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A FRAMEWORK FOR CLINICAL DECISION SUPPORT IN INTERNAL MEDICINE – A PRELIMINARY VIEW

Kopecky D[1], Adlassnig K-P[1]

Abstract

MedFrame provides a medical institution with a set of software tools for developing knowledge bases and inference mechanisms and applying them as expert systems in clinical routine. CADIAG-IV—a data-driven fuzzy expert system for computer-assisted consultation in internal medicine—is entirely based on MedFrame. MedFrame's core components have been implemented; the implementation realization of CADIAG-IV and its application in clinical rheumatology is currently in progress. The achieved results confirm the applicability and scalability of the MedFrame/CADIAG-IV approach.

Keywords *– **Medical expert system, MedFrame, CADIAG, Fuzzy logic, Rheumatology***

1. Introduction

CADIAG-II and -III [2, 10] are data-driven fuzzy expert systems for the purpose of computer-assisted consultation in internal medicine. They provide diagnostic hypotheses as well as confirmed and excluded diagnoses, if possible, explain their indication, and propose further useful examinations in response to the input of a list of symptoms, signs, laboratory test results, and clinical findings pertaining to a patient. A PC-based medical expert system shell named MedFrame [4, 9] will be developed as the basis of a newly designed CADIAG-IV [6], the successor of the IBM-host-computer-system-based CADIAG-II and -III. Its purpose is to substantially extend the application of fuzzy concepts.

2. Methods

2. 1. MedFrame

Expert systems are required to contain at least three components: a knowledge base using particular knowledge representation formalism, an inference engine, and a dialog component for communication between system and user. A knowledge acquisition component and a component for explaining the established results are also desirable. This is especially true for medical expert systems whose purpose is to provide the physician with fully transparent diagnostic and/or therapeutic proposals.

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1 Section for Medical Expert and Knowledge-Based Systems, Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Austria

Expert system shells offer the user specific knowledge representation formalism and an adequate inference mechanism for building knowledge bases. Therefore, it is no longer necessary to reimplement or adapt various parts of an existing expert system when a new knowledge base is installed. However, expert system shells usually have the following drawbacks:

- only a single knowledge representation formalism and inference mechanism (e.g., predicate logic) is provided; therefore, only a certain class of problems can be modeled;
- knowledge acquisition components are rarely targeted to the needs of domain experts, and thus specially trained knowledge engineers are required;
- the implementation of reusable dialog and explanation components is usually not supported;
- the possibility to provide reference cases for automatic validation of the knowledge base after a modification is commonly not available;
- the storage of external information such as patient data is usually not possible.

These concerns prompted us to define a set of requirements for an expert system shell to be used in medicine. We decided to implement an expert system shell named MedFrame that will include the following functions:

- various representation formalisms for knowledge and inference mechanisms;
- interfaces to add further inference mechanisms;
- concepts for modeling and handling uncertainty in medical terminology and relations;
- mechanisms for storing patient data and history;
- a graphical user interface providing the four essential components of expert systems: (a) a knowledge acquisition component, (b) a component allowing the definition of a set of test patients with approved gold-standard diagnoses, (c) an interface for the input of patients' administrative and examination data, and (d) a component for displaying the inferred diagnostic and/or therapeutic hypotheses and proposals for further examination;
- interfaces to adapt the GUI components to the requirements of particular medical domains.

By offering this functionality, MedFrame provides the end user with a set of tools for developing knowledge bases and also allows the application programmer to extend the expert system shell components by implementing a set of interfaces and using a collection of libraries. Therefore, MedFrame significantly reduces the time and cost of building new expert systems. A discussion of the core components of MedFrame, a flexible object model for storing clinical data as well as medical knowledge, can be found in [9]. Further components of the expert system shell, such as knowledge acquisition systems and inference mechanism are considered in [6, 9].

2. 2. CADIAG-IV

CADIAG-IV will be the first expert system to be entirely based on MedFrame. Its predecessors CADIAG-II and -III are data-driven fuzzy medical expert systems providing diagnostic hypotheses as well as confirmed and excluded diagnoses, if possible, explaining their indications, and proposing further useful examinations in response to the input of a list of symptoms, signs, laboratory test results, and clinical findings pertaining to a patient. To deal with the inherent vagueness of boundaries in medical linguistic terms and the uncertainty of medical relationships, CADIAG-II and -III rely on the theory of fuzzy sets, particularly on the concepts of linguistic variables and fuzzy logic [12]. A comprehensive discussion of CADIAG-II is provided in [1].

As in CADIAG-II and -III, a clear distinction is also made in CADIAG-IV between patient data on a detailed observational level on the one hand (detailed history items, signs from physical examinations, quantitative laboratory test results, etc.), and interpreted and aggregated data (symptoms, pathological signs, abnormal laboratory test results, etc.) on the other hand. At the beginning of a consultation, a transformation step known as data-to-symbol conversion which abstracts and aggregates medical information measured or provided by the physician into this internal representation is applied. In CADIAG-II and -III this transformation process assigns a real number in [0, 1], a "degree of presence", to every symptom, where a value of 1 means that the corresponding symptom is fully present, while values in (0, 1) mean that the symptom is present in the patient to a certain degree. Symptoms that can definitely be excluded are assigned the value of 0. The transformation process is formally defined by a set of linguistic variables and their corresponding membership functions (cf.,[2, 10]).

However, this methodology can only express total exclusion of a medical entity. It is unable to provide so-called negative evidence, thus indicating the absence of a particular medical entity to a certain degree. To overcome this limitation, CADIAG-IV assigns two values to every medical entity: (a) strength of evidence and (b) strength of counter-evidence. Both values are—to overcome the criticism of rather sharp and therefore not very fuzzy point values in CADIAG-II and -III—fuzzy truth values in [0, 1]. The interpretation of these values is as follows: a fuzzy truth value representing 0 means that we have no evidence (or counter-evidence) regarding this medical entity while a fuzzy truth value representing 1 is interpreted as evidence (or exclusion). Intermediate values denote evidence that is not sufficient to prove or rule out the entity in question. Therefore, the data-to-symbol conversion is adapted so that every symptom is assigned two fuzzy truth values instead of a single point value. In addition, the process has been enhanced to deal with context-sensitive as well as pathophysiologically interdependent data. A more detailed examination of the data-to-symbol conversion in CADIAG-IV may be found in [5].

In CADIAG-II and -III, relationships between medical entities are represented as rules being defined by (a) the strength of confirmation and (b) the frequency of occurrence. The occurrence value describes the certainty with which the left-hand side of the rule will occur in patients already showing the right-hand side, while the confirmation value describes the certainty with which the consequence of the rule occurs in patients already showing the antecedent, i.e., how much evidence the antecedent provides for the consequence. In CADIAG-IV, this type of rule relationship is only to be used to model evidence for a medical entity. A second type of rule is used to model counter-evidence; this rule is defined by (a) the strength of disconfirmation and (b) the frequency of absence, which function in a diametrically opposed manner. In CADIAG-IV, all of these values are expressed by a fuzzy number in [0, 1] while point values are used in CADIAG-II and -III.

The basic concept upon which the inference mechanisms of both systems rely is the compositional rule of fuzzy inference [12]. A comprehensive description of the inference in CADIAG-II and -III is given in [2, 10]. The main advancement in CADIAG-IV is its handling of the newly introduced concept of counter-evidence and the computation of evidence and counter-evidence with fuzzy numbers. Further improvements are the realization of patient-specific adaptation of the rule base during inference, the possibility to use different fuzzy operators for the evaluation of symptom combinations, and the operators used for the compositional inference rule. Theoretical considerations regarding inference in CADIAG-IV may be found in [4].

3. Results

After the implementation of the components that transform MedFrame into a fully-featured expert system shell, in a first step the knowledge base of CADIAG-II/RHEUMA including all available patient data from the relevant clinics was transferred from the record-oriented representation of the previously used IBM host system WAMIS to the object-oriented model of MedFrame. For this purpose a set of converter components were implemented. These contain two parser components as an integral part: one for CADIAG-II- and one for CADIAG-IV-rules. Therefore, both the syntax of CADIAG-II and CADIAG-IV-rules have been set up in Backus-Naur Form (BNF) (as shown in *Figure 1*) and automatically converted into parser components by the Java parser generator JavaCC. As a result, two MedFrame modules—the equivalent of a knowledge base in MedFrame—were created: CADIAG-II/RHEUMA and CADIAG-IV/RHEUMA.

<table>
<tr><td><Rule></td><td>::=</td><td><Symptom> :- <Symptom>, <StrengthOfRelation>, <FrequencyOfRelation>, <Relationship></td></tr>
<tr><td></td><td></td><td>| <Disease> :- <Symptom>, <StrengthOfRelation>, <FrequencyOfRelation>, <Relationship></td></tr>
<tr><td></td><td></td><td>| <Disease> :- <Disease>, <StrengthOfRelation>, <FrequencyOfRelation>, <Relationship></td></tr>
<tr><td></td><td></td><td>| <Disease> :- <SYC-Name>, <StrengthOfRelation>, <FrequencyOfRelation>, <Relationship></td></tr>
<tr><td></td><td></td><td>| <Therapy> :- <Disease>, <StrengthOfRelation>, <FrequencyOfRelation>, <Relationship></td></tr>
<tr><td></td><td></td><td>| <Therapy> :- <Therapy>, <StrengthOfRelation>, <FrequencyOfRelation>, <Relationship></td></tr>
<tr><td></td><td></td><td>| <Symptom> :- <Disease>, <StrengthOfRelation>, <FrequencyOfRelation>, <Relationship></td></tr>
<tr><td></td><td></td><td>| <Symptom> :- <Therapy>, <StrengthOfRelation>, <FrequencyOfRelation>, <Relationship></td></tr>
<tr><td></td><td></td><td>| <Disease> :- <Therapy>, <StrengthOfRelation>, <FrequencyOfRelation>, <Relationship></td></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td><Symptom-Combination></td><td>::=</td><td><SYC-Name> := <SYC-Expression></td></tr>
<tr><td><SYC-Expression></td><td>::=</td><td><SYC-Term> {∨ <SYC-Term>}*</td></tr>
<tr><td><SYC-Term></td><td>::=</td><td><SYC-Factor> {∧ <SYC-Factor>}*</td></tr>
<tr><td><SYC-Factor></td><td>::=</td><td>[¬] <SYC-Variable></td></tr>
<tr><td><SYC-Variable></td><td>::=</td><td><Symptom></td></tr>
<tr><td></td><td></td><td>| <Disease></td></tr>
<tr><td></td><td></td><td>| <Therapy></td></tr>
<tr><td></td><td></td><td>| <IC-Name></td></tr>
<tr><td></td><td></td><td>| (<SYC-Expression>)</td></tr>
<tr><td></td><td></td><td>| <SYC-MIMA-Term></td></tr>
<tr><td><SYC-MIMA-Term></td><td>::=</td><td>{fzatleast | fzatmost}(<Part-Whole>, <SYC-Variable-List>)</td></tr>
<tr><td><SYC-Variable-List></td><td>::=</td><td><SYC-Expression> {, <SYC-Expression>}*</td></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td><StrengthOfRelation></td><td>::=</td><td><Fuzzy-Degree></td></tr>
<tr><td><FrequencyOfRelation></td><td>::=</td><td><Fuzzy-Degree></td></tr>
<tr><td><Relationship></td><td>::=</td><td>[+ | -]</td></tr>
<tr><td><Symptom></td><td>::=</td><td>S<Integer></td></tr>
<tr><td><Diagnosis></td><td>::=</td><td>D<Integer></td></tr>
<tr><td><Therapy></td><td>::=</td><td>T<Integer></td></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td><SYC-Name></td><td>::=</td><td>SYC<Integer></td></tr>
<tr><td><IC-Name></td><td>::=</td><td>IC<Integer></td></tr>
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<tr><td><Fuzzy-Degree></td><td>::=</td><td>PI(<Degree>,<Degree>,<Degree>,<Degree>)</td></tr>
<tr><td></td><td></td><td>| Lambda(<Degree>,<Degree>,<Degree>)</td></tr>
<tr><td></td><td></td><td>| Singleton(<Degree>)</td></tr>
<tr><td><PartWhole></td><td>::=</td><td><Integer>/<Integer></td></tr>
<tr><td><Degree></td><td>::=</td><td>0.{<Digit>}+ | 1.0</td></tr>
<tr><td><Integer></td><td>::=</td><td>{<Digit>}+</td></tr>
<tr><td><Digit></td><td>::=</td><td>0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9</td></tr>
</table>

Figure 1: The Syntax of CADIAG-IV Rules in BNF

Based on the components developed for MedFrame, the inference mechanism of CADIAG-II/-III was reimplemented in Java. For this purpose, a general set of inference components was developed inside of MedFrame, which are capable of dealing with CADIAG rules and other types of rules as well. These components were used as a foundation on which the CADIAG-II/-III-inference process was implemented. The outcomes were compared to the results generated by the original CADIAG.

Tests have confirmed the applicability, accuracy, and performance of the MedFrame concept and the CADIAG reimplementation: the inference engine produces the same results as the original CADIAG-II and -III [7]. A consultation takes only about a second and is thus considered to be fast. MedFrame provides all functionalities needed for implementing expert systems like CADIAG-II.

4. Discussion

Besides the CADIAG systems, three other major decision support systems for internal medicine have been developed in the past: DXplain [3], Iliad [11], and QMR [8]. DXplain [3] interprets clinical findings (signs, symptoms, laboratory results) to infer a sorted list of diagnoses which might explain (or be associated with) the clinical manifestations. The system applies a modified form of Bayesian logic to derive clinical interpretations and provides justifications as to why each of these diseases might be considered. Iliad [11] uses Bayesian reasoning to calculate the posterior probabilities of various diagnoses under consideration, given the findings present in a case. Iliad is also part of an expert system shell that can be used to develop and evaluate knowledge bases.

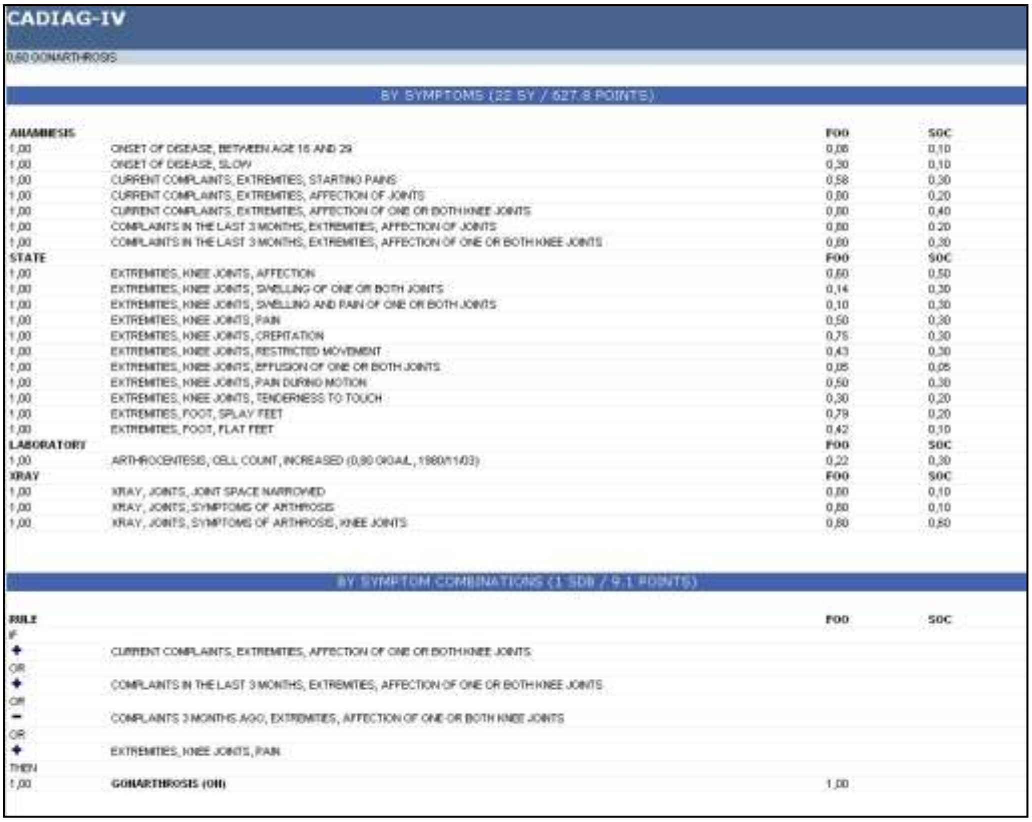

Figure 2: Screenshot of the Explanation for an Inferred Diagnosis

Finally, in QMR [8] which is the successor of INTERNIST-I, data input includes signs, laboratory data, and aspects of the patient’s history. The inference is based on a ranking algorithm to produce a list of ranked diagnoses based on disease profiles. The heuristic rules rely on a partitioning algorithm to create problem areas, and exclusion functions to eliminate diagnostic possibilities.

Although the overall design is similar in all described systems, they differ in respect of one major aspect, namely knowledge representation. While DXplain and Iliad apply Bayesian logic, QMR relies on hierarchical decision-tree logic. In our opinion, systems based on Bayesian logic are not equipped with the necessary power to provide the physician with a comprehensive explanation as to why a specific diagnosis has been inferred. The hierarchical or taxonomic decision-tree logic of QMR on the other hand, which links each disease profile to only one “parent” disease class, misses the power to model all of the complex cases of internal medicine. The rule-based approach of the CADIAG systems combines the power to model complex cases and relations with the possibility to clearly explain the reasons for the proposed inference result. Using the concepts of fuzzy set theory and fuzzy logic, an additional level of expressiveness is introduced into clinical decision support.

5. Outlook and Conclusion

Currently the realization of the CADIAG-IV inference engine is in progress, as are the consultation user interfaces. Modern web technologies are applied for the latter, including Java Server Faces

(JSF), the IceFaces component library, and the SEAM application framework. *Figure 2* shows a typical user interface in MedFrame and CADIAG-IV. It explains why CADIAG has inferred a particular diagnosis by showing the relevant medical information that led to the decision. After implementation of the rule-based inference engine, MedFrame now serves as a solid framework for building medical expert systems. In addition, MedFrame is equipped with two additional knowledge representation formalisms and inference mechanisms: decision graphs and lookup tables. At present these three formalisms constitute the basis of MedFrame.

6. References

[1] ADLASSNIG, K.-P., A Fuzzy Logical Model of Computer-Assisted Medical Diagnosis. Methods of Information in Medicine 1980;19:141–8.

[2] ADLASSNIG, K.-P., KOLARZ, G., SCHEITHAUER, W., GRABNER, H., Approach to a Hospital-Based Application of a Medical Expert System. Medical Informatics 1986;11:205–23.

[3] BARNETT, G.O., CIMINO, J.J., HUPP, J.A., HOFFER, E.P., Dxplain – An Evolving Diagnostic Decision-Support System. JAMA 1987;258:67–74.

[4] BOEGL, K., ADLASSNIG, K.-P., HAYASHI, Y., LEITICH, H., Knowledge Acquisition in the Fuzzy Knowledge Representation Framework of a Medical Consultation System. Artificial Intelligence in Medicine 2004;30:1–26.

[5] BOEGL, K., LEITICH, H., KOLOUSEK, G., ADLASSNIG, K.-P., Clinical Data Interpretation in MedFrame/ CADIAG-4 using Fuzzy Sets. Biomedical Engineering—Applications, Basis & Communications 1996;8:488–95.

[6] BREIN, L., ADLASSNIG, K.P., KOLOUSEK, G., Rule Base and Inference Process of the Medical Expert System CADIAG-IV, in: R. Trappl (ed.), Cybernetics and System '98, Austrian Society for Cybernetic Studies, Vienna 1998, pp. 155–9.

[7] LEITICH, H., KIENER, H.P., KOLARZ, G., SCHUH, C., GRANINGER, W., ADLASSNIG, K.-P., A Prospective Evaluation of the Medical Consultation System CADIAG-II/RHEUMA in a Rheumatological Outpatient Clinic. Methods of Information in Medicine 2001;40:213–20.

[8] MYERS, J.D., The Background of INTERNIST-I and QMR, in: B.I.Blum, K. Duncan (eds.), A History of Medical Informatics, ACM Press, New York 1990, pp.427–33.

[9] SAGEDER, B., BOEGL, K., ADLASSNIG, K.-P., KOLOUSEK, G., TRUMER, B., The Knowledge Model of MedFrame/CADIAG-IV, in: C. Pappas (ed.), Medical Informatics Europe '97, IOS Press, Amsterdam 1997, pp. 629–33.

[10] VETTERLEIN, T., CIABATTONI, A., On the (Fuzzy) Logical Content of CADIAG-2. Fuzzy Sets and Systems 2010;161(14):1941–58.

[11] WARNER, H.R., BOUHADDOU, O., Innovation Review: Iliad – A Medical Diagnostic Support Program, Topics in Health Information Management 1994;14:51–8.

[12] ZADEH, L.A., The Concept of a Linguistic Variable and Its Application to Approximate Reasoning-I. Information Sciences 1975; 8:338–53.

Corresponding Author

Dieter Kopecky
Section for Medical Expert and Knowledge-Based Systems
Center for Medical Statistics, Informatics, and Intelligent Systems
Medical University of Vienna, Spitalgasse 23, A-1090 Vienna
Email: dieter.kopecky@meduniwien.ac.at