SOFT DEDUCTION RULES IN MEDICAL DIAGNOSTIC PROCESSES

by

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The methodology we propose for medical decision making is based on possibility theory and fuzzy logic. Three types of imprecise concepts involved in medical diagnosis processes are taken into account: evaluation of diagnostic indicators, medical knowledge and computed results. Moreover, this method allows the setting of a hierarchy among diagnostic indicators by means of what we call the suggestion value and the disconfirmation value associated with each diagnosis. Two soft deduction rules are proposed, that, in some sense, may be viewed as extensions of Modus Ponens and Modus Tollens. These rules act on fuzzy propositions and yield fuzzy degrees of presence and absence of a diagnosis which are then simultaneously interpreted. A concrete application to the classification of hyperlipoproteinemias, currently used in a conversational mode, is finally described.

Keywords: possibility distributions, fuzzy logic, deduction rules, suggestion, disconfirmation, medical diagnosis, classification.

1. INTRODUCTION

In medical reasoning, it is common to encounter qualitative descriptions of symptoms, diagnoses and pathological situations. In fact, many propositions state properties of attributes that may be viewed as labels of fuzzy sets because of vague boundaries, subjectivity, linguistic relationships, approximate descriptions, etc. Fuzziness appears to be inherent in most concept-formation and human reasoning processes, especially in the setting of some classes of medical diagnoses. Thus, handling of thresholds in biological tests is a difficult task for, in automatic procedures, acceptance or disconfirmation of a result can be a close decision in borderline cases. Can one say that a patient with a glycemia of 1.21 g/ℓ. is diabetic and that he/she is healthy with a glycemia of 1.19 g/ℓ? Another common example of imprecision is a patient's condition which is not either a healthy or a pathological state; instead there exists a gradual transition between these two states.

A sentence like "cholesterol is slightly increased" can be considered as a fuzzy proposition, of the form "X is A", inducing a possibility distribution $\Pi_X = A$. The theory of possibility distributions introduced by Zadeh is a simple and well adapted tool for handling such imprecise propositions. We shall widely use it in this paper to describe some deduction methods in fuzzy reasoning.

Our exposition is divided into three sections.

First, we propose two soft deduction rules for inference from fuzzy propositions. These rules are referred to as "Extended Modus Ponens" (EMP) and "Extended Modus Tollens" (EMT). Each is decomposed into two steps: matching (or not) of attributes by means of possibility measures, and final computation of the result by means of the bounded sum. A basic idea which we use throughout this paper involves the use of a functional correspondence between numbers in [0, 1] and possibility distributions of fuzzy subsets of [0, 1].

Second, the two soft deduction rules are employed as a basis for a methodology of computer-assisted medical decision-making. In particular, two notions of suggestion and disconfirmation which relate diagnostic indicatorsand diagnosis are introduced. These notions allow the setting of a hierarchy among diagnostic indicators, which relates to their importance with respect to the presence or absence of diagnoses. Suggestion and disconfirmation concepts are treated simultaneously to obtain a result.

Finally, a concrete application of this methodology to the classification of hyperlipoproteinemias is presented, an application which is simple to use with a computer in a conversational mode. Parameters defining fuzzy membership functions can be easily modified and the computed results are very informative.

2. SOFT DEDUCTION RULES

Let us first recall two basic concepts and definitions in possibility theory, Zadeh [21], namely possibility distribution and possibility measure.

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Let X be available which takes values in a universe of discourse U and let A be a fuzzy subset of U; then the proposition "X is A" associates a possibility distribution, Π_X, with X which is postulated to be equal to A. Instead of the possibility assignment equation "$\Pi_X = A$", we here simply write Π^A, i.e.

$$X \text{ is } A \rightarrow \Pi^A,$$

where, on the right hand side, the variable X_A is implicit, and the symbol "$\rightarrow$" indicates that Π^A is induced by "X is A."

Manipulation of possibility distributions is then derived from the basic operations in fuzzy set theory and fuzzy logic, e.g. if B is a fuzzy subset of U, then

$$X \text{ is } A \text{ and } X \text{ is } B \rightarrow \Pi^{A \cap B},$$

if

$$X \text{ is } B \rightarrow \Pi^B.$$

Assume now that Π^B is a reference possibility distribution in the sense that it will serve as a basis for characterizing a pattern with which other possibility distributions may be compared. Then, the possibility measure, $\pi(A)$, of A is defined as a number in [0, 1] given by[1]

$$\pi(A) \triangleq \sup_{u \in U} \mu_A(u) \wedge \mu_B(u),$$

where μ_A and μ_B are the respective membership functions of A and B.

We recall now that $\pi(A)$ expresses "the possibility that X is A given X is B," which we denote by $\pi(A|B)$, yielding

$$\pi(A|B) \triangleq \sup \Pi^{A \cap B},$$

where, equivalently, the right hand side is expressed in terms of compound possibility distributions.

In this definition, A and B are fuzzy sets in the same universe of discourse, U, so that they can be directly be compared in regard to their meaning.

Let us now introduce two new deduction rules, (I) and (II), involving fuzzy propositions.

[1] The symbol $\triangleq$ stands for "denotes" or "is equal by definition to."

$$\text{(I)} \quad \begin{cases} p_1 \triangleq X \text{ is } A \\ q_1 \triangleq \text{If } X \text{ is } B \text{ then } Y \text{ is } C \\ \hline r_1 \triangleq Y \text{ is } D \end{cases}$$

where X and Y are variables that take values in the universes of discourse U and V, respectively; A and B are fuzzy subsets of U; C and D are fuzzy subsets of V.

Several authors, e.g. Bellman and Zadeh [3], Mizumoto et al. [11], Baldwin [2], proposed and investigated methods to handle (I), i.e. how to derive proposition r_1 from the knowledge of propositions p_1 and q_1. The deduction rules we present here (see [17] for a more detailed description) are different; they are in fact very much oriented towards applications in the spirit of the one shown at the end of this paper. They involve normal[2] fuzzy sets either expressing concepts like "around a" where a is a number (or an interval), or fuzzy subsets of the unit interval [0, 1] expressing truth-values.

Strictly speaking, q_1 does not correspond to a logical implication, rather it expresses some dependence of C from X that emphasizes the "importance" of "X is B" in connection with a characterization of Y. For example, q_1 may have the form "If X is B_Y then Y is C_X," which means "If X is B (for a given Y) then Y is C (where C is defined in connection with X)." Further interpretations will be given with an application in this paper.

Returning now to (I), here is what we require in the deduction process. If A matches B, in the sense of $\pi(A|B) = 1$ (A not being necessarily equal to B, instead we may have $A \subseteq B$), then the inferred D is precisely C. In the particular particular case where A = B, (I) can be written as follows:

$$\begin{cases} X \text{ is } A \\ \text{If } X \text{ is } A \text{ then } Y \text{ is } C \\ \hline Y \text{ is } C \end{cases}$$

which explains the reference to (I) as the "extended Modus Ponens" or EMP, for short.

Before defining C, let us turn to (II) which will be referred to as "Extended Modus Tollens" or EMT.

[2] A fuzzy subset A of U is said normal iff $\sup_{u \in U} \mu_A(u) = 1$. Moreover, in our examples, the supremum is attained.

$$\text{(II)}\quad \begin{cases} p_2 \triangleq X \text{ is } A \\ q_2 \triangleq \text{If } Y \text{ is } C \text{ then } X \text{ is } B \\ \hline r_2 \triangleq Y \text{ is } D. \end{cases}$$

As in (I), X and Y are variables that take values in U and V, respectively; A and B are fuzzy subsets of U; C and D are fuzzy subsets of V. q_2 is interpreted in the same spirit as q_1. But here is now what we required in the deduction process. If A does not match B, i.e., if A is totally disjoint from B (A not being necessarily related to the complement B' of B) in the sense of $\pi(A|B) = 0$, then the inferred D in r_2 is precisely the complement C' of C.

In order to define fuzzy sets D in r_1 and in r_2, let us recall some definitions of fuzzy truth values.

In fuzzy logic [3], a fuzzy truth value is a fuzzy subset of [0, 1], where [0, 1] in association with the logical connectives constitutes the base logic.

Fuzzy truth values <u>true</u> and <u>false</u> are defined as follows, Zadeh [20], as in the work of Baldwin [2], Tsukamoto [18].

$$\forall x \in [0,1],\ \mu_{\underline{\text{true}}}(x) = x,\ \mu_{\underline{\text{false}}}(x) = 1-x.$$

From these fuzzy truth values, by using linguistic modifiers such as <u>fairly</u>, <u>very</u>, other fuzzy truth values are defined. For example, $\forall x \in [0,1]$,

$$\mu_{\underline{\text{very true}}}(x) = x^2,\ \mu_{\text{fairly true}}(x) = x^{1/2},$$

$$\mu_{\underline{\text{very false}}}(x) = (1-x)^2, \text{ etc.}$$

Moreover, the fuzzy truth values <u>absolutely true</u> (τ) and <u>absolutely false</u> (ϕ) are defined as:

$$\mu_\tau(x) = \begin{cases} 1 & \text{if } x = 1 \\ 0 & \text{otherwise} \end{cases};\ \mu_\phi(x) = \begin{cases} 1 & \text{if } x = 0 \\ 0 & \text{otherwise} \end{cases}$$

a fuzzy truth value T does not provide a precise characterization of the truth value of a proposition; rather it yields a possibility distribution Π^T of this truth value, which allows to take into account the imprecision in the assignment of a truth value to a proposition.

In this paper we treat separately two families of truth values: T associated with TRUTH, and F associated with FALSEHOOD as illustrated in Fig. 1.

When two fuzzy truth values A and B either both belong to T or either both belong to F, and only in these two cases, we here use the distance

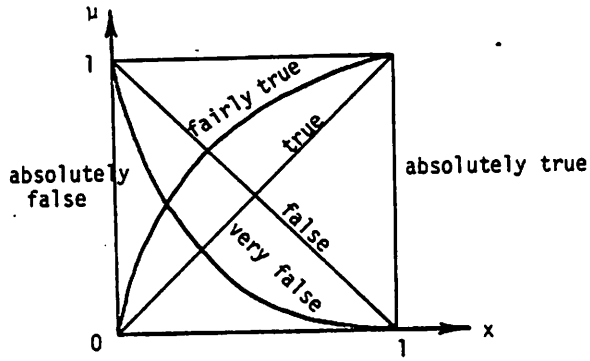

Fig. 1. Possibility distributions of fuzzy truth and fuzzy falsehood values.

d, [10], defined on possibility distributions as follows.

$$d(\Pi^A,\Pi^B) = \int_0^1 |\mu_A(x)-\mu_B(x)|dx .$$

In particular, if $A \in T$, $d(\Pi^A,\Pi^\tau) = \int_0^1 \mu_A(x)dx = a \in [0,1]$; if $B \in F$, $d(\Pi^B,\Pi^\phi) = \int_0^1 \mu_B(x)dx = b \in [0,1]$.

From now on, we shall assume that for all $\alpha \in [0, 1]$, there exists one and only one $A \in T$ and, one and only one, $B \in F$ such that

$$\alpha = d(\Pi^A,\Pi^\tau) = d(\Pi^B,\Pi^\phi).$$

This functional correspondence between numbers in [0, 1] and possibility distributions in T (or in F) is a basic assumption in the sequel. For example, the elements of T (or of F) can be defined as being generated by powers of <u>true</u> (or of <u>false</u>) but we do not have to impose, here, precise definitions of the elements of T (or of F).

We are now able to define the fuzzy sets D in r_1 (I) and in r_2 (II). In (I) as well as in (II) two steps are needed to compute the corresponding D's. In all cases it is of course assumed that fuzzy propositions induce corresponding possibility distributions.

<u>(I) EMP - Step 1</u>. Matching of A and B.

Define $M \in T$ such that $d(\Pi^M,\Pi^\tau) = 1-\pi(A|B)$. Thus, comparison of A with B by means of a possibility measure, yields a truth value M in the family T, as illustrated in Figure 2.

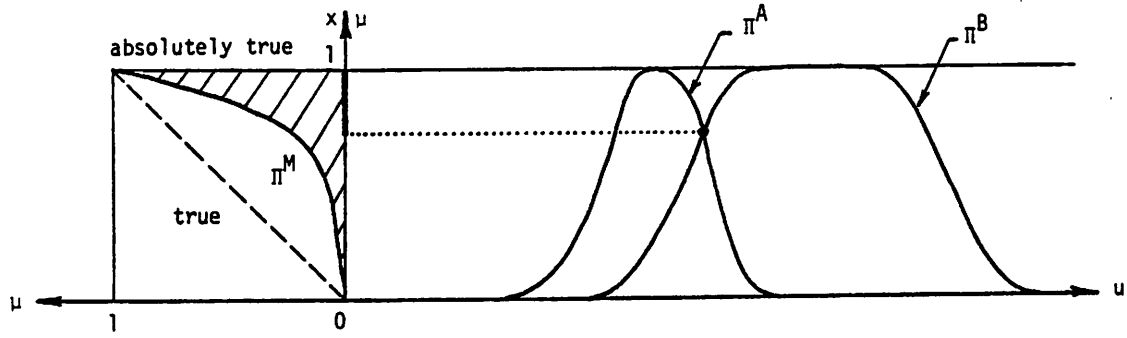

Fig. 2. Illustrative example of matching for A and B

Note that if $\pi(A|B) = 1$, e.g. when $A \subseteq B$, then $M = \tau$, i.e., absolutely true.

(I) EMP - Step 2. Definition of D.

$$\forall v \in V,\ \mu_D(v) \triangleq \mu_C(v) \oplus \mu_M(\mu_C(v)),$$

where for a and b in [0, 1], $a \oplus b = \min(a+b,1)$, i.e., $\oplus \triangleq$ bounded sum. See in Fig. 3 an illustration for the deduction of D in EMP.

Note that in all cases, deduction by EMP yields a fuzzy set D such that $C \subseteq D$.

Moreover, if $A = B$ then $C = D$, for when $A = B$, $\pi(A|A) = 1$ (recall that fuzzy sets are assumed to be normal), $M = \tau$, $\mu_D(v) = \mu_C(v) \oplus 0$ (if $\mu_C(v) < 1$) or $\mu_D(v) = \mu_C(v) \oplus 1 = 1$ (if $\mu_C(v) = 1$).

SPECIAL CASE. When the C's belong to a family with a structure akin to the families of truth values, deduction processes can be defined in a slightly different, but more homogeneous form. This is the case when Y takes values in [0, 1] to handle concepts like beauty, pain, etc. All C's are then generated from a basic term and its antonym like true and false, for example handsome and ugly in the case of beauty, presence and absence in the case of pain. Moreover, all C's are characterized by the distance of their respective possibility distributions to the extremal possibility distribution ($\Pi^{\text{absolutely handsome}}$, for example) which we generally denote by Π^E. In the deduction process, first step is unchanged but, in second step, D, or equivalently Π^D, is now defined as follows.

$$d(\Pi^D,\Pi^E) = d(\Pi^M,\Pi^\tau) \oplus d(\Pi^C,\Pi^E).$$

(II) EMT - Step 1. "Nonmatching" of A and B.

The goal here is to determine to what extent A does not match B. The result of the comparison is $N \in F$ such that

$$d(\Pi^N,\Pi^\phi) = \pi(A|B),$$

as illustrated in Fig. 4.

Note that if $\pi(A|B) = 0$, then $N = \phi$, i.e., absolutely false.

(II) EMT - Step 2. Definition of D.

$$\forall v \in V,\ \mu_D(v) \triangleq \mu_{C'}(v) \oplus \mu_N(\mu_C(v)),$$

where we recall that $\mu_{C'}(v) = 1-\mu_C(v)$ and $\oplus$ is the bounded sum. See in Fig. 5 an illustration for the deduction of D in EMT.

Note that in all cases, deduction by EMT yields a fuzzy set D such that $C' \subseteq D$.

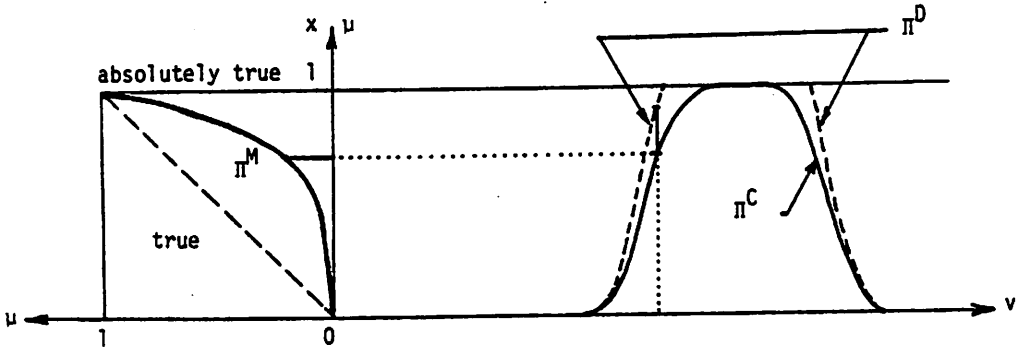

Fig. 3. Illustrative example for deducing D in EMP.

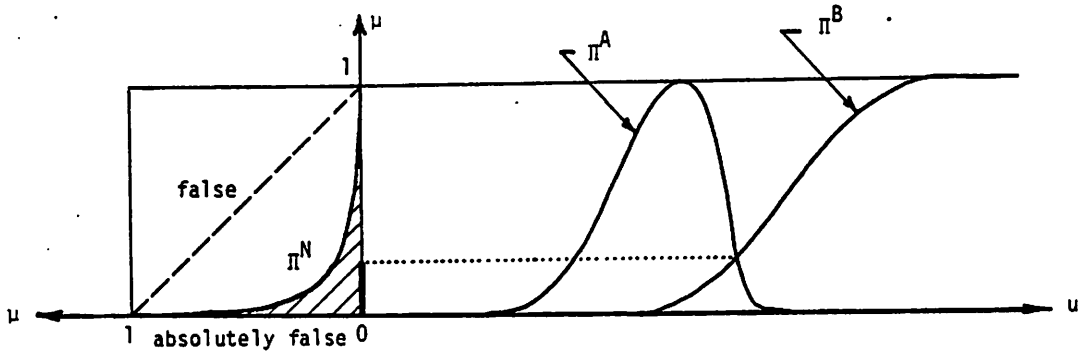

Fig. 4. Illustrative example of "nonmatching" for A and B.

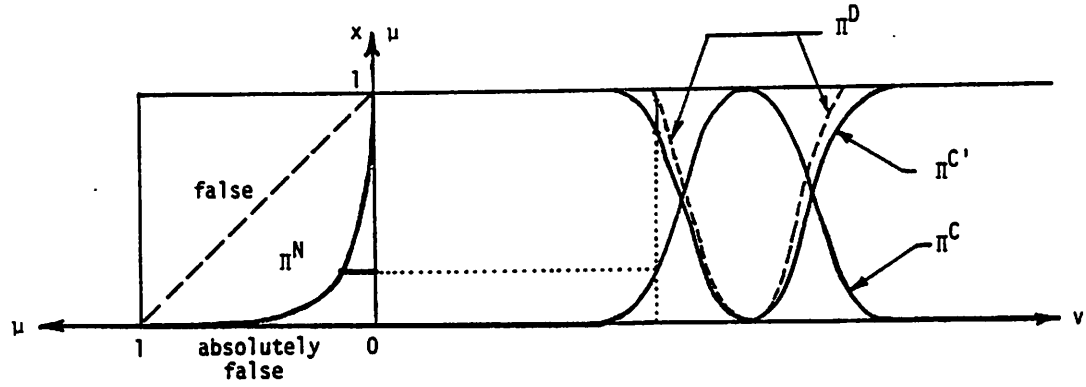

Fig. 5. Illustrative example for deducing D in EMT.

Moreover, if A is totally disjoint from B, in the sense of $\pi(A|B) = 0$, then $N = \phi$, $\mu_D(v) = \mu_{C'}(v) \oplus 0$ (if $\mu_C(v) > 0$) or $\mu_D(v) = \mu_{C'}(v) \oplus 1 = 1$ (if $\mu_C(v) = 0$, i.e., $\mu_{C'}(v) = 1$), hence $D = C'$.

SPECIAL CASE. When the C's belong to a family with a structure akin to the families of truth values, deduction processes can again be defined in a slightly different, but more homogeneous form. If we still denote by Π^E the extremal possibility distribution like in (I), the first step is unchanged but, in the second step, D, or equivalently, Π^D, is now defined as follows.

$$d(\Pi^D,\Pi^E) = d(\Pi^N,\Pi^\phi) \oplus d(\Pi^{C*},\Pi^E),$$

where $\forall v \in [0, 1]$, $\mu_{C*}(v) = \mu_C(1-v)$.

3. MEDICAL DECISION PROCESSES

The methodology we propose for computer-assisted medical decision making is based on the two soft deduction rules EMP and EMT which we have introduced in the preceding section. It can also be applied in other domains to fault diagnosis or to fuzzy logic controllers, for example.

Within a given pathology we consider a set of diagnostic indicators or symptoms and a set of diagnoses (or groups, or types, or syndromes, etc.). Fuzziness will be considered in the three domains of evaluation of diagnostic indicators, medical knowledge representation, and computation of results.

i) Evaluation of diagnostic indicators. In most cases, subjectivity and imprecision are associated with evaluation of diagnostic indicators for some of the following reasons.

- Difficulty of quantifying symptoms like "pain" for example.
- Errors due to technical measurement procedures.
- Poor conditions of observation.
- Change in symptoms in the course of a disease.

In all cases, the imprecision in the evaluation of a diagnostic indicator will be interpreted by means of a fuzzy proposition of the form: The diagnostic indicator is around a or close to a

where a is a numerical value. A fuzzy set labeled around a will be denoted by $\underset{\sim}{a}$, and it will be assumed that fuzzy propositions translate into corresponding possibility distributions. For example,

John's triglycerides are 6.3 mmol/ℓ is transformed into

Triglycerides (John) = $\underset{\sim}{6.3}$

which translates into a possibility distribution of the type shown in Figure 9, with $a_j = 6.3$.

ii) Medical knowledge. Three concepts are taken into account by means of finite matrices expressing relationships between diagnoses (rows) and diagnostic indicators (columns).

The pattern matrix G is such that its entries express the theoretical nature of diagnostic indicators associated with diagnoses. For examples, in the case of poorly defined dosage thresholds, G reflects fuzzy propositions such as (in the context of a given diagnosis) diagnostic indicator is slightly higher than ..., or clearly lower than ...

The suggestion matrix H is such that its suggestive values reflect the subjectivity associated with each diagnostic indicator in relation to the corresponding diagnoses. This matrix allows the setting of a hierarchy among signs to induce a diagnosis. The entries stand for properties like high suggestive value or low suggestion value, etc.

The disconfirmation matrix J is such that its entries represent how subjectively the diagnostic indicators disconfirm diagnoses in order to eliminate them in the deduction process. This matrix also allows a setting of a hierarchy among diagnostic indicators, but to reject diagnoses. Entries are exemplified by translation of properties like low disconfirmation value of very low disconfirmation value, etc.

These matrices, G, H, J, are filled up by physicians according to their experience and how subjectively they feel about the different relationships. They can be modified after some training and further experience.

iii) Computed results. With the exception of specific cases, it is uncommon for the combination of observed diagnostic indicators over patients and medical knowledge to yield precise results. The yes-or-no membership of a patient in relation to a pathological condition is less often encountered than a graded membership which represents a transition stage between a normal and a pathological condition. Hence, each patient is characterized by a graded membership in each possible decision which reflects both suggestion and disconfirmation values.

ALGORITHM. Each observed diagnostic indicator on a patient is first transformed into a possibility distribution, and compared with each entry in G (a possibility distribution) by means of the possibility measure which yields the possibility distributions of matching and non-matching fuzzy sets, i.e., Π^M and Π^N respectively. These possibility distributions -- which determine whether or not the patient matches the theoretical pattern G -- are respectively combined with each entry in the suggestion matrix H by EMP, and with each entry in the disconfirmation matrix J by EMT (see Figure 7). Let us rewrite the deduction rules in terms suited for medical applications, assuming that diagnoses are characterized over [0, 1] (cf. V).

Let S_j be a diagnostic indicator or symptom taking values in a set U_j (usually a real interval) and let $\mathcal{D}_i$ be a diagnosis taking values in V = [0, 1]; S_j and $\mathcal{D}_i$ are viewed as variables (cf. X and Y, respectively).

$G_{ij} \triangleq$ fuzzy subset of U_j expressing a (reference) relationship between $\mathcal{D}_i$ and S_j; it is the (i,j)-th entry in the pattern matrix G (cf. B in (I) and (II)).

$H_{ij} \triangleq$ fuzzy subset of V expressing how $\mathcal{D}_i$ is suggested by S_j; it is the (i,j)-th entry in the suggestion matrix H (cf. C in (I)).

$J_{ij} \triangleq$ fuzzy subset of V expressing how $\mathcal{D}_i$ is disconfirmed by S_j; it is the (i,j)-th entry in the disconfirmation matrix J (cf. C in (II)).

Assume now that a measurement of S_j in U_j yields a value "a_j" which is then transformed into $\underset{\sim}{a}_j$ (cf. A in (I) and (II)), expressing "around a." By EMP, a fuzzy subset D^I_{ij} of V is inferred and, by EMT, a fuzzy subset D^{II}_{ij} of V is also inferred.

(I) or EMP

S_j is $\underset{\sim}{a}_j$	: observed diagnostic indicator
If S_j is G_{ij} then $\mathcal{D}_i$ is H_{ij}	: medical knowledge (pattern & suggestion)
$\mathcal{D}_i$ is D^I_{ij}	: fuzzy degree of presence

D^I_{ij} will be determined by a possibility distribution characterized by the distance $d(\Pi^{D^I_{ij}}, \Pi^{AP})$ (cf. $d(\Pi^D, \Pi^E)$), where AP $\triangleq$ absolutely present, see Figure 6 for illustration.

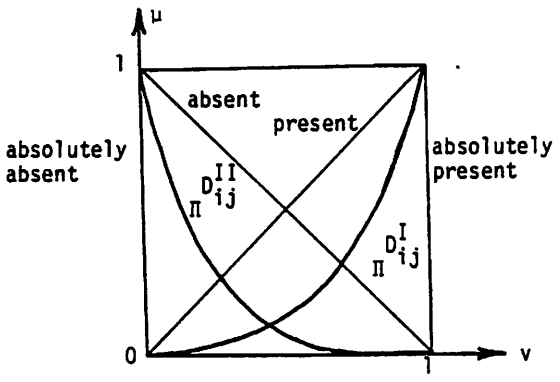

Fig. 6. Possibility distributions of fuzzy presence and fuzzy absence values.

We briefly recall definition of D^I_{ij}, or, equivalently, its possibility distribution (cf. special case, in (I)).

$$d(\pi^{D^I_{ij}},\pi^{AP}) = (1-\pi(\underline{a}_j|G_{ij})) \oplus d(\pi^{H_{ij}},\pi^{AS}),$$

where AS $\triangleq$ absolutely suggestive

(recall that $M \in T$ is defined by $d(\pi^M,\pi^\tau) = 1 - \pi(\underline{a}_j|G_{ij})$).

(II) or EMT.

S_j is $\underline{a}_j$		observed diagnostic indicator
If $\mathcal{D}_i$ is J_{ij} then S_j is G_{ij}	:	medical knowledge (pattern & disconfirmation)
$\mathcal{D}_i$ is D^{II}_{ij}	:	fuzzy degree of absence

D^{II}_{ij} will now be determined by the distance $d(\pi^{D^{II}_{ij}},\pi^{AA})$, where AA $\triangleq$ absolutely absent, see Figure 6 for illustration.

Let us briefly recall, too, the definition of D^{II}_{ij}, or, equivalently, its possibility distribution (cf. special case, in (II)).

$$d(\pi^{D^{II}_{ij}},\pi^{AA}) = \pi(\underline{a}_j|G_{ij}) \oplus d(\pi^{J^*_{ij}},\pi^{AD}),$$

where $\forall v \in [0, 1]$, $\mu_{J^*_{ij}}(v) = \mu_{J_{ij}}(1-v)$ and AD $\triangleq$ absolutely disconfirmed (recall that $N \in F$ is defined by $d(\pi^N,\pi^\phi) = \pi(\underline{a}_j|G_{ij})$).

For each patient, the entries in the two computed matrices D^I and D^{II} are fuzzy degrees of presence (D^I) and fuzzy degrees of absence (D^{II}) for each possible diagnosis $\mathcal{D}_i$. The elements of D^I and D^{II} are finally combined by means of aggregation operators whose choice is application-dependent. Here, we have chosen the minimum operator acting on possibility distributions. For each $\mathcal{D}_i$, then, we obtain two possibility distributions π^{P_i} and π^{A_i} which express a fuzzy degree of presence and a fuzzy degree of absence of $\mathcal{D}_i$. They are defined and combined as follows, [17].

$$d(\pi^{P_i},\pi^{AP}) \triangleq \min_j d(\pi^{D^I_{ij}},\pi^{AP}) = \alpha_i,$$

$$d(\pi^{A_i},\pi^{AA}) \triangleq \min_j d(\pi^{D^{II}_{ij}},\pi^{AA}) = \beta_i.$$

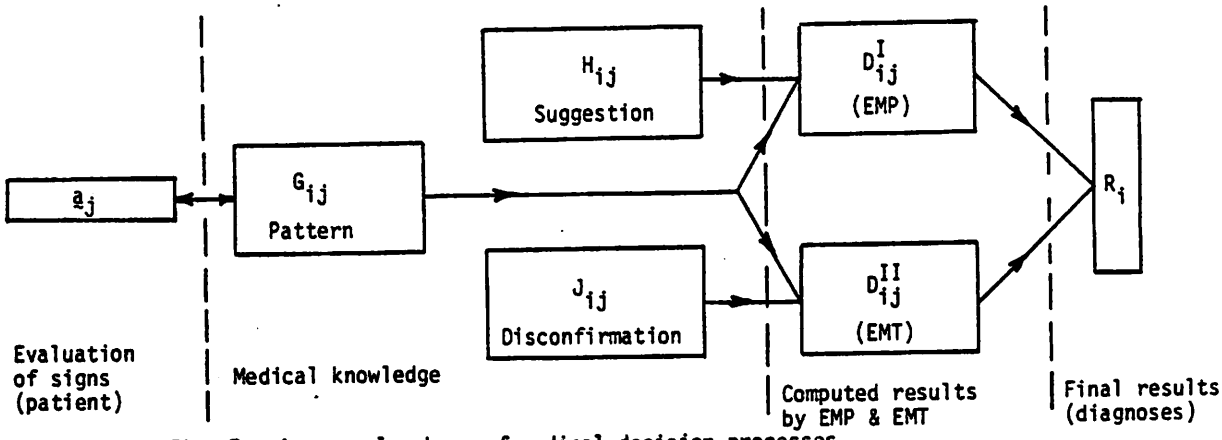

Fig. 7. A general schema of medical decision processes.

For each diagnosis $\mathcal{D}_i$, the solution R_i is derived from a simultaneous analysis of the fuzzy degree of presence and the fuzzy degree of absence. We express it by the variation range $[1-\alpha_i, \beta_i]$ or $[\alpha_i', \beta_i]$, when $\alpha_i' \leq \beta_i$, which is the condition of existence of a solution. This condition of existence expresses consistency and homogeneity in the observed diagnostic indicators on a patient. Homogeneity depends on both suggestion diagnostic indicators and disconfirmation diagnostic indicators in relation to a diagnosis $\mathcal{D}_i$.

If condition of existence for a diagnosis $\mathcal{D}_i$ is not satisfied, it is defined as a degree of heterogeneity $h_i \triangleq \alpha_i' - \beta_i$.

In summary, for each diagnosis $\mathcal{D}_i$, we specify either a variation range $[\alpha_i', \beta_i]$ or the value of β_i, associated with a heterogeneity degree h_i.

4. APPLICATION TO THE CLASSIFICATION OF HYPERLIPOPROTEINEMIAS

Hyperlipoproteinemias are a major metabolic perturbation and their etio-pathogenic role on vascular atherosclerosis has been documented during the past years. A synthesis of these abnormalities was first given by Fredrickson and, later on, a classification was proposed by the W.H.O. [22]. This classification relies upon respective values of lipidemia, cholesterolemia, triglyceridemia, electrophoresis and/or electrocentrifugation of lipoproteins.

Description of these abnormalities and criteria for their classification remain imprecise; they are expressed by means of propositions such as "Plasma cholesterol is normal or increased," "β-lipoproteins markedly decreased," "triglycerides are clearly increased," "broad band suspected on electrophoresis" [22]. There is no information on thresholds in these propositions, which are fuzzy indeed, so that a wide and subjective interpretation is permissible.

Moreover, there exists a hierarchy among the variables entering in the classification, according to their degree of importance. For example, total cholesterol and triglycerides are basic factors in the definition of what we call primary classes (they play the role of "diagnoses" in the general study), i.e. the "normal" class and classes II_a, II_b and IV. To the contrary, the three remaining variables entering in this classification, i.e., percentage of β lipoproteins, percentage of pre-β lipoproteins and total lipidemia, are less important and their presence confirms membership of a patient in a class or determines so-called minor classes, i.e., minor II_a, minor II_b and minor IV.

In the present application, classes I, III, and V that appear in the international classification are not introduced since they correspond to uncommon genetic abnormalities and they are determined by specific variables, i.e., by the conjunction of presence, or absence of chylomicrons and/or broad β lipoproteins suspected on electrophoresis. Moreover, percentage of α lipoproteins is not taken into account since it follows from the constraint α + β + pre β = 100 and it does not provide additional information regarding the classification.

In summary, this application deals only with seven classes: Normal, II_a, minor II_a, II_b, minor II_b, IV and minor IV. These classes are characterized by the variations of five variables (diagnostic indicators): total lipids, total cholesterol, triglycerides, β lipoproteins and pre-β lipoproteins.

In practice, the method runs in a conversational mode and comprises two stages, initialization and computation, as follows.

INITIALIZATION. In this first stage, the three componentsof the medical knowledge are determined.

The pattern matrix G reflects the theoretical description of the W.H.O. classification, derived from fuzzy propositions taking into account the constructed classes and giving the possible values of the five biological tests. Here are some examples of fuzzy propositions, the corresponding fuzzy sets are to be seen in Table I. "In class IIa ($\mathcal{D}_j$), cholesterol (S_j) is markedly increased (G_{ij})," "In class minor IIa, triglycerides are normal," "In class IV, lipids are very increased," etc. Fuzzy sets in Table I are built from one of the two types of parametrized curves shown in Figure 8; they are derived from the S-membership function [3] which is piece-wise quadratic.

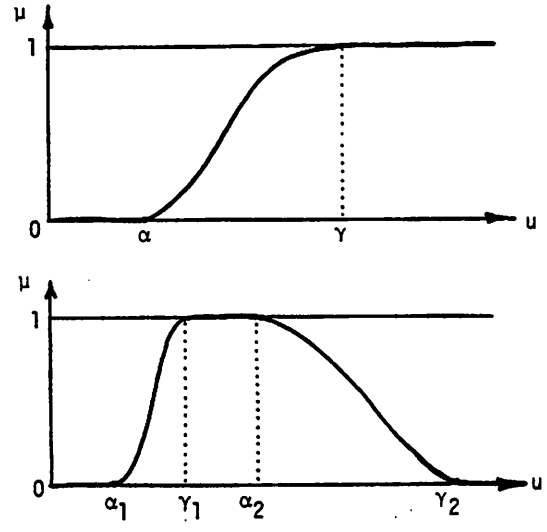

Fig. 8. The two types of curves used in G.

Suggestion matrix H and disconfirmation matrix J are also specified by the biologist to introduce the notion of hierarchy into diagnostic indicators, either to determine the membership (using H) or the non-membership (using J) of a patient in a class. Suggestion and disconfirmation values are, of course, imprecise and based on the biologist's experience. They reflect fuzzy properties like very suggestive value or weakly suggestive value, by possibility distributions in the universe of discourse [0, 1]. Such possibility distributions are characterized by their respective distances to the possibility distribution of absolutely suggestive. As the suggestion value increases, the distance decreases and conversely, so that the biologist determines the suggestion (and the disconfirmation) values with respect to the associated distances. Suggestion matrix and disconfirmation matrix are respectively reproduced in Table II and Table III where, for the sake of simplicity, the entries stand not for the value of a distance but for the complement of this value. For example, the higher the suggestion value, the higher the entry in the matrix (the corresponding distance has a low value).

Finally, the imprecision attached to the result "a_j" of a biological test is translated into fuzzy propositions such as "percentage of pre-β lipoproteins (S_j) is around a_j." Every test performed on a patient will be defined by a curve, which is a combination of an S and an S' = (1-S)-membership functions, and which depends on two parameters a_j (the measured value) and, b_j that depends only on the nature of S_j and not on the measured values, and take into account the fuzziness of "around" (see Figure 9). In our application, the b_j's we use are reproduced in Table IV.

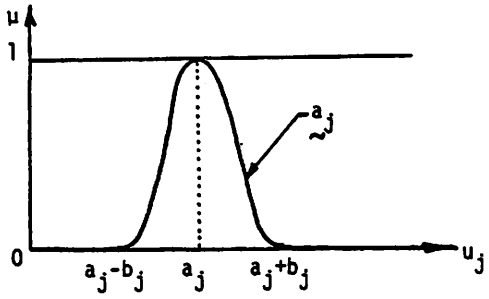

Fig. 9. Representation of the result of a biological test S_j.

COMPUTATION. The application of the proposed method to a classification process which depends on the biological tests performed on a patient presents no difficulty. It is necessary only to provide the computer with the results of five tests. The method yields intervals (cf. $[\alpha_i', \beta_i']$) associated with each of the seven predetermined classes (the $\mathcal{D}_i$'s). The boundaries and the range of the intervals represent the membership of a patient in a class. If necessary, heterogeneity degrees are determined on request.

If the condition of existence of a solution is satisfied (cf. $\alpha_i' \leq \beta_i$), the variation ranges are interpreted as follows.

- Two bounds close to 1 indicate full membership to a group, e.g. [0.9, 1];
- Two bounds close to 0 indicate non membership to a group, e.g. [0, 0.1];
- The narrower the variation range, the more accurate the result;
- The larger the variation range, the more inaccurate the result (the limit case is [0, 1]).

An example with some results is shown in Table V.

5. CONCLUSION

In practive, clinicians and biologists were substantially satisfied with the classification of patients in the different classes, and by now more than a thousand patients have been examined by means of this methodology. To summarize, the application of the method to the classification of hyperlipoproteinemias yields:

A clinician's personal and clearer perception of the definition of more or less subjective classes of medical knowledge;

Similar and stable results of the same tests; this prevents misclassifications due to a collaborator's lack of experience and prevents any evolution of the subjectivity inherent to the interpretation;

A graded classification in many classes allowing a gradation of lipid analyses. In particular, the existence of intermediate classes allows one to assume, in absence of any prevention or therapy, a final evolution towards a crisper class. This is of great interest in epidemiologic studies.

Finally, let us mention that, in our Department, fuzzy set theory has been applied in problems of thyroid pathology, of cardiac insufficiency [9], of anemias and of the classification of some icterias [15], and is now used in the treatment of diabetes.

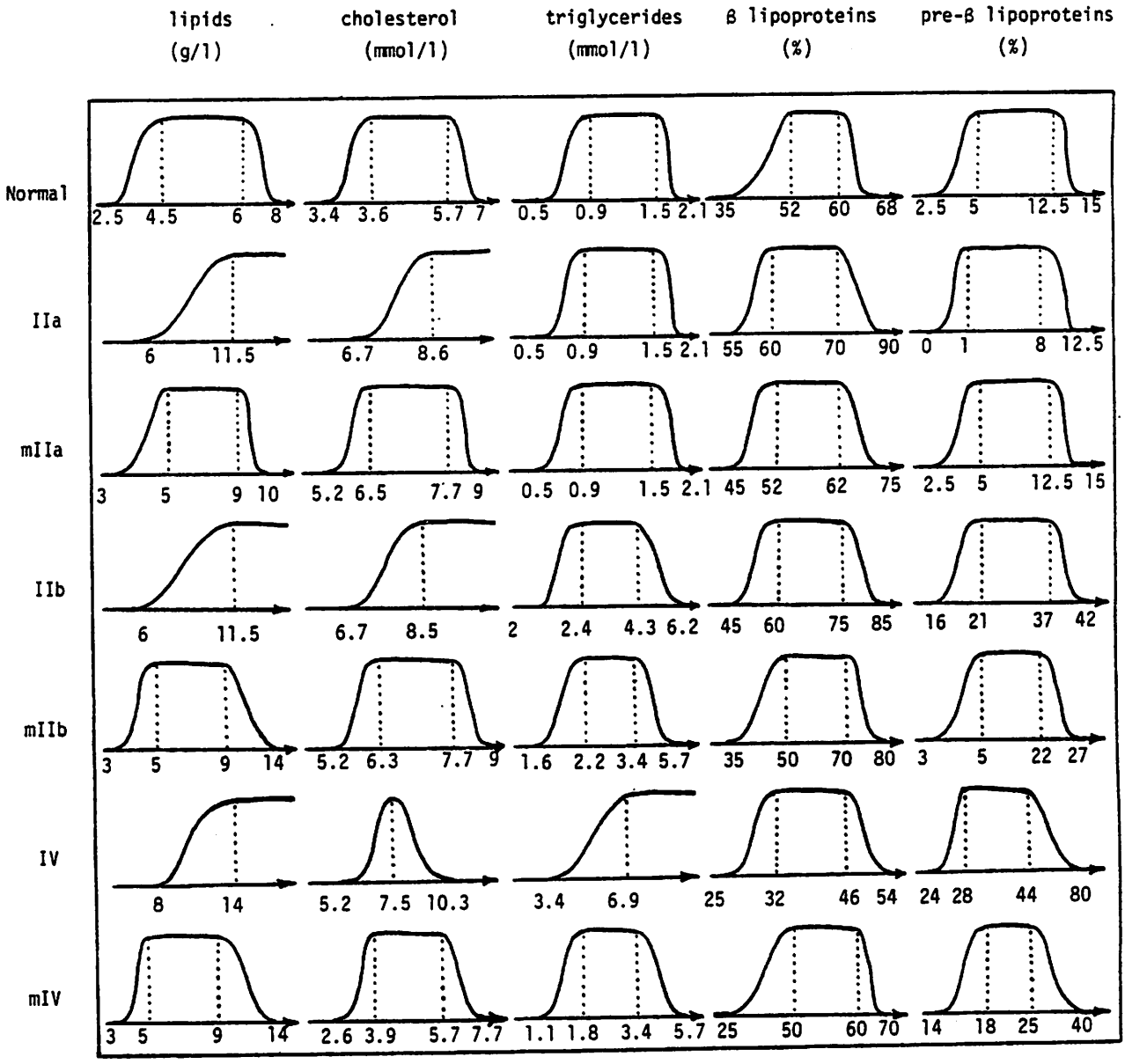

Table I. Classification of hyperlipoproteinemias: Pattern matrix G.

	Lipids	Chol.	Trigl.	β-lip.	pre-β lip.
Normal	0.7	1	1	0	0
IIa	0	1	0	0.9	0
mIIa	0	1	0	0.9	0
IIb	0	1	1	0.8	0.8
mIIb	0	1	1	0.8	0.8
IV	0.7	0	1	0	0.9
mIV	0.5	0	1	0	0.9

Table II. Suggestion values.

	Lipids	Chol.	Trigl.	β-lip	pre-β lip.
Normal	0.8	0.9	0.9	1	1
IIa	0.5	0.8	0.7	0.9	0.6
mIIa	0.5	0.8	0.7	0.9	0.7
IIb	0.5	0.9	0.8	0.7	0.8
mIIb	0.5	0.9	0.9	0.7	0.7
IV	0.6	0.5	0.8	0.6	0.9
mIV	0.5	0.9	0.8	0.9	0.7

Table III. Disconfirmation values.

S_j	Lipids	Chol.	Trigl.	β-lip.	pre-β lip.
b_j	1.8 g/ℓ	1.5 mmol/ℓ	0.6 mmol/ℓ	10%	10%

Table IV. Fuzziness attached to the biological tests.

Results of biological tests on patients

patients	lipids	cholesterol	triglycerides	β	pre-β
1	9	7.5	1.6	75	6
2	12	5.93	3	39	38
3	4.3	3.3	0.6	53	11
4	12	5.93	3	39	42
5	15	7.7	4.8	60	32

Final Results

patients	N	IIa	mIIa	IIb	mIIb	IV	mIV
1	β=0.1 h=0.9	[0.8,1]	β=0.5 h=1	β=0.2 h=0.6	β=0.6 h=0.4	[0,0.1]	β=0.2 h=0.8
2	β=0 h=1	[0.1,0.1]	β=0.2 h=0.7	β=0.2 h=0.8	β=0.3 h=0.7	β=0.2 h=0.7	β=0.8 h=0.2
3	[0.9,0.9]	β=0.2 h=0.3	β=0.2 h=0.7	β=0.1 h=0.5	β=0.1 h=0.7	[0,0.1]	β=0.2 h=0.2
4	β=0 h=1	[0.1,0.1]	β=0.2 h=0.7	β=0.2 h=0.8	β=0.3 h=0.7	β=0.2 h=0.7	β=0.5 h=0.5
5	β=0 h=0.1	β=0.3 h=0.6	β=0.3 h=0.7	[0.9,1]	β=0.5 h=0.5	β=0.5 h=0.4	β=0.4 h=0.3

Table V. Examples of Classification.

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