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DETECTION OF INACCURACY IN A MEDICAL KNOWLEDGE BASE USING A CLASSICAL THEOREM PROVER

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Abstract

CADIAG-2 is a medical expert system to assist differential diagnosis in several sub-specialties of internal medicine. A patient's symptoms, signs, laboratory test results, and various clinical findings constitute the starting point of the computer-assisted differential diagnostic process. Lists of confirmed and excluded diagnoses as well as diagnostic hypotheses are the output. In this paper we logically verify CADIAG-2's knowledge base which consists of about 20,000 rules, by using a classical theorem prover. We identified ten inaccuracies in the present knowledge base. One of the inaccuracies is presented and discussed here.

Keywords – medical expert system, verification, knowledge base, first-order logic

1. Introduction

The expert systems CADIAG-1 and its successor CADIAG-2 – "CADIAG" stands for "computer-assisted diagnosis" – have been developed to support the diagnostic procedure in internal medicine. The system was developed by K.-P. Adlassnig's research group at the Medical University of Vienna. One of the many reasons for transforming CADIAG-1 into CADIAG-2 was to introduce graded notions for the presence or absence of the included medical entities, such as symptoms, signs, laboratory test results, and diagnoses. In all of these cases, a rational number between 0 and 1 is assigned. Each of the two CADIAG systems contains about 300 diseases from various medical specialties such as rheumatology [6, 7] and gastroenterology [3]. Both expert systems are data-driven rule-based systems. Whereas CADIAG-1's knowledge base was checked and 17 errors were found in [10], this was not done for CADIAG-2. Our aim was to check the knowledge base of CADIAG-2.

In this article we use the translation from CADIAG-2's rules into CADIAG-1's rules proposed in [1, 2, 4] and their formalization in first-order classical logic of the translated rules introduced in [10]. We then apply the theorem prover *Prover9* developed by McCune [9] to the large number of obtained logical formulas.

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2. Rules of CADIAG-1 and CADIAG-2

As regards the rules of CADIAG-1, five types of relationships are defined between medical entities in CADIAG-1 (see *Table 1*).

Table 1: Five essential relationships between medical entities in CADIAG-1

Rule type	Natural language	IF-THEN statements
α FC β	facultative occurring and confirming	if α then β
α ON β	obligatory occurring and non-confirming	if not α then not β
α EX β	excluding	if α then not β
α FN β	facultative occurring and non-confirming	if α then possibly β
α OC β	obligatory occurring and confirming	if α then β and if not α then not β

In both CADIAG-1 and CADIAG-2, compound statements are formed from symptoms and diagnoses by means of conjunction, disjunction, and negation. An antecedent α of a rule may possibly be compound and a consequent β is either a symptom or a diagnosis.

We briefly explain each type of rule. FC stands for facultative occurring and confirming. α does not have to be present in order to establish β (meaning that β does not imply α), but β is confirmed by the presence of α. ON stands for obligatory occurring and non-confirming. In this case, the absence of α excludes β. EX stands for excluding. The presence of α excludes β. FN stands for facultative occurring and non-confirming. FN rules may generate diagnostic hypotheses. Finally, OC stands for obligatory occurring and confirming. α has to be present in order to establish β; if α is absent, β is excluded. However, if α is present, β is confirmed.

Here is an example of an FC rule:
IF *intracellular uric acid crystals are detected in joint effusion* THEN confirm the diagnosis *gout.*

CADIAG-2 is the successor of CADIAG-1; the relationships between medical entities in CADIAG-2 are treated differently. In contrast to CADIAG-1, CADIAG-2 contains only one uniform type of rule. A rule in CADIAG-2's knowledge base is of the following type:

$$\text{IF } \alpha \text{ THEN } \beta \text{ WITH } soc, foo; \tag{1}$$

where *soc* (*strength* of *confirmation*) and *foo* (*frequency* of *occurrence*) are numbers in the real unit interval [0, 1]. The values *soc* and *foo* represent the strength of relationship between α and β. The larger *soc* (or *foo*) is, the stronger is the implication from α to β (or from β to α).

The inference engine of CADIAG-2, when applying a rule *r*, computes from *soc*, *foo*, and the value assigned to the antecedent α - the graded presence/absence value - is a value for the consequent β. For a detailed description of CADIAG-2's inference engine see [11].

3. Formal representation of CADIAG-2's rules

We present the rules of CADIAG-2 as first-order formulas in two steps. We first translate the rules into the form of CADIAG-1's rules and then apply the formalization of CADIAG-1's rules introduced in [10].

The rules of CADIAG-2 are divided into five groups (see *Table 2*) and associated with a specific type of CADIAG-1 rule. In [1], the following translation from CADIAG-2's rules into CADIAG-1 rules was proposed:

Table 2: Translation of five types of CADIAG-2 rules into five CADIAG-1 relationships

CADIAG-2 rule	specified by		CADIAG-1 rule
c1	soc = 1	0 < foo <1	FC
ao	0 < soc <1	foo = 1	ON
me	soc = 0	foo = 0	EX
cd	0< soc <1	0 < foo <1	FN
oc	soc = 1	foo = 1	OC

In [10], the formalization of the rules FC, ON, EX, FN, and OC was given in first-order logic. We identify each medical entity (symptom, sign, laboratory test result, clinical finding, or diagnosis with a one-place predicate S (resp. D), e.g., the formula $\forall xS(x)$ means that "all patients x have symptom S". We represent the antecedent α, which is possibly a compound statement of symptoms and diagnoses, by the formula $A(x)$ which is formed with the respective predicates. We represent the consequent β by the formula $B(x)$ which is either of the form $S(x)$ or $D(x)$. We denote a formula representing CADIAG-2's rule by the same symbol enclosed in parentheses, e.g., (c_d) and the translation above leads to the formulas presented below.

(KB) would be a set of formulas of first-order logic obtained by instantiating the formulas below with the entities of CADIAG-2, according to the system's knowledge base:

(c_1) $\forall x(A(x)\rightarrow B(x)) \wedge \exists xA(x) \wedge \exists x(\neg A(x) \wedge B(x))$
(ao) $\forall x(B(x)\rightarrow A(x)) \wedge \exists xB(x) \wedge \exists x(A(x) \wedge \neg B(x))$
(me) $\forall x(A(x)\rightarrow \neg B(x)) \wedge \exists xA(x) \wedge \exists xB(x)$
(c_d) $\exists x(A(x) \wedge B(x)) \wedge \exists x(A(x) \wedge \neg B(x)) \wedge \exists x(\neg A(x) \wedge B(x))$
(oc) $\forall x(A(x)\rightarrow B(x)) \wedge \forall x(B(x)\rightarrow A(x)) \wedge \exists xA(x)$

The formulas (KB) model the rules of CADIAG-2 in a semantically meaningful manner. We introduce the interpretation of *soc* and *foo* to support the chosen logical representation provided in [1]. Given a set of patients P, let us assume that every symptom and every diagnosis is assigned either 1 or 0. This assignment produces a system of subsets on P. We identify an antecedent α (or a consequent β) with a subset of patients to whom α (resp. β) applies. We denote a set of this type also with α (resp. β). We then define the following interpretation of *foo* and *soc*:

$$soc = \frac{F(\alpha \cap \beta)}{F(\alpha)} \tag{2}$$

$$foo = \frac{F(\alpha \cap \beta)}{F(\beta)} \tag{3}$$

where $F(\alpha)$, $F(\beta)$ and $F(\alpha\cap\beta)$ denote the frequency of patients in α, β, and α∩β, respectively.

This interpretation is a basis for explaining the formalization of CADIAG-2's rules as formulas (KB). As an example, we discuss the rule c_1 in a stepwise manner. The line of reasoning in the other cases is analogous.

The fact that *soc* and *foo* are defined, i.e., that the denominators in equations (2) and (3) are different from zero, can be represented by a formula $\exists x A(x) \wedge \exists x B(x)$ which we denote (DEF). For the rule c_1, *soc* is equal to one and *foo* is strictly less then one. From *soc* = 1 and equation (2), we conclude $F(\alpha \cap \beta) = F(\alpha)$, which means that α is a subset of β. This is formalized by formula $\forall x(A(x) \rightarrow B(x))$. From *foo* <1 and equation (3) we conclude $F(\alpha \cap \beta) < F(\beta)$. Hence, at least one patient in β does not belong to α. This is represented by the formula $\exists x(\neg A(x) \wedge B(x))$, which implies the right conjunct of (DEF). Thus, the resulting formula for c_1 is $\forall x(A(x) \rightarrow B(x)) \wedge \exists x A(x) \wedge \exists x(\neg A(x) \wedge B(x))$.

4. Consistency checking

We introduce a notion of inaccuracy in the knowledge base of CADIAG-2 and relate it to the set of formulas (KB) from the previous section. We say that a set of patients *P* together with an assignment to symptoms and diagnoses *models* a rule *r* (cf. (1)) of CADIAG-2 if *soc* and *foo* are calculated according to equations (2) and (3). *P* models CADIAG-2's knowledge base if it models all its rules. We say that there is an *inaccuracy* in CADIAG-2's knowledge base if a set of patients *P* that models it does not exist.

However, to check KB for inaccuracies in this manner is computationally infeasible. Instead, we transfer the check to the formulas representing the rules and check the consistency of the formulas. A relationship exists between the consistency of formulas (KB) and our notion of inaccuracy. If a set of patients *P* models CADIAG-2's knowledge base, it would mean that a model of the formulas (KB) exists. Hence, an inconsistency in (KB) would signify an inaccuracy in CADIAG-2's knowledge base.

The consistency check of (KB) was implemented using the theorem prover *Prover9* developed by McCune at the University of New Mexico; see [9]. *Prover9* identifies unsatisfiable formulas by proving the negation of their conjunction. However, an input such as (KB) is too extensive for *Prover9,* as CADIAG-2's KB contains more than 20,000 rules. Therefore, we represented CADIAG-2's KB as a graph whose vertices are the medical entities of the system, and whose edges connect two entities if there is a rule in the KB in which they both appear. Two entities are connected by a *k*-path, when there is a path between them containing at most *k* edges. We iterated through every medical entity *X* and natural number *k*. As input to Prover9, the formulas of (KB) containing at least one predicate representing the medical entity connected to *X* by a *k*-path were given. In applying this procedure, we detected ten sets of inconsistent formulas and thus ten inaccuracies in the KB.

Here is an example of one of these (the degree *foo* is omitted for the sake of simplicity):

(r1) IF *histology, connective tissue, fibrosarcoma*
THEN *fibrosarcoma*
with soc = 1.

(r2) IF *fibrosarcoma*
THEN *malign neoplastic cartilage-bone disease*
with soc = 1.

(r3) IF *histology, connective tissue, fibrosarcoma*
THEN *malign neoplastic cartilage-bone disease*
with soc = 0.1.

Rule (r1) states that a positive histology of fibrosarcoma in connective tissue (which is a proposition at the level of data collection) implies the diagnosis of fibrosarcoma. Furthermore, rule (r2) tells us that a fibrosarcoma is a form of malignant neoplastic cartilage-bone disease (a sub-super-term relationship). Thus, the proven positive histology also directly implies the disease super-term of a malignant neoplastic cartilage bone disease. The value soc = 0.1 is incorrect and must be substituted by 1.0. This mistake is probably due to a simple error in data entry error.

5. Discussion and conclusion

In [8], a consistency checking method based on similarity and affinity measures was introduced. The authors describe the consistency checker CCFE which is able to tackle mixed fuzzy and non-fuzzy terms. A further approach is described in [5]; the author suggests the use of directed acyclic graphs for representing the knowledge base. The arcs are weighted with certainty factors of the rules. An algorithm for finding all of the execution paths is presented. It also serves as a method of detecting inconsistencies.

By interpreting the relationships in CADIAG-2's KB by equations (2) and (3), we simplify the procedure of consistency checking. Note that equations (2) and (3) did not take gradedness into account. Symptoms and diagnoses involved in the rules of CADIAG-2 are fuzzy, i.e., values from the real unit interval [0, 1] are assigned to them. In this context, more precise interpretations of *soc* and *foo* are the following:

$$soc = \frac{\sum_x \min\{\alpha(x), \beta(x)\}}{\sum_x \alpha(x)}, \tag{4}$$

$$foo = \frac{\sum_x \min\{\alpha(x), \beta(x)\}}{\sum_x \beta(x)}, \tag{5}$$

where $\alpha(x)$ and $\beta(x)$ are numbers in [0,1], representing the degrees to which the entities α and β apply to a patient x, and the sum $\sum_x$ encompasses all considered patients.

However, this interpretation leads to formulas of first-order fuzzy logic and a search algorithm for inconsistent formulas is yet to be developed. Nevertheless, when we restrict the antecedents to single medical entities (i.e., formula $A(x)$ in (KB) is atomic), the satisfiability of the resulting first-order fuzzy logic formulas is equivalent to the satisfiability of the formulas presented here. How the satisfiability will change with compound antecedents yet to be determined, and will be investigated in future work.

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7. References

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