

## A SURVEY ON MEDICAL DIAGNOSIS AND FUZZY SUBSETS

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Fuzzy set theory with its capability of defining inexact medical entities as fuzzy subsets, with its linguistic approach providing an excellent approximation to medical texts as well as its power of approximate reasoning seems to be perfectly appropriate for designing and developing computer-assisted diagnostic, prognostic and treatment recommendation systems. The detailed survey of fuzzy approaches to medical decision making shows the wide and deep interest of researchers all over the world to find a solid fuzzy theoretical basis for the representation of medical knowledge as well as for the diagnostic process and to use it in practical applications.

Keywords: fuzzy set theory, medical diagnosis, survey.

### 1. INTRODUCTION

Since the very beginning of developing computer-assisted diagnostic methods and medical decision aids in the years 1958 /1/ and 1959 /2/, a great number of medical diagnostic models applied in different medical fields with varying results (bibliographies in computer-assisted diagnosis can be found in /3-5/) have been proposed and a certain number of them has been tested.

The first logical approach to medical decision making (as opposed to numerical models <sup>1)</sup> based on Bayes' Theorem, likelihood ratio, linear and nonlinear discriminant analysis, clustering methods, factor and principal component analysis, decision analysis, adaptive threshold logic unit, perceptron algorithm, etc.) has been suggested by LEDLEY and LUSTED in 1959 /2/ (see also

LEDLEY /6/).

Since that year, several systems using Boolean logic to express functional and etiological relationships between symptoms and diseases have been proposed /7/ and established /8-16/. In 1969 GANGL, et al. /11/ proved the usefulness of such approaches. The described batch system considered 82 liver diseases and 323 symptoms (history, physical examination, laboratory tests, X-ray findings, special tests). In each of the 20 test cases the clinically confirmed diagnosis was put out as diagnostic hypothesis (among 3-6 others). These results were very encouraging.

Later then, as a logical consequence, the symptoms and diagnoses were not only considered to be present or absent as in two-valued systems but the truth-values "present", "absent", or "not

examined" were assigned to symptoms and "present" (confirmed), "absent" (excluded), and "possible" (hypothesis) to diagnoses. Thus tri-valued logic was introduced as a means for the representation of medical knowledge /17-20/.

In the report about the computer-assisted medical diagnostic consultation system CADIAG-1 /19/, the tri-valued logical system of KLEENE /21/ seems to be adequate to formalize medical judgement in an abstract and computable way, understandable by and acceptable to the medical community. This system has now been established for 308 diseases from internal medicine (rheumatology, hepatology, coagulation defects and pancreatic diseases) and takes about 2.500 symptoms into account.

The possibility of expressing medical knowledge in terms of predicate logic was also mentioned in /19/.

In the last ten years, some very powerful computer-based medical decision and consultation systems have been developed by researchers working in the field of artificial intelligence. SHORTLIFFE, et al. give in /22/, among others, an excellent introduction to these symbolic reasoning approaches.

The MYCIN system (see /22,23/) has been designed to assist physicians in the detection of the cause of infectious diseases and to recommend therapies. The medical knowledge about the diseases considered is represented in IF-THEN production rules associated with certainty factors.

CASNET /22,24,25/ offers associational links between Boolean combinations of tests and single pathophysiological

causal states that carry confidence factors. Furthermore, state network rules associated with a given likelihood for the effect  $S_j$  to follow from the occurrence of the cause  $S_i$  are used in CASNET. Finally, classification rules that are Boolean combinations of confirmed or denied states implying diagnostic statements are incorporated in order to represent medical knowledge. CASNET was created for glaucoma consultation.

The EXPERT system /26-28/ permits the definition of rules with confidence levels and hierarchical concepts to convert medical knowledge into a computable form. It has been applied in rheumatology, endocrinology and ophthalmology /29/.

A further system applicable in the field of internal medicine is called INTERNIST /22,30,31/. Symptom-disease (frequency of occurrence) as well as disease-symptom relationships (evoking strength) are stored on the basis of an ad hoc scoring method.

MYCIN, CASNET and EXPERT are logical in the sense that relationships between all kinds of observations on the patient form the basis for IF-THEN inferences (modus ponens in classical logic, implication in terms of logical operations) but the inferences do not necessarily have a definite character. They are associated with certainty factors, confidence factors, likelihoods, or confidence levels that express the fuzziness, the non-definiteness of the relationships. The "evoking strength" of the INTERNIST system also belongs into this category.

Other authors who use IF-THEN statements



sets is less natural and clear. A subjective (patient or physician) assignment of the observed symptom value (patient's pain, or blue discoloration) in the fuzzy subset is needed.

PEREZ-OJEDA /39/ and MOON, et al. /40/ use linguistic modifiers (also termed hedges /42-44/) to calculate the degree of membership of a test result in the fuzzy subset  $S_2$  out of the degree of membership in  $S_1$ . Linguistic modifiers are for example very, more or less, not, etc. By using them, MOON, et al. /40/ compute the degree of membership of the result  $x$  of the urine sodium concentration test in the fuzzy subset very high urine sodium concentration  $\mu_{S_2}(x)$  out of high urine sodium concentration  $\mu_{S_1}(x)$  by performing

$$\mu_{S_2}(x) = \mu_{\text{very } S_1}(x) = [\mu_{S_1}(x)]^2. \quad (2)$$

In /41/, ESGBUE and ELDER introduce fuzzy subsets to determine diseases or disorders in the patient's past history which might be missed or remain undiagnosed. The presence or absence of such diseases might then be decided on from past undiagnosed symptoms, but the physician only considers the "prominent" symptoms of past diseases. The fuzzy subset  $\Sigma_j$ , containing the prominent symptoms of past disease  $j$  is defined as

$$\Sigma_j = \{(x_{ij}, \mu_{\Sigma_j}(x_{ij})) / x_{ij} \in \beta_j, \mu_{\Sigma_j}(x_{ij}) \geq \alpha\} \quad (3)$$

where  $\mu_{\Sigma_j}(x_{ij}) \in [0, 1]$  and  $0 \leq \alpha \leq 1$ .

The set of possible symptoms for past undiagnosed disease  $j$  is  $\beta_j$ , where  $1 \leq j \leq p$  and  $p$  is the number of undiagnosed diseases in the patient's past history. Wherever the physician designates the membership function  $\mu_{\Sigma_j}(x_{ij})$  of symptom  $x_{ij}$  for disease  $j$  over a specified level  $\alpha$ , the symptom of  $\beta_j$  becomes a "promi-

nent" symptom.

## 2.2. Diseases/diagnoses and fuzzy subsets

SMETS, et al. /45/ mention the fuzziness of diagnostic terms like arterio-sclerosis or angina pectoris. Mostly, diseases are not clearly defined entities. It is often impossible to determine precisely the symptoms related to a disease. Diagnoses are defined to be fuzzy subsets with symptoms as elements. The symptoms are combined with a degree of membership which characterizes the intensity of belonging to the fuzzy subset that represents the disease under consideration.

ALBIN /38/ considers patients suffering from a certain disease as points in the  $n$ -dimensional symptom space  $S$ , where  $n$  is the number of symptoms taken into account. Now, every given patient with disease  $D_j$  exhibiting symptoms  $(S_1, \dots, S_n) \in S$  is combined with a degree of membership  $\mu_{D_j}(S_1, \dots, S_n) \in [0, 1]$  that shows the affiliation of the patient in  $D_j$ . Because  $\mu_{D_j}(S_1, \dots, S_n)$  is not necessarily 1 for  $i=j$  and 0 for  $i \neq j$ , patients suffering from the same disease do not form clusters with sharp boundaries.

## 2.3. Fuzzy relations between symptoms and diseases

In /39/, PEREZ-OJEDA proposes a network presentation of medical knowledge (associative memory, semantic network) in which the facts, symptoms, diseases, etc., are linked by relations. Six types of nodes are considered: disease-complex nodes, disease nodes, symptom-complex nodes, symptom nodes, statement nodes (relations) and test nodes. PEREZ-OJEDA

translates medical statements like

"Acute pyelonephritis usually presents bladder irritation and infection." and "Acute pyelonephritis presents occasionally fever, or chills, and malaise." into

OR (usually (acute pyelonephritis, AND (bladder irritation, infection)), occasionally (acute pyelonephritis, AND (OR (fever, chills), malaise))).

The relations used in this information structure (usually, occasionally, always, almost always, etc.) are frequency or probabilistic modifiers. They are represented as fuzzy subsets, e.g.

always=0.1/0.7+0.3/0.8+0.6/0.9+1.0/1.0,

of the universe of discourse

U= 0+0.1+0.2+0.3+0.4+0.5+0.6+0.7+0.8+0.9+1.0.

A network in the fashion described above has been built which consists of 23 disease-complex and disease nodes, 101 symptom nodes and 227 statements.

SANCHEZ /46,47/ starts by considering the introduction of a fuzzy relation  $R \subset S \times D$  between symptoms  $S$  and diseases  $D$ . SANCHEZ calls this "medical knowledge" expressing associations between symptoms and diseases. Let, further,  $A$  be a fuzzy subset of  $S$  related to the patient, then the computation of the max-min<sup>2)</sup> composition  $B = A \circ R$ <sup>3)</sup> is assumed to describe the state of the patient in terms of diagnoses as a fuzzy subset  $B$  of  $D$ , characterized by its membership function

$$\mu_B(d) = \max_{s \in S} \min\{\mu_A(s); \mu_R(s,d)\}, \quad d \in D. \quad (4)$$

If we consider several patients belonging

to a set  $P$  and define a relation  $Q \subset P \times S$ , equation (4) becomes

$$\mu_T(p,d) = \max_{s \in S} \min\{\mu_Q(p,s); \mu_R(s,d)\}, \quad (5)$$

where  $p \in P$  and  $T$  is a fuzzy relation on  $P \times D$ . The composition is written as

$$T = Q \circ R. \quad (6)$$

In fuzzy logic, (6) is called a compositional rule of inference (ZADEH /44/, BELLMANN and ZADEH /42/ or a fuzzy meta-implication (KAUFMANN /48/).

Moreover, the composition  $B = A \circ R$  of a fuzzy subset  $A$  with a fuzzy relation  $R$  corresponds to the concept of the fuzzy conditional statement: IF  $A$  THEN  $B$  BY  $R$  (see /42,44,52,53/).

Applied in the field of medical diagnosis, the conditional statement allows to infer medical diagnoses  $B$  out of patient's symptoms  $A$  by means of the "medical knowledge"<sup>4)</sup> which is presented in a relation matrix  $R$  established by medical specialists.

If the relationships between symptoms and diseases are considered to be either 0 (no relationships) or 1 (strong relationship), e.g.  $\mu_R(s,d) \in \{0,1\}$ , and patient's symptoms can be evaluated as 0 (absent) or 1 (present), e.g.  $\mu_A(s) \in \{0,1\}$ , then the max-min composition (4) or (5), respectively, is reduced to a Boolean sum-product composition (see also /46-48/).

JOLY, et al. /54/ report an application of the max-min composition in the field of cardiopathies. Cardiologists have determined a fuzzy relation  $R$  in order to reflect the degrees of association between five cardiological symptoms and

the diagnoses normal<sup>5)</sup>, left ventricular hypertrophy and valvular cardiopathy. Five symptoms have been partitioned into classes (7 binary and 16 quantitative symptoms). The results obtained by the diagnostic procedure carried out for 21 patients with disparate cardiopathies were used "to confirm the classical concepts about cardiac function."

Another problem treated by SANCHEZ is related to equation (6). Knowing R and Q in (6), it is easy to find T. However, it is often as interesting to find R from given T and Q. In medicine, the problem frequently arises to determine degrees of association between symptoms and diseases from real patient data in Q and known diagnoses in T that have been established by medical specialists.

SANCHEZ presents in /46,47/ a solution of the problem by obtaining the greatest R for  $T=Q \circ R$  (see also DUBOIS and PRADE /43/). But because of getting the greatest solution for R from the solution set, which also can be void, R may contain degrees of association between symptoms and diseases that are stronger than in reality. Thus it depends on the control structure of the computer-based diagnostic system that uses the computed R in which way results are interpreted: "diagnostic hypotheses or confirmed diagnoses".

The problem to find Q from given T and R can be considered in analogy to the problem mentioned above. This task presents itself when studying different fuzzy subsets of S, i.e. patient's symptom evaluations contained in Q that keep the composition  $T=Q \circ R$  without changing T and R. The corresponding

medical question would be: "How far can patients' data vary until other diagnoses have to be made?".

Obtaining the greatest Q of possible Q's is demonstrated by SANCHEZ in /46, 47/. In /46,47,55/ the converse problems of (6) treated in the last two sections are also investigated by SANCHEZ in terms of Brouwerian logic.

An application of a converse problem of (6) to the differential diagnosis of icterus is given by SOULA, et al./56/. In this example four diseases and ten symptoms are taken into account.

Furthermore, in /57/, SANCHEZ has investigated the applicability of inverses of fuzzy relations in medical diagnosis.

SANCHEZ and SAMBUC /53/ and SAMBUC, et al. /58/ propose an interesting application of  $\phi$ -fuzzy sets<sup>6)</sup> to the medical diagnostic problem.  $\phi$ -fuzzy sets take their values in the set of intervals of the form  $[a_1, a_2]$  that are included in the real interval  $[0,1]$ . To illustrate how symptoms are represented in this way, we will quote an example from /58/ for the sign "pain on palpation" in patient p

$\neg(p)=[0,0]$  absence of pain on palpation  
 $\mu(p)=[0.8,0.8]$  marked pain  
 $\nu(p)=[0,1]$  totally indeterminate value  
 $\lambda(p)=[0.2,0.6]$  there is hesitation between mild and relatively marked pain.

After defining suitable connectives for  $\phi$ -fuzzy variables,  $\phi$ -fuzzy functions of the form hyperthyreoidism = (tachycardia OR weight loss) AND (thermophobia OR increased thirst) AND (in-

creased seric T4 values OR increased seric T3 values) are evaluated. The following possible results are noted in /58/:

hyperthyroidism=[0,1]: Impossible to determine from the available signs whether or not the patient is hyperthyroid.

hyperthyroidism=[0.7,0.8]: The patient suffers from frank hyperthyroidism.

hyperthyroidism=[0.35,0.45]: The patient presents a tableau of border-line hyperthyroidism.

ADLASSNIG proposes in /59/ an approach to computer-assisted medical diagnosis using fuzzy subsets that is based on two different relationships between symptoms  $S_i$  and diseases  $D_j$ :

- 1)  $S_i D_j$ -occurrence relationships and
- 2)  $S_i D_j$ -confirmability relationships.

Occurrence and confirmability are considered to be linguistic variables with always, almost always, very very often, very often, rather often, often, more or less often, unknown, more or less seldom, seldom, rather seldom, very seldom, very very seldom, almost never, never as elements (see BELLMAN and ZADEH /42/). Single  $S_i D_j$ -indications can be deduced from the  $S_i D_j$ -occurrence and  $S_i D_j$ -confirmability relationships. Examples for fuzzy subsets used to determine single  $S_i D_j$ -indications are strong and weak. Finally, one obtains total indications of the patient's symptom pattern to disease  $D_j$  by consolidating the single  $S_i D_j$ -indications.

TUSCH /60,61/ uses this model /59/ in a slightly modified form for the cranial computer tomography. The application

considers five tumor diagnoses: malignomata, semimalignomata, metastases, malformation tumors and benignomata. 25 symptoms gathered by seven different examinations describe every case: number of foci, structure of foci (native), edemata, localisation of edemata, form and position of ventricles, sulci and cisterns. The symptoms are dichotomous, with "symptom present" and "symptom absent/not investigated" as the two distinct values. TUSCH examines different algorithms in order to calculate total indications of the patient's symptom pattern to diseases  $D_j$ . The efficiency of the procedures lies between 55 and 76% compared to physicians' diagnoses. 802 tumor cases were used to perform this calculation. The  $S_i D_j$ -occurrence and  $S_i D_j$ -confirmability relationships have been documented linguistically by a neuroradiologist.

#### 2.4. Symptom combinations and fuzzy subsets

ALBIN /38/ proposes a fuzzy linguistic approach to medical diagnosis. In /38/, it is said that physicians normally try to fit patients to certain prototypes of diseases. As a first approximation to such an approach, disease prototypes can be defined as shown in Table 1.

The definition of fuzzy membership functions for long  $S_1$ , decreased  $S_2$ , normal  $S_2$ , etc., then allows the calculation of degrees of membership in the fuzzy subset long  $S_1$ , decreased  $S_2$ , normal  $S_2$ , etc. given symptom values measured on the patient. Fuzzy disease membership values of patients can now be computed by using the MAX definition

Table 1: Disease prototype definitions for two hemorrhagic disorders (from /38/, p. 128).

Disorder	S <sub>1</sub> IVY Bleeding Time	S <sub>2</sub> Platelet Count	S <sub>3</sub> QUICK Time	S <sub>4</sub> Partial Thromboplastin Time	S <sub>5</sub> Thrombin Time
D <sub>1</sub> <u>Thrombocytopenia</u>	<u>Long</u>	<u>Decreased</u>	<u>Normal</u>	<u>Normal</u>	<u>Normal</u>
D <sub>2</sub> <u>Von Willebrand's Disease</u>	<u>Long</u>	<u>Normal</u>	<u>Normal</u>	<u>Normal</u> or <u>Long</u>	<u>Normal</u>

for fuzzy set union and MIN definition for fuzzy set intersection, for example:

$$\begin{aligned} \mu_{D_1}(p) &= \mu_{\text{long}} S_1(12 \text{ min.}) \\ &\wedge \mu_{\text{decreased}} S_2(60\,000/\text{mm}^3) \\ &\wedge \mu_{\text{normal}} S_3(12 \text{ sec.}) \\ &\wedge \mu_{\text{normal}} S_4(37 \text{ sec.}) \\ &\wedge \mu_{\text{normal}} S_5(18 \text{ sec.}) \\ &= 0.95 \end{aligned}$$

Patient p, in our example, fits the prototype definition of D<sub>1</sub> almost exactly and if additionally computed fuzzy disease membership values  $\mu_{D_i}(p)$ , where  $i \neq 1$ , are much smaller than  $\mu_{D_1}(p)$ , diagnosis D<sub>1</sub>=thrombocytopenia is presumably the correct diagnosis for patient p.

In /62/, SANCHEZ, et al. propose a similar linguistic approach to the classification of hyperlipoproteinemias. But in the diagnostic procedure described, predetermined bandwidths of the symptoms depending on the measuring accuracy of the laboratory performing the tests are additionally taken into account. The application involves five lipoprotein tests determined by electro-

phoretic methods. The degrees of membership in three types of dyslipoproteinemia were calculated for five test cases.

MOON, et al. /40/ present symptom combinations as AND and OR functions. The calculation of the symptom combinations is performed using the fuzzy intersection for AND and the algebraic sum for OR. A different way of presenting the OR function is mentioned: MOON, et al. use the convex combination

$$\mu_D(S_1, \dots, S_k) = \frac{\sum_{i=1}^k w_i \mu_{S_i}}{\sum_{i=1}^k w_i} \quad (7)$$

where  $\mu_{S_i}$  is the ceiling function of  $\mu_{S_i}$  and the weights  $w_i$  are set equal to the posterior probabilities  $p(D/S_i)$  calculated for the single symptom  $S_i$ .

CERUTTI and PIERI /63/ also use linguistic variables as an alternative to numerical variables in order to characterize complex relationships between symptoms and diseases. Primary linguistic terms (small, medium, large)



that express intervals on the numerical symptom scale compounded with linguistic hedges (very, slightly, more or less) are connected by AND and OR to compose fuzzy logical combinations. By evaluating the fuzzy logical combination, a membership function is obtained that calculates non-fuzzy values (for details see /63/).

#### 2.5. Medical diagnosis using procedural fuzzy concepts

In /64/, WECHSLER proposes a procedural knowledge base system using fuzzy concepts. Instead of using fuzzy membership degrees, classes of functions  $f_i^p$  are established whose task is to define implicitly fuzzy sets. A class is related to a concept and it contains one or more functions  $f_i^p$  where  $p$  stands for the property to be checked and  $i$  relates to some context, e.g. to the observer  $i$ . For example:

$$f_i^{\text{age}}(\text{teenage}) = (\text{age } 12, \text{age } 18)$$

$$f_i^{\text{age}}(\text{young}) = (\text{age } 17, \text{age } 30)$$

Subsequently, two kinds of order-decisions that determine whether or not a given object has the property in question are presented:

- 1) Middle order: The closer the value of the property of a given object is to the middle of the interval defined by  $f_i^p$  the better it fits the property to be checked. For example:  
Age 18 fits "teenage" better than "young".
- 2) LB order: The first member of the interval defined in  $f_i^p$  is the best.

Then the medical knowledge is embedded in procedures and a possible program

checking for ulcers may look like <sup>7)</sup>:

```
(LAMBDA(+D ULCERS)
  (PROGRAM ()
    (EXISTS Patient pain-location slightly
      below the top of
      xiphoid process  $f_u^{p1}$ )
    (EXISTS Patient time of pain breakfast  $f_u^{p2}$ ))).
```

#### 2.6. Fuzzy cluster analysis in medical diagnosis

In /38/, ALBIN has developed a fuzzy clustering approach using an elliptic metric to define distance in the symptom space  $S_1 \times \dots \times S_n = S \in R^n$ . The proposed fuzzy clustering method is compared with a Bayesian approach on the basis of some test patients.

FORDON /65/, and FORDON and BEZDEK /66/ present a very interesting application of fuzzy clustering techniques to the diagnosis of hypertensive patients. Different distance measurements are used. In one example, a fuzzy k-means algorithm diagnosed 218 essential and renovascular hypertensive cases described by four continuous parameters. The overall efficiency of the algorithm was 80.7%.

In /67/, BEZDEK applied the fuzzy ISODATA clustering algorithm to feature selection of medical data. In the numeric example, 11 binary symptoms of 107 stomach disease patients who had either hiatal hernia or gallstones were considered.

A further paper proposing the use of fuzzy clustering methods in medical diagnosis is the one by ESOGBUE and ELDER /68/. That paper gives an instructive example of applying a criterion function that is a modified form of the minimum MINKOWSKI metric to

rheumatic valvular heart diseases.

### 2.7. Fuzzy decision analysis in medical diagnosis

Imprecision in decision analysis is modeled using fuzzy set theory in NOMURA, et al. /69/ and MISHIMA, et al. /70/. These reports propose an interesting model that represents probability or utility by a membership function. The model selects an optimal treatment by comparing among degrees of truth of some propositions on expected utilities. This method is applied to managing patients with pancreatic diseases centered around primary cancer. The decision process starts from a point at which a patient is very likely to be suffering from any one of four pancreatic diseases taken into account. In clinical practice the procedure helps to decide whether or not a radical operative invasion against the supposed disease should be performed.

### 2.8. Bayesian approach and fuzzy subsets

In /38/, ALBIN argued that it is entirely reasonable to assign

$$\mu_{D_i}(S_1, \dots, S_n) = P(D_i/S_1, \dots, S_n) \quad (8)$$

under the condition that good Bayesian values can be obtained for the probability indices  $P(D_i/S_1, \dots, S_n)$ .

"Calling  $P(D_i/S_1, \dots, S_n)$  the value of the membership function  $\mu_{D_i}$  at  $(S_1, \dots, S_n)$  in  $R^n$  is much more reasonable than calling it a probability, since the manner of estimating  $P(D_i/S_1, \dots, S_n)$  is very inexact. Physicians' estimates based on their own medical knowledge have also been used in computing  $P(D_i/S_1, \dots, S_n)$

from  $P(S_1, \dots, S_n/D_i)$  and  $P(D_i)$ , so these estimates should be used with equal validity for  $\mu_{D_i}(S_1, \dots, S_n)$ ."

quoted from /38/, p. 84

### 2.9. Miscellaneous

CHENG and McINNIS describe in /71/ an algorithm for multiple attribute (symptoms), multiple alternative (diagnoses) decision problems (see also KICKERT /72/). The relative importance of a symptom  $j$  denoted by  $\mu_{W_j}$ , and the rating  $\mu_{r_{ij}}$  that indicates the importance of the symptom  $j$  with respect to disease  $i$  have been established for 12 blood chemistry tests considering 78 diseases. On this basis the computer program calculates possible diseases which are ranked and arranged in descending order.

In FOX /73/, some critical remarks concerning WECHSLER's paper /64/ are put forward. FOX emphasizes that clinical and professional acceptability of computer-based medical consultation systems is of primary importance. Technology should be planned with this in mind.

OHSATO, et al. /74/ established a fuzzy relation in a preoperative nursing care system. The relation between preoperative patient's state and postoperative state is determined by using patient's attributes before and after the operation estimated by a nurse, e.g. degree of seriousness of preoperative and postoperative patient's states.

### 3. FINAL REMARKS

The detailed survey of fuzzy approaches to medical decision making shows the wide



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