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FUZZY SET THEORY AND FUZZY LOGIC IN MEDICINE

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Abstract

The linguistic vagueness of medical terms and expressions, uncertainty in the occurrence and co-occurrence of medical entities, and incompleteness of medical data and medical theories are well-known features of patient data and medical knowledge. These factors need to be taken into account when designing practical medical knowledge-based systems. We found that fuzzy set theory and fuzzy logic are enormously powerful theories in this regard. Fuzzy set theory and fuzzy logic were applied in the following systems: CADIAG-II and MedFrame/CADIAG-IV, FuzzyTempToxopert, FuzzyKBWean, and FuzzyARDS. CADIAG-II and MedFrame/CADIAG-IV are framework programs for consultation systems to aid in differential diagnosis in internal medicine. FuzzyTempToxopert interprets toxoplasmosis serology test results automatically. It uses fuzzy concepts for temporal distance checking between ordered tests. FuzzyKBWean is an open-loop fuzzy control program for optimization and quality control of the ventilation and weaning process of patients after cardiac surgery at the intensive care unit (ICU). FuzzyARDS is an intelligent online program for monitoring data of patients with acute respiratory distress syndrome (ARDS) at the ICU. It employs fuzzy trend detection and fuzzy automata.

1. Introduction

Medical expert and knowledge-based systems are designed to provide expert-level, problem-specific advice in the areas of medical data interpretation, patient monitoring, diagnosis, treatment selection, disease prognosis, and patient medical management. They capture and make available the knowledge of experts and—by applying the knowledge to patient data—assist in decision-making on the part of medical personnel. Research in medical expert and knowledge-based systems and the development of such systems is of great importance in terms of quality assurance and cost curtailment in medicine. The growing complexity of the fund of knowledge makes the application of such systems indispensable. Provided that they are used correctly, the systems can reduce much of the repetitive and specialized mental effort made by the treating physician and enable him/her to devote attention to patient care.

Medical knowledge is processed by expert and knowledge-based systems, using stored medical knowledge and the current data of a patient. On this basis, the systems provide a range of alternative suggestions for patient care.

For those concerned with the construction of medical expert and knowledge-based systems, fuzzy set theory and fuzzy logic have a number of features that make them highly suitable for modeling uncertain information, which medical concepts, interpretation of patient status, and diagnostic as well as therapeutic decision-making are usually based upon.

First of all, medical entities such as symptoms, signs, test results, diseases and diagnoses, therapy proposals, prognostic information items, and patient medical management decisions may be defined as fuzzy sets. The usual inherent vagueness of these entities will thus be conserved. Secondly, fuzzy logic offers reasoning methods capable of drawing strict as well as approximate conclusions. Medicine demands such a wide range of possibilities because the body of medical theory includes definitional, causal, statistical, and heuristic knowledge. Practical medicine has to accept incomplete patient medical data and even incomplete medical theories. In such situations, vague and uncertain empirical information guides medical decisions and the diagnostic and therapeutic procedures they are based upon. Finally, fuzzy controller and fuzzy automata can be used as intelligent high-level patient control and monitoring devices employing real-time access to the various medical information systems.

A number of methods and computer systems using the theory of fuzzy sets and fuzzy logic and off-spring concepts (or fuzziness theory, for short, cf. [SADEGH-ZADEH 2001], p. 1) have been developed and applied over the last 30 years. A number of overviews, editorials, and books on this subject have been published [ADLASSNIG 1982; MAIERS 1985; STEIMANN 1997; TEODORESCU ET AL. 1999; ADLASSNIG 2000; MORDESON ET AL. 2000; SZCZEPANIAK ET AL. 2000]. Most recently, a special issue of the journal *Artificial Intelligence in Medicine* entitled Fuzzy Theory in Medicine dedicated to LOTFI A. ZADEH on the occasion of his 80th birthday was also published [STEIMANN 2001].

2. Medical domains

The results of these research activities have influenced a number of computer applications in medicine:

- *Clinical patient management*: Helping to monitor the patient's measured and derived medical data and generate reminders, warnings, and alerts during the automatic processing of medical protocols and guidelines.
- *Laboratory medicine*: Providing knowledge-based interpretive reports of laboratory test results and having alerting modules check for notifiable, noteworthy, contradictory, or otherwise remarkable laboratory data.
- *Anesthesia and intensive care*: Building monitoring systems for summarizing and abstracting patient data, disease prevention and early detection of diseases, observing entry criteria for therapies, and building knowledge-based adaptive control systems for medical devices.
- *Internal medicine*: Providing knowledge-based filtering, abstraction, and aggregation of medical data under consideration of their context dependency and temporal course, offering the physician widely applicable consultation systems for differential diagnosis and therapy in difficult cases, and providing electronic text tools for rare syndromes and rare pathological constellations by means of knowledge-based searching routines.
- *Image generating and processing medicine*: Introducing systems for knowledge-based navigation and monitoring of diagnostic and surgical procedures including routines to avoid undesired events or critical anatomical regions, providing differential diagnostic support during image interpretation, and offering clinical data of patients after previous knowledge-based filtering in order to assist the image-diagnosing physician in his/her decision.

3. CADIAG-II and MedFrame/CADIAG-IV: Fuzzy systems in internal medicine

3.1. CADIAG-II: A diagnostic consultation system for internal medicine

Computer-assisted diagnostic (CADIAG) projects are long-term efforts aimed to set up consultation systems able to extensively assist in differential diagnosis and eventually in the therapeutic process in internal medicine. CADIAG-II, a consultation system formally based on fuzzy set theory and fuzzy logic, was developed and tested in 1979/80 [ADLASSNIG 1980]. The clinical issues underlying CADIAG-II are as follows:

- *Indication of all possible disease hypotheses* that can explain the given symptoms from the patient history, signs from the physical examination, pathological test results obtained in the laboratory, and findings from clinical investigations such as ultrasonography, radiography, biosignal tests, endoscopy, and histology.
- *Proposals for further useful questions to and examination of the patient* to confirm or exclude postulated diagnostic hypotheses or to find corroborative or discorroborative support for them.
- *Search for pathological findings present in the patient that are not yet accounted for* by CADIAG-II's diagnostic hypotheses, then triggering the continuation of differential diagnostic—possibly in a different medical area—until all pathological findings in the patient are accounted for.

CADIAG-II was described in various stages of development [ADLASSNIG 1986; ADLASSNIG 1988] and applied in different areas of internal medicine [LEITICH ET AL. 1996; ADLASSNIG & AKHAVAN-HEIDARI 1989; ADLASSNIG & SCHEITHAUER 1989]. It is fully integrated into the medical information system (Wiener Allgemeines Medizinisches Informationssystem, WAMIS) of the Vienna General Hospital [ADLASSNIG ET AL. 1986]. A prospective medical study concerning CADIAG-II and rheumatic diseases was recently published [LEITICH ET AL. 2001].

3.2. MedFrame/CADIAG-IV: An internet-based framework for diagnostic and therapeutic decision support

MedFrame/CADIAG-IV is the present successor of the former CADIAG systems. MedFrame is intended to construct a broad platform for the development of various knowledge-based systems in medicine: differential diagnosis or differential therapy in the entire field of internal medicine, for subspecialty areas of internal medicine such as cardiology, angiology, gastroenterology, hepatology, nephrology, rheumatology, pulmology, neurology, endocrinology, metabolic diseases, or for smaller subspecialties of medicine such as differential diagnosis of abdominal pain, headaches, vertigo, etc. It can also host knowledge-based systems for the interpretive analysis of laboratory test results. An integrated patient data and medical knowledge base, knowledge base editor modules, differential diagnosis and therapy modules, and an immediate case evaluation module will constitute the core of MedFrame.

MedFrame/CADIAG-IV will be upward compatible with respect to the available medical knowledge bases contained in the former CADIAG systems. Improved data-to-symbol conversion with extended context dependency, stepwise abstraction of high-level medical concepts including temporal concepts, extended frame and rule-based knowledge representation, inference procedures able to infer positive and negative diagnostic hypotheses as well as positive and negative therapy proposals are features of MedFrame/CADIAG-IV. Parts of the system have been described in the past [BOEGL ET AL. 1996; BOEGL 1997; KOLOUSEK 1997; BREIN ET AL. 1998; ROTHENFLUH ET AL. 2000].

The development of CADIAG systems, the integration of CADIAG-II into the medical information system WAMIS, and their extended retrospective and prospective case evaluations with patient records from the Vienna General Hospital constitute a broad and basic foundation of theoretical and practical knowledge to develop a new and extended system for the ambitious task of assisting in the mental diagnostic and therapeutic activities of physicians, nurses, and laboratory personnel. The MedFrame/CADIAG-IV system—presently in an active developmental phase—will eventually signify a major step towards support in decision-making and computer-based automation of subspecialties of medical practice.

4. FuzzyTempToxopert—A fuzzy system in laboratory medicine

FuzzyTempToxopert interprets toxoplasmosis serology test results obtained in the course of screening for *Toxoplasma gondii* infections in pregnant women. This screening program is obligatory for all pregnant women in Austria. The antibody tests are performed at the toxoplasmosis laboratory of the Department of Pediatrics and Adolescent Medicine at the Vienna General Hospital. FuzzyTempToxopert interprets them in the course of time and automatically provides a diagnostic interpretation and, most importantly, therapeutic recommendations to avoid fetal damage or subsequent harm to the child.

FuzzyTempToxopert contains a knowledge base in the form of a decision graph. Decision rules control the transition from one decision node to the next; each transition step is activated by obtaining a further serological test result. In order to arrive at correct diagnostic interpretations, a minimal temporal distance from one test to the next has to be observed. These minimal distances are checked by applying fuzzy sets modeling temporal concepts such as 'at least three weeks'. Recent tests [KOPECKY ET AL. 2000a] confirmed the applicability of FuzzyTempToxopert for routine use in the toxoplasmosis laboratory. Steps preceding the FuzzyTempToxopert have also been published [NAGY 1996; NAGY ET AL. 1997; KOPECKY 1999; RAPPELSBERGER ET AL. 1999; KOPECKY ET AL. 2000b].

5. Fuzzy systems in intensive care medicine

5.1. FuzzyKBWean: Knowledge-based weaning from artificial ventilation

FuzzyKBWean is an open-loop fuzzy control system for optimization and quality control of the ventilation and weaning process in patients after cardiac surgery at one of the ICUs of the Vienna General Hospital, the main teaching hospital of the University of Vienna Medical School.

The system is directly connected to the patient data management system (PDMS) of the ICU and is run on bedside computers, as previously described [SCHUH ET AL. 1998]. At one-minute intervals, it actively accesses the PDMS data base and transfers the patient's medical data required for ventilation and weaning decisions.

According to the well-known structure of fuzzy control systems, a fuzzification step is followed by a fuzzy rule evaluation. The fuzzy rules in FuzzyKBWean contain linguistically expressed physiological parameters of the patient and actual ventilator settings in their antecedents, yet crisp proposals for new settings of the ventilator in the consequences of the rules. Thus, it is possible to apply the Sugeno control method to combine rule output of the same kind [SCHUH 1998]. Moreover, a fuzzy set and a fuzzy rule editor known as FuzzyKBWEdit have been programmed. They enable the cooperating physicians to directly carry out changes in the knowledge base at the ICU.

An early study concerning FuzzyKBWean was published in 1993 [HIESMAYR ET AL. 1993]. A recent clinical trial showed that a number of appropriate proposals for ventilator settings are given at stages of the weaning process, earlier than the attending personal would react. Thus the proposed adjustments to stabilize the ventilated patient, to start and end the weaning process, and finally to extubate the patient caused less suffering for the patient and reduced costs.

5.2. FuzzyARDS: Knowledge-based patient monitoring and therapy entry criteria decision support

FuzzyARDS/MONITOR is an intelligent online monitoring program for the intensive care data of patients with acute respiratory distress syndrome (ARDS) [STELTZER ET AL. 1999]. Its clinical aim is to detect ARDS in patients as early as possible and to provide appropriate therapeutic advice.

ARDS is an ill-defined medical entity and is modeled using the concept of fuzzy automata. States in these automata are considered to be a patient's pathophysiological state or entry criteria for different forms of ARDS therapy. Patients may be partially assigned to one or several states in such an automaton at the same point in time. Transitions in the automata carry fuzzy conditions that have to be true or partially true to transit from one state to another. Fuzzy conditions are usually high-level medical concepts such as 'low', 'normal', or 'high F_iO_2', 'hypoxemia', or linguistically expressed trend information, e.g., 'rapidly improving oxygenation'. These high-level concepts are permanently evaluated in a data-to-symbol conversion step according to adjustable time granularity. Detailed descriptions of these formal concepts have been published [STEIMANN & ADLASSNIG 1994b; STEIMANN 1996].

In the present phase of development, an international study has been conducted to compare and eventually improve the various definitions of ARDS used at medical study centers and compare the respective entry criteria used for therapeutic decisions. A web-based system known as FuzzyARDS/STUDY was programmed, allowing patient data entry at the study centers, the definition of fuzzy criteria, the calculation of fuzzy scores with respect to fuzzy criteria in various stages of disease, and patient data evaluations based on interval techniques to consider missing variables in the given patient data sets. Most of the work done so far has been summarized in two publications [STELTZER ET AL. 1996; TRUMMER ET AL. 1998].

Based on the available FuzzyARDS/STUDY system, patient data sets are entered at the various study centers and evaluated in ARDS consensus meetings. The results led to a better understanding of ARDS as a life-threatening disease as well as to a better understanding of its treatment [STELTZER ET AL. 1999]. Based on these results, FuzzyARDS/MONITOR is continuously adjusted to newly derived medical knowledge. A prototype application of FuzzyARDS/MONITOR is available for clinical tests [STEIMANN & ADLASSNIG 1994a]. Some problems still have to be solved, e.g., the definition and incorporation of idle and delay functions in the online monitor to avoid oscillations in the patient states.

6. Discussion

Fuzzy set theory and fuzzy logic provide a highly suitable and broadly applicable basis for developing medical expert and knowledge-based systems in medicine, where the tasks include interpretation of sets of medical findings, single or differential diagnosis of diseases in various areas of medicine, optimal selection of medical therapy, and real-time monitoring of patient data for various purposes.

The clinical studies conducted so far show the appropriateness of the respective patient data and fuzzy knowledge representation and the selected fuzzy inference mechanisms with respect to the necessary medical applicability and the achieved correctness of the results. They further revealed the immediate intuitive understanding of the basic ideas of fuzzy set theory and fuzzy logic by the medical users. Thus, it is easily understood that the transition from healthy to ill and from normal to pathological, which is modeled by fuzzy sets in the above-mentioned knowledge-based systems, is a gradual transition and not a crisp one, or that the partial firing of rules with partially valid antecedents naturally diminishes the validity of the resulting consequence—a mechanism inherent to fuzzy logic.

Fuzzy set theory and fuzzy logic in medical expert and knowledge-based systems will become a standard methodology of medical computer systems based on computational intelligence. Eventually, there will be a time when medical expert and knowledge-based systems will be ubiquitously applied as natural tools in any medical setting [WYKE 1997].

The above-mentioned computer systems have reached the state of extensive clinical integration and testing at the Vienna General Hospital. The obtained results show the applicability and usefulness of these systems.

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