Use of Intelligent Agents in the Diagnosis of Cardiac Disorders

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Abstract

Diagnosis of cardiac disorders requires the combination of many different types of data, including family and patient histories, laboratory results, physical findings, genetic information, electrocardiogram analysis, and imaging results. Computer-assisted decision support systems must be able to combine these data types into a seamless system. Intelligent agents, an approach that has been used chiefly in business applications, provides a structure that can combine not only data types but also a variety of reasoning methodologies in the same decision support system. The user is included as an agent in the system and can interact directly with any of the components. The authors have used this approach to develop a decision aid for dementia evaluation. The adaptation of this methodology to the diagnosis of cardiac disorders is presented here.

1. Introduction

The basic paradigm of the intelligent agent approach is the use of communication protocols that permit diverse types of intelligent components to work cooperatively. Intelligent agents have their origins in distributed artificial intelligence and have been used successfully in a number of business applications [1]. Each agent is an independent methodology with reasoning capabilities working on a prescribed task. The goal of the overall system is to provide a cooperative environment in which two or more agents can be combined to solve a problem through the use of a mediator or facilitator. The use of intelligent agents in biomedical systems has been limited, with the major focus on health care delivery [2,3], although some complex medical decision making problems have been addressed [4,5]. The research described here uses the intelligent agent framework to develop a computer-assisted aid for diagnosis of cardiac disorders, allowing the combination of existing decision support systems and new components. The resulting structure is an expansion of the hybrid system approach for the development of comprehensive computer-assisted medical decision support aids that can use differing methodologies to address different aspects of the overall problem [6]. In the following sections, the general methodology is explained, followed by the customization to diagnostic support in cardiology.

2. Methodology

The system contains five specific agents in addition to the medical professional, who is agent 0. The overall structure is shown in Figure 1. The five agents are defined in the following sections.

2.1. Knowledge-based model (EMERGE)

The first agent, EMERGE, is a knowledge-based system developed by the authors for chest pain analysis [7]. It uses a modified production rule that incorporates approximate reasoning techniques with partial substantiation and weighting of antecedents. The general evidence aggregation formula is based on substantiation of proposition P determined by assuming there is some subset C of V such that either the number of elements in C satisfies Q; or that each element in C satisfies the property A. The degree S to which C satisfies P is:

$$S = \max_{C\, \varepsilon A} \{V_P(c)\} \tag{1}$$

where

$$V_P(c) = \max[(Q \sum_{i=1}^{n} c_i \wedge a_i) \wedge \min_{i=1,\dots,n} (w_i^{\,c_i \wedge a_i})] \tag{2}$$

where ^ indicates minimum, w_i and a_i are the weighting factor and degree of substantiation of the i^{th} antecedent, $c_i \in \{0,1\}$, Q is a linguistic quantifier, and n is the number of antecedents. The initial rule base for EMERGE concentrated on evaluation of chest pain in the emergency room and has since been used in additional applications [8]. New methods aligned with evidence based medicine techniques handled by agent 2 are used to update the knowledge base.

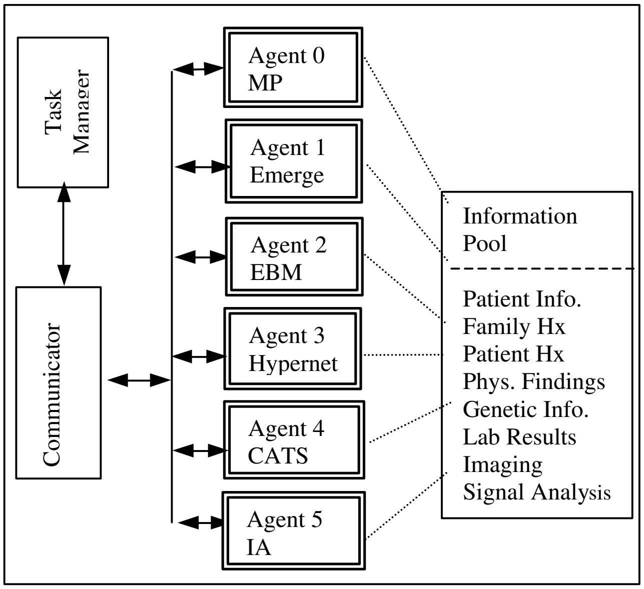

Figure 1. Computational Architecture

2.2. Evidence-based medicine (EBM)

The knowledge base for EMERGE was expanded through both expert input and evidence based medicine techniques [9] to insure inclusion of the latest available information. Evidence-based medicine focuses on the use of relevant medical literature to assist in clinical decision making. The intent of EBM is to supply information to a physician to aid in the decision process, not as a source of information of computer-assisted clinical support systems. However, this information can be used to augment both knowledge-based and data-based automated decision aids.

2.3. Data-based model (Hypernet)

The third agent is based on Hypernet [10], a neural network model developed by the authors and subsequently used as a classification tool in a number of medical applications, including analysis of exercise treadmill tests. Hypernet uses an expanded potential function approach in a supervised learning algorithm resulting in a nonlinear network structure with three or more layers. Input parameters can be any type of ordered data. Output is in the form of a decision function:

$$D(\mathbf{x}) = \sum_{i=1}^{n} w_i x_i + \sum_{i=1}^{n} \sum_{j=1\ (i\neq j)}^{n} w_{ij} x_i x_j \qquad (3)$$

where x_i represents the value of ith input node, w_i is the weighting factor for the node, and w_{ij} is the weighting factor for the interaction of nodes i and j. If $D(\mathbf{x})$ exceeds a pre-specified threshold value the condition holds. The normalized value of $D(\mathbf{x})$ provides a degree of certainty in the decision.

2.4. Signal analysis (CATS)

Signal analysis data are important in many medical domains, but none as important as the electrocardiogram in cardiology. The signal analysis agent uses a methodology based on nonlinear dynamics developed by the authors [11]. The package, denoted CATS for chaotic analysis of time series, utilizes second-order difference plots. For the nth point in a time series, denoted T_n the second-order difference A_n, is defined as:

$$A_n = T_n - T_{n-1} \qquad (4)$$

The second-order difference plot is generated by plotting A_{n+1} vs. A_n. This plot gives a useful graphical display of the degree of variability in the time series. In order to be useful in data-based decision tools, the plot needs to be summarized numerically. This is accomplished through the use of the Central Tendency Measure (CTM) computed by selecting a circular region around the origin of radius r, counting the number of points that fall within the radius, and dividing by the total number of points. Let t = total number of points, and r = radius of central area:

$$\text{CTM} = \left[\sum_{i=1}^{t-2} \delta(d_i)\right]/(t-2) \qquad (5)$$

where $\delta(d_i) =$ 1 if $[(T_{i+2}-T_{i+1})^2+(T_{i+1}-T_i)^2]^{.5} < r$
0 otherwise.

2.5. Image analysis (IA)

Imaging of all types are accessible using picture archiving and computer storage (PACS) systems. While many pattern recognition algorithms have been developed for automated interpretation of images, these are in general supplemental to radiologist interpretation. For this implementation, natural language descriptions of abnormalities are used. In this situation, the radiologist can also be considered an agent.

2.6. Agent interactions

The principal components of the control structure are the task manager and the communications interface. The task manager breaks the problem into subtasks that are then directed toward the appropriate agents. It also combines results from agents, including the client, for the overall response to the problem. The communicator presents input to each agent in an understandable form and interprets output from each agent so that other relevant agents can understand it. The main components are the symbolic-numeric converter and the common language generator that interprets output in a form that can be communicated to each agent. The objective is to overlay the conversion similarly to a human user interface so no agent modification is required.

3. Application to cardiology

The implementation of the agents in terms of defining the agent knowledge algorithms and knowledge bases is explained in this section. Section 4 illustrates the use of these agents in the diagnostic mode.

3.1. Agent 1: EMERGE

The knowledge bases for EMERGE are developed through a combination of expert consultation and evidence-based medicine techniques. The production rule format allows for partial presence of symptoms and weighting of antecedents. Rules are substantiated by evidence aggregation using equation 1. A rule is substantiated if the accumulated evidence exceeds the rule threshold. Table 1 shows one rule for determining patient status. Degree of presence for the ith symptom, d_i, is determined by agent 0, the medical professional.

Table 1. Sample Rule for EMERGE.

Antecedent	Wt. Factor	° of presence
Atrial fibrillation	0.15	d_1
BP < 100/60	0.25	d_2
Abnormal mental status	0.05	d_3
Cold, clammy skin	0.05	d_4
Gray, cyanotic skin	0.05	d_5
Weak peripheral pulses	0.05	d_6
Urinary output < 30 cc/hr	0.05	d_7
Continuing chest pain	0.25	d_8
Heart rate > 120	0.10	d_9
Admit	Threshold 0.6	

3.2. Agent 2: EBM

Development and maintenance of knowledge bases is very time consuming and normally requires the cooperation of one or more experts. In order to facilitate the process, especially of updating knowledge, online searching using keywords and Mesh headings is used. In addition, intelligent searching agents that are specifically geared to the application locate recent publications that may augment the knowledge base. Incorporation of publication-based knowledge must involve evaluation of the study based on standard techniques of evidence evaluation [12].

3.3. Agent 3: Hypernet

Hypernet generates decision surfaces based on databases containing values for specific cases. For example, in a differential diagnosis application in cardiology, data were collected on patients in three categories: heart failure, other cardiac disease, and controls. Table 2 contains a list of clinical parameters. Hypernet using its imbedded learning algorithm selects relevant parameters from this list plus output from agent 4 that analyzes Holter recordings.

Table 2. Clinical parameters.

Demongraphics: ID, Age, Sex
Hx : Bypass, MI
Presence of symptoms: Dyspnea, Orthopnea, PND
Duration of Symptoms
Physical Findings: Resting HR, edema, rales,
gallup, mitroregurgitation
Functional Impairment (NYHA)
LV Ejection Fraction
Echo
ETT Data: Resting HR & BP
Time to max ST↓ & angina
Total exercise time
HR, BP at end of test
Reason for stopping
Electrolytes (Na, K, Mg, BUN, Cr)
Drugs: Digitalis, diuretic, ACE inhibitor, vasodilator,
anti-arrhythmic
URI/Viral Syndrome

3.4. Agent 4: CATS

Twenty-four hour Holter recordings from patients in the three categories mentioned in section 3.3 were used. Each patient recording contains approximately 100,000 points consisting of R-R intervals representing the time between successive heartbeats. The nth R-R interval is T_n in equation 4. Computation of the CTM for a file containing in excess of 100,000 points takes approximately 30 seconds on the SUN SPARCserver 470 which is used for the CTM calculation as well as Hypernet. Both algorithms can also be run on PCs. The general pattern of the CTM indicates the degree to which points are centered around the origin, with a low number indicating a low level of variability. Low variability is associated with normal subjects.

3.5. Agent 5: IA

Relevant imaging techniques for cardiac disorders include echocardiography, ultrasound, MRI, and standard chest radiographs. In the current implementation, radiologists perform image evaluation, interacting with the system as an agent. Future work will focus on using partially automated image analysis.

4. Results

The model has been used as a decision aid in a number of applications, including differential diagnosis of cardiac disorders, identification of specific cardiac diseases, and survival analysis. In the decision mode, the agents are invoked for data that is relevant to each model. EMERGE attempts to substantiate rules by combining degrees of presence of symptoms that are entered by the medical professional (agent 0). Hypernet provides information regarding the confirmation of conditions, the results of which are feed to the EMERGE system to be processed by additional rules. The CATS system determines a numeric value indicating the degree of variability in the Holter recording and passes this result to both Hypernet and EMERGE. Imaging results are entered directly into EMERGE. The model has been used in studies to diagnosis heart failure [13], to differentiate heart failure from other cardiac disorders [14], and to determine prognostic factors in heart failure. Results for the evaluation of prognostic factors in congestive heart failure using this model based on chaotic heart rate variability combined with clinical parameters resulted in sensitivity, specificity, and accuracy of 80%, 94%, and 88%, respectively.

5. Conclusion

The intelligent agent approach offers the advantage of free communication among differing methodologies, including using output from one agent as input to another. For example, output from the chaotic analyzer can be used as input to either the neural network model or the knowledge-based model. The model can incorporate both new domain knowledge as well as the addition on new methodologies without structural changes to the overall system. In complex diagnostic systems, many data types are important for complete evaluation of a patient, resulting in the necessity for different methodologies to interact in a seamless fashion. Intelligent agents are particularly important in cardiac diagnosis as virtually all data types found in medicine are important for thorough evaluation. Future work will include testing on larger populations with a broader range of cardiac disorders.

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