Simulating Patients with Parallel Health State Networks

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The American Board of Family Practice is developing a computer-based recertification process to generate patient simulations from a knowledge base. Simulated patients require a stochastically generated history and response to treatment, suggesting a Monte Carlo-like patient generation process. Knowledge acquisition experiments revealed that description of a patient's overall health as a node in a Monte Carlo model was difficult for domain experts to use, severely limited knowledge reusability, and created a plethora of awkwardly defined health states. We explored a model in which patients traverse several parallel health state networks simultaneously, so that overall health is a vector describing the current nodes from every Parallel Network. This model has a reasonable biological basis, more easily defined data, and greatly improved reuse potential, at the cost of more complex simulation algorithms. Experiments using osteoarthritis stages, weight classification, and absence or presence of gastric ulcers as three Parallel Networks demonstrate the feasibility of this approach to simulating patients.

INTRODUCTION

Computer-based testing holds promise as a technology that could add educational content to the testing process[1] while yielding different, and perhaps more important, information about examinees than paper-based tests.[2-6] Some computer-based tests use traditional multiple choice item formats. Other tests simulate patient care experiences. [7-9] Some elegant simulation programs generate patient data from systems of equations,[10] but most outpatient medical problems still require empiric description. Some programs embed the logic of the simulation in code,[2,3,7] although reuse and knowledge maintenance may be difficult.

The American Board of Family Practice (ABFP) is developing a computer-based recertification process based on an editable knowledge base. [11-13] This empiric simulation project (ESP) could yield practically endless numbers of high quality cases at an affordable cost per case. Variability in case presentations should help the ABFP maintain a secure test. Conversely, modeling decisions which restrict the details of case histories may reduce security.

The ESP development team designed an entity-relationship model of medical concepts and algorithms to create patient simulations from the data model. These algorithms create patient histories and evolve patients during simulated medical care. The central concept in the history generation algorithm is that patients with some health states evolve to experience other health states.

The assumptions underlying early ESP algorithms and data models were similar to those of a Monte Carlo process. A simulated patient would have partially completed a path through a Monte Carlo network. A physician's management decisions would influence the remainder of the path. Nodes along this path represented the patient's overall health during a period of time, that is, all simultaneous medical problems are represented in a single Monte Carlo node. Arcs between nodes represent the patient's transitions between conglomerate health states. Other common decision modeling techniques, such as Markov processes and decision trees, employ similar models of health states.

The Department of Family Medicine at Duke University and the affiliated Cabarrus Family Medicine Program conducted knowledge acquisition experiments for a variety of problems common in family practice. These included alcohol abuse, ankle sprains, diabetes mellitus, hypertension, osteoporosis, otitis media, peptic ulcer disease, pregnancy, reactive airway disease, and smoking. These domains involve addictions and behavioral problems; acute illness; acute illness superimposed on chronic predisposing illness; and non-systemic illnesses. The ESP development team advised the domain experts, and simultaneously modeled osteoarthritis of the knee and normal health.

These experiments demonstrated many serious difficulties with the conceptual model. First, to

1091—8280/98/$5.00

obtain variable histories required modeling many nodes in a Monte Carlo simulation. In several domains a chronic progressive systemic illness (e.g. osteoporosis) combined with recurrent acute site-specific exacerbations or complications (e.g. fractures of various bones). The original model implied the need for a large number of conglomerate health states, for instance to define multiple paths from "Normal health" to "Ex-smoker with Severe osteoporosis and healed second left hip fracture." The number of conglomerate health states can expand quickly, and data required to define these conglomerate health states (e.g. age specific incidence) is often speculative and redundant.

Second, identical information may be collected in several testing domains. For instance, highly redundant obesity descriptions would appear in tests of osteoarthritis, diabetes, and hypertension.

Third, relations between health problems are unclear. Conglomerate health states do not compartmentalize disease processes, obscuring whether domain experts consider hyperthyroidism or nicotine addiction as direct precursors of osteoporosis, or risk factors, or distracters.

Fourth, modeling one therapeutic complication adds many nodes and arcs. Therapeutic complications are typically new illnesses superimposed on any of several antecedent conglomerate health states. For instance, a patient in any of the osteoporosis nodes might develop uterine cancer while taking unopposed estrogen. The number of nodes required in the Monte Carlo model may double, with an equal number of new arcs. Historical distracters, such as randomly appearing colds or a history of appendicitis might require still more conglomerate states.

Finally, a computer-based test needs to specify the anatomy of disease, so that it can correctly present findings to the examinee. In some diseases the anatomy is erratic. A typical osteoarthritis patient will have joints afflicted to different degrees.

Thus, Monte Carlo modeling techniques have an appealing ability to generate multiple temporal sequences of events. However, the ABFP's need for finer anatomic detail, reusable information, and manageable knowledge acquisition and maintenance required some revision of the Monte Carlo approach.

METHODS

The ESP model was revised to define Parallel Networks of Health States, while discarding conglomerate health states. A Parallel Network includes a sequence of distinguishable, mutually exclusive Health States. These typically reflect the medical literature's descriptions of stages of progression or severity of a disease. If the literature does not provide a staging definition for a disease, Health States can usually be defined as absent, mild, moderate, and severe.

A parallel health state network connects these health states with "Leads To" objects, e.g. mild disease leads to moderate disease. A Leads To object associates specific collections of risk factors and treatments with a fuzzy rate of progression from the preceding to succeeding Health States. The risk factors may be Health States from other Parallel Networks, activities (e.g. work, play, and habits), and family history. Treatments may be interventions prescribed by the examinee, or some simulated previous provider.

Separate collections of Leads To objects manage history generation and evolution. In history generation, the ESP creates a life history and context for the examinee's encounter with the simulated patient. The examiner may want an unremarkable story compatible with many simulated medical problems, or a story that is virtually pathognomonic. In evolution, an efficient test might routinely simulate rapid progression of disease or complications of the examinee's treatments, regardless of the likelihood of these events in practice.

Each Parallel Network defined in a simulation imposes its Health States on one or more anatomic sites, which evolve simultaneously. For instance, a rheumatoid arthritis simulation could name a single Parallel Network and all of the joints affected. An osteoarthritis simulation might use two copies of a knee osteoarthritis Parallel Network, applying one to each knee. Different presenting Health States at each knee and independent evolution of the knees would be typical of osteoarthritis. Systemic diseases involve the entire body of a simulated person.

Health States may recursively contain Parallel Networks representing more acute exacerbations of the parent Health State. For instance, moderate osteoarthritis may include a Parallel Network

describing transitions between baseline and flare Health States. A simulated patient cycling between these Health States will display or recount episodes of worsening arthritis symptoms.

The algorithms for history generation and evolution were adapted from Monte Carlo techniques. A request for a simulation identifies the presenting Health State in each Parallel Network. Using incidence and prevalence information, the age, sex and race of the simulated patient are selected. The time of the next (or, in history generation, the preceding) event in each Parallel Network is predicted. In history generation, this may require assertions regarding the activities of the simulated patient. The temporally closest event from all of the Parallel Networks is instantiated. In history generation, the process of predicting the most recent preceding Health State change proceeds backward through time until no further transitions are defined by the Parallel Networks. In evolution, this process of predicting the next event continues until one of the events initiates another encounter with the physician.

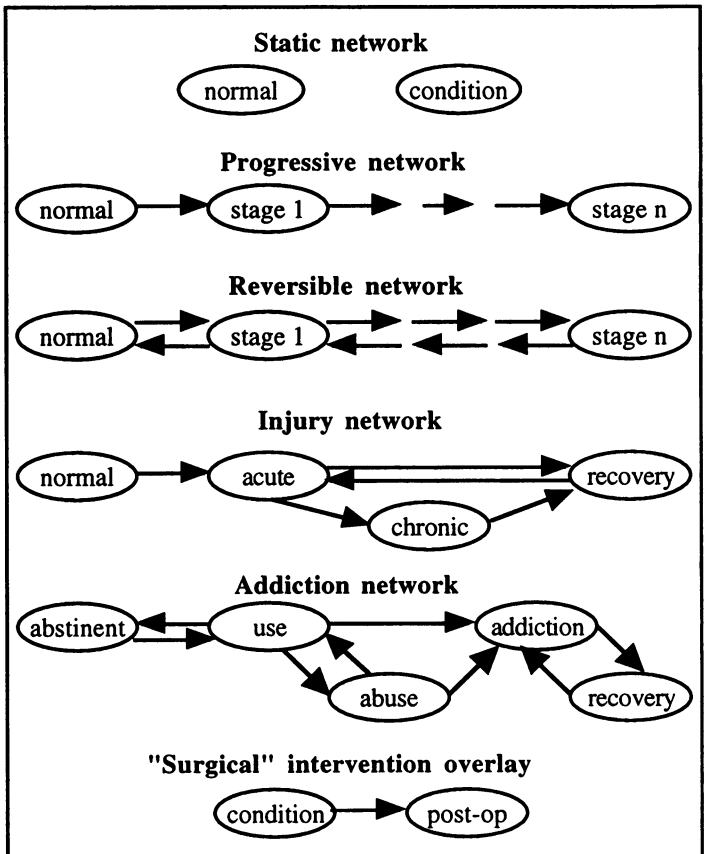

Figure 1. Basic types of Parallel Networks used to describe disease evolution.

The revised ESP model was tested by additional knowledge acquisition experiments, implementation of a Poet™ object oriented database and supporting algorithms, and generation of simulated osteoarthritis cases. The database was used to generate cases of osteoarthritis of the knee with obesity as a risk factor, and gastric ulcers induced by non-steroidal anti-inflammatory drugs prescribed without misoprostel.

RESULTS

Knowledge acquisition

Simple illustrations of their medical domains helped content experts understand the scope of their knowledge acquisition tasks. Initially intricate domain models were decomposed into much less threatening Parallel Networks. Figure 1 illustrates common Parallel Network structures. The simplest network is a collection of one or more static states, typical of genetic (Downs syndrome) and some congenital conditions (anencephaly). The progressive network is a series of states with no cycles, typical of degenerative illnesses such as osteoarthritis. The reversible network illustrates chronic but reversible conditions, such as essential hypertension and weight disorders. In the injury network an acute insult evolves to either recovery or a chronic condition with a later recovery. Injury networks describe many infectious diseases and trauma. The addiction network illustrates that a person may abstain from, use, abuse, or become addicted to a substance. In the scheme shown here, a previously addicted person can only be addicted or recovering, but can not return to abstinence, use or abuse. The surgical intervention overlay illustrates that new states can be added to the above networks using irreversible therapies such as radiation or surgery. Domain experts adapted these networks to their needs by eliminating unwanted nodes and arcs, or replacing nodes with another network.

Domain experts began with a primary Parallel Network to sketch the diseases defining their domain, such as stages of diabetes mellitus. Parallel Networks of comorbid conditions were identified in most domains, typically including risk factors for

progression through the primary network, such as obesity. Most domains included one recursive layer of Parallel Networks representing exacerbations of the Health States in the primary Parallel Network. Most domains also identified one or more Parallel Networks representing complications of Health States in the primary network, such as retinopathy, or of treatment of primary Health States, such as gastric ulcers.

Experts were asked to estimate 1) how long a risk factor should exist before it could influence a transition between states in a primary network, 2) the time required for transitions in the primary network, given different combinations of risk factors, and 3) the number of passes an individual patient should be allowed to make through a cycle (e.g. from acute injury to recovery and back). Although these data were often non-existent in the literature, domain experts could comfortably estimate a range of values from clinical experience. Although the data to gather remained imposing in volume and dauntingly quantitative, Parallel Networks in the revised ESP model appeared to successfully guide segmentation of data into intellectually plausible sets.

Data model and algorithm implementation

The osteoarthritis experiment continued with development of an object oriented database structured after the ESP model. The database was populated with information about four stages of osteoarthritis, three weight conditions, and 2 ulcer states.

The algorithms mentioned above were implemented, but without support for acute exacerbations or multiple Parallel Network copies afflicting different anatomic sites. Conditional probabilities were managed with a simple scripting language. The scripting language has since been replaced by Bayesian networks.

Instantiation of the model confirmed the expected difficulty in authoring a family of cases with the same underlying disease process, but different details in presentation. In particular, giving attention to conditional probabilities slows knowledge acquisition considerably. Memories of individual clinical cases were helpful in authoring a narrowly defined simulation, but much more attention was required to produce Health States generation methods and Leads To objects that were robust to changing assumptions about sex, race, and obesity. In spite of these difficulties, data entry in a data base founded on Parallel Networks was accomplished.

Experimental Verification

The prototype ESP simulator generated a series of patients for demonstration at the American Board of Medical Specialties meeting on computer-based testing in Chicago, March 21-22, 1996. Approximately 30 patients were generated and stored over a four day period, including several during the meeting. Each patient generation required about 10 minutes. After generating a variety of male and female patients, data in the knowledge base were skewed to generate middle aged overweight white females. These patients were typically 55 to 65 years old and complained of recently worsening pain in one or both knees. Patients had been morbidly obese for 1 to 3 years prior to presentation, and had at least a 5 year history of mild arthritis in the affected knees. Their health problems began with either obesity or mild osteoarthritis 10 to 30 years prior to presentation.

During the demonstration, most history and laboratory requests returned graphs of values over the simulated patient's lifetime, enabling viewers to see how variables such as weight, uric acid, or osteophyte numbers had changed since birth. These graphs demonstrated concurrent histories of worsening osteoarthritis and obesity.

Demonstration patients were managed interactively. Patients managed with high doses of non-steroidal antiinflammatory drugs without misoprostel would develop ulcers sometime during a 2 year follow up period. Weight loss was also possible. Optimal management of weight and prescription of strengthening exercises would slow the inexorable progression of knee osteoarthritis, but progression from moderate to severe knee arthritis would inevitably occur within 10 years.

DISCUSSION

The simulations demonstrated that the prototype system could generate patients with plausible medical histories; appropriate symptoms, signs, and laboratory values; and could evolve patients over time. The separation of data controlling osteoarthritis, obesity, and ulcer histories and presentations suggests that these components would be reusable with modest modification, if any, in new disease domains. Substantially different osteoarthritis simulations could be produced by replacing a few history controlling Lead To objects.

Limitations

We are currently developing a simulator with acute exacerbations, past medical interventions, and use of multiple copies of one Parallel Network's data. The new model and algorithms replace simple scripts with Bayesian networks. Although the next generation simulator is not yet functional, no fatal conceptual difficulty is evident.

The knowledge acquisition problem for the ESP model remains daunting. One vexing problem is that the history generation algorithms require solutions to multiple temporal constraints. These constraints may not always have a solution, and it is not yet clear how to react if a history generating step fails, or how to guarantee temporal solutions while reusing data.

The cartesian product of N parallel networks creates an N dimensional grid whose nodes represent conglomerate health states. This grid is a complex Monte Carlo model with many low probability paths that would never have been considered in an explicit Monte Carlo model. Conditional probabilities within Parallel Network's Leads To objects could provide a means of pruning the N-dimensional space. This mechanism may not work, as it places further burdens on knowledge acquisition and reusable object design.

These limitations must be considered in context. In the absence of mathematical models of the diseases of interest, the ABFP requirements for secure tests, realistic temporal and clinical features, and defensible credentialling decisions, complex data is an inevitable feature of a computerized problem generation process.

CONCLUSION

Parallel Networks facilitate some aspects of knowledge acquisition for a patient simulation knowledge base, and appropriate algorithms support generation of patients. The data required are relatively reusable, in contrast to data explicitly describing global health. Further experimentation is required to demonstrate that this approach remains tractable with more complex scenarios. Parallel Networks may have application in other endeavors that traditionally describe global health, such as decision analysis.

Acknowledgements

The American Board of Family Practice funded this work. Lloyd Michener, David Lobach, and the Duke and Cabarrus Departments of Family Medicine provided invaluable feedback. Mark Musen assisted with conceptual models. Rovinelli Associates implemented the knowledge base and algorithms.

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