

Fuzzy Medical Diagnosis

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Abstract: Despite all standardization efforts, medical diagnosis is still considered an art. Much of this status is owed to the fact that medical diagnosis requires a proficiency in coping with uncertainty simply not found in today's computing machinery. Offering a generic and powerful framework for the remodelling of existing systems and the paradigms they are based on, fuzzy set theory promises to be a valuable contribution to the advancement of medical computing, particularly as implementations begin to proliferate. With our work we provide an overview of fuzzy medical systems covering three different aspects of diagnosis: scoring, consultation, and diagnostic monitoring.

Keywords: problems of medical diagnosis, medical scores, consultation systems, diagnostic monitoring

1. Introduction

Medical diagnosis is the art of determining a person's pathological status from an available set of findings. Why is it an art? Because it is a problem complicated by many and manifold factors, and its solution involves literally all of a human's abilities including intuition and the subconscious.

If it is an art, is it at all susceptible to information processing? Although it appears to be among the most demanding problems ever to be approached by the information processing community, there is strong evidence that it is. It does, however, require an integration of results from most of the many subdisciplines of information processing and, especially, AI.

1.1. Problems of medical diagnosis

The functioning of the human body is characterized by the complex and highly interactive interplay of its organs and the psyche. The goal of this concerted effort is homeostasis, the equilibrium of all physiological quantities. While the actual level at which the balance is maintained varies --- within physiological bounds --- from individual to individual, deviations from it are indicative of some kind of perturbation, be it of internal or of external cause. The identification of these perturbations is the goal of medical diagnosis.

With the diagnostic means available today it is often impossible to look inside a sick patient and determine the primary cause that led to the (series of) effects and reactions the patient complains about. More often than not, diagnosis is therefore based on indirect evidence, the presence of symptoms, and the knowledge of the medical mechanisms that relate presumed causes to observed effects. The problems of diagnosis do not only arise from the incompleteness of this knowledge, but also and most immediately from the theoretical and practical limitations associated with the reversal of the chain of implications that lead from an initial cause to its observable effects.

First of all, medical cause-effect relationships, the relations between diagnoses and their symptoms, are hardly ever one-to-one. Differentiation of diagnoses that share an overlapping range of symptoms is therefore inherently difficult. Secondly, all observation is subject to error: the correction of this error, stochastic in nature, requires strong assumptions that do not hold in practice. Lastly, the required observations can often not be made on a continuous basis. Quite the contrary: Because many diagnostically meaningful observations can only be obtained at

rather high risk or cost, one has to make do with significantly less than desirable information. This is especially a problem for the diagnosis of dynamic perturbations that evolve over an extended period of time: gapless recording of the time course of physiologically decisive parameters is still more a desideratum than reality. Diagnosticians are left with a lot to speculate about.

Although taken alone none of the problems is unique to the medical domain, taken together they add to an intricacy surpassing that of even the most sophisticated man-made systems known today. It is therefore realistic to expect that medical diagnosis will for a long time remain problematic.

1.2. How fuzzy sets can help

It seems quite clear that system theoretic, analytic solutions to the problems of medical diagnosis are very hard to find. On the other hand, the intelligence of a human diagnostician is sufficient to achieve satisfactory results in the vast majority of diagnostic problems posed. Certainly, this performance cannot be explained by non-reproducible processes such as guessing or intuition. There must be some structure to diagnosis susceptible to formalization and automated reproduction. The identification of such structure and associated methods is a key goal of medical AI.

AI has brought out two basic approaches to diagnosis. One, referred to as heuristic diagnosis, is associative in nature and relies on the formalized experience of experts in the field (which is often phenomenological or case-based). The other, called model-based diagnosis, builds on a deeper understanding of the matter of discourse and uses models to reproduce the diagnosed subject's behaviour. The former is an attempt to reverse the physiologic cause-effect relationships directly, while the latter tries to derive the observed symptoms from hypothesized diagnoses, simulating the known relationships and so determining the cause indirectly.

It is not difficult to see how fuzzy set theory can help with heuristic diagnosis. Every trustworthy expert knows that his/her medical knowledge and the resulting diagnoses are pervaded by uncertainty. Uttered expert knowledge therefore abounds with imprecise formulations. This imprecision is not a consequence of rhetorical inability, but an intrinsic part of expert knowledge acquired through laborious experience. Any formalism disallowing uncertainty is therefore inapt to capture this knowledge --- stripping it of its uncertainty entails the danger of fallacies due to misplaced precision.

Fuzzy set theory on the other hand was conceived with the formalization of vague knowledge in mind. Together with appropriate rules of inference it provides a powerful framework for the combination of evidence and deduction of consequences based on knowledge specified in syllogistic form.

Not so obvious is the suitability of fuzzy set theory for model-based diagnosis. Yet, an intrinsic need for fuzziness in the models themselves has been observed: "Indeed, the complexity of biological systems may force us to alter in radical ways our traditional approaches to the analysis of such systems. Thus, we may have to accept as unavoidable a substantial degree of fuzziness in the description of the behaviour of biological systems as well as in their characterization. This fuzziness, distasteful though it may be, is the price we have to pay for the ineffectiveness of precise mathematical techniques in dealing with systems comprising a very large number of interacting elements or involving a large number of variables in their decision trees." [Zadeh 69], p. 200. No doubt, in model-based diagnosis, precision would be as misplaced as in heuristic diagnosis.

The generality of fuzzy set theory allows literally all models, as well as the ontologies within which they are created, to be fuzzified; resultant is a treatment of uncertainty that lies at the intersection of qualitative and quantitative methods.

1.3. A brief history

The first logic-based approach (as opposed to several earlier approaches based on numerical methods) to medical diagnosis was pursued by Ledley and Lusted in 1959 [Ledley 59]. Due to the undeniable uncertainty of the problem domain pure binary logic was soon found to be inadequate as a language of medical problem formulation and solving. Three-valued logic, binary logic extended by "unknown" as a third logical value, was accepted as a first remedy [Salamon 76]. For example, the ternary logic of Kleene [Rescher 69] provided the logical basis of CADIAG-I [Adlassnig 80 b].

Progress in the field was characterized by the presentation of different alternatives of inexact reasoning, many of which used continuous, probability-related measures of (un)certainty. The MYCIN [Shortliffe 76], PIP [Szolovits 78], CASNET [Weiss 78], EXPERT [Kulikowski 82] and INTERNIST [Pople 82] systems were among the more prominent. The certainty factor model of MYCIN, which could also be found in many expert system shells developed in the sequel, has only recently been superseded by the theory of Bayesian nets [Pearl 88, Heckerman 92].

At the same time, but widely unnoticed, first investigations examining the suitability of fuzzy sets in overcoming the inadequacies of symbolic reasoning in medical domains were undertaken (eg [Albin 75, Wechsler 76, Perez-Ojeda 76, Moon 77, Esogbue 79]). Generalized fuzzy approaches to medical diagnosis followed, eg a fuzzy quantification of the decision making process [Cerutti 81] or a fuzzy interpretation of MYCIN's certainty factors [Pis 89]. With [Adlassnig 80a], the theoretical groundwork of CADIAG-2, the most prominent fuzzy medical expert system to date, was laid. While the work on this and other systems continues, more and more of the many different aspects of medical diagnosis are covered, so that it is possible to identify distinct categories of fuzzy diagnostic systems.

In the following, we give an overview over fuzzy systems in three different diagnostic contexts: scoring, consultation, and diagnostic monitoring.

2. Scoring

A medical score is a numeric scheme for the combination of different observable variables into a single parameter reflecting a certain physiological or pathophysiological condition. Evaluating a score may thus be regarded as a simple form of diagnosis.

Scores are omnipresent in psychology. Other disciplines also make occasional use of scores; examples are Apgar's score for the assessment of neonates, the definition of entry criteria for highly invasive or expensive therapies, survival indices for the critically ill, etc. The general ability of scores to combine the information from different sources into a single value has been recognized and exploited in PIP, an early medical decision support system, which uses scores as a replacement of logical connectives¹ [Szolovits 78].

Most scoring schemes specify a weighted sum of the involved variables. Because the weighting is not necessarily linear and because not all parameters are quantitative in nature, scores are usually defined in the form of tables. However, tabular mappings are discontinuous, and their utility suffers from the handling of borderline cases which is inevitably perceived as arbitrary. Scores have therefore been fuzzified.

The definition of fuzzy scores usually follows the fuzzification/inference/defuzzification approach that is also the basis of fuzzy control. Such a fuzzy score effectively implements a continuous function whose shape can be adjusted to approximate the modelled medical relationship (of which the nonfuzzy score is a coarser and, in particular, discontinuous approximation) by tuning the fuzzy sets it is based on. The advantage of the fuzzy score over other

¹ Scores include the logical *and* and *or* connectives as well as the more general *n-out-of-m* operators as special cases.

specifications of continuous mappings lies in its intuitive formulation: the original rules or tables can be retained, a fuzzy score thus requires minimum remodelling.

However, one of the biggest advantages of scores, that they handle quantitative and qualitative information in a uniform way, is not easily retained in their fuzzified versions: while the fuzzification of quantitative input (heart rate, blood pressure etc.) which is (near) continuous by nature is straightforward, qualitative descriptions as obtained from percussion, auscultation, radiography etc. are themselves fuzzy concepts such as hollow, rattle, or diffuse shadows. To allow that such observations are integrated into a fuzzy score, their qualitative descriptions are arranged on a linear scale (say, from 0 to 10) and the observer is requested to quantify his observation on that scale. While being a little clumsy, this procedure also allows it to state borderline observations in a natural way.

2.1. An example

To evaluate the vitality of neonates immediately after birth, the American physician Apgar devised a simple scoring system which is named after her and is now in use the world over. The Apgar score evaluates five variables: heart rate, respiratory effort, muscle tone, reflex irritability, and colour of skin, each of which is given as score of 0, 1, or 2 (cf. Table 1). Normal Apgar scores range between 8 and 10. With only three classes for each variable, the effect of arbitrary assignment to one of two neighbouring classes in borderline cases is necessarily momentous.

Table 1: Apgar's score.

VARIABLE/SCORE	0	1	2
heart rate	absent	< 100	>100
respiratory effort	absent	slow, irregular	good, crying
muscle tone	flaccid	tone of extremities	active motion
reflex irritability	no	grimace	cough or sneeze
colour of skin	pale	body pink, extremities cynaotic	pink

Note that only the heart rate is observed in quantitative form.

In a fuzzified version of the Apgar score [Shono 92], all input is made on a continuous scale. The problem of arbitrary class assignment is hence replaced by that of subjective deviation from the objective value, which has, in most cases, less impact on the outcome of the score.

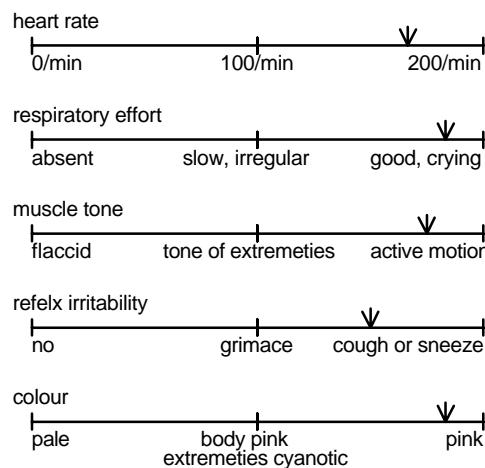


Figure 1: Continuous input to the fuzzy Apgar score

The correspondence of a value on the continuous scales to the three classes per variable is specified through fuzzy sets. The correspondence of a combination of class assignments to a particular valuation, also defined as a fuzzy set, is in turn specified in the form of rules: the total fuzzy score assigned to a neonate is derived from the observations following the fuzzification/inference/defuzzification approach (using center of gravity for defuzzification) that is heavily employed in fuzzy control.

The fuzzy Apgar score effectively specifies a continuous function from observations to a outcome. The advantage over other conceivable specifications of this function is its closeness to the original tabular scheme of Table 1, and hence its relative ease of formulation.

2.2. Bibliography

Only few fuzzy scoring systems have been described in the literature. Among those that have are the following: AFES, the Apgar fuzzy expert system assessing the vitality of neonates [Shono 92]; a fuzzy scoring system of liver scintigrams designed to differentiate chronic hepatitis from cirrhosis [Shiomi 95]; and a system to assess the severity of dysphagia (impaired coordination of the swallowing act) based on acceleration, swallowing pressure and the number of attempts to swallow [Suryanarayanan 95]. All systems have been evaluated in clinical trials and have been found to perform better than their conventional relatives.

An alternative approach employing distance measures between fuzzy numbers to calculate the position of a patient in a continuum between normal and pathologic has also been suggested [Duckstein 95].

3. Consultation

The consultation system paradigm requires that there is an acute informational need and a set of data that can be drawn upon to satisfy this need. The diagnosis of a consultation system changes only as new data are entered into the system, be it at a later time and session, be it as the system prompts for additional information in a running session.

Consultation systems always reason over a snapshot of the posed problem, even though this snapshot may and usually will include historical data. Technically, a consultation system is characterized by its relative ignorance of time, as opposed to diagnostic monitoring systems, which focus on the exploitation of temporal information.

3.1. Sanchez' approach

The basic idea presented by Sanchez et al. is that medical knowledge is simply a flat relation between the set of symptoms and the set of diseases [Sanchez 79]. Because medical knowledge is inherently fuzzy and the degree to which the symptoms are present as well as the degree to which the diagnoses apply can be mapped to a scale from 0 to 1, it seems a natural choice to regard the set of symptoms found in a patient, the relation representing the medical knowledge, and the set of diagnoses derived, as fuzzy sets. This is, however, ignoring the underlying mechanisms such as causality and resorting to a purely observational standpoint.

Let S and D be the set of symptoms and diagnoses, respectively, and $\tilde{\wp}(S)$ and $\tilde{\wp}(D)$ be the fuzzy power sets of S and D . Medical knowledge is then the relationship between symptoms and diagnoses expressed by a fuzzy relation $\tilde{R} \in \tilde{\wp}(S \times D)$, and the diagnosis $\tilde{D}_i \in \tilde{\wp}(D)$ of an individual patient i presenting with symptoms $\tilde{S}_i \in \tilde{\wp}(S)$ is derived by the composition

$$\tilde{D}_i = \tilde{R} \circ \tilde{S}_i$$

which is evaluated as

$$\mu_{\tilde{D}_i}(d) = \max_{s \in S} (\min(\mu_{\tilde{S}_i}(s), \mu_{\tilde{R}}(s, d))) \quad d \in D,$$

the compositional rule of inference.

Although there are medical applications of this principle (eg [Joly 80]), the main interest of research has been in the discovery of the "medical knowledge" R , which remains difficult.

3.2. The CADIAG-2 systems

The CADIAG systems, which go back to the work of Spindelberger and Grabner [Spindelberger 68], have been designed to support diagnostic and therapeutic decisions in various subdomains of internal medicine. They are among the first fuzzy expert systems and follow the consultation system paradigm. The latest offspring of the family, MEDFRAME/CADIAG-4, integrates a fuzzy reasoning framework with contemporary software engineering concepts. To understand CADIAG's general fuzzy reasoning, however, it suffices to take a look at CADIAG-2.

CADIAG-2 employs fuzzy set theory and fuzzy logic to capture:

- uncertainty as to whether a patient's symptoms (signs, laboratory test results) are pathological or normal;
- uncertainty as to whether symptoms necessarily have to occur with a disease; and
- uncertainty as to whether symptoms sufficiently confirm or exclude a diagnosis.

The uncertainty in the presence of a symptom is expressed as a degree of compatibility, ie as the degree to which the actual observation is compatible with the semantic concept of the symptom. For example, whether or not a patient is icteric depends on the tone of skin and its compatibility with the conception of icteric. Formally, the collection of such degrees establishes a fuzzy binary relationship between the patient P and the symptoms S_i , $\mu_{PS}(P, S_i)$. Each degree is either derived subjectively, as in the example above, or determined objectively. The latter is possible when answering questions such as whether or not the serum glucose level is elevated in a patient, because the serum glucose level is an objectively measurable quantity and elevated is defined by pathological ranges resulting from epidemiological studies. Because elevated shows gradual transitions to its adjacent concepts normal and highly elevated, it is ideally modelled as a fuzzy set.

Uncertainty concerning the confirmation or exclusion of diagnoses D_j in a patient P is also modelled by degrees of compatibility, denoted as $\mu_{PD}(P, D_j)$. They express the degree to which the diagnosis logically follows from the given medical evidence. Ranging from 0 to 1, a degree of 0 means excluded and one of 1 means confirmed. Degrees other than 1 and greater than or equal to a certain threshold identify diagnostic hypotheses.

Fuzzy logical inference in CADIAG-2 follows two basic relationships between medical entities. These are:

- the necessity of occurrence or, as denoted in CADIAG-2, the frequency of occurrence O of a symptom with a disease;
- the sufficiency of occurrence or, as denoted in CADIAG-2, the strength of confirmation C of a symptom for a disease.

From the statistical point of view, the frequency of occurrence may be interpreted as the sensitivity of the finding (the rule antecedent) with the disease (the consequent). Conversely, the strength of confirmation can be interpreted as the positive predictive value of the finding for the disease. This interpretation is particularly useful for the semi-automatic detection of both relationships from existing clinical databases [Adlassnig 86].

On the other hand, statements about the necessity and sufficiency found in textbooks usually contain terms such as mostly, seldom, very often, or strongly, which are mapped to fuzzy quantifiers in CADIAG-2's knowledge representation. Examples of this are: "mostly acute pancreatitis is accompanied by vomiting" or "highly elevated amylases in serum and urine strongly indicate acute pancreatitis". These fuzzy quantifiers are translated into the fuzzy binary

relationships $\mu_O(S_i, D_j)$ and $\mu_C(S_i, D_j)$. The entities and the relationships between them are represented in the form of rules as a general form of knowledge representation. Their format is:

IF *antecedent* THEN *consequent* WITH (O, C).

The tuples (O, C) contain linguistic and/or numerical values. An antecedent is a sufficient criterion for concluding a consequent if the numerical value of the strength of confirmation is 1; it is a necessary criterion if the numerical value of the frequency of occurrence is 1; and it is an excluding criterion if both the numerical value of the frequency of occurrence and of the strength of confirmation are 0. Relationships with intermediate degrees are supportive criteria. Graded adverse criteria are not considered in CADIAG-2.

Example 1 (supportive):

IF elevated pancreatic oncofetal antigen (POA) in serum
THEN MAYBE pancreatic cancer
WITH ($\lambda_O = \text{often}[\mu_O = 0.80]$, $\lambda_C = \text{strong}[\mu_C = 0.70]$).

Example 2 (necessary and sufficient):

IF (IF NOT) rheumatoid arthritis, and
splenomegaly, and
leukopenia under 4 giga/l
THEN (THEN NOT) Felty's syndrome
WITH ($\lambda_O = \text{always}[\mu_O = 1.00]$, $\lambda_C = \text{always}[\mu_C = 1.00]$).

Rules that render taxonomic knowledge and mutual exclusions among symptoms and among diseases are also included in CADIAG-2's knowledge base. The entirety of CADIAG-2's medical knowledge has been acquired

- from medical experts, who provide definitional, judgmental, and statistical knowledge from textbooks and their own clinical experience; and
- semi-automatically, which is possible through a numerical interpretation of CADIAG-2's medical relationships, and which can be carried out if computerized patient records with known diagnoses are available.

The inference process of Cadiag-2 aims at generating one or more differential diagnoses and, at the same time, at excluding some or all remaining diagnoses. Its mechanism basically relies on the compositional rule of inference. This rule accepts fuzzy descriptions of a patient's symptoms, expressed by $\mu_{PS}(P, S_i)$, and infers corresponding degrees to which the diagnoses can be concluded from the given evidence, denoted as $\mu_{PD}(P, D_j)$. For this purpose, the frequency of occurrence and the strength of confirmation are combined through different syllogisms. One of them is a fuzzy modus ponens applied to infer diagnoses from given symptoms under exploitation of the strength of confirmation. The formal representation is:

if P has with $\mu(P, S_i)$, and
if S_i implies D_j with $\mu_C(S_i, D_j)$,

then P has D_j with $\mu(P, D_j)$.

As with Sanchez' approach, application of this syllogism to a given set of symptoms yields

$$\mu_{PD}(P, D_j) = \max_i (\min(\mu_{PS}(P, S_i), \mu_C(S_i, D_j)))$$

for any given D_j .

The compositional rule of inference is also applied for drawing conclusions from combinations of symptoms, and inferences from symptoms to symptoms and from diagnoses to diagnoses are equally arrived at. Inferences based on absent symptoms as well as on the frequency of

occurrence are performed in a similar manner. The results are confirmed diagnoses, excluded diagnoses, and diagnostic hypotheses.

Because the outcome of the diagnostic process is independent of the number of present symptoms in support of a diagnostic hypothesis, CADIAG-2 resorts to a heuristic function designed to accumulate evidential support. It calculates support scores SS_{D_j} that indicate how strongly the various hypotheses are supported by the medical evidence. The scoring scheme provides the possibility of assigning weights to the values of the frequency of occurrence and strength of confirmation to vary the impact of these relationships on the final score. The exact formula is:

$$SS_{D_j} = 100 \sum_{i=1}^m (\alpha \min(\mu(P, S_i), \mu_O(S_i, D_j)) + \beta \min(\mu(P, S_i), \mu_C(S_i, D_j)))$$

where m is the number of findings present or present to a certain degree with supportive relationships to the diagnosis D_j . Practically, $\alpha = 0.09$ and $\beta = 0.91$ have proven reasonable values. The multiplication by 100 is introduced to obtain easily readable scores.

A complete on-line consultation session with CADIAG-2 includes:

- access and transfer of patient data from the central patient database;
- abstraction and aggregation of patient data by the patient data fuzzy interpreter;
- review of patient data by the consulting physician who may add, update, or delete data;
- the diagnostic fuzzy inference process establishing confirmed and excluded diagnoses as well as diagnostic hypotheses;
- display of the diagnostic results and their explanations; and
- input of some further patient data according to the examination proposals of Cadiag-2.

The practicality of CADIAG-2's concept of knowledge representation and fuzzy inference was confirmed by applying the expert system to about 500 clinical cases. These cases included up to 800 symptoms, signs, and laboratory test results, which were either present, present to a certain degree, or definitely absent. The analysis of the CADIAG-2 diagnoses compared with clinical and pathological diagnoses yielded an accuracy of up to 93%. Such an accuracy is considered to be sufficient for a computer based diagnostic system, applied as diagnostic aid and diagnostic information system.

Today, CADIAG-2 is in routine use and its successor, CADIAG-4, is near completion.

3.3. Bibliography

The following is an excerpt of the available English literature addressing fuzzy diagnosis following the consultation system paradigm; the presented choice is necessarily incomplete, yet does not reflect the preferences of the authors.

The CADIAG-2 systems for the diagnosis of rheumatic and pancreatic diseases [Adlassnig 85] as well as for the gall bladder and bile duct [Adlassnig 89]; RENOIR, another expert system in the field of rheumatology [Belmonte-Serrano 94]; AMDIS (for automated medical diagnosis with intelligent systems) for the early diagnosis of postmenopausal osteoporosis [Binaghi 93]; EPEXS to analyse and interpret evoked potentials [Brai 94]; assessment of iron deficiency [Causer 94]; the computerized analysis of electrocardiographic signals [Degani 90]; MEDUSA for the diagnosis of acute abdominal pain [Fathi-Torbaghan 94]; the application of MILORD to the medical domain [Godo 88]; DREAM [Kuncheva 92]; LITO, a system for the assessment of liver function and the diagnosis of hepatic diseases [Lesmo 89]; the FLORIDA expert system for intensive medicine [Pilz 95]; and ABVAB for the diagnosis of abnormal vaginal bleeding [Wong 90].

4. Diagnostic monitoring

Much more than systems following the consultation system paradigm, diagnostic monitors must regard the fact that the human body is a dynamic system exhibiting highly complex behaviour. In particular, this means that the body's current state is almost never sufficiently described by the instantaneous values of its observable parameters or any time-ignorant derivation thereof. A diagnostic monitor must therefore be aware of the disease or state history of the monitored subject. Such awareness is achieved through internal state variables serving as a memory to the monitor. In a fuzzy diagnostic monitor, these state variables are fuzzy.

Fuzzy state variables offer immediate advantages over non-fuzzy ones: They can represent the patient's being in between states and, dynamically, the gradual and continuous transition from one state to another. By doing so, they can report the tendency of the patient to change state and the change's continuous progress to the observer so that timely countermeasures can be taken.² At the same time, fuzzy state variables allow it that a patient never fully reaches one state, representing the fact that the present condition is only to a certain degree compliant with what the state stands for.

Requiring the autonomous surveillance, integration and interpretation of temporally evolving data, diagnostic monitoring is technically a more general problem than that of consultation. On the other hand, the medical subject of monitoring is usually much more confined than any topic of consultation: monitoring of the cardiovascular state of a patient undergoing surgery for example involves far fewer physiological variables and relationships than a consultation system covering the field of cardiovascular diseases.

Because of the technical complexity, diagnostic monitors are usually composed of separate modules, each solving a particular subproblem. Here, we present two such modules the combination of which results in a configurable system capable of transforming on-line data into fuzzy states comprising the disease history of the monitored patient. One, also referred to as trend detection, covers the transformation of incoming data streams into sequences of events. The other is basically a fuzzified deterministic automaton designed to assign interpretations to such sequences.

4.1. Fuzzy trend detection

It is common practice in medical AI that, for reasons of abstraction and subsequent symbolic processing, instantaneous quantitative data is transformed into qualitative terms or symbols such as *high*, *low*, or *normal*. Otherwise known as qualitative abstraction, in the context of fuzzy systems this process is referred to as fuzzification of continuous data. Trend detection resembles this process in principle, the main difference being that the qualitative terms are extended by a temporal dimension covering the time course of a parameter rather than its instantaneous value.

Following this idea, a trend may be defined as a fuzzy set of time courses all having identical meaning with respect to a given monitoring problem. Deciding whether or not an observed course follows a specified trend is then a matter of determining the degree of membership of the course in that trend. This reduces the problem of trend detection to two subproblems: finding an efficient representation of membership functions, and adequate treatment of the gaps between samples, ie the uncertainty resulting from sparse sampling.

To understand the following examples (which are taken from the dense sampling domain) it suffices to regard a fuzzy trend \tilde{C} as a fuzzy relation in the time-value space. $\mu_{\tilde{C}}(t_i, v_i)$ denotes the degree of membership of an observation (represented by a time/value-pair (t_i, v_i)) in \tilde{C} . The

² In fuzzy control, the composition of diagnosis and therapy, these countermeasures are taken automatically.

degree of match of \tilde{C} with a series $\langle(t_i, v_i)\rangle$ of time-stamped values relative to a time of onset t_Ω is then defined as $\min_i \mu_{\tilde{C}}(t_i - t_\Omega, v_i)$.³

To illustrate the functioning of trend detection based on fuzzy time courses we use data from a real case.⁴ Our examples focus on the monitoring of arterial oxygen saturation (SaO_2), a physiologic indicator of patient oxygenation that is measurable non-invasively and on-line. In the given case, the focus of interest is on a certain procedure repeated approximately every two hours: to deliver a bronchodilating aerosol, continuous mechanical ventilation was interrupted and the patient was ventilated manually (through a hand bag). During that time, the inhaled gas was replaced by pure oxygen. The expected effect of this procedure is an immediate increase in SaO_2 to values near 100% and a lasting improvement in oxygenation.

Table 2 defines a number of trends considered to be relevant to the presented monitoring case. It gives a verbal and a graphical description of each trend. Numbers present thresholds for full compliance (membership grade equals 1), while numbers in parentheses indicate the bounds beyond which membership grades are defined to be 0. The interspersing transition zone is assumed to be linear.

Table 2: Definition of trends

TREND	DEFINITION	DEPICTION
<i>adequate oxygenation</i>	SaO_2 above 97% (93%) for 5 minutes	
<i>hypoxemia</i>	SaO_2 between 90% and 93% (87% and 97%) for 2 minutes	
<i>rapidly improving oxygenation</i>	SaO_2 increasing from 87–95% (85–99%) to 97–100% (93–100%) within 30–90 seconds (5–120 seconds)	
<i>slowly decreasing oxygenation</i>	SaO_2 above 96% (91%) steady or decreasing to 94% (89%) within 25 minutes	

Figure 2 depicts the results of trend detection applied to the provided data sample. In each frame, the upper half displays SaO_2 in a range of 80–100%, while the lower half depicts the concurrent degree of match (ranging from 0–1) with the corresponding trend. SaO_2 of *adequate oxygenation*, *hypoxemia*, and *slowly decreasing oxygenation* was smoothed by a moving average filter of two, one, and five minutes, respectively.

³ A more elaborate version of this theory covering first derivatives even in sparse samples is presented in [Steimann 95, 96, 97].

⁴ This data set was provided by the American Association of Artificial Intelligence and served as benchmark for the 1994 Stanford Spring Symposium on Artificial Intelligence in Medicine [Steimann 94b].

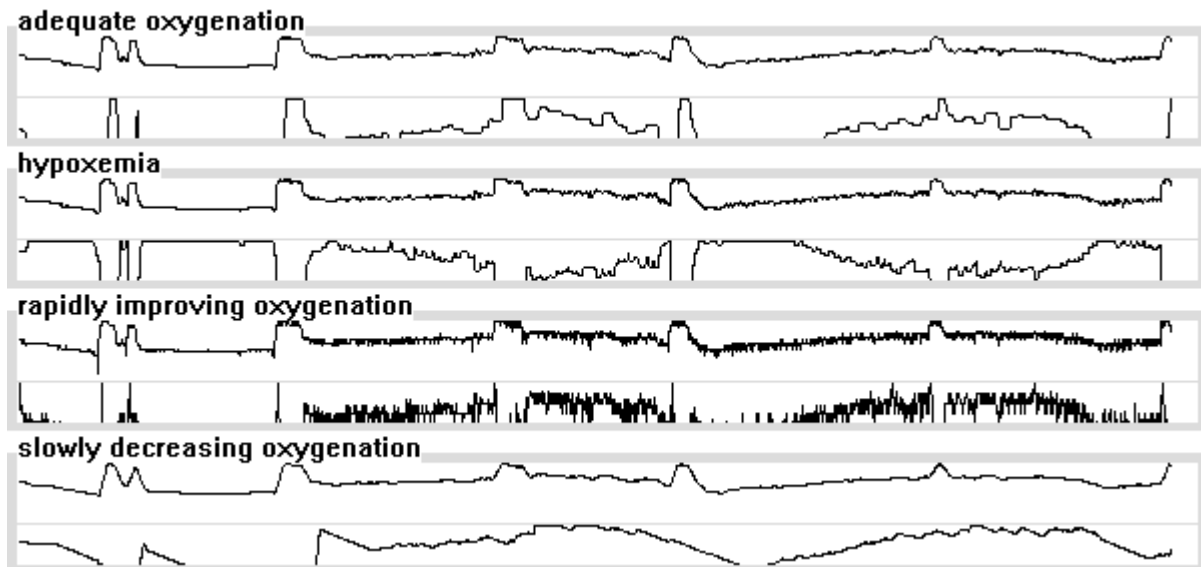


Figure 2: Trend detection applied to SaO_2 (in part filtered through moving average), 12-hour period

The example demonstrates the sensitivity of the proposed method: all sudden increases in SaO_2 (rapidly improving oxygenation) were correctly identified. It also shows that trend detection has a smoothing effect on the data: the longer the trend to be detected, the less volatile is the curve indicating the degree of match.

4.2. Tracing disease histories

While the occurrence of a clinically significant trend has some diagnostic value in itself, its correct and exhaustive interpretation usually depends on the state the patient is currently in and the disease history. The detection of a trend can trigger a new assessment of the patient's condition, technically corresponding to the transition from one state to another.

Deterministic finite automata are capable of analysing sequences of events or symbols. If an automaton is designed as a model of the system under observation, then its current state reflects the actual status of that system. Applied to diagnostic monitoring, an automaton can model possible courses and complications of a disease and its treatment, allowing it to follow the state of a patient on an abstract level.

In the given case of critical care we focus on the states and transitions related to the change of mode of ventilation from mechanical ventilation to hand bagging (an event in the examples referred to as high FIO_2) and vice versa (low FIO_2). The expected effect of hand bagging along with delivery of pure oxygen is an immediate increase in oxygenation reflected in a rise of SaO_2 to values close to 100%. In addition, if manually exerted higher pressures and the effects of the bronchodilator helped in recruiting occluded alveolar spaces, a persistent improvement in oxygenation may be expected.

Tables 3 and 4 present the states and transitions used to obtain the results presented in Fig. 4. Figure 3 graphically depicts the modelled transitions in a state transition diagram.

Table 3: Definition of states under consideration

STATE	INTERPRETATION (DIAGNOSIS)
<i>start</i>	initial state, system warm up, undecided
<i>normal</i>	oxygenation is satisfactory without additional effort such as increased FIO_2
<i>hypoxic</i>	oxygenation is too low and should be improved
<i>responding to high FIO_2</i>	high FIO_2 has affected oxygenation positively

<i>not responding to high FIO₂</i>	high FIO ₂ does not have the desired effect
<i>improved after hand bagging</i>	hand bagging has persistently improved oxygenation
<i>not improved after hand bagging</i>	hand bagging shows no satisfactory effect

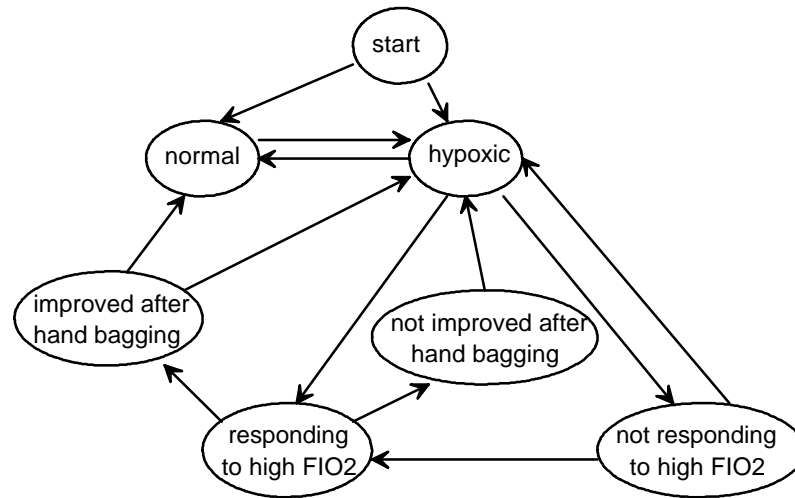


Figure 3: State transition diagram of the automaton

The automaton employed is fuzzy deterministic automaton described in [Steimann 94a]. It is best characterized as the superposition of a fuzzy and a crisp automaton maintaining a current state (called *active*) as well as a set of gradually satisfied states. It transitions on fuzzy events, fuzzy sets associating a degree with every event of the automaton's input alphabet. To obtain fuzzy events, the trends and the degrees to which they have been detected during trend detection are comprised in one fuzzy set.

Table 4: Definition of transitions

FROM STATE	ON EVENTS	TO STATE
<i>start</i>	<i>adequate oxygenation</i>	<i>normal</i>
	<i>hypoxemia</i>	<i>hypoxic</i>
<i>normal</i>	<i>hypoxemia</i>	<i>hypoxic</i>
<i>hypoxic</i>	<i>low FIO₂ ∧ adequate oxygenation</i>	<i>normal</i>
	<i>high FIO₂ ∧ rapidly improving oxygenation</i>	<i>responding to high FIO₂</i>
	<i>high FIO₂ ∧ hypoxemia</i>	<i>not responding to high FIO₂</i>
<i>responding to high FIO₂</i>	<i>low FIO₂ ∧ slowly decreasing oxygenation</i>	<i>improved after hand bagging</i>
	<i>low FIO₂ ∧ hypoxemia</i>	<i>not improved after hand bagging</i>
<i>not responding to high FIO₂</i>	<i>low FIO₂ ∧ hypoxemia</i>	<i>hypoxic</i>
	<i>high FIO₂ ∧ adequate oxygenation</i>	<i>responding to high FIO₂</i>
<i>improved after hand bagging</i>	<i>adequate oxygenation</i>	<i>normal</i>
	<i>hypoxemia</i>	<i>hypoxic</i>
<i>not improved after hand bagging</i>	<i>hypoxemia</i>	<i>hypoxic</i>

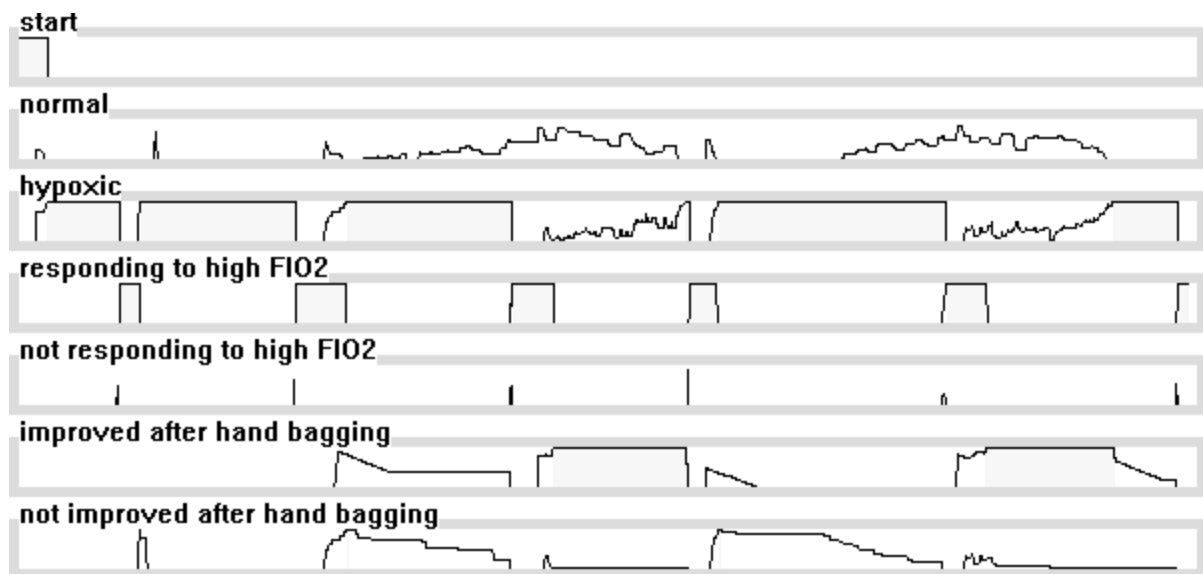


Figure 4: Distribution of states over time

Note that in Figure 4 there is always one (active) state with a membership grade of 1, which is a consequence of the automaton "waiting" for a full transition to a successor state being triggered by sufficient evidence. At the same time, candidate successors may show rising membership grades reflecting a change in the patient's condition. This behaviour models human decision making naturally: once a decision has been made, it is usually pursued rather uncritically until there is sufficient evidence for another to be favoured.

4.3. Bibliography

As stated above, diagnostic monitoring is technically more demanding than consultation. In particular, the adequate treatment of time poses many nontrivial problems, which are, in general, not solved and, in particular, not directly related to fuzzy set theory. Thus, it comes as no surprise that fuzzy diagnostic monitors are few and far between.

Among the few systems described in the literature are: fuzzy grammar-based classification of heart beat sequences to detect cardiac arrhythmia [Barro 91]; monitoring routinely sampled physiological data for cardiopulmonary emergencies [Goldman 94]; and the DIAMON-1 monitoring framework [Steimann 96].

5. Concluding remarks

With the conception of fuzzy set theory, *symbolic* and *discrete* are no longer synonymous: symbolic systems may now exhibit continuous behaviour and thus address medical problems more adequately. Therefore, automated diagnostic support based on fuzzy set theory does not have to break with symbolic tradition: the theory of fuzzy set is not an alternative to, but an enhancement of classical AI approaches.

However, fuzzy set theory is not the only approach to extending AI concepts with uncertainty and gradation: in recent years, uncertainty in AI has become one of the most flourishing sub-disciplines in the field, and fuzzy set theory is only one of many alternatives competing for the favour of the community. Likely criteria for the success of each competitor are: tractability, scalability, and ease of integration with temporal reasoning, the other as yet unsolved problem of the field.

Ironically, in today's clinical practice the output of fuzzy systems will sometimes be discretized "so as to follow medical usage and human brain processing capability" [Duckstein 95]. This is

inconsistent with the claim that fuzzy and, thus, continuous systems are closer to medical reality, but seems to be a consequence of our complete spiritualization of Aristotelian dichotomous logic. If not for our limited brain processing capability, then, continuity is certainly a problem for the evaluation of fuzzy systems: compliance with the gold standard, the ultimate standard for medical decisions, is no longer a matter of yes or no, but one of more or less. New, fuzzy measures of quality (sensitivity, specificity, positive and negative predictive value) are therefore needed. Ultimately, claiming that a fuzzy diagnostic system is more natural may even impose a critical revision of the gold standard itself: is the gold standard naturally crisp or has it inaptly been forced into strict categories?

6. References

- [Adlassnig 80a] KP Adlassnig "A fuzzy logical model of computer-assisted medical diagnosis" *Methods of Information in Medicine* 19:3 (1980) 141--148.
- [Adlassnig 80b] KP Adlassnig, G Grabner "The Viennese computer assisted diagnostic system. Its principles and values" *Automedica* 3 (1980) 141--150.
- [Adlassnig 85] KP Adlassnig, G Kolarz, W Scheithauer, H Effenberger, G Grabner "CADIAG: Approaches to computer-assisted medical diagnosis" *Comput Biol Med* 15:5 (1985) 315--335.
- [Adlassnig 86] KP Adlassnig, G Kolarz "Representation and semiautomatic acquisition of medical knowledge in CADIAG-1 and CADIAG-2" *Computers and Biomedical Research* 19 (1986) 63--79.
- [Adlassnig 89] KP Adlassnig, M Akhava-Heidari "CADIAG-2/GALL: An experimental expert systems for the diagnosis of gallbladder and biliary tract diseases" *Artificial Intelligence in Medicine* 1 (1989) 71--77.
- [Albin 75] MA Albin *Fuzzy Sets and Their Application to Medical Diagnosis* (Doctoral Dissertation, University of California, Berkley 1975).
- [Barro 91] Barro S, Ruiz R, Presedo J, Mira J: "Grammatic representation of beat sequences for fuzzy arrhythmia diagnosis", *International Journal of Bio-Medical Computing* 27:3-4 (1991) 245--59.
- [Belmonte-Serrano 94] Belmonte-Serrano M, Sierra C, Lopez de Mantaras R: "RENOIR: an expert system using fuzzy logic for rheumatology diagnosis", *International Journal of Intelligent Systems* 9:11 (1994) 985--1000.
- [Binaghi 93] Binaghi E, De Giorgi O, Maggi G, Motta T, Rampini A: "Computer-assisted diagnosis of postmenopausal osteoporosis using a fuzzy expert system shell.", *Computers and Biomedical Research* 26:6 (1993) 498--516.
- [Brai 94] Brai A, Vibert J-F, Koutlidis R: "An expert system for the analysis and interpretation of evoked potentials based on fuzzy classification: application to brainstem auditory evoked potentials", *Computers and Biomedical Research* 27:5 (1994) 351--66.
- [Causar 94] MB Causar, GA Findlay, CR Hawes, DR Boswell "Assesment of a Computerized System for the diagnosis of iron deficiency" *Pathology* 26:1 (1994) 37--39.
- [Cerutti 81] S Cerutti, Timo Pieri C: "A method for the quantification of the decision-making process in a computer-oriented medical world.", *Int J Biomed Comput* 12:1 (1981) 29-57.
- [Degani 90] R Degani "Methodology of ECG interpretation in the Padova program", *Methods of Information in Medicine* 29:4 (1990) 386--392.
- [Duckstein 95] L Duckstein, A Blinowska, J Verroust: "Fuzzy classification of patient state with application to electrodiagnosis of peripheral polyneuropathy", *IEEE Transactions on Biomedical Engineering* 42:8 (1995) 786--792.
- [Esogbue 79] AO Esogbue, RC Elder "Fuzzy sets and the modelling of physician decision processes, Part I: The initial interview-information gathering session" *Fuzzy Sets and Systems* 2 (1979) 279--291.
- [Fathi Torbaghan 94] Fathi Torbaghan M, Meyer D: "MEDUSA: a fuzzy expert system for medical diagnosis of acute abdominal pain.", *Methods of Information in Medicine* 33:5 (1994) 522--9.

- [Godo 88] Godo LL, Lopez de Mantaras R, Sierra C, Verdaguer A: "Managing linguistically expressed uncertainty in MILORD application to medical diagnosis" *AI Communications* 1:1 (1988) 14--31.
- [Goldman 94] JM Goldman, MJ Cordova "Advanced clinical monitoring: considerations for real-time hemodynamic diagnostics" in: *Proceedings of the 18th Symposium on Computer Applications in Medical Care* (AMIA 1994) 752--755.
- [Heckerman 92] DE Heckerman, EH Shortliffe "Form certainty factors to belief networks" *Artificial Intelligence in Medicine* 4 (1992) 35--52.
- [Joly 80] H Joly, E Sanchez, J Gouvernet, J Valty "Applications of fuzzy set theory to the evaluation of cardiac function", in: DAB Lindberg, S Kaihara (eds) *Proceedings of the MedInfo'80* (North Holland, Amsterdam 1980) 91--95.
- [Kulikowski 82] CA Kulikowski, SM Weiss "Representation of expert knowledge for consultation: the CASNET and EXPERT projects" in: P. Szolovits (ed), *Artificial Intelligence in Medicine* (Westview Press, Colorado, 1982) 21--55.
- [Kuncheva 93] L Kuncheva, K Andreeva: "DREAM: a shell-like software system for medical data analysis and decision support", *Computer Methods and Programs in Biomedicine* 40:2 (1993) 73-81.
- [Ledley 59] RS Ledley, LB Lusted "Reasoning foundations of medical diagnosis" *Science* 130 (1959) 9--21.
- [Lesmo 89] Lesmo L, Saitta L, Torasso P: "Dealing with uncertain knowledge in medical decision-making: a case study in hepatology", *Artificial Intelligence in Medicine* 1:3 (1989) 105--16.
- [Moon 77] RE Moon, S Jordanov, A Perez, IB Turksen "Medical diagnostic system with human-like reasoning capability" In: DB Shires, H Wolf (eds) *MedInfo'77* (North-Holland, Amsterdam 1977) 115--119.
- [Pearl 88] J Pearl *Probabilistic Inference in Intelligent Systems: Networks of Plausible Inference* (Morgan Kaufmann, San Francisco 1988).
- [Perez-Ojeda 76] A Perez-Ojeda *Medical Knowledge Network: A Database for Computer-Aided Diagnosis* (Thesis, University of Toronto, Toronto 1976).
- [Pilz 95] U Pilz "Structure and basic functional mode of the FLORIDA expert system for intensive medicine", *Elektrie* 49:10-12 (1995) 399--406.
- [Pis 89] Pis P, Mesiar R: "Fuzzy model of inexact reasoning in medicine", *Computer Methods and Programs in Biomedicine* 30:1 (1989) 1--8.
- [Pople 82] HE Pople "Heuristic methods for imposing structure on ill-structured problems: the structuring of medical diagnostics" in: P. Szolovits (ed), *Artificial Intelligence in Medicine* (Westview Press, Colorado, 1982) 119--190.
- [Rescher 69] N Rescher *Many-valued Logic* (McGraw-Hill, New York 1969).
- [Salamon 76] R Salamon, M Bernadet, F Gremy "Ternary algebra: theoretical aspects and possible applications" in: FT Dombal, F Gremy (eds) *Decision Making and Medical Care: Can Information Science Help?* (North-Holland, Amsterdam 1976) 505--513.
- [Sanchez 79] E Sanchez "Medical diagnosis and composite fuzzy relations" in: MM Gupta, RK Ragade, RR Yager (eds) *Advances in Fuzzy Set Theory and Applications* (North-Holland, Amsterdam 1979) 437--444.
- [Shiomi 95] Shiomi S, Kuroki T, Jomura H, Ueda T, Ikeoka N, Kobayashi K, Ikeda H, Ochi H: "Diagnosis of chronic liver disease from liver scintiscans by fuzzy reasoning.", *J Nucl Med* 36:4 (1995) 593--598.
- [Shono 92] H Shono, M Oga, K Shimomura, M Yamasaki, Y Ito, M Muro, H Sugimori "Application of fuzzy logic to the Apgar scoring system" *International Journal of Bio-Medical Computing* 30 (1992) 113--123.
- [Shortliffe 76] EH Shortliffe *Computer-based medical consultations: MYCIN* (Elsevier, New York 1976).
- [Spindelberger 68] W Spindelberger, G Grabner "Ein Computerverfahren zur diagnostischen Hilfestellung" in: K Fellinger (Hrsg) *Computer in der Medizin -- Probleme, Erfahrungen, Projekte* (Verlag Brüder Hollinek, Wien 1968) 189--221.

- [Steimann 94a] F Steimann, KP Adlassnig "Clinical monitoring with fuzzy automata", *Fuzzy Sets and Systems* 61:1 (1994) 37--42.
- [Steimann 94b] F Steimann, KP Adlassnig "Two-stage interpretation of ICU data based on fuzzy sets" in: *Working Papers of the AAAI 1994 Spring Symposium on Artificial Intelligence in Medicine*, AAAI Technical Report (AAAI, Menlo Park 1994).
- [Steimann 95] F Steimann *Diagnostic Monitoring of Clinical Time Series* (Doctoral Dissertation, Technische Universität Wien, Wien 1995).
- [Steimann 96] F Steimann "The interpretation of time-varying data with DIAMON-1", *Artificial Intelligence in Medicine* 8:4 (1996) 343--57.
- [Steimann 97] F Steimann, M Hayde: "A method to derive the time of onset of infection from serological findings", *Methods of Information in Medicine* 36:1 (1997) 51--58.
- [Suryanarayanan 95] Suryanarayanan S, Reddy NP, Canilang EP: "A fuzzy logic diagnosis system for classification of pharyngeal dysphagia", *International Journal of Bio-Medical Computing* 38:3 (1995) 207--15.
- [Szolovits 78] P Szolovits, SG Pauker "Categorical and probabilistic reasoning in medical diagnosis" *Artificial Intelligence* 11 (1978) 115--144.
- [Wechsler 76] H Wechsler "A fuzzy approach to medical diagnosis" *International Journal of Bio-Medical Computing* 7 (1976) 191--203.
- [Weiss 78] SM Weiss, CA Kulikowski, S Amarel, A Safir "A model-based method for computer-aided medical decision-making" *Artificial Intelligence* 11 (1978) 145--172.
- [Wong 90] Wong WSF, Leung KS, So YT: "The recent development and evaluation of a medical expert system (ABVAB)", *International Journal of Bio-Medical Computing* 25:2-3 (1990) 223--229.
- [Zadeh 69] LA Zadeh, Biological application of the theory of fuzzy sets and systems, in: *Proc. Int. Symp. Biocybernetics of the Central Nervous System* (Little, Brown & Co., Boston 1969) 199--212.