systems. This challenge has been variously described as the "pixel-to-predicate" or "signal-to-symbol" transformation problem.

Both classes of models (logical and evolution) are subject to incremental review and change over time. Treatment protocols are updated, new chemical process models are discovered, new forms are required for patient monitoring and reporting, analytical accuracy and detail of radiographical results change with improvement in equipment. Various research thrusts revolve around the determination of how to represent and incrementally adapt the degree of confidence we have in the accuracy of the models being examined.

2 Our approach for overcoming a fundamental constraint in integration of medical models

We propose a new approach for coupling of numeric and symbolic computation which is based on *unification* of trusted models instead of *experimentation* with trusted models [2]. This new approach eliminates the dichotomy in models by representing the state of the system as a point in a manifold (explained below) which admits both logical and evolution models.

Recent medical informatics work by Dr. Nicholas DeClaris has addressed unifying dynamical system models and phenomenological algorithms for medical decision making. He has introduced a novel conceptual scheme based on "Disease-Therapeutic Dynamics" which involves computer-aided reasining from the outset. There are five essential medical elements in this conceptualization: pathophysiological dynamics, immunological and allergic dynamics, pharmacokinetics, observations and measurements, and iatrogenics. The medical elements are conceptualized by means of analytical (differential equations, random processes, etc.) and algorithmic techniques (data structures, etc.) as well as phenomenological associations involving skill and specialized knowledge based on training and experience.

We have developed preliminary ideas concerning use of Multiple Agent Declarative Control Architecture (MA-DCA) with Dr. DeClaris' results from medical informatics. The MA-HCA architecture is based on a theory developed by Wolf Kohn and Anil Nerode over the past 3 years. This theory extends the concepts, principles and algorithms of Single Agent Declarative control theory, and merges them with the principles of concurrent computing and dynamical hybrid systems. The multiple agent architecture is a collection of these agents and an inter-agent connectivity network. The central concept for MA-DCA is that an on-line restrictive mechanical theorem prover will exist within each agent. The theorem prover of each agent consists of five elements: a Knowledge Base, a Planner, an Inferencer, an Adapter, and a Knowledge Decoder. The Knowledge Base stores the goal for the agent, system constraints, inputs and inference operations. The Planner generates the theorem which represents the goal. For some agents, this goal will govern the behavior local to that agent. For other agents, the goal will also include behaviors global to the system. The Inferencer proves the theorem. If the theorem is true, control actions, computed during inferencing, are issued to the plant. If the theorem is false, the Adapter processes the failed terms in the theorem for replacement or modification. Data from other agents is provided to the Planner for incorporation as constraints into the theorem and passes through the Knowledge Decoder for entry into the Knowledge Base. The MA-DCA has several key capabilities:

- *Reactive*: The theorem proving function of each agent on the architecture operates according to a first principles feedback paradigm.
- *Adaptive*: The knowledge base of each agent is open and modifiable by sensory data. Theorem failure triggers tuning and corrective action.
- *Distributive with Coordination*: The theorem proving is carried out distributively over the agents. The coordination scheme is implicit without umpire.
- *Dynamic Hierarchization*: The architecture can operate simultaneously at different levels of abstraction.
- *Figure of Merit*: The behavior of the closed loop distributive system is determined by proving that there exists a command trajectory that minimizes a goal functional.
- *Real-Time*: Constraints for real-time performance are explicit and part of the knowledge base. This is important because real time constraints cannot be fully instantiated at design time.

2.1 Hybrid System State

For purposes of our exposition, there are three cases which need to be considered in the characterization of unified-medical-information represented in the computer. These cases collectively contain the kinds of information that describe the *state of the system*. The cases are:

- information derived from monitoring continuous variables,
- information derived from monitoring variables which normally evolve continuously but which may exhibit logical changes (jumps), and

- information which is derived from logical variables.

The Kohn-Nerode approach for unification of logical and evolution models is based on introducing the idea of continuity of the hybrid state representation. The continuity argument and the constructive extraction of automatons which comply with the continuity constraint is accomplished by using the mathematics of manifolds (see Figure 2). A point in a manifold supports unification of logic and evolution models. T-zero topologies have a one-to-one correspondence with horn clauses of logical representations. This enables us to model the Discrete-Event Dynamic System (DEDS) sampling rule models. Lie algebra infinitesimals allow us to consider all the standard evolution models of differential operators and DEDS evolution models. We embed logical models in continuous models in order to construct automatons which comply with logical and continuum constraints. This is discussed more fully in the white paper [2]. We assert and emphasize here that for systems which meet the conditions for creation of a hybrid system state, the revolutionary nature of our approach has two benefits:

- Creation of a unified mathematical foundation for analysis and synthesis of models which for decades have been treated separately, and
- Creation of a rigorous process for incremental expansion of trusted systems which must comply with stringent safety and performance constraints.

Dr. DeClaris' previous work in unification of models in medical system informatics has focused on applying the notion of discriminants (implementable as neural networks) to develop a unified treatment of the two kinds of models. A discriminant is subject to rigorous mathematical analysis yet at the same time it accommodates very well phenomenological associations. More precisely, given the need to form cognitive associations between elements in a feature space, a *framework* for supporting analysis and selection of elements from the feature space is:

Associations: Known Ordered Pairs $\{x_i, q_j\}$

where: $x_i \in X^m \subset \mathbf{R}^m$, $q \in Q^n \subset \mathbf{R}^n$

Classification: Given x_i, find q_j

Feature Space: $\Omega \subset \mathbf{R}^s$

Discriminant: For a known association there exists a $W \in \Omega$ such that

$$F[x_i, W, \phi(x_i, w_i)] = q_j$$

where

$$\phi(\,) \in \mathbf{R} \quad \text{and} \quad F[\,] \in \mathbf{R}^n$$

Discriminants from a mathematical *approach* for using learning algorithms for feature selection and generalization:

Set-up: F and ϕ

Choose initial: $W_0 = W + \epsilon_0$

Compute: $F(x_i, W_0, \phi) = q_i + \epsilon_0$

Choose: $W_{k+1} = W_k + \Delta_k(\epsilon_k)$

So that: $F(x_i, W_{k+1}, \phi) = q_i + \epsilon_{k+1}$

And: $|\epsilon_{k+1}| < |\epsilon_k|$

We are interested in solving these problems by laying the foundations for integration of scalable information systems for quality health care delivery. Our approach is to implement a global coordination scheme which is implicit without umpire yet cooperates at each local level to analyze situations which are *compositions* of: high-level logical models of decisions concerning diagnosis and patient management, and low-level evolution models of pharmacology, quantitative pathophysiology, and immunology. This general approach will take the results Dr. DeClaris has achieved in using discriminants to develop cognitive associations between elements in medical feature spaces and place them in the framework described below.

2.2 Medical Information System Framework

We would not replace the existing medical information systems. The medical information system framework we envision would rely on a telecommunications network to integrate existing medical systems.

Telecommunications Process Model

Our model for medical information system processes relies on a *hierarchical organization* of the network

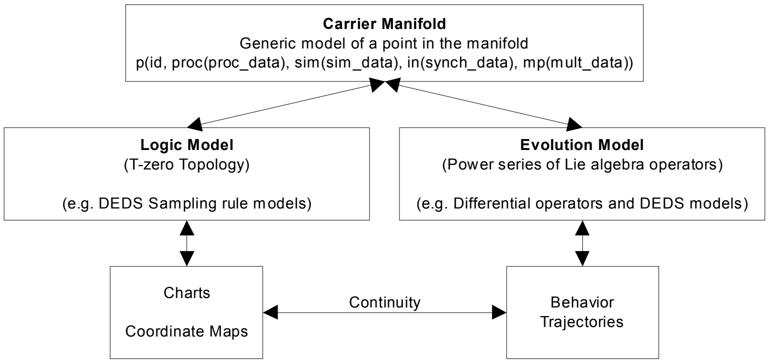

Figure 2: Continuity in the Topology of the Representation

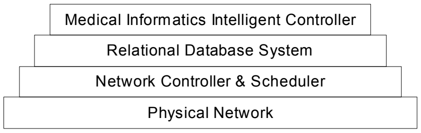

Figure 3: Hierarchical Organization of the network

operation, and a logic distribution of *decision agents* controlling these processes. We proceed to discuss these two aspects next.

Hierarchical Organization

The hierarchical organization of the network system is similar to the ISO model. An aggregated version of this organization is depicted in the diagram of Figure 3. The bottom of the hierarchy contains the *Physical Network*, composed of the primary and secondary network links, switching nodes, interfaces, etc. A typical primary heterogeneous network is illustrated in Figure 4.

The next level of the hierarchy, the *Network Controller and Scheduler* processes requests from the network for medical informatics services and queries the relational data base system for setups and status for those requests. It also receives state information from the network and processes it to generate updates to an aggregated operational network model that resides in the database. The *Relational Database System* ex-

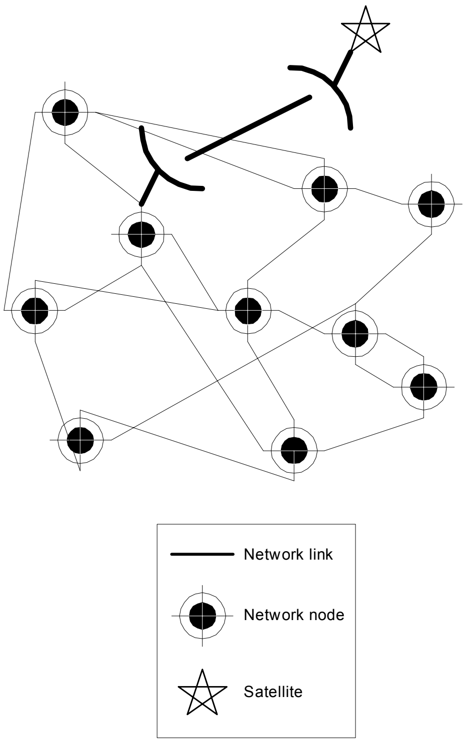

Figure 4: Logic Communication Network example

ecutes the operational model of the network at a level of aggregation compatible with the needs of the Medical Informatics Intelligent Controller. The relational database System includes interactive interfaces with the network and medical informtics controllers. At the top of the hierarchy, the *Medical Informatics Intelligent Controller* generates control actions to initiate, facilitate, monitor, and adaptively regulate medical informatics processes. The medical informatics controller is composed of a (varying) number of devices called Decision Agents (or agents for short) implicitly coordinated through a variable (over time) configuration *Logic Communication Network* (Figure 4) implemented through the hierarchy of Figure 4. We provide a discussion of the operational characteristics of the agents in [2]. An example of the logic communication network is presented in Figure 4.

Logic Distribution of Decision Agents

The medical informatics controller domain of action is a *Hybrid Distributed Model* of active medical informatics processes through the network (Figure 4). The model is termed hybrid because its structure is an amalgamation of logic and evolution elements. The evolution elements are encoded in the network model stored in the relational data base. The logic elements are encoded in the knowledge bases of the agents of the controller. We propose to model the medical informatics process dynamics in terms of the conservation of the flow of a commodity called *Service Demand* (demand for short) through the logic communication network. This network is composed of connection links and agents. The agents are allocated at the nodes of the network. As a function of time (t), the network configuration varies because new agents are *spawned* and become part of the network or old ones drop out.

The agents in the logic communication network are of two types: *Permanent* and *Transitory* agents. Permanent agents are those associated with medical informatics processes. They remain active even if the process they control becomes inactive. Transitory agents, which are spawned by the permanent agents, remain part of the network as long as the process in which they participate is active. Transitory agents are spawned as a response, among others, to increased demand, satisfaction of service requirements, and network malfunctions.

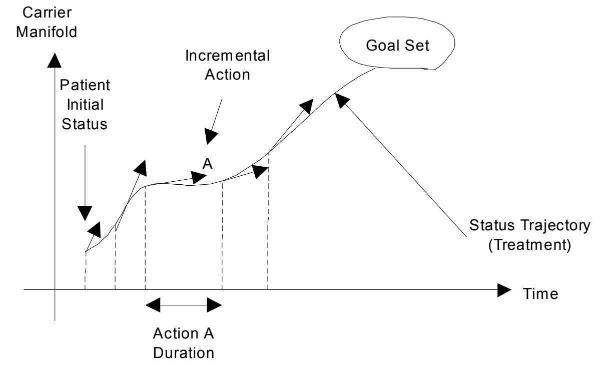

Figure 5: Example of Status Trajectory

2.3 Operational Characteristics of an Agent

An *agent* is a care provider or a specialized Data Base System. The purpose of an agent is to achieve coordination of specialized heterogeneous information systems to support clinical activities. MA-DCA will achieve this implicitly (without umpire) by capturing the status of medical activity (i.e., patient diagnostic or treatment, institutional resource allocation, hospital beds, diagnostics facilities, ambulance service, insurance) of the care system as *continuous* status trajectories (functions from the time axis to the manifold – see Figure 5) on a manifold called the carrier manifold whose algebraic structure carries the *evolution information* of diagnosis, treatment, tests, institutional planning and scheduling, etc., and whose topological structure carries the *current knowledge* about the system. A point in the carrier manifold is a data structure whose entries are parameters characterizing the system. Continuity of trajectories in the carrier manifold corresponds to status evolution logically compatible with respect to current knowledge. Equivalently, discontinuity corresponds to status not logically compatible with current knowledge.

The *action* generated by an agent at any time interval is given by a *chattering combination* of primitive vector fields in the tangent bundle of the carrier manifold. The agent generates an action by time multiplexing one or more of the primitive vector fields and determining the duration that it stays active. Each agent has its own *basis* of primitive actions. The set of status trajectories for each agent are integral curves corresponding to this basis. These curves define a submanifold of the carrier manifold; the status manifold of the agent.

Information of other agents and goal information (translated to the current time) is represented as vector fields. They are additively added to the action field of the agent to determine the current *total action.* A more complete discussion of this analytical approach, as well as the constructive algorithm for choosing actions at each update interval which simultaneously complies with logical and evolution constraints is contained in [2].

3 Conclusion

We have provided an overview of a significant, decades-old barrier to successful attainment of intelligent integration of medical information systems: the need to conduct exhaustive experiments in order to integrate dissimilar models. We have discussed the ability of our multiple-agent, declarative control architecture (MA-DCA) to construct automatons which simultaneously comply with logical model constraints and evolution model constraints. We intend to investigate the integration of existing dissimilar medical information systems to demonstrate the applicability of this new technology.

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