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ON INCORPORATION OF TIME IN MEDICAL EXPERT SYSTEMS

Tatiana Kiseliova — Claudio Moraga

ABSTRACT. Medical expert system have the purpose of supporting the diagnosis work of physicians. Most medical expert systems consider facts and symptoms to provide a diagnosis. There is an obvious necessity for the representation of time in medical diagnoses. This paper introduces various ways of incorporation of time in the inference mechanism within the formalism of fuzzy logic.

1. Introduction

Medical expert systems constitute one of the most challenging projects in Artificial Intelligence and aim to assist physicians in diagnosing certain kinds of diseases. Medical expert systems use knowledge about the diseases and facts about the patients to suggest a diagnosis. However, time dependencies are not yet included and constitute the core of the present paper. In the rest of this section some basic aspects of medical expert systems are discussed. Inclusion of time in an inference mechanism is the subject of Section 2. Appropriate mathematical models are discussed in the 3rd section. The paper is finished by some concluding remarks.

1.1 Medical expert systems

Starting with the pioneering paper on MYCIN [10], the way was open to the development of medical expert systems.

The diapason of the theoretical backgrounds and practical applications of these systems are very wide. The power of Computational Intelligence allows to solve different problems in many branches of medicine.

Among the best known projects in this area, the systems CADIAG [1] developed at the University of Vienna and Pneumonia/Milord [4] developed at the Artificial Intelligence Research Institute (IIIA), a center of the Spanish Scientific Research Council (CSIC) have shown impressive results in support of the

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diagnosis work of physicians. CADIAG-**II** (**C**omputer **A**ssisted **DIAG**nosis) is a rule-based medical expert system designed for internal medicine. **MILORD II** was developed as a target programming environment of an example in biological identification. These two medical expert systems use the formalism of fuzzy logic.

The main components of a medical expert systems are: a knowledge base, which contains the specific knowledge related to the area of application of the system; a rule base that supports the work with the knowledge to obtain a diagnosis; an explanation component, making the user know how the system arrived to the suggested diagnosis, and a user interface for adequate communication between consulting physicians and the system. Most medical expert systems consider facts and symptoms to provide a diagnosis. However, time aspects are missing.

1.2 Acquisition of medical knowledge

A knowledge acquisition system must be capable to obtain information on medical entities and relationships between them. Medical information can be acquired at least in two ways:

1. through numerical or linguistic evaluation by medical experts,
2. through statistical evaluation of a database containing medical data on patients with confirmed diagnoses.

1.3 Notations, relations

To represent *patient-symptoms* relationships, the symbol R_{PS} (or $R(P_i, S_j)$) is used.

$R(P_i, S_j)$ is defined to be a degree to which it is true that the patient P_i has the symptom S_j. Stress here again, that this relation $R(P_i, S_j)$ is based on the definition of **fuzzy relations.**

Another kind of relations are relations between *symptoms and diagnoses*, R_{SD} (or $R(S_i, D_j)$). They can be based on **statistical interpretation** of relations.

Two binary relations R^c_{SD}, R^o_{SD} were introduced to express symptom-diseases relationships.

> *A confirmation relation* R^c_{SD} represents the so called *strength of confirmation* (c),

while

> *an occurrence relation* R^o_{SD} represents the so called *frequency of occurrence* (o).

The relationships between medical entities are given in the form of rules:

$$\text{IF (antecedent) THEN (consequent) WITH } (o, c)\,.$$

1.4 An inference mechanism.

Let

$$R(P_q, S_i) =_{\text{def}} S'_i\,,$$
$$R(P_q, D_j) =_{\text{def}} D'_j\,,$$

The Generalized Modus Ponens (CRI) is presented as follows:

$$\begin{array}{lllll} \text{IF} & S = S_i & \text{THEN} & D = D_j \\ & S = S'_i & & \\ \hline & & & D = D'_j\,. \end{array} \tag{1}$$

The Compositional Rule of Inference was transformed by Sanchez [9] into medical diagnoses and adopted as an inference mechanism. In fact, it means an application of the max-min composition of fuzzy relations:

$$R_{PD} = R_{PS} \circ R_{SD}\,, \tag{2}$$

$$R(P_q, D_j) = \max_{S_i \in \sum} \min\bigl(R(P_q, S_i), R(S_i, D_j)\bigr)\,, \tag{3}$$

where Σ is a set of all symptoms.

Remark. We will follow this interpretation of composition of fuzzy relations in medical diagnoses, although in recent investigations other t-norms and t-conorms are used correspondingly (see, for example, [5]).

Because of features of physicians' thinking and of distinguishing confirmation and occurrence relations, there are three types of inference rules/compositions:

1. confirmation (by present symptoms) $R^1_{PD} = R_{PS} \circ R^c_{SD}$,
2. exclusion (by present symptoms) $R^2_{PD} = R_{PS} \circ (1 - R^c_{SD})$,
3. exclusion (by absent symptoms) $R^3_{PD} = (1 - R_{PS}) \circ R^o_{SD}$.

All three inference rules/compositions are max-min compositions as in equation (3).

Analogous rules are defined for symptom combination-disease (R^4_{PD}, R^5_{PD}, R^6_{PD}), symptom-symptom (R^7_{PD}, R^8_{PD}, R^9_{PD}) and disease-disease relationships (R^{10}_{PD}, R^{11}_{PD}, R^{12}_{PD}).

1.5 A diagnostic process

The results of the inference process (examined diagnoses) can be interpreted as:

1. confirmed,
2. excluded,
3. possible

diagnoses [1].

- A *confirmed diagnose* is established when

$$\begin{cases} R^1(P_q, D_j) = 1.00 \\ \text{or} \\ R^4(P_q, D_j) = 1.00\,. \end{cases} \tag{4}$$

- An *excluded diagnose* is established when

$$\begin{cases} R^2(P_q, D_j) = 1.00 \\ \text{or} \\ R^3(P_q, D_j) = 1.00 \\ \text{or} \\ R^5(P_q, D_j) = 1.00 \\ \text{or} \\ R^6(P_q, D_j) = 1.00\,. \end{cases} \tag{5}$$

- A *possible diagnose* is established

$$\text{in other cases}\,. \tag{6}$$

2. Time-factor in the inference mechanism

Let S, T, D be linguistic variables denoting symptom, time, and disease correspondingly. $S_i, S_i', \mathcal{T}_S, \mathcal{T}_S', D_j, D_j'$ are fuzzy sets defined on universes $\mathcal{S}, \mathcal{T}, \mathcal{D}$, respectively.

One of the possible ways to introduce a time-factor to (1) is the following:

$$\begin{array}{llllll} \text{IF} & S = S_i & \text{and} & \mathcal{T} = \mathcal{T}_S & \text{THEN} & D = D_j \\ & S = S_i' & \text{and} & \mathcal{T} = \mathcal{T}_S' & & \\ \hline & & & & & D = D_j'\ . \end{array} \tag{7}$$

It means: if $S = S_i$ at time $T = \mathcal{T}_S$ then the disease is $D = D_j$; if $S = S_i'$ was observed at time $T = \mathcal{T}_S'$, it follows that the disease will be $D = D_j'$.

Note.

- Index s in $\mathcal{T}_S$ and $\mathcal{T}_S'$ shows that time is connected with symptoms, e.g., symptoms were measured, watched, felt at this time.
- $\mathcal{T}_S$ and $\mathcal{T}_S'$ differ slightly. “Slightly” means that within an appropriate metric the distance between $\mathcal{T}_S$ and $\mathcal{T}_S'$ is small enough for (7) to be

meaningful. If $\mathcal{T}_S$ and $\mathcal{T}'_S$ are represented as fuzzy sets, then "slightly" means that the intersection between $\mathcal{T}_S$ and $\mathcal{T}'_S$ is not empty. For instance the case when $\mathcal{T}_S$ is "around 5.30" and $\mathcal{T}'_S$ is "mid-April" will not be considered.

Let it be mentioned here that $\{\mathcal{T}_S, \mathcal{T}'_S\}$ are not only exact time-points, but they can be imprecise and uncertain, namely, fuzzy time-points, dates, intervals.

This fuzzy temporal knowledge can be processed, for example, as described in [3], one of the fundamental papers on the processing of fuzzy temporal knowledge. In this paper, *dates* (precisely known, imprecisely known, fuzzily known), *time periods after/before* (possibly before, strictly after, necessary strictly before, possibly before), *time-intervals* and reasoning with these fuzzy temporal knowledge based on possibility theory are considered. This branch was developed by many authors, and there are different approaches to this subject (see, for example, the references to the literature).

We will consider some theoretical aspects of "fuzzy time" interesting for us later. We use these different approaches to construct mathematical models of (7) where

- atemporal components (like D_j) are combined with time dependent components (as S_i, S'_i) (compare with [11]);
- there are combined pieces of information whose date is known with total precision (data from clinical tests or data from clinical explorations) with pieces which are imprecisely located (subjective symptoms or vaguely remembered previous facts) (compare with [4]).

Consider the following examples.

Example 2.1.

IF the *Fever* is strong every day from 12 till 14 o'clock
THEN the patient has a *Cold.*

<u>A patient has a strong *Fever* in the middle of the day every day</u>.
Very likely, he has a *Cold.*

Example 2.2.

IF the *Asthenia* appears every two days during the last 3 months
THEN it is a *Retrograde Circulatory Failure.*

<u>A patient has an *Asthenia* every day in the evening during the last month</u>
It is a *Retrograde Circulatory Failure* with a confidence of 0.7.

Example 2.3.

IF *Community-acquired and Bacterial Pneumonia* and *Contacts with Birds*
THEN the patient is affected by a *Pneumococcus.*

Community-acquired and Bacterial Pneumonia and *Contacts with Birds* for the last 3 months.
Quite sure, the patient is affected by a *Pneumococcus*.

Examples of these types are very often used in medical diagnostics and can be easily presented in the scheme (7).

3. Mathematical models

3.1 Non separated fuzzy time

Due to above mentioned characteristics, the following possible interpretations of a time-factor can be done:

$$\begin{array}{llll} \text{IF} & S = S_i(T) & \text{THEN} & D = D_j \\ & S = S_i'(T) & & \\ \hline & & & D = D_j' \quad . \end{array} \tag{8}$$

A notation $S_i(T)$ shows that this fuzzy set depends on S_i as well as on T.

3.2 Dutta's method

According to Dutta's method (see [2, 3, 8]): given an event S_i, $\mu_I(S_i)$ represents the degree to which S_i occurs within the interval I, where time is described using a set of precise disjoint intervals, which can be of different length.

In our case $S_i(T)$ in (8) can be interpreted as a representation of the degree to which S_i is associated to time T. $S_i(T)$ strongly generalizes S_i in (1) and further manipulations (3) will be done with $S_i(T)$.

3.3 Time operator

Another interpretation is based on a notion of a *time operator* (TO) [6]. In [6] two types of time are considered: *an instant* and *an interval.* A fuzzy instant is presented by means of a possibility distribution, a fuzzy time interval is derived from the fuzzy instants which delimit the time span during which an event occurs.

In our case a TO can be used to define $S_i(T)$ as follows:

$$\text{TO}\colon (\mathcal{T}_S \otimes S_i)(t, x) = \min\Big(\max_{l \leq x+\delta} S_i(l)\,,\ \max_{r \geq x-\delta} S_i(r) \Big)\,, \tag{9}$$

where $\delta = w \times \big(1 - \mathcal{T}_S(t)\big)$, w is the cardinality of fuzzy set S_i and t, x are crisp values, $t \in \mathcal{T}$, $x \in \mathcal{S}$.

Due to results presented in [6], the TO and Gödel implication[1] applied in CRI give good results from the theoretical point of view as well as from practical applications, for example, in a societal system.

The TO adopted in our case, as was shown in (9), helps to avoid the case when every element of the fuzzy set S_i changes the membership value on the time interval, therefore practical cases, as presented in examples before, can be easily described with this methodology.

EXAMPLE 3.1. The results of a TO for fuzzy sets $\mathcal{T}_S$ and S_i defined in crisp instants t_0, t_1, t_2 (see Figure 3).

Figure 1 shows the fuzzy set S_i, Figure 2 shows the fuzzy set $\mathcal{T}_S$ and Figure 3 shows the result of TO for $t = t_0, t_1, t_2$.

If $\mathcal{T}_S(t) = 0$, an event $S_i(T)$ at the crisp instant will be unchanged. If the membership value of the fuzzy time interval is smaller $(\mathcal{T}_S(t_0) < \mathcal{T}_S(t_1) < \mathcal{T}_S(t_2))$, the vagueness of an actual event $S_i(T)$ will be larger.

For t_0 δ is bigger than for t_1.

This example shows, that TO gives the possibility to change the fuzzy set S_i not abruptly, although time has influence on S_i. But there are some points on the universe where S_i stays unchanged. This reflects practical cases when, if time changes slightly, the symptom cannot jump from one stage to completely different one. It evolves gradually.

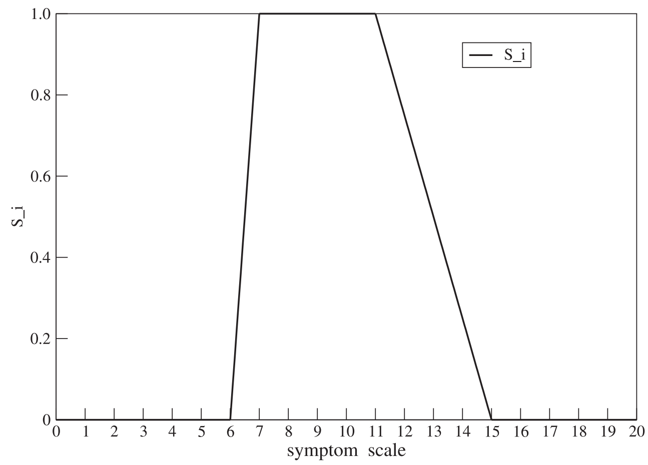

FIGURE 1. Symptom.

[1] $R_{SD}(x, d) = \begin{cases} 1, & S_i(x) \le D_j(d) \\ D_j(d), & S_i(x) > D_j(d) \end{cases}$

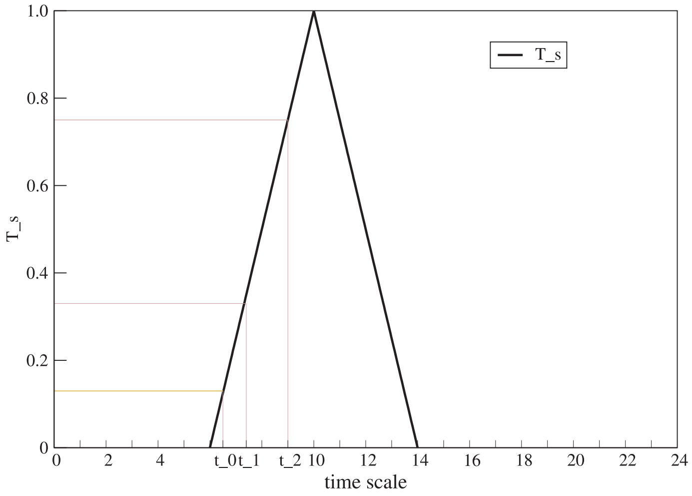

Figure 2. Time.

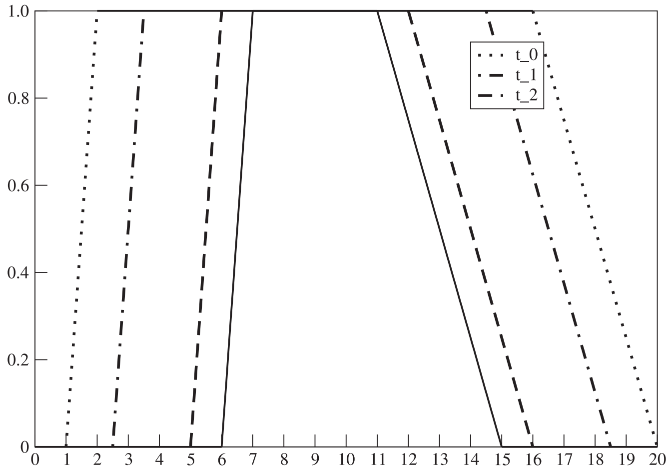

Figure 3. Time operator.

3.4 Temporal descriptor

Qian's approach [7] can be also used to model scheme (8), because it gives a clear formalization of a representation of fuzzy time and its integration with fuzzy propositional reasoning.

Qian uses *a time point* and *a time interval* in the *operator* TD (*Temporal Descriptor*) for modelling fuzzy time. Time point and time interval in Qian's approach correspond to fuzzy instant and fuzzy interval of [6]. Qian uses not only time descriptors based on real clock time coordinates (for example, S_1 is about 5 o'clock), but relative time descriptors (for example, S_1 is 2 minutes earlier than S_2) and *before/after* chain descriptors (for example, S_1 before/after S_2). With the help of *before/after* descriptors, *contain, during, overlap* time-descriptors can be defined as well.

Adapting formulas from [7] for (8), conclusion D_j is calculated with respect to three thresholds: *temporal, numeric and overlap* that are calculated from rule IF $S_i(T)$ THEN D_j in a special way; $R(P_q, D_j)$ is restricted by these three values.

Qian' s approach allows to interpret examples presented above and like Example 3.2:

EXAMPLE 3.2.

IF *Fever* is observed *before Cough*
THEN it is an *Influenza*.
<u>*Fever* appeared 5 days before</u>.
Sure, it is an *Influenza*.

IF *Fever* is observed *before Cough*
THEN it is an *Influenza*.
<u>*Fever* appeared 7 days before</u>.
Possibly, it is an *Influenza*.

IF *Fever* is observed *before Cough*
THEN it is an *Influenza*.
<u>*Fever* appeared 20 days before</u>.
No *Influenza*.

3.5 Separated fuzzy time

Because our purpose is to introduce time to the already existing inference mechanism of medical expert systems, mathematical models manipulated with temporal entities independently of the domain facts associated with them can be used. Therefore the following model

$$R_{PD} = \tau\big(R_{PS} \circ R_{SD}, \mathcal{T}''(\mathcal{T}_S, \mathcal{T}'_S)\big), \tag{10}$$

where τ is a t-norm, seems more appropriated.

$\mathcal{T}''(\mathcal{T}_S, \mathcal{T}'_S)$ can be interpreted in different ways as, for example, normalized similarity, compatibility or indistinguishability, or else normalized distance or difference (see, for example [11]). Depending on the kind of relation used for $\mathcal{T}''$, the semantic of (10) will change accordingly (see below).

EXAMPLE 3.3. If τ is the product t-norm, then

$$R_{PD} = (R_{PS} \circ R_{SD}) \times \mathcal{T}''(\mathcal{T}_S, \mathcal{T}'_S)\,, \tag{11}$$

where $\times$ is an operation of multiplication.

In our case $\mathcal{T}''$ will be considered as a similarity index and a distance, because these notions were already used in some medical applications (see, for example, [2] or [8]).

3.5.1 Similarity index

Adopted from [8], a similarity index, an index for measuring likeness of time fuzzy sets is defined as follows:

$$\mathcal{T}''(\mathcal{T}_S, \mathcal{T}'_S) = \sup\bigl\{\min\bigl(\mathcal{T}_S(t), \mathcal{T}'_S(t)\bigr):\ t \in \mathcal{T}\bigr\}\,. \tag{12}$$

If it is necessary, cylindrical extensions of $\mathcal{T}_S$ and $\mathcal{T}'_S$ are considered.

$\mathcal{T}''(\mathcal{T}_S, \mathcal{T}'_S)$ in (12) is a number from $[0,1]$ and can be used in inference mechanism of medical expert systems as shown in (11). In this case interpretations (4)–(6) of a diagnose is stated without changes.

Other interpretations of a similarity index can be found, for example, in [12].

3.5.2 Distances

Additional to *dates* [3], concepts of *time-extents* and *intervals* are considered in [2]. In Fuzzy Temporal Constraint Satisfaction Network (FTCSN) in [2] date-date, date-interval, interval-interval relations (that could be considered as $\mathcal{T}''(\mathcal{T}_S, \mathcal{T}'_S)$ in our case) are defined through the concept of a *distance*, based on possibility theory. This differs from the approach [3] by testing the temporal relations. The approach in [2] is interesting in our case, because

- it is oriented to medical applications;
- in FTCSN many of the possible fuzzy time cases are considered and described;
- the authors separate the handling of the time from the treatment of the domain variables. (It should be mentioned here that this assumption is based on the analogy with processes in physics, where time is considered as independent variable).

In the case of (10), one identifies the appropriate case from FTCSN and makes correspondent calculations of $\mathcal{T}''(\mathcal{T}_S, \mathcal{T}'_S)$.

4. Conclusions

Medical expert systems development constitutes a long term effort to assist in the differential diagnostic processes in internal medicine by a computer program.

Some of these medical expert systems are based on fuzzy set theory and fuzzy logic. The inference mechanism is based on a composition of fuzzy relations. But there is no explicit presentation of a time in these systems, although a representation of a time in medical diagnoses is a very important task.

The aim of this paper is to consider some possibilities to include time to the existing inference mechanism of medical expert systems, that a priori should make a diagnostic procedure more precise.

All possibilities of an application of a time to medical expert systems can be classified to 2 groups:

1. a time is **not separated** from the treatment of the domain variables, and
2. **separated** time.

In both cases the problem of a combination of temporal and atemporal components arise.

Following this classification, two types of inference mechanism were extended by time from those developed by [9] for CADIAG-II-like systems.

For "time-non separated" case, Dutta's approach, time-operator and time-descriptor were used in the inference mechanism of medical expert systems and explained.

For "time-separated" case, the powerful theory of fuzzy temporal knowledge can be used. We have considered similarity index and distance as already tested examples in medical applications for expert systems.

In all cases, time was presented as a fuzzy set (date, interval, time-extent and others).

From a theoretical point of view, all these approaches can be explained and applied.

The next step is to prove these results in practice.

REFERENCES

[1] ADLASSNIG, K. P.: *Fuzzy set theory in medical diagnosis*, IEEE Transactions on Systems, Man, and Cybernetics **16** (1986).

[2] ADLASSNIG, K. P.: *Fuzzy set theory and fuzzy logic in medicine*, in: MIF '99: The International Symposium on Medical Informatics and Fuzzy Technology, Hanoi, Vietnam, Vol. 1, August, 26–29, 1999, pp. 134–138.

[3] HUNG, D. H.—OTHERS: *Development of an expert system for lung diseases using fuzzy logic*, in: MIF '99: The International Symposium on Medical Informatics and Fuzzy Technology, Hanoi, Vietnam, Vol. 1, 1999, pp. 51–62.

[4] BARRO, S.—MARIN, R.—MIRA, J.—PATON, A.: *A model and a language for the fuzzy representation and handling of time.*, Fuzzy Sets and Systems (1994).

[5] DUBOIS, D.—PRADE, H.: *Processing fuzzy temporal knowledge*, IEEE Transactions on Systems, Man, and Cybernetics **19** (1989), 729–744.

[6] GODO, L. ET AL.: *MILORD: The Architecture and Management of Linguistically Expressed Uncertainty, Chapter 23*, Wiley Computing Publishing, John Wiley and Sons, INC, New York, 1990, pp. 357–387.

[7] DANIEL, M.—HÁJEK, P.—NGUYEN, P. H.: CADIAG-*2 and MYCIN-like Systems*, Artificial Intelligence in Medicine **9** (1997), 241–259.

[8] MAEDA, M.—ASAOKA, S.—MURAKAMI, S.: *Dynamical fuzzy reasoning and its application to system modelling*, Fuzzy Sets and Systems **80** (1996), 101–109.

[9] TSANG, E. C. C.—LEE, J. W. T.—YEUNG, D. S.: *Similarity based fuzzy reasoning methods for fuzzy production rules*, Fuzzy Sets and Systems **444** (1992), 444–888.

[10] QIAN DA GUN: *Representation and use of imprecise temporal knowledge in dynamic systems*, Fuzzy Sets and Systems **50** (1992), 59–77.

[11] RAHA, S.—RAY, S.: *Approximate reasoning with time*, Fuzzy Sets and Systems **107** (1999), 59–79.

[12] SANCHEZ, E.: *Medical diagnosis and composite fuzzy relations*, in: Advances in Fuzzy Set Theory and Applications (R. K. Ragade M. M. Gupta and R. R Yager, eds.), North-Holland, Amsterdam, 1979, pp. 437–444.

[13] SHORTLIFFE, E.: *MYCIN: A Rule-Based Computer Program For Advising Physicians Regarding Antimicrobial Therapy Selection*, PhD thesis, Stanford University, 1974.

[14] TRILLAS, E.—VALVERDE, L.: *On implication and indistinguishability in the settings of fuzzy logic*, in: Readings in Fuzzy Sets for Intelligent Systems (D. Dubois, H. Prade, and R. Yager, eds.), Morgan Kaufmann Publishers, Inc, California, 1992, pp. 97–104.

[15] VIRANT, J.—ZIMIC, N.: *Attention to time in fuzzy logic*, Fuzzy Sets and Systems **82** (1996), 39–49.

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University of Dortmund
Department of Computer Science I
D–44221 Dortmund
GERMANY

Tbilisi State University
Department of Applied Mathematics
and Computer Science
380028 Tbilisi
GEORGIA

E-mail: kiseliov@ls1.informatik.uni-dortmud.de