Medical Knowledge, Fuzzy Sets, and Expert Systems

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Abstract. The term medical knowledge is a superimposed concept for the relationships between symptoms and diagnoses a physician may find in books, journals, monographs, but also in practical experience. In the second half of the 20th century medical knowledge was also stored in computer systems. To assist physicians in medical decision-making and attendance medical expert systems have been constructed that use the theory of fuzzy sets, which was founded in 1965 by Lotfi A. Zadeh. The present article delineates two specific pathways resulting from a bifurcation in the history of applied fuzzy expert systems in medicine. This bifurcation occurred in the 1970's in the history of the theory of fuzzy systems, when Zadeh published the "rule of max-min composition" and other researchers applied this rule in different areas. This was the origin of two research areas: fuzzy control, initiated by Sedrak Assilian and Ebrahim Mamdani in London, and fuzzy relations, introduced by Elie Sanchez in Marseille. Later on both concepts were used to construct medical knowledge-based systems in medicine. We present two Viennese systems representing these concepts: the "fuzzy version" of the Computer-Assisted DIAGnostic System (CADIAG) which was developed at the end of the 1970s, and a fuzzy knowledge-based control system, FuzzyKBWean, which was established as a real-time application based on the use of a Patient Data Management System (PDMS) in the intensive care unit (ICU) in 1996.

1 Medical Knowledge

The history of computerized medical diagnosis is a history of intensive collaboration between physicians and mathematicians respectively electrical engineers or computer scientists. In the late 1950s Ledley and Lusted published *Reasoning Foundations for Medical Diagnosis* [1], Lipkin and Hardy [2], and Ledley [3], wrote on the methods for the use of card and needle systems for storage and classification of medical data and systematic medical decision-making. In the 1960s and 1970s various approaches to computerized diagnosis arose using Bayes rule [4, 5], factor analysis [6], and decision analysis [3]. On the other side artificial intelligence approaches came into use, e.g., DIALOG (*Diagnostic Logic*) [7] and PIP (*Present Illness Program*) [8], which were programs to simulate the physicians reasoning in information gathering and diagnosis using databases in form of networks of symptoms and diagnoses.

We use the term "symptom" for any information about the patient's state of health, anamnesis, signs, laboratory test results, ultrasonic results, and X-ray findings. Based on this information a physician has to find a list of diagnostic possibilities for the patient. To master this process he had to study many relationships of obligatory or facultative proving or excluding symptoms for diagnosis in books and journals and in his practical experience. These certain information about relationships that exist between symptoms and symptoms, symptoms and diagnoses, diagnoses and diagnoses and more complex relationships of combinations of symptoms and diagnoses to a symptom or diagnosis are formalizations of what is called medical knowledge.

In 1976 in Toronto, Canada, Alonzo Perez-Ojeda called this network linked by logical relations "medical knowledge". The basic conception of his master thesis *Medical Knowledge Network. A Database for Computer Aided Diagnosis* was the representation of "medical knowledge" using an associative model of the human memory. Perez-Ojeda designed a prototype system to be used in the search for an adequate strategy to simulate an approximate reasoning model in medical decision-making and he gave examples of typical elements of medical knowledge ([9], p. 3.2):

- "A runny nose is *almost always* present in a common cold."
- "Acute pyelonephritis *usually* presents bladder irritation and infection."
- "Acute pyelonephritis presents *occasionally* fever, or chills, and malaise."

The diseases *common cold* and *acute pyelonephritis* are presented by the abbreviations D_1 and D_2 and *runny nose*, *fever*, *bladder irritation*, *infection*, *chills*, and *malaise* by S_1 to S_6. Therefore the network of medical knowledge could be graphically constructed by elementary knots and arcs. However, Perez-Ojeda modeled the relations (*usually*, *occasionally*, and *almost always*) by mathematical probability modifiers:

$$D_1 \xrightarrow{\textit{almost always}} S_1$$

$$D_2 \xrightarrow{\textit{usually}} S_3 \text{ AND } S_4$$

$$D_2 \xrightarrow{\textit{occasionally}} (S_2 \text{ OR } S_5) \text{ AND } S_6$$

Figure 1. Examples of elements of the network of medical knowledge

2 Computer-Assisted Diagnostic

In the nineteen-sixties and -seventies, the Department of Medical Computer Sciences of the University of Vienna Medical School at the Vienna General Hospital envisaged the development of a computer-assisted diagnostic system that did not use stochastic methods. "It was intended to develop a system which is not based on statistical assumptions like normal distribution, mutual independency of symptoms, constant probabilities of symptoms in different populations and at different observation times. There is no need for information about the frequency or lack of certain symptoms with the sick or the healthy. Therefore rare complaints are considered as well as frequent diseases" [10, p. 141].

To systemize and formalize medical knowledge and to store it in a suitable form, Georg Grabner (professor of gastroenterology and hepatology and both head of the University Department of Medical Computer Sciences and, at the same time, head of the University Clinic of Gastroenterology and Hepatology) and the IBM information scientist W. Spindelberger started to use a computer for medical diagnosis in the late 1960's. This was followed by intensive collaboration between physicians and mathematicians, and engineers constructed a first *c*omputer-*a*ssisted *diag*nostic system based on two-valued logic in 1968 [11]. One year later Gangl, Grabner, and Bauer published their first experiences with this system in the differential diagnostics of hepatic diseases [12].

In 1976, the second generation of the system was developed on the basis of three-valued logic. Here, in addition to symptoms and diagnoses being considered to be 'present' or 'absent', 'not examined' or 'not investigated' symptoms and 'possible' diagnoses are also included. For this system known as CADIAG-I (*C*omputer-*A*ssisted *DIAG*nostis, version I), the following relationships between symptom (S_i) and disease (D_j) have been defined:

- OP: S_i is *obligatory occurring and proving* for D_j.
- E: S_i forces *obligatory exclusion* of D_j.
- FP: S_i is *facultative occurring and proving* for D_j.
- ON: S_i is *obligatory occurring and not proving* for D_j.
- FN: S_i is *facultative occurring and not proving* for D_j.
- NK: A specific relationship between the symptom and the disease is *not known*.

With three-valued logic these relationships could be expressed in the form of three-valued logic operators: the symptom's values could be *present* (1), *absent* (0), or *not investigated* (½), whereas the possible diagnoses' values could be *present* (1), *absent* (0), or *possible* (½).

As an example we show here the three-valued logic truth table of the relationship OP (S_i is *obligatory occurring and proving*. S_i must be present for D_j and S_i proves D_j; $S_i \Leftrightarrow D_j$.)

D_j / S_i	0	½	1
0	1	½	0
½	½	½	½
1	0	½	1

Figure 2. Three-valued logic truth table of OP: $S_i \Leftrightarrow D_j$

3 Hardware History

The Viennese CADIAG-system was a system in the tradition of the work of biomedical investigators in the USA after the second World War using automatic data processing techniques to study correlations of signs and symptoms with diseases. This was a result of the rapid accumulation of data from medical research. M. Lipkin and J. D. Hardy tried to classify and correlate all the data of a medical case (diagnosis of hematological diseases) with the use of a mechanical apparatus [2].

In order to record data from which the diagnoses of hematological diseases had been made, standard textbooks were consulted to choose 26 diseases and to list all characteristics of each disease. Storage and sorting of these medical data were first performed with the use of marginal punch cards. The periphery of these cards had been divided into numbered spaces, and a single hole was punched in each of the spaces. Each of the 138 available spaces had the significance of an item of information, and each card represents a given body of information. One margin of the card consisted of data derived from the case history and a second side consisted of data derived from physical examination. Information relating to peripheral blood examination was assigned to a third side, and bone marrow examination and other laboratory work to the fourth side.

The information of a given disease represented by one single card was transferred to the card in the following way. Where a given positive finding had been previously listed for a disease, a triangular wedge was punched in the appropriate space on the disease card.

"Thus, if one wished to find all the diseases characterized by a single item found under physical examination, for example 'large spleen', one would place this set of cards front to back and place a metal or plastic rod into the hole to which that item had been assigned. When the rod was raised, cards representing diseases characterized by a large spleen would fall, because the triangular wedge would have been punched into that space. Cards without the wedge would be raised" ([2], pp.116 f).

4 Software History

This hardware origin of the system was complemented by the software developed during the same period. It was published in *Science* in 1959 by Lee B. Lusted and Robert S. Ledley. Their article entitled *Reasoning Foundations of Medical Diagnosis* reached a large circle of medical researchers [1].

In April 1955, when Lusted was an instructor at the University of California School of Medicine and assistant at the University of California Hospital he wrote in the *New England Journal of Medicine* an article entitled *Medical Electronics*: "Members of the medical profession and electronic engineers have shown increasing interest in the field of medical electronics, with the result that electronic instrumentation has contributed to recent advances in some fields of medicine. Greater application of electronic instrumentation to medical problems will result from teamwork between the engineer and physician" ([13], p. 584).

In 1960, Robert S. Ledley, a professor of electrical engineering at George Washington University, Washington D. C. and the founding president of the National Biomedical Research Foundation (NBRF), wrote a book on *Digital Computer and Control Engineering*. In his introduction he stressed that: "It has been recognized that electronic computers can aid certain aspects of medical diagnosis. For example, the computer can (1) produce a list of possible diagnoses, consistent with medical knowledge, for a given set of symptoms presented by a patient; (2) indicate further diagnostic tests which best differentiate between remaining diagnostic possibilities; (3) calculate probabilities for the alternate diagnostic possibilities;" and other things [14].

In their 1959 *Science* paper, Ledley and Lusted saw two logical concepts inherent in medical diagnosis: medical knowledge, that is the physicians knowledge about relationships between the symptoms and the diseases, and the signs and symptoms presented by a particular patient, which give further information associated with this patient. Here only a brief review may show their logical analysis of this diagnosis process:

- x, y, ... are used to represent 'attributes'. A patient may have an attribute
  such as, for instance, a sign 'fever' or a disease 'pneumonia'.
- Corresponding capital letters X, Y, ... are used to represent statements about
  these attributes.
- For example: Y represents the statement "The patient has attribute y."
- Negation $\neg Y$: "The patient does not have attribute y."
- The combination $X{\cdot}Y$ represents the combined statement
  "The patient has the attribute x *and* the attribute y."
- The combination $X{+}Y$ represents the combined statement
  "The patient has attribute x *or* attribute y *or* both."
- The statement "If the patient has attribute x then he has attribute y"
  is symbolized by $X \Rightarrow Y$.

With only two attributes, symptoms (S) and diseases (D), they defined

$S(i)$ means "The patient has symptom i." $i = 1, ..., n$,
$D(j)$ means "The patient has disease j." $j = 1, ..., m$.

From a diagnostic textbook they took abstract example statements:

If a patient has disease 1 and not disease 2,
then he cannot have symptom 2 $D(1) \cdot \neg D(2) \Rightarrow \neg S(2)$

If a patient has either or both of the symptoms,
then he must have one or both of the diseases $S(1) + S(2) \Rightarrow D(1) + D(2)$

To consider, in general, more than two attributes, and more complicated expressions Ledley and Lusted used 'Boolean functions' $f(X, Y, ...)$.

After the section on logical concepts Ledley and Lusted continued with a section on probabilistic concepts. They argued that in many cases our medical knowledge is not exact but in the form "If a patient has disease 2, then there is only a certain chance that he will have symptom 2 — that is, say, approximately 75 out of 100 patients will have symptom 2. [...] Since »chance« or »probabilities« enter into »medical knowledge«, then chance, or probabilities, enter into the diagnosis itself" ([1], p. 13).

Six years later, it seemed that Lusted had given up the program to use methods of exact mathematics in medicine; in his contribution to a volume on *Computers in Biomedical Research* [15] he was agreeing with a very new claim: "Research on medical diagnosis has served to emphasize the need for better methods of collecting and coding medical information and to demonstrate the inadequacy of conventional mathematical methods for dealing with biological problems. In a recent statement Professor L. A. Zadeh (1962) summed up the situation as follows: »In fact, there is a fairly wide gap between what might be regarded as 'animate' system theorists and 'inanimate' system theorists at the present time, and it is not at all certain that this gap will be narrowed, much less closed, in the near future.

There are some who feel that this gap reflects the fundamental inadequacy of the conventional mathematics — the mathematics of precisely-defined points, functions, sets, probability measures, etc. — for coping with the analysis of biological systems, and that to deal effectively with such systems, which are generally orders of magnitude more complex than man-made systems, we need a radically different kind of mathematics, the mathematics of fuzzy or cloudy quantities which are not describable in terms of probability distributions. Indeed, the need for such mathematics is becoming increasingly apparent even in the realm of inanimate systems, for in most practical cases the *a priori* data as well as the criteria by which the performance of a man-made system is judged are far from being precisely specified or having accurately-known probability distributions.«" ([16], p. 321).

5 Fuzzy Sets, Fuzzy Relations, and Fuzzy Control

Lotfi Zadeh, a Professor of electrical engineering at Berkeley, founded a mathematical theory of such fuzzy sets about two years after his demand quoted by Lusted. By generalization of usual set theory an object can not only be an element of a set (membership value 1) or not an element of this set (membership value 0) but it can also have a membership value between 0 and 1. Therefore he defined fuzzy sets by their *membership function* μ which is allowed to assume any value in the interval [0,1] instead of their *characteristic function* which is defined to assume the values 0 *or* 1 only (fig. 3) [17].

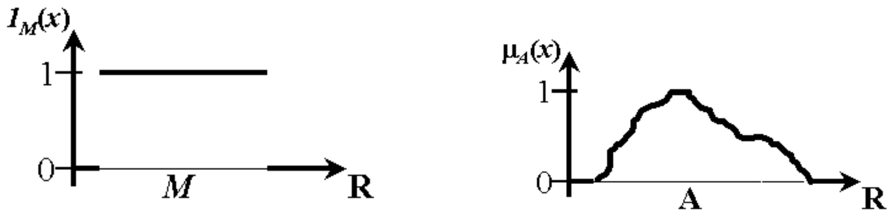

Figure 3. Characteristic function of a set *M*, membership function of a fuzzy set *A*

Relating to fuzzy sets *A*, *B* in any universe of discourse *X*, Zadeh defined *equality*, *containment*, *complementation*, *intersection*, and *union* (for all $x \in X$):

- $A = B$ if and only if $\mu_A(x) = \mu_B(x)$,
- $A \subseteq B$ if and only if $\mu_A(x) \leq \mu_B(x)$,
- $\neg A$ is the complement of A if and only if $\mu_{\neg A}(x) = 1 — \mu_A(x)$,
- $A \cup B$ if and only if $\mu_{A \cup B}(x) = \max(\mu_A(x), \mu_B(x))$,
- $A \cap B$ if and only if $\mu_{A \cap B}(x) = \min(\mu_A(x), \mu_B(x))$.

The space of all fuzzy sets in *X* becomes a Boolean algebra; thus, a propositional logic with fuzzy concepts constitutes "fuzzy logic".

Zadeh introduced "fuzzy systems" in system theory if input, output, and state of a system or "any combination of them ranges over fuzzy sets" and he argued that "the difference between stochastic and fuzzy systems is that in the latter the source of imprecision is nonstatistical in nature and has to do with the lack of sharp boundaries of the classes entering into the descriptions of the input, output or state" ([18], p. 33).

In 1973, Zadeh defined *fuzzy* relations: If $L(A \times B)$ is the set of all fuzzy sets in the Cartesian product $A \times B$ of crisp sets A and B, then a fuzzy relation is a subset of $L(A \times B)$ [19]. Having three sets A, B, and C, to compose fuzzy relations $Q \subseteq L(A \times B)$ and $R \subseteq L(B \times C)$ to get another fuzzy relation $T \subseteq L(A \times C)$, Zadeh introduced the combination rule of a *max-min-composition*: $T = Q * R$ is defined by the following membership function

$$\mu_T(x,y) = \max_{y \in B} \min\{\mu_Q(x,y); \mu_R(y,z)\}, \; x \in A \; y \in B \; z \in C.$$

Using this composition formula as an inference rule, Assilian and Mamdani developed the concept of *fuzzy control* in the early 1970s [20, 21]. Fuzzy control can be described as "control with sentences rather than equations". In many cases, it is more natural to use sentences, or rules, for instance in operator-controlled systems, with the control strategy written in terms of if-then clauses. If the controller further adjusts the control strategy without human intervention, it is *adaptive*. The adaptive *fuzzy* controller, invented by Assilian and Mamdani, is known as the *self-organising fuzzy controller*. An adaptive controller is a controller with adjustable parameters and a mechanism for adjusting the parameters [22]. Despite the lack of a formal definition, an adaptive controller has a distinct architecture consisting of two loops: a control loop and a parameter adjustment loop (see figure 4).

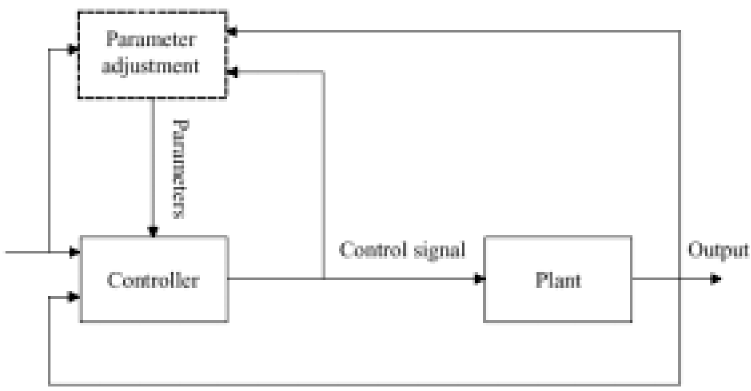

Figure 4. Adaptive control system

In other words, fuzzy control is based on an I/O function that maps each very low-resolution quantization interval of the input domain into a very low-low resolution quantization interval of the output domain. As there are a few fuzzy quantization intervals covering the input domains, the mapping relationship can be very easily expressed using the "if-then" formalism. (In some applications this leads to a simpler solution in less designing time.) The overlapping of these fuzzy domains and their usually linear membership functions will eventually allow a rather high-resolution I/O function between crisp input and output variables to be achieved. Mamdani's development of fuzzy controllers in 1974 [21] gave rise to the utilization of these fuzzy controllers in ever-expanding capacities.

6 Expert Systems, Medical Diagnosis and Control

Some of the first knowledge-based systems to be introduced were medical knowledge-based systems, namely MYCIN, INTERNIST, CASNET, PIP, EXPERT, and CADIAG. The latter is one of the first to use the theory of fuzzy sets. It was developed to assist the physician in diagnostics. Representation and processing of medical knowledge was a very difficult and complex task for computer systems when the first fuzzy expert system, CADIAG, arose in the late seventies.

Here we delineate two specific pathways through an eventful history. They result from a bifurcation in the development of fuzzy systems developed to assist the physician in medical science. This branching occurred in the 1970's in the history of the theory of fuzzy sets and systems, when Lotfi A. Zadeh's "rule of max-min composition" was applied in different areas. *Fuzzy control* was initiated by Sedrak Assilian and Ebrahim Mamdani in London, UK, [20], whereas *fuzzy relations* were generally introduced by Zadeh [19] and into medical sciences by Elie Sanchez in Marseille, France [23, 24].

Today, both concepts are used to construct knowledge-based systems in medicine. The branch of fuzzy relations has been used to model "medical knowledge" expressing associations between symptoms and diseases. Using this approach, a "fuzzy version" of the *C*omputer-*A*ssisted *DIAG*nostic System was developed in 1980 at the University of Vienna Medical School in collaboration with the Vienna General Hospital. The version is based on Klaus-Peter Adlassnig's *Fuzzy Logical Model of Computer-Assisted Medical Diagnosis* [25].

The branch of fuzzy control is being implemented in medical application systems since the 1990's, as real-time applications are being adequately executed by computers since this time. Scientists and physicians at the University of Vienna Medical School and the Vienna General Hospital established the fuzzy knowledge-based control system FuzzyKBWean as a real-time application, based on the use of a Patient Data Management System (PDMS) in the intensive care unit (ICU) in 1996.

Four years after the publication of *Fuzzy Sets*, Zadeh suggested their application in medical science. He wrote: "A human disease, e.g., Diabetes, may be regarded as a fuzzy set in the following sense. Let $X = \{x\}$ denote the collection of human beings. Then diabetes is a fuzzy set, say D, in X, characterized by a membership function $\mu_D(x)$ which associates with each human being x his grade of membership in the fuzzy set of diabetes" ([26], p. 205).

Merle Anne Albin, a mathematician in Berkeley wrote her doctoral thesis *Fuzzy Sets and Their Applications to Medical Diagnosis and Pattern Recognition* in 1975 [27], and a year later in Toronto, Canada, Alonso Perez-Ojeda wrote his master thesis [8]. Harry Wechsler published his *Applications of Fuzzy Logic to Medical Diagnosis* [28] while Augustine O. Esogbue and Robert C. Elder published two parts of a *fuzzy model* of a physician's decision process in the new journal *Fuzzy Sets and Systems* in 1979 and 1980 [29, 30].

7 Medical Knowledge as a Fuzzy Relation

A more far-reaching concept of modeling relationships between symptoms and diseases was introduced in 1974 by Elie Sanchez from Marseille, France, in his human biological doctoral thesis *Equations de Relations Floues* [23]. Sanchez planned "to investigate medical aspects of fuzzy relations at some future time" ([24], p. 47). In 1979 he introduced the relationship between symptoms and diagnoses by the concept of 'medical knowledge': "In a given pathology, we denote by S a set of symptoms, D a set of diagnoses and P a set of patients. What we call "medical knowledge" is a fuzzy relation, generally denoted by R, from S to D expressing associations between symptoms, or syndromes, and diagnoses, or groups of diagnoses" ([31], p. 438). Sanchez adopted Zadeh's max-min-compositional rule as an inference mechanism. It accepts fuzzy descriptions of the patient's symptoms and infers fuzzy descriptions of the patient's diseases by means of the fuzzy relationships described earlier. If a patient's symptom is S_i then the patient's state in terms of diagnoses is a fuzzy set D_j with the following membership function:

$$\mu_{D_j}(d) = \max_{s \in S} \min \{\mu_{S_i}(s); \mu_R(s,d)\}, \; s \in S, \; d \in D.$$

$\mu_R(s,d)$ is the membership function of the fuzzy relation "medical knowledge".

With P, a set of patients, and a fuzzy relation Q from P to S, and by 'max-min composition' we get the fuzzy relation $T = Q * R$ with the membership function

$$\mu_T(p,d) = \max_{s \in S} \min \{\mu_Q(p,s); \mu_R(s,d)\}, \; p \in P, \; s \in S, \; d \in D.$$

Adlassnig in Vienna was aware of the theory of fuzzy sets and the fact that it had been used in computer-aided diagnosis. In his first paper together with Grabner, *The Viennese Computer-Assisted Diagnostic System. Its Principles and Values* in 1980 [11], he referred to the medical diagnostic systems using the concept of fuzzy sets by Tautu and Wagner [32] and by Moon et al. [33]. He now proposed to integrate this concept into a more suitable version of the system CADIAG: "Fuzzy set theory with its capability of defining inexact medical entities as fuzzy sets, 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" ([34], p. 205).

This new fuzzy version of the computer-assisted diagnostic system, CADIAG-II, appeared in 1980. In Adlassnig's *fuzzy logical model of computer-assisted medical diagnosis* [25], all symptoms $S_i \in S$ are considered to be fuzzy sets of different universes of discourse X with membership functions $\mu_{S_i}(x)$, for all $x \in X$, indicating the strength of x's affiliation in S_i, while all diagnoses $D_j \in D$ are considered to be fuzzy sets in the set P of all patients under consideration, with $\mu_{D_j}(p)$ assigning the patient p's membership to be subject to D_j.

To describe medical knowledge as the relationship between symptom S_i and disease D_j Adlassnig found two fuzzy relationships, namely *occurrence* — how often does S_i occur with D_j ? — and *confirmability* — how strongly does S_i confirm D_j? — ([35], p. 225). These functions could be determined by

- linguistic documentation by medical experts and
- medical database evaluation by statistical means or a combination of both.

In both ways to determine these fuzzy relationships between symptoms and diagnoses, *occurrence* and *confirmation*, they have been defined as fuzzy sets. When physicians had to specify these relationships by only giving answers like *always*, *almost always*, *very often*, *often*, *unspecific*, *seldom*, *very seldom*, *almost never*, and *never*, they chose fuzzy sets which have been defined by Adlassnig's determination of their membership functions. In the case of medical databases, the membership functions' values of *occurrence* and *confirmability* could be defined as relative frequencies.

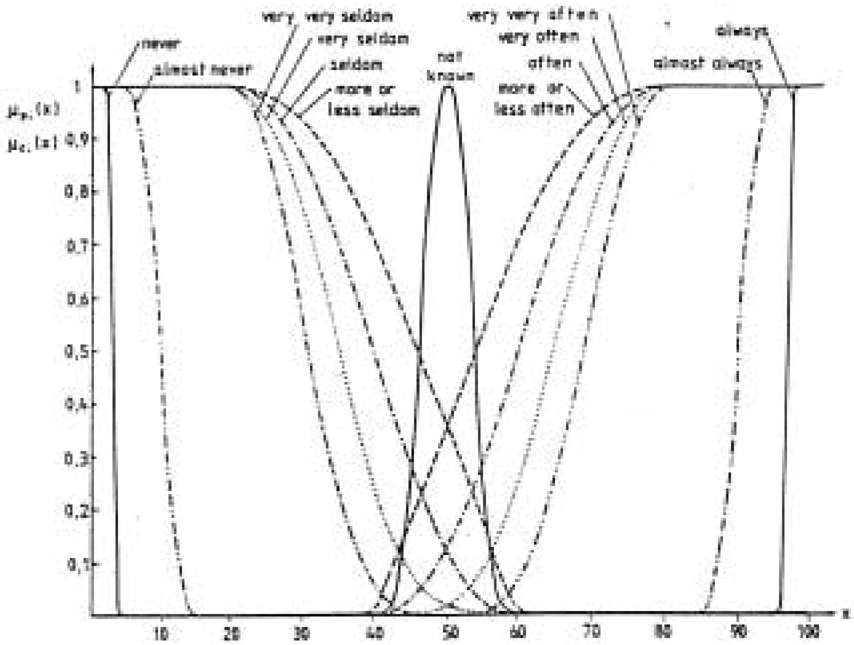

Figure 5. Membership functions of the fuzzy sets *occurrence o (former presence p)* and *confirmability (former conclusiveness c)* ([25], p. 145)

Thus, in CADIAG-II, the fuzzy relationships between symptoms (or symptom combinations) and diseases are given in the form of rules with associated fuzzy relationship tupels (*frequency of occurrence o*, *strength of confirmation c*); their general formulation is ([36], p. 262):

- IF antecedent THEN consequent WITH (o, c)

In particular, the following fuzzy relationships exist ([36], p. 262; K = set of symptom combinations SC_i):

- S_i, D_j (occurrence relationship) $R^o_{SD} \subset \Sigma \times \Delta$
- S_i, D_j (confirmation relationship) $R^c_{SD} \subset \Sigma \times \Delta$
- SC_i, D_j (occurrence relationship) $R^o_{SCD} \subset K \times \Delta$
- SC_i, D_j (confirmation relationship) $R^c_{SCD} \subset K \times \Delta$
- S_i, S_j (occurrence relationship) $R^o_{SS} \subset \Sigma \times \Sigma$
- S_i, S_j (confirmation relationship) $R^c_{SS} \subset \Sigma \times \Sigma$
- D_i, D_j (occurrence relationship) $R^o_{DD} \subset \Delta \times \Delta$
- D_i, D_j (confirmation relationship) $R^c_{DD} \subset \Delta \times \Delta$

To deduce diseases $D_j \in D$ suffered by patient $P_k \in P$ from the observed symptoms $S_i \in S$ in CADIAG-II we use three max-min-compositions as inference rules:

- hypotheses and confirmation $R_{PD}^1 = R_{PS} \circ R_{SD}^c$
  defined by
  $$\mu_{R_{PD}^1}(P_k, D_j) = \max_{S_i} \min\{\mu_{R_{PS}}(P_k, S_i); \mu_{R_{SD}^c}(S_i, D_j)\}$$
- exclusion (by present symptoms) $R_{PD}^2 = R_{PS} \circ (1 - R_{SD}^c)$
  defined by
  $$\mu_{R_{PD}^2}(P_k, D_j) = \max_{S_i} \min\{\mu_{R_{PS}}(P_k, S_i); 1 - \mu_{R_{SD}^c}(S_i, D_j)\}$$
- exclusion (by absent symptoms) $R_{PD}^3 = (1 - R_{PS}) \circ R_{SD}^o$
  defined by
  $$\mu_{R_{PD}^3}(P_k, D_j) = \max_{S_i} \min\{1 - \mu_{R_{PS}}(P_k, S_i); \mu_{R_{SD}^o}(S_i, D_j)\}$$

CADIAG-II was very successful in partial tests, e.g., in a study of 400 patients with rheumatic diseases, CADIAG-II elicited the correct diagnosis in 94.5 % ([36], p. 264). More results can be found in [35, 36].

8 Fuzzy Control in Medicine

Fuzzy control techniques have recently been applied in various medical processes, such as pain control [37] and blood pressure control [38]. Fuzzy control compared to classical control theory (PID control), which is a fuzzy logic approach to control, offers the following advantages [39, 40]:

- It can be used in systems, which cannot be easily modeled mathematically. In particular, systems with non-linear responses that are difficult to analyze may respond to a fuzzy control approach.
- As a rule-based approach to control, fuzzy control can be used to efficiently represent an expert's knowledge about a problem.
- Continuous variables may be represented by linguistic constructs that are easier to understand, making the controller easier to implement and modify. For instance, instead of using numeric values, temperature may be characterized as "cold, cool, warm, or hot".
- Fuzzy controllers may be less susceptible to system noise and parameter changes; in other words, they will be more robust.
- Complex processes can be controlled by relatively few logical rules, permitting an easily comprehensible controller design and faster computation for real-time applications.

In other words, fuzzy control can be best applied to production tasks that heavily rely on human experience and intuition, and which therefore rule out the application conventional control methods. The use of *Patient Data Management Systems* (PDMS) in *Intensive Care Units* (ICU) since 1992 has made it possible to apply fuzzy control applications in real-time in this medical field.

Mechanical ventilation is such an example. One purpose of mechanical ventilation is to achieve optimal values of arterial O_2-partial pressure (pO_2) and arterial CO_2-partial pressure (pCO_2) while ensuring careful handling of the lung:

- $FiO_2 < 60$ (else oxygen toxicity)
- low inspiratory pressures $P_I < 35$ (else barotrauma)
- small shear forces equivalent to small tidal volumes (else volume trauma)
- prevent atelectasis formation (else shear forces at reopening)

In addition, the patient has to be carefully handled in order to avoid cardiac failure and respiratory muscle fatigue. Both of these conditions have to be observed if the heart rate or the respiratory rate increases. The value pO_2 states whether the oxygenation is sufficient. pO_2 is not continuously available because it would entail taking a blood sample. O_2-saturation (SpO_2) provided by pulsoximetry is more convenient because SpO_2 is permanently available. pCO_2 states whether alveolar ventilation is sufficient. Similarly, the end-tidal CO_2 ($EtCO_2$) is permanently available, but at the disadvantage of being an indirect measure of pCO_2. Thus, the main physiological input parameters of the weaning system are SpO_2 and $EtCO_2$.

For instance, the *Biphasic Positive Airway Pressure* (BIPAP) controlled mode is an integrated mode of ventilation of Evita ventilators (Evita, Dräger, Lübeck, Germany). This mode allows spontaneous inspiration during the whole respiratory cycle and thus permits a very smooth and gradual transition from controlled to spontaneous breathing. Ventilatory adjustments are based on two pressure levels: inspiratory pressure (P_I or P_{high}) and expiratory pressure (P_E or P_{low}); on two durations, inspiration time (t_I) and expiration time (t_E), as well as on the fraction of inspired O_2 (F_IO_2). Within this mode, five parameters can be adjusted.

BIPAP was first described in a study published in 1989 by a group led by M. Baum and H. Benzer and it was incorporated in the Evita ventilator in the same year [41]. Earlier studies conducted by Stock et al. used the term APRV (Airway Pressure Release Ventilation) [42] to describe a method of ventilation, which used the same mechanical principle as BIPAP, but started from a different premise. The authors describe BIPAP as pressure-controlled ventilation with freedom of respiration and spontaneous breathing on two levels (see figure 6).

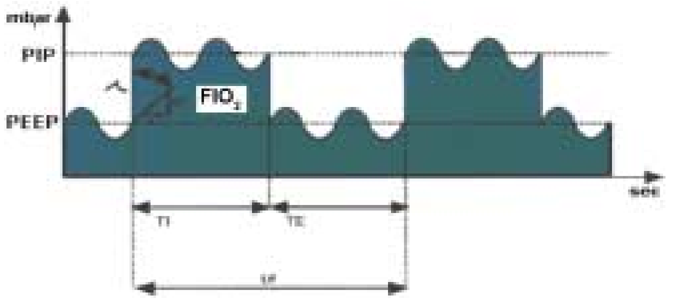

Figure 6. BIPAP ventilation mode

The workgroup of Baum represented a new approach to ventilation techniques. Before 1989, though ventilation modes employed a mixture of mechanical ventilation and spontaneous breathing (augmented ventilation), they were all based on the same principle for maintaining minimum ventilation, namely mechanical breaths alternating with spontaneous breaths. The clinical problems which arose from alternating between mechanical ventilation and spontaneous breathing were the starting point for the development of BIPAP: patients often failed to accept the enforced respiratory rate or the interruption of their spontaneous breathing by the mandatory breaths. Baum and Benzer realized that BIPAP was particularly important from the clinical point of view because ventilation was accurately matched to the patient's spontaneous breathing and because it was straightforward to use. These advantages were thought to be particularly significant for weaning, because there was no alternation between pure mechanical and augmented ventilation. Decisions about when to start the weaning process became totally unnecessary — with the new BIPAP mode weaning is possible right from the start.

Some recent examples are: VentPlan, a ventilator management advisor that interprets patients' physiological data to predict the effect of proposed ventilator changes [43]; ESTER, a program which assesses the patient's pathophysiological state using modified APACHE-II criteria, then offers suggestions for weaning from intermittent mandatory ventilation [44]; NEOGANESH, a program for automated control of assisted ventilation in ICUs [45]; KUSIVAR, a program which describes a comprehensive system for respiratory management during all phases of pulmonary disease [46]; and FuzzyKBWean, a system for weaning patients from artificial ventilation [47]. Although many such expert systems have been described, only a few have been tested in clinical patient care. For example, studies of computer-controlled optimization of positive end-expiratory pressure and computerized protocols for the management of adult respiratory distress syndrome were explored by East and Bohm [48]. A computerized ventilator weaning system for postoperative patients was tested by Strickland and Hasson [49] and Schuh et al. [47].

The procedure for weaning a patient with respiratory insufficiency from mechanical ventilation is a complex control task and requires expertise based on long-standing clinical practice. Fuzzy knowledge-based weaning (FuzzyKBWean) is a fuzzy knowledge-based control system that proposes stepwise changes in ventilator settings during the entire period of artificial ventilation at the bedside in real time.

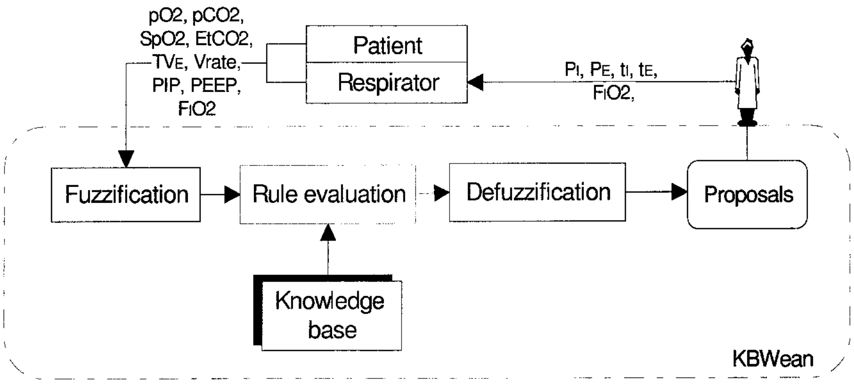

Figure 7. The FuzzyKBWean control process

Information is obtained from a PDMS operating at the ICU with a time resolution of one minute. The system is used for postoperative cardiac patients at the Vienna General Hospital. A large part of the explicitly given and implicitly available medical knowledge of an experienced intensive care specialist could be transferred to the fuzzy control system. Periods of deviation from the target are shorter using FuzzyKBWean.

9 Outlook

In medicine, two fields of fuzzy applications were developed in the nineteen-seventies: computer assisted diagnostic systems and intelligent patient monitoring systems. Both developments of Zadeh's "rule of max-min composition", namely fuzzy relations and fuzzy control, have been applied in these areas.

For obvious reasons, the available body of medical data (on patients, laboratory test results, symptoms, and diagnoses) will expand in the future. As mentioned earlier, computer-assisted systems using fuzzy methods will be better able to manage the complex control tasks of physicians than common tools.

Most control applications in the hospital setting have to be performed within critical deadlines. Decisions have to be made locally and promptly. This is a setting that requires a local hospital intranet rather than the possibilities of the world-wide internet.

Using current web technology, integrated systems of both types of fuzzy systems described above can be easily implemented as internet and intranet applications.

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