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Fuzzy theory approach for temporal model-based diagnosis: An application to medical domains

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Summary

Objective: The aim of this work is to provide a theoretical framework which is sufficiently expressive to describe temporal evolution of diseases, and also to propose a diagnostic process for building explanations of patient's observed temporal evolution based on these disease descriptions.

Background: Model-based diagnosis (MBD) tackles the problem of troubleshooting systems by starting from a description of their structure and function (or behaviour). It is in this area where the use of deep causal models, as part of MBD systems, has shown its greater efficiency over classical rule based systems. From its beginnings, the temporal dimension was considered as an important component in MBD, since it makes it possible to define the dynamic behaviour. Several approaches have been proposed to represent time in MBD, enabling the representation of temporal concepts and relations, as well as the use of temporal reasoning mechanisms.

Methodology: We first propose a temporal behavioural model (TBM), which allows us to capture the dynamics underlying temporal evolution of diseases and to include contextual information. Contextual information is required to model how contextual factors change the temporal evolution of diseases. The temporal component is modelled by fuzzy temporal constraints networks (FTCN), which makes the representation of quantitative and qualitative imprecise temporal information possible. We also provide a diagnostic process, which is based on a temporal adaptation of classical cover and differentiate method.

Results: The TBM and diagnostic process proposed provides a unique framework which addresses three problems not dealt with together so far: (a) the inclusion of contextual information, (b) the expressivity of the solution provided, and (c) the evaluation of the diagnostic hypotheses. This proposal demonstrates that the FTCN

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formalism provides mechanisms sufficiently expressive to cope with the intrinsic imprecision in the description of diseases' temporal evolution. The explanation generated provides the user with a complete picture of the temporal evolution of diseases and its causal links, thus allowing the appearance of repeated instances of the same disease through time. Mechanisms are provided which evaluate the credibility of alternative hypotheses, based on possibility theory. A prototype is presented along with a knowledge acquisition tool that guides medical experts in the model building process.
Conclusions: In this paper, we propose a model that tightly couples methods from MBD area with constraint-based temporal reasoning techniques. The proposed model allows us to model complex contextual relationships in a compact way as well as providing solutions expressive enough to be used for decision support purposes. The solution provided conforms a causal network entailing the abnormal observations, including pathophysiological and etiological states. Furthermore, different instances of the same diagnostic hypotheses, located at different time instants, are also possible in the final solution. Finally, we provide an analysis of related and future works.

1. Introduction

Since the early days of Artificial Intelligence, the design of intelligent systems for medical diagnosis has been one of the most prolific areas. Deep causal models have been pioneered in this area, showing the advantages of modelling domain knowledge in this way and in contrast to the classical rule-based systems [1]. During the last decade, research in this area has paid increasing attention to the use of deep causal models, especially if they are considered as integrated in model-based diagnostic (MBD) techniques, which have proved their efficiency in the design of intelligent diagnostic systems [2].

MBD tackles the problem of troubleshooting systems by starting from a description of their structure and function (or behaviour) [3]. From its beginning, the temporal dimension was considered as an important component in MBD (especially in medical domains if it is considered as part of patient monitoring), since it makes the definition of the dynamic behaviour possible. This is especially important in Artificial Intelligence in Medicine which has shifted its research interest from static consultation systems to dynamic ones, which capture the patient's evolution over time better [4,5]. It is in the Intensive Care Unit (ICU) where temporal dimension is the key element in diangosis. However, the inclusion of the temporal dimension in MBD has increased the complexity of the diagnostic process. Different formalisms have been proposed to represent time in MBD, ranging from totally qualitative approaches [6,7], based on Allen's interval logic [8], to totally quantitative approaches [5,9–11]. An exhaustive review of temporal MBD (TMBD) can be seen in [3], together with a general characterization for TMBD at knowledge level.

Despite the intense research activity in this area, there are three issues that have still not been analysed together: (a) the interaction between contextual knowledge and behavioural models, (b) evaluation of hypotheses, and (c) the structure of the explanation provided. Contextual knowledge can be defined as knowledge, which plays the role of premises instead of consequences of some hypotheses. In most MBD proposals, contextual knowledge is modelled as preconditions in the antecedents of temporal formulas defining causal relations between diseases and their associated findings [3,12]. However, there are situations in which a certain combination of contextual factors may modify the normal evolution of a disease. These modifications may range from a simple change in the causal relations between the diseases and a given finding, to removing a causal relation or adding a new one. This kind of contextual knowledge is not easy to model using the classical TMBD approaches. The other two issues are related to the capacity of the diagnostic process to be integrated in the decision making process. In this sense, the solution must include all the information required for justification purposes and not be limited to the presentation of a set of hypotheses. It would be also desirable to include a hypothesis evaluation process which takes into account medical information, such as that provided by evidence-based medicine (EBM) [13].

In this paper, a TMBD approach, which provides solutions to the issues outlined above, is proposed. The proposed model is based on the definition of temporal patterns. These temporal patterns capture the temporal and causal relations between the elements, which describe the physiological processes associated to the evolution of the diseases. Mechanisms are also provided to model complex interactions between contextual factors and the temporal behaviour model. The diagnostic solutions are presented in the form of a causal network, which allows the causal chain from the observations to the hypotheses to be analysed. Finally, a hypotheses evaluation process based on the possibility theory [14] is also provided. All this is possible thanks to the fuzzy temporal constraints network (FTCN) [15,16] used to manage the temporal component.

The structure of the paper is as follows: the underlying temporal framework is laid out in a concise manner in Section 2. In Section 3, the temporal behavioural model is presented. The elements that constitute the inputs for temporal MBD and the structure of the diagnostic solution are presented in Section 4, which also introduces the definition of the fuzzy temporal diagnostic problem. In Section 5, we outline the process for building a diagnostic explanation. Section 6 illustrates the hypotheses evaluation and discrimination process. System implementation is outlined in Section 7. Finally, we discuss the proposed approach and provide some conclusions.

2. The temporal framework

In this proposal for TMBD, the temporal dimension is modelled by means of the so-called FTCN formalism [16]. An FTCN is a pair $\mathcal{N} = \langle \mathcal{T}, \mathcal{L} \rangle$ consisting of a finite set of temporal variables, $\mathcal{T} = \{T_0, T_1, \ldots, T_n\}$, and a finite set of binary temporal constraints, $\mathcal{L} = \{L_{ij}, 0 \leq i, j \leq n\}$ defined on the variables of $\mathcal{T}$. An FTCN can be represented by means of a directed constraint graph, where nodes represent temporal variables and arcs represent binary temporal constraints.

Each binary constraint L_{ij} on two temporal variables T_i and T_j is defined by means of a fuzzy number, i.e., a convex possibility distribution $\pi_{L_{ij}}$, whose discourse universe is $\mathbb{Z}$, and which restricts the possible values of the time elapsed between both temporal variables. In the absence of other constraints, the assignments $T_i = t_i$ and $T_j = t_j$ are possible if $\pi_{L_{ij}}(t_j - t_i) > 0$ is satisfied. T_0 represents an arbitrary time origin. A convex possibility distribution can be represented by means of a five-tuple fuzzy number (a, b, c, d, h), as shown in Fig. 1, which indicates that the event associated to it necessarily occurs in interval $[a - c, b + d]$ (referred to as support), but possibly occurs in interval $[a, b]$ (referred to as kernel), with a possibility of h.

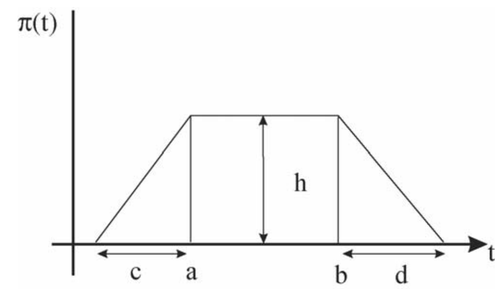

Figure 1 Possibility distribution associated to the fuzzy number (a, b, c, d, h).

An n-tuple $S = (t_1, \ldots, t_n) \in \mathbb{Z}^n$ is a σ-possible solution of an FTCN network $\mathcal{N}$ if $\pi^{S_{\mathcal{N}}} = \sigma$, where $\pi^{S_{\mathcal{N}}} = \min\{\pi_{L_{ij}}(t_j - t_i), 0 \leq i, j \leq n\}$. The possibility distribution $\pi^{S_{\mathcal{N}}}$ defines the fuzzy set $S_{\mathcal{N}}$ of the σ-possible solutions of the network, with $\sigma \geq 0$. An FTCN network $\mathcal{N}$ is *consistent* if and only if $S_{\mathcal{N}}$ is not empty given a previously established threshold Π_{th} for σ.

The inference of unknown relations is carried out by applying a constraint propagation algorithm. By means of constraint propagation, a new FTCN that is equivalent to the original one is obtained. The equivalence property states that both networks have the same solution set. However, the new constraints are included in the corresponding constraints of the original FTCN. The new FTCN, although containing the same fuzzy set of solutions, describes the differences between variables in a more precise way. Constraint propagation removes impossible values from the original constraints. A constraint is minimal when all the impossible values have been removed. A minimal constraint contains the smallest degree of imprecision. A network whose constraints are all minimal is called a minimal network. The minimal network makes all the implicit constraints in the network explicit, and always corresponds to a complete graph. There are some efficient algorithms to propagate constraints. It may be proved that, when the possibility distributions are convex, the well-known shortest-path algorithm is complete for the FTCN model, i.e., it obtains the minimal constraints for consistent networks and it detects inconsistent networks. One of the main advantages of obtaining the minimal network is that it provides the most precise temporal information consistent with the temporal information provided [16].

In order to interact with this theoretical framework a high-level temporal language has been proposed and implemented in FuzzyTIME [17].

FuzzyTIME is a general-purpose temporal reasoner providing reasoning capabilities on fuzzy temporal constraints between temporal variables, which can represent both instants and interval. Nevertheless, intervals are not considered in the diagnostic model presented here. FuzzyTIME provides procedures for maintaining and querying temporal information at FTCN level, which is given as high-level temporal sentences.

The key element in FuzzyTIME high-level language is the temporal relation. A wide range of qualitative and quantitative temporal relations between temporal entities is allowed in the high level language. There are five kinds of basic relations [18—22]:

- *Qualitative interval—interval relations (QII)*: BEFORE, MEETS, STARTS, DURING, FINISHES, OVERLAPS, their inverses and the equality relation EQUAL.
- *Qualitative point—interval relations (QPI) and Qualitative interval—point relations (QIP)*: BEFORE, STARTS, DURING, FINISHES and AFTER.
- *Qualitative point—point relations (QPP)*: AFTER, BEFORE and EQUAL.
- *Metric point—point relations (MPP)*, which specifies the temporal gap between two temporal instants in some temporal unit (minutes, hours, days, months and years) which can be specified as a fuzzy number. For the sake of simplicity, hereinafter an MPP relation between two temporal variables is represented by $C(t_i, t_j)$.

All convex disjunctions of basic relations are admitted and are expressed as subsets of each set of basic relations. Unary operators such as APPROX, LESS THAN and MORE THAN can be included as part of any temporal relations. Thus, there are six QPP and 181 QII admissible relations [21]. As can be observed, non-convex relations are not allowed in the high level language.[1] Expressions based on convex relations have a direct mapping to the FTCN formalism and can be translated to equivalent MPP relations [17]. This is performed in two steps: (1) convex temporal relations are decomposed into a conjunction of QPP relations, and (2) this conjunction of QPP relations is then also translated into a conjunction of MPP relations by applying a fuzzy generalization of the QUAN operator proposed in [20]. The unary operators previously mentioned only modified the support of the corresponding possibility distributions by applying a previously established percentage.

[1] Consistency checking for non-convex relations networks is NP-hard. In our experience, convex relations suffice to capture temporal knowledge in medical domains.

In order to represent patients' evolution in FuzzyTIME, a new temporal entity, referred to as *events*, has been considered. Events are defined by the 4-tuple (m, s, v, t), where m stands for clinical concepts (pain, st-level, ...), s and v for an attribute-value pair (location-precordial, intensity-moderate, ...) and t for the corresponding temporal variable representing a time instant. For example, expression (1) can be used to represent the temporal evolution of a patient suffering from *dehydration* (formally this manifestation is internally represented as (dehydration,presence,true, t_1)) approximately 1 hour before a *precordial pain* and, approximately 2 minutes after the *precordial pain*, a *moderate st_level elevation* has been detected.

$$\begin{aligned}&(\textit{dehydratation}, t_1)\ \text{APPROX 1 HOUR BEFORE}\\&\quad(\textit{pain}, \textit{location}, \textit{precordial}, t_2)\\&\quad(\textit{st\_level}, \textit{intensity}, \textit{moderate}, t_3)\\&\text{APPROX 2 MINUTES AFTER}\ t_2\end{aligned} \tag{1}$$

The process of answering queries is based on the possibility theory [14]. Therefore, there are two types of queries: queries about possibility $\Pi(F)$ and about necessity $N(F)$, where F is a formula constructed with the logical connectives (conjunction, disjunction and negation) applied to admissible temporal expressions. A query answered with $\Pi(F) = 0$ means that F is impossible, i.e., is certainly false. $\Pi(F) = 1$ means that F is completely possible. $N(F) \in (0, 1)$ means that F is somewhat certain ($N(\neg F)$ is certainly false) and therefore $\Pi(F) = 1$. $F = 0$ means that F is completely false. The process for answering temporal queries is explained in [17].

Logical expression (2) shows an example of a temporal query on the possibility of an *Acute Myocardial Infarction* (AMI) occurring approximately 1 hour before precordial pain and 2 minutes before the *ST elevation*.

$$\begin{aligned}&\Pi((\text{AMI}, t_1)\ \text{APPROX 1 HOUR BEFORE}\\&\quad(\textit{pain}, \textit{location}, \textit{precordial}, t_2)) \wedge\\&\quad(t_1 \text{APPROX 1 MINUTE BEFORE}\\&\quad(\textit{st\_changes}, \textit{intensity}, \textit{moderate}, t_3)))\end{aligned} \tag{2}$$

3. The temporal behavioural model

In this proposal, temporal behavioural model (TBM) is based on an abnormal behavioural model in which only the causal and temporal relations between diseases and their abnormal findings are represented. These relations are defined by *diagnostic fuzzy temporal patterns* (DFTPs). Besides this, each DFTP includes knowledge about how the context affects the temporal evolution of the disease — referred to as *contextual temporal meta-knowledge* — and information about the temporal relations between contextual elements. Each DFTP is therefore composed of:

1. A main hypothesis, H, which represents the disease being described and a temporal variable t_h indicating its approximate time appearance. Formally, H is given by the pair $(\hbar, t^{\hbar})$.
2. A set of implied abnormal manifestations, IM, which represents the set of events describing disease evolution. Each abnormal manifestation is defined by the tuple $im = (m, s, V, t)$ where, in contrast to the definition of events, V stands for the set of event values admitted for the abnormal manifestation.
3. A set of implied hypotheses, IH, which specifies the set of diseases caused by the diseases H under description. By means of these causal links, from H to elements in IH, the TBM conforms a causal network of diseases. This type of causal relation allows us to model existing causal relations between the etiological and pathophysiological diagnoses.
4. A consistent FCTN, $\mathcal{R}^{\mathrm{DFTP}} = \langle \mathcal{T}^{\mathrm{DFTP}}, \mathcal{L}^{\mathrm{DFTP}} \rangle$, whose temporal variables, $\mathcal{T}^{\mathrm{DFTP}}$, are those associated to the main hypothesis, implied manifestations and implied hypotheses. The set $\mathcal{L}^{\mathrm{DFTP}}$ represents the set of fuzzy binary temporal constraints between temporal variables, $\mathcal{L}^{\mathrm{DFTP}} = \{C(t_i, t_j); t_i, t_j \in \mathcal{T}^{\mathrm{DFTP}}\}$. These constraints are obtained from temporal information provided by medical experts (see Section (7)). They are stored as a set of MPP relations between temporal variables.

DFTPs allow us to capture all kinds of causal knowledge which can be extracted from medical domains [9]: pathophysiological knowledge (causal relations between pathophysiological states), evidential causal knowledge (causal relations between external manifestations and either pathophysiological or etiological states) and diagnostic knowledge (relations between pathophysiological states and etiological states). As well as the previous elements, two functions have to be considered in a DFTP definition:

- $S_1 : \mathrm{H} \times (\mathrm{IM} \cup \mathrm{IH}) \rightarrow [0, 1]$, is a function that defines the necessity degree associated to the causal relation between $\hbar$ and its implied manifestations and hypotheses, $N(\hbar \rightarrow mh) = S_1(\hbar, mh)$ (where mh represents an implied manifestation or hypothesis). In order to simplify the notation, we will use $S_1(mh)$ instead of $S_1(\hbar, mh)$.
- $S_2 : (\mathrm{IM} \cup \mathrm{IH}) \times H \rightarrow [0, 1]$, is a function that defines the necessity degree associated to the causal relation $mh \rightarrow \hbar$ that is, $N(mh \rightarrow \hbar) = S_2(mh, \hbar)$. In order to simplify the notation, we will use $S_2(mh)$ instead of $S_2(\hbar, mh)$.

One of the main problems in the configuration of the DFTPs, that conforms the TBM, lies in the expert's capacity to define each DFTP element. Our experience in medical domains reveals that the definition of S_1 and S_2 functions is one of the most complex points. Accordingly, useful information can be extracted from EBM literature [13]. In EBM, given a disease $\hbar$ and a manifestation or implied hypothesis mh_k, the causal relationship between them can be quantified by means of two values:

- Sensitivity, which measures the proportion of all patients suffering the disease who present the manifestation. In probabilistic terms, this can be formulated as $P(mh_k/\hbar)$, i.e. $P(\hbar \rightarrow m_k)$.
- Specificity, which measures the proportion of all patients not suffering from that disease who do not present the manifestation. In probabilistic terms, this can be formulated as $P(\neg mh_k/\neg\hbar)$, i.e. $P(\neg\hbar \rightarrow \neg mh_k) = P(mh_k \rightarrow \hbar)$

S_1 and S_2 necessity functions can be determined from sensitivity and specificity measures. To this end, we must take into account that probabilistic measures are particular cases of necessity and possibility measures [14]:

$$\Pi(x) \geq P(x) \geq N(x) \tag{3}$$

In the particular case of DFTPs, the causal relationships $\hbar \rightarrow mh_k$ and $mh_k \rightarrow \hbar$ are considered completely possible, then:

$$\Pi(\hbar \rightarrow mh_k) = \Pi(mh_k \rightarrow \hbar) = 1 \tag{4}$$

Using formulae (3) and (4), it is possible to define the following relationships:

$$1 = \Pi(\hbar \rightarrow mh_k) \geq P(\hbar \rightarrow mh_k) \geq N(\hbar \rightarrow mh_k) = S_1(mh_k) \tag{5}$$

$$1 = \Pi(mh_k \rightarrow \hbar) \geq P(mh_k \rightarrow \hbar) \geq N(mh_k \rightarrow \hbar) = S_2(mh_k) \tag{6}$$

Table 1 Sensitivity categories and S_1 values

Category	Probability interval	S_1
Occurs in essentially all cases of the disease	[0.80,1]	0.80
Occurs in the substantial majority of the cases	[0.60,0.80)	0.60
Occurs in roughly one-half of the cases	[0.40,0.60)	0.40
Occurs in a substantial minority of the cases	[0.20,0.40)	0.20
Occurs rarely in cases	[0.10,0.20)	0.10
Unknown	—	0

Table 2 Specificity categories and S2 values

Category	Probability interval	S_2
Manifestation is pathognomic for the disease	[0.80,1]	0.80
Disease is the overwhelming cause of the manifestation	[0.64,0.80)	0.64
Disease is the most common cause	[0.48,0.64)	0.48
Disease causes a substantial minority of manifestation instance	[0.32,0.48)	0.32
Disease is a rare or unusual cause	[0.16,0.32)	0.16
Manifestation occurs too commonly in disease instances	[0.10,0.16)	0.10
Unknown	—	0

From the previous expressions it is easy to deduce that necessity functions S_1 and S_2 are upper bounded by sensitivity and specificity, respectively. However, in some cases, information about sensitivity and specificity is often not available. For this reason, and to facilitate the interaction with experts and users, especially for knowledge acquisition purposes, the domains of S_1 and S_2 functions [0,1], are discretized into several categories with their corresponding linguistic labels. The definition of the linguistic labels is based on those definitions described in [23] for the discretization of sensitivity and specificity. The different categories defined for sensitivity and specificity, together with the corresponding intervals, can be seen in Tables 1 and 2. Another category, referred to as *Unknown*, is necessary to represent the lack of information on specificity and sensitivity. The *Unknown* value sets the value 0 for S_1 and S_2, stating that nothing can be said about the necessity of both $\hbar \rightarrow mh$ and $mh \rightarrow \hbar$ (in other words, the causal relations $\neg(\hbar \rightarrow mh)$ and $\neg(mh \rightarrow \hbar)$ are completely possible). The corresponding S_1 and S_2 values for the rest of categories are also shown and are calculated according to expression (6). As can be seen in the last but one rows of Tables 1 and 2, both categories are defined as an open interval on 0. This is due to the fact that the 0 value is used to indicate the lack of information. Hence, the value 0.10 is used as the closest approximation to 0, given the precision used.

3.1. Description of a real clinical case

We will take the following case as an example[2] in order to illustrate the diagnostic process and to show the expressive power of the model presented:

A male, middle-aged patient is admitted at the ICU at 00:10:00 with symptoms of dehydration and complaining of an acute precordial pain. Solinitrine (nitro-glycerine) is subsequently administered and a TNK (thrombolytic) at 00:20:00. Monitoring of the patient begins and the following abnormal events were registered: Bradycardia at 00:38:00 h; re-elevation of the ST segment at 00:38:40 and 01:07:15; and a sharp decline in arterial pressure (hypotension) at 00:33:35. Capillary refill time was observed to be slow at 00:36:55 and moments later (00:37:00) paleness was observed.

Table 3 shows the set of events using the formalism introduced in Section 2. In a clinical case, we can also find atemporal events such as (*demographical_data, sex, male*) and (*demographical_data, age, middle-aged*). To illustrate the steps of the diagnostic process more clearly, we have chosen a threshold value of $\Pi_{\text{th}} = 0$. This value implies the condition that establishes the temporal inconsistency of an

[2] The example is a simplification of the real medical case and, therefore, should not be interpreted as a real medical situation. Nevertheless, the temporal relations taken from observations in real medical records have been maintained.

Table 3 Sequence of temporal events in the example

Manifestation	Attribute	Value	Time (h:m:s)
Pain increment	Presence	True	00:10:00
Dehydration	Presence	True	00:10:00
Drug-administration	Solinitrina	True	00:20:00
Drug-administration	TNK	True	00:20:00
Hypotension	Variation	Sudden	00:33:35
Capillary refill	Velocity	Slow	00:36:55
Paleness	Presence	True	00:37:00
Bradycardia	Presence	True	00:38:20
ST re-elevation	Presence	True	00:38:40
ST re-elevation	Presence	True	01:07:15

FTCN $(\min\{\pi_{L_{ij}}(t_j - t_i), 0 \leq i, j \leq n\} = 0)$, i.e., an FTCN is only considered as inconsistent if the constraint propagation process infers a temporal constraint which is totally impossible. Fig. 2 depicts part of the causal network used throughout this article to illustrate the presented concepts. In this figure, etiological (AMI) and pathophysiological (DS) diseases are represented by ovals. The definition of the temporal pattern representing AMI is shown in Fig. 3, in which all the elements introduced in Section 3 are used.

Table 4 represents the minimal temporal constraints between temporal variables. For example, given the temporal information provided in Fig. 3, the default temporal constraint between AMI and DS is $C(\text{AMI}, \text{DS}) = \{before\} = (1, \infty, 0, \infty, 1)$. After constraint propagation, we obtain the minimal equivalent constraint $C(\text{AMI}, \text{DS}) = (103, 137, 2, 2, 1)$, which can be interpreted as DS necessarily occurring between 101 and 139 seconds after AMI, but it is completely possible that DS occurs between 103 and 137 seconds after AMI, since maximum possibility is 1.

As indicated in Section 2, fuzzy numbers represent the possibility distribution indicating the approximate elapsed time between two temporal variables. FuzzyTIME provides temporal information

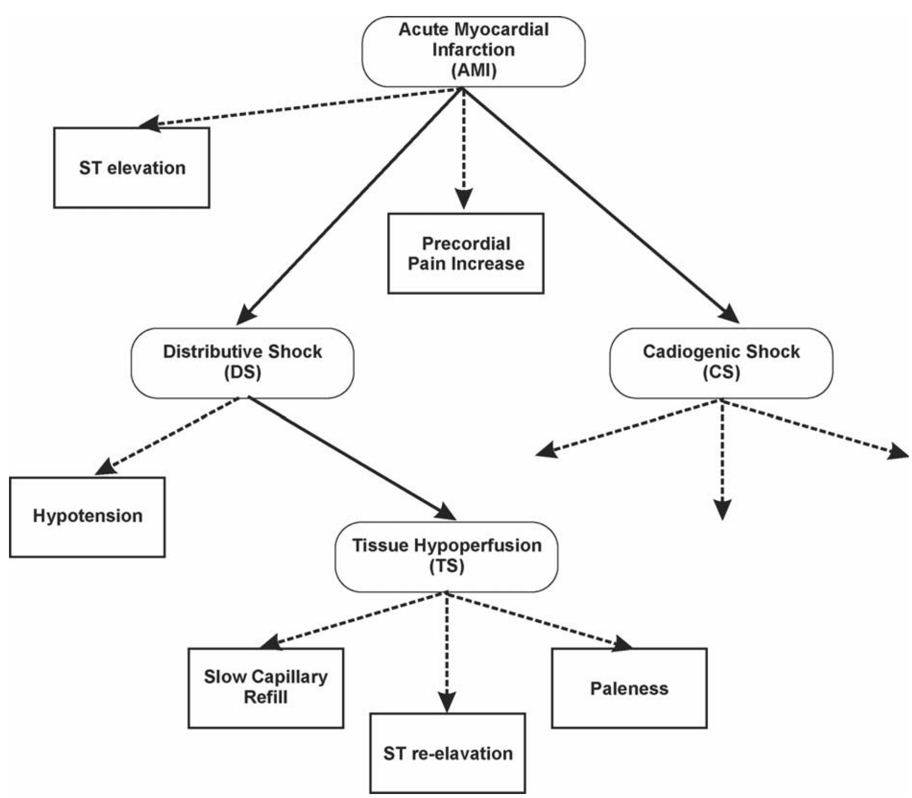

Figure 2 Part of the causal network used as example.

- Main Hypothesis: (AMI,$t_\hbar$)
- Implied Manifestations
  - (ST-elevation,Intensity,Moderate,t_1) $[S_1 = 0.8, S_2 = 0.8]$
  - (Precordial Pain Increase,Presence,true,t_2) $[S_1 = 0.8, S_2 = 0.8]$
- Implied Hypotheses
  - (DS,t_3) $[S_1 = 0.6, S_2 = 0.64]$
  - (CS,t_4) $[S_1 = 0.6, S_2 = 0.64]$
- Temporal Constraints
  - Explicit Temporal Constraints
    * t_1 approx 2 mins after $t_\hbar$
    * t_2 approx 40 secs after t_1
    * t_3 aprox at t_1
    * t_4 aprox at t_1
  - Default Temporal Constraints
    * $t_\hbar$ before t_1
    * $t_\hbar$ before t_2
    * $t_\hbar$ before t_3
    * $t_\hbar$ before t_4

Figure 3 Description of AMI temporal pattern.

on the lowest granularity used in the diseases description, in our example seconds. However, internally all the temporal information is converted to milliseconds. In other words, milliseconds are the lowest granularity that can be used in DFTP definitions.

The default temporal constraints are introduced to fulfill a standard axiom which states that a disorder precedes the onset of its manifestations. How these default constraints are used in the model building process will be explained in Section 7.

3.2. Contextual temporal meta-knowledge

In MBD, contextual data correspond to data that have not to be accounted for by diagnosis, unlike findings that have to be accounted for [3,12]. In order to add contextual knowledge in a TBM using this definition, atoms (not included in the observations set) can be added in the antecedent of causal rules defining some diagnostic hypotheses. We used a different approach, which we describe in this section.

The use of contextual information is especially important in medical domains, since it is very difficult to explain a real-world patient evolution using theoretical descriptions of diseases. This is mainly due to the presence of contextual factors that affect theoretical patient evolution. For example, at ICUs, it is very common to increase a patient's blood pressure (when it is excessively low) by means of the corresponding therapy. If, in this context, a rise in blood pressure is detected, it should not be considered as an abnormal manifestation, since the rise is expected. In our model, an event associated to a manifestation in a given hypothesis can play the role of a contextual factor in another hypothesis.

Therefore, it is necessary to provide a representational framework to model how contextual factors affect DFTP's definitions. In our proposal, this is done by means of one or more temporal contexts, TC, associated to a given DFTP [24]. TCs specify the different modifications that have to be accomplished in a DFTP definition if a certain context is present. To define a TC the following elements are necessary:

- A set of atemporal concepts, A_i, describing information such as patient's demographics (age, sex, ...), risk factors (smoker, diabetes, ...) and all the relevant information that have no temporal dimension.
- A set of temporal concepts, T_i, mainly related to the administration of drugs.
- A consistent FTCN, $\mathcal{R}_i^{ct}$, that specifies the temporal constraints between the hypothesis H and the temporal concepts T_i.
- $MF_i = \{mf_1, \ldots, mf_m\}$ is a set of modification functions (mf_i) that describes how the context changes the basic DFTP definition. These functions create, delete and modify elements of the IM, IH sets, and the R^{DFTP} network:
  - *modify_values*$(\mathrm{DFTP}, im, V_m^{\mathrm{new}})$ substitutes the set *V_m* for the allowed values of the implied manifestation *im*.
  - *modify_necessity*$(\mathrm{DFTP}, mh, S_1^{\mathrm{new}}, S_2^{\mathrm{new}})$ modifies the necessity degree associated to causal implication.
  - *add_implication*$(\mathrm{DFTP}, mh^{\mathrm{new}}, S_1^{\mathrm{new}}, S_2^{\mathrm{new}}, C^{\mathrm{new}}(t^h, t^{mh}))$ adds a new implied manifestation or implied hypothesis mh to DFTP. It also assigns the necessity degree values of the corresponding causal relationships and a temporal con-

- **Temporal Concepts**
  - $(\mathrm{AMI},t_\hbar)$
  - $(\mathrm{solinitrine},t_1)$
  - $(\mathrm{dehydratation},t_2)$
- **Temporal Constraints**
  - t_1 aprox 45 min after $t_\hbar$
  - t_2 aprox 1 hour before $t_\hbar$
- **Modifying function**
  - $add\_implication((bradycardia, t_3),$
    $, 0.4, 0.48, C(t_3 \text{ aprox 5 min after } t_\hbar))$

Figure 4 Temporal Context associated to AMI temporal pattern.

straint between the added manifestation or hypothesis and the pattern main hypothesis.

- *remove_implication*(DFTP, *mh*) deletes the implied manifestation or implied hypothesis *mh*, its necessity degree value from the DFTP and the associated temporal variable and constraints.

For example, let us suppose that a patient has suffered AMI and, approximately 1 hour earlier, has suffered dehydration. Let also suppose that 45 minutes after the infarction (on arrival at the ICU), he or she has been administered Solinitrine (nitro-glycerine). This context causes a bradycardia approximately 5 minutes after AMI-a finding that in normal condition are not expected. This context can be modelled by means of the TC described in Fig. 3, associated to the temporal pattern describing AMI (Fig. 3).

If the TC described in Fig. 4 is present, the corresponding modification has to be applied before using the temporal pattern describing AMI to explain a given event. This approach for modelling context interaction allows more complex relations between TBM and context to be modelled than those described in classical temporal MBD models [3,9]. In logical terms, TC can be interpreted as some kind of metaknowledge that specifies how logical formulation of diagnostic hypotheses has to be modified if elements defining the TC are present. Once contextual contexts are applied to a given DFTP, it is referred to as *Contextualized* DFTP. This contextualization implies modifications in DFTP definition (if any) and its temporal localization, which is needed to test the temporal constraints stated in TCs. In the rest of the paper, when the term DFTP is used, it should be considered as a reference to a contextualized DFTP. Of course, several contextualizations of the same DFTP may be possible. In this case, the hypotheses discrimination process (HDP), described in Section 6, will evaluate the credibility of each contextualization.

4. Fuzzy temporal diagnostic problem

The aim of the diagnostic process is to generate a possible explanation of an observed behaviour. The observed behaviour is provided as a set of events.

In most cases, we know the precise absolute dates at which each event occurs, since these are collected from clinical information systems. In other words, the temporal variable t_i in each event tuple (m, s, v, t_i) is only subject to a constraint relative to time origin $C(t_0, t_i) = C_{0i}$, and this constraint is given by means of a precise possibility distribution $\pi_{C_{0i}} = (a, a, 0, 0, h)$. This was the case in the example shown in Table 3. In this case, a chronological ordering can be established on the set of events, and we could represent it as a sequence of events. However, this is not required in our model. The diagnostic process can also cope with events defined by means of imprecise absolute dates or by means of relative dates. In the first case, $C(t_0, t_i)$ is a true fuzzy number and, in the second case, there are constraints $C(t_i, t_j)$ relative to different events, as in the example corresponding to expression (1).

There are also special events which have no temporal reference. These events represent concepts which are always present during patient evolution, such as demographical data of the patient (age, sex, ...), anamnestic information (previous heart problems) and risk factors (hypertension, smoker, diabetic, ...). These atemporal events will be compared to the atemporal concepts referred in TCs.

Table 4 The FTCN of an AMI temporal pattern after minimization

	t_h	t_1	t_2	t_3	t_4
t_h	(0,0,0,0,1)	(105,135,1,1,1)	(140,180,2,2,1)	(103,137,2,2,1)	(103,137,2,2,1)
t_1	(− 135, − 105,1,1,1)	(0,0,0,0,1)	(35,45,1,1,1)	(− 2,2,1,1,1)	(− 2,2,1,1,1)
t_2	(− 180, − 140,2,2,1)	(− 45, − 35,1,1,1)	(0,0,0,0,1)	(− 47, − 33,2,2,1)	(− 47, − 33,2,2,1)
t_3	(− 137, − 103,2,2,1)	(− 2,2,1,1,1)	(33,47,2,2,1)	(0,0,0,0,1)	(− 4,4,2,2,1)
t_4	(− 137, − 103,2,2,1)	(− 2,2,1,1,1)	(33,47,2,2,1)	(− 4,4,2,2,1)	(0,0,0,0,1)

Taking the above considerations into account, diagnostic process input is defined as:

- The set of events to be explained $\mathrm{EVT} = \{\mathrm{evt}_i | i = 1, \cdots, n_{\mathrm{obs}}\}$. As introduced in Section 2, events are represented by the tuple $\mathrm{evt}_i = (m_i, s_i, v_i, t_i)$, except for atemporal events which have no temporal variable associated.
- $\mathcal{R}^{\mathrm{in}} = \langle \mathcal{T}^{\mathrm{in}}, \mathcal{L}^{\mathrm{in}} \rangle$ is a consistent FTCN, where temporal variables in $\mathcal{T}^{\mathrm{in}}$ are associated to events in EVT, and their corresponding temporal constraints are defined in $\mathcal{L}^{\mathrm{in}}$.

Once the diagnostic process finishes, the set of input/initial events will be divided into two disjunctive sets, EVT^- in which will be included those events explained by DFTP in the TBM, and EVT^+, which will include the remaining events. Besides, the elements of EVT can be used as temporal concepts in some TCs.

We will use the elements introduced in this section and Section 3 in the following definition:

Definition 1. Fuzzy temporal diagnostic problem (FTDP). Given a TBM, a set of events EVT and a consistent FTCN $\mathcal{R}^{\mathrm{in}}$, a fuzzy temporal diagnostic problem can be defined as the tuple: $\mathrm{FTDP} = \langle \mathrm{TBM}, \mathrm{EVT}, \mathcal{R}^{\mathrm{in}}, \Pi_{\mathrm{th}} \rangle$, with Π_{th} defining the minimum possibility degree for hypotheses in diagnostic explanation to be accepted.

All those hypotheses which are not sufficiently supported by the observed behaviour that is their possibility degree is lower than Π_{th}, can be pruned from the explanation generated. The HDP is shown in Section 6.

The diagnostic process output (i.e., the explanation provided) is an instantiated causal network containing the diagnostic hypotheses that survive the HDP. In classical diagnostic systems, the output is merely a set of abducibles (see, for example [3,6]). In our proposal, the output includes physiopathological and etiological diagnosis, linked by means of causal relations. Moreover, the network can include several diagnostic hypotheses at the top level (etiological diagnosis), thus providing the user with alternative explanations for the observed behaviour.

Therefore, the diagnostic algorithm output can be formally defined as the tuple $\mathrm{EXP} = \langle \mathrm{CN}_{\mathrm{exp}}, \mathcal{R}^{\mathrm{exp}} \rangle$ where:

- $\mathrm{CN}_{\mathrm{exp}} = \langle \mathcal{N}, \mathcal{A}, \Pi_{\mathrm{cn}}, N_{\mathrm{cn}} \rangle$ is the graph that represents the causal network.
  - $\mathcal{N}$ is the set of nodes of the causal network, where each node is composed by the pair: $\langle n_i, t_i^{\mathrm{cn}} \rangle$, where n_i represents a manifestation or a hypothesis concept, and t_i^{cn} is the temporal variable associated to this node. The leaf nodes are associated to the events in EVT^-.
  - $\mathcal{A}$ is the set of links between causal network nodes.
  - $\Pi_{\mathrm{cn}}, N_{\mathrm{cn}} : \mathcal{N} \to [0, 1]$ are functions that indicate the possibility and necessity degree associated to each node. The process for determining these degrees will be explained in Section 6.
- $\mathcal{R}^{\mathrm{exp}} = \langle \mathcal{T}^{\mathrm{exp}}, \mathcal{L}^{\mathrm{exp}} \rangle$ is a consistent FCTN, where $\mathcal{T}^{\mathrm{exp}}$ is the set of temporal variables associated to the $\mathrm{CN}_{\mathrm{exp}}$ nodes, and $\mathcal{L}^{\mathrm{exp}}$ is the binary temporal constraint sets between nodes temporal variables, given as a fuzzy number representing the approximated duration of the time elapsed between the temporal variables.

Different interpretation of temporal diagnostic explanations have been proposed. In our proposal, an intermediate model has been chosen in which an abductive component is applied to explain the subset EVT^- of the inputs events (those considered as abnormal by the TBM). A consistency component is applied for both the rest of events, EVT^+ (events not explained by the TBM) and the temporal dimension. This intermediate interpretation of diagnostic explanation can be formally stated as follows:

Definition 2. FTDP explanation. Given a $\mathrm{FTDP} = \langle \mathrm{TBM}, \mathrm{EVT}, R^{\mathrm{in}}, \Pi_{\mathrm{th}} \rangle$, $\mathrm{EXP} = \langle \mathrm{CN}_{\mathrm{exp}}, R^{\mathrm{exp}} \rangle$ is a possible explanation of FTDP if:

1. $\mathrm{DFTP}(\mathrm{EXP}) \bigcup TC \models \mathrm{EVT}^- \subseteq \mathrm{EVT}$,
2. $\mathcal{R}^{\mathrm{in}} \cap \mathcal{R}^{\mathrm{exp}}$ is temporally consistent.
3. $\forall D_i \in \mathrm{DFTP}(\mathrm{EXP}), \Pi(D_i) \geq \Pi_{\mathrm{th}}$

where $\mathrm{DFTP}(\mathrm{EXP})$ stands for all the temporal patterns (contextualized or not) included in the explanations.

In other words, the explanation generated must: (1) logically entail those observations considered abnormal (EVT^-) taking into account the TBM and the current TC, (2) be consistent with the temporal information observed, and (3) be consistent with the the rest of observations, EVT^+. This condition is checked by means of the hypotheses possibility and necessity degree, as discussed in Section 6. This definition of temporal diagnosis imposed some requirements on the design of the diagnostic process in the sense that two sequential processes are necessary. The first process must abductively build the explanation taking into account temporal information, and the second process must evaluate hypotheses consistency and prune, from the explanation, those hypotheses which are inconsistent or not sufficiently supported by the observed behaviour.

5. Diagnostic process

The goal of the diagnostic process is to build a diagnostic explanation, as described in Section 4, for a FTDP (Definition 1). The diagnostic process is based on an extension of the classical method *cover and differentiate* [25,26] which has been adapted to deal with: (a) temporal component, (b) possibility theory [14] based hypotheses evaluation, and (c) the TBM described in Section 3. The main characteristics of the diagnostic process are:

- *Multiple hypotheses solution*. Several hypotheses may be found in a solution, even at the top level, representing alternatives or complementary explanation for the observed behaviour. Furthermore, different instances of the same hypothesis (the same hypothesis located at different time instants) can be included in a solution. This makes it possible to cope with *general temporal diagnosis* [3], which can be defined as an assignment of faults over time which explains both the temporal, and time-varying behaviour of patient evolution from admission to the ICU, τ_0, to time of the diagnosis, τ_{now}.
- *Parsimonious covering based diagnosis*. The proposed process explains those events considered abnormal, EVT^-, through parsimonious covering. New hypotheses are included in the final explanation to explain a given event if and only if there is no alternative instantiated hypotheses which can explain that event.

Essentially, our proposal is composed of two phases: first, a causal network (temporally consistent) is built using an abductive strategy to explain the set of events. This phase is carried out by the *temporal covering process* (TCP), described in Section 5.1. Second, some hypotheses are pruned from this causal network through HDP which will be described in Section 6. Thus, the diagnostic explanation obtained fulfills the conditions described in Definition 2.

5.1. Temporal covering process

The main objective of TCP is to build an explanation for the set of input events, EVT, which satisfies conditions 1 and 3 in Definition 2. To this end, TCP tries to explain all the events abductively, maintaining the temporal consistency of the temporal information asserted in the solution. The final explanation will explain those events in EVT considered abnormal by the TBM, and taking into account the current TC.

In addition to the input events, the generation of the complete causal network implies creating new events that are associated to each hypothesis included in the explanation, and these must be explained in the same way as the normal input events (i.e., those events in EVT marked as event to be explained). These new events make it possible for TCP to extend the explanation upwards through the causal dimension until abducibles are reached by applying TCP recursively. The algorithm finishes when it is not possible to find a higher level hypothesis that can explain any of the EVT events. These hypotheses conform the set of abducibles of the solution. TCP can be described, as follows (Algorithm 1):

- First, an event evt_i is selected from those elements in EVT which are marked as events to be explained. This event can represent either an observation or a hypothesis, as TCP works recursively. As can be deduced, the solution is incrementally built.
- Second, TCP tries to find (*evoke*, line 4) the set $\mathcal{D}$ of all possible temporal patterns in TBM that can explain event evt_i.
- Finally, the algorithm tries to explain evt_i by means of each temporal pattern in $\mathcal{D}$, and adds both the event and the temporal patterns into the solution as follows:
    - First, TCP tries to contextualize (lines 8–10) the temporal pattern. If contextualization is possible, a new instance of the temporal pattern is created and included in the explanation, and the corresponding temporal constraints are asserted in R^{exp}. Then, evt_i is associated to the new temporal pattern instance and TCP proceeds with a new event. As indicated above, a new event associated to the new instance is created and marked as an event to be explained.
    - If the contextualization is not possible, TCP tries to subsume (*subsume*( ), line 15) the event in any of the already instantiated patterns that exist in the partial solution ($\text{DFTP}^{\text{evt}_i} = \mathit{evoke}(\text{evt}_i, \text{EXP})$).
    - When the subsumption is not possible, a temporal shifting process (TSP) is applied (*temporal shifting* ( ), line 16).
    - Only if all the previous processes fail to explain evt_i, will TCP generate a new instance of the temporal pattern in the solution (generate new( ), line 19). Of course, a new event associated to the new instance is created and marked as an event to be explained.

In the following subsections, these processes will be described in detail.

Algorithm 1. The temporal covering process

```
Function TemporalCovering(TBM, EVT) return EXP
Mark all events in EVT as event to be explained
while Unexplained events remain do
  for each evt_i ∈ EVT do
    D = evoke(evt_i, TBM)
    if D ≠ ∅ then
      Mark evt_i as belonging to EVT^-
      for each dftp_i ∈ D do
        if contextualisable(dftp_i, EVT, EXP) then
          Contextualize dftp_i for each valid context
          Add to EXP each contextualized pattern that explains evt_i
        else
          DFTP^{evt_i} = evoke(evt_i,EXP)
          if DFTP^{evt_i} ≠ ∅ then
            for each dftp_j ∈ DFTP^{evt_i} do
              if possible subsume(evt_i, dftp_i, EXP)
              else try temporal_shifting(evt_i, dftp_i, EXP)
            end for
          else
            dftp_new = generate_new(evt_i, dftp_i, EXP)
            Generate a new event evt_j associated to the new hypothesis
            Mark evt_j as an event to be explained
          end if
        end if
      end for
      Mark evt_i as belonging to EVT^-
    else
      Mark evt_i as belonging to EVT^+
    end if
  end for
end while
```

5.2. New hypotheses generation

The process of generating a new hypothesis is the simplest task of TCP. A given event can be explained by a temporal pattern if it is included in the set of the pattern implied manifestations or hypotheses. Let us suppose that TCP has to explain the first event representing an *increase in precordial pain*, $\mathrm{evt}_{\mathrm{pain}}$ (see Section 3.1). Since it is the first event, TCP cannot find an instance of a temporal pattern in the explanation which explains it ($evoke(\mathrm{evt}_{\mathrm{pain,EXP}}) = \varnothing$). Hence, TCP will try to locate in the TBM those temporal patterns which might explain the event. In our example, the only temporal pattern which might explain it is AMI, defined in Section 3. In order to include this hypothesis in the explanation, a new instance of the pattern will be generated and associated to the given event. Finally, the temporal constraint $C(t_{\mathrm{AMI}}, t_{\mathrm{pain}})$ will be asserted in R^{exp}. When this constraint is propagated, a temporal constraint $C(\tau_0, t_{\mathrm{AMI}})$, which will indicate the approximate time of the appearance of the AMI, will be generated.

5.3. Subsumption

The main objective of the subsumption process is to avoid an excessive proliferation of temporally close

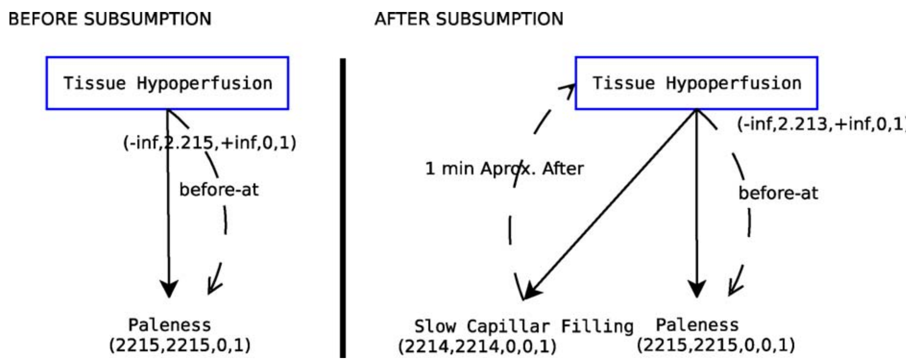

Figure 5 Subsumption process.

hypotheses. Thus, before creating a new instance of a temporal pattern in the explanation (to explain a given event), the subsumption process tries to include it in one of the already instantiated patterns, particularly those patterns in DFTP(EXP) which also explain the event.

Continuing with the example, let us suppose that TCP wishes to explain the event *slow capillary refill*, $evt_{capillary}$. In this situation, TCP will look for all the temporal patterns already instantiated in the solution which may explain this event. Suppose that the only temporal pattern instance which explains it is *tissue hypoperfusion* pattern ($TH = evoke(evt_{capillary}, EXP)$), since this was created to explain the event $evt_{paleness}$. Thus, before creating a new instance of the pattern D_{TH}, an attempt will be made to subsume the event in the existing instance.

In order to check that the subsumption is possible, it must be verified that the temporal constraints defined in D_{TH}, which involves the elements associated to the pattern in the explanation and to the new event, are consistent with the temporal location of $evt_{capillary}$. In our case, the only event associated to the D_{TH} instance is $evt_{paleness}$, and so the temporal constraints $C_{D_{TH}}(t_{capillary}, t_{TH})$ and $C_{D_{TH}}(t_{capillary}, t_{paleness})$ would need to be taken into account. The temporal query made on R^{exp} to determine whether the subsumption is possible is given in expression (7).

$$\Pi(C_{D_{TH}}(t_{capillary}, t_{TH}) \wedge C_{D_{TH}}(t_{capillary}, t_{paleness})) \qquad (7)$$

If the result of this query is greater than Π_{th} (see Definition 1), the subsumption is possible and $evt_{capillary}$ is associated to the instance TH of the temporal pattern D_{TH}. Of course, R^{exp} and CN_{exp} are also updated to take into account the new event and the associated temporal information. Fig. 5 shows the resulting causal network after subsumption. Below each element the fuzzy number representing the possibility distribution of the temporal constraint with τ_0 is shown.

5.4. Temporal shifting

Continuing with the example, let us suppose that TCP wishes to explain the event associated to the *re-elevation of the* ST *segment*, $evt_{STre\text{-}elevation}$, detected at 00:38:40 h. TCP will look for all those patterns which may explain the event. One of the patterns able to explain the event is the *tissue hypoperfusion* pattern. Since an instance of this pattern exists in the explanation ($TH = evoke(evt_{STre\text{-}elevation,EXP})$), TCP will try to subsume the event in this instance. In this case, the subsumption fails because of the temporal inconsistency of $evt_{STre\text{-}elevation}$ with some of the elements already associated to the instance. Thus, the only way of explaining the event lies in creating a new instance, $\overline{TH}$, of the temporal pattern TH at another time instant (that which is temporally consistent with $evt_{STre\text{-}elevation}$) and in associating the event to that instance. Nevertheless, it must be taken into account that the new instance may explain some of the events associated to the TH instance. Accordingly, some of the events, already associated to TH, could also be explained by the new instance of the pattern. In conclusion, TSP will produce two instances of the same pattern (at different time instants), whose hypotheses individually explain at least one different event and, perhaps, some common events. Fig. 6 shows the result of the TSP in which it has been possible to subsume only the event $evt_{paleness}$ in the new instance of the temporal pattern, $\overline{TH}$. HDP will decide which of the two instances is the more plausible, or whether they are equally plausible.

Algorithm 2 shows TSP in detail. This procedure returns a new instance of an existing pattern of the explanation. As can be shown, TSP reduces the algorithm's efficiency because of the large amount of calculi for temporal consistence checking, in spite of the local propagation of temporal constraint. In [17], the local propagation process of fuzzy temporal constraints (a fuzzy adaptation of

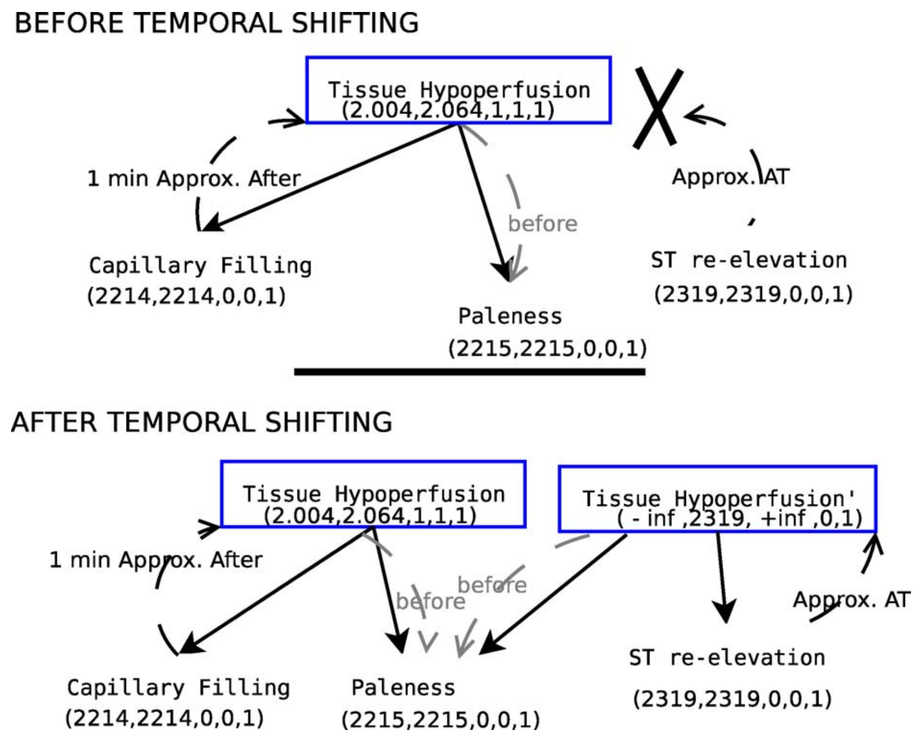

Figure 6 Temporal shifting process.

the one presented in [27]) is deeply analysed. Furthermore, this process could imply new subsumptions. This problem can be solved using some heuristics, which determine whether the hypothesis must be shifted or not. In this work, we suggest a heuristic in which only the latest temporal instance of a given pattern can be shifted. This heuristic increases the probability of finding at least one hypothesis that can explain the event. As can be deduced, temporal shifting may produce different alternative explanations for the same set of events. The alternative hypotheses of the solution must be evaluated by HDP. If TSP is applied to all the temporal instances of a given pattern, the order in which the set of inputs event are processed has no influence on the solution provided. However, due to the computational cost associated to temporal shifting, we apply the previous heuristic, which guarantees at least one temporal shifting per temporal pattern.

Algorithm 2. The temporal shifting procedure

Function $temporal\_shifting(evt_i, dftp_i, EXP)$ **return** D_{new}

$D_{new} = generate\_new(evt_i, dftp_i, EXP)$
$\mathcal{E} = associated\_events(dftp_i)$
for each $evt_i \in \mathcal{E}$ **do**
  $subsume(evt_i, dftp_i, EXP)$
end for
return $dftp_{new}$

5.5. Temporal pattern contextualization

Contextualization can be defined as the process of verifying whether the conditions that describe each TC, together with their temporal constraints, are present when a temporal pattern is selected to explain a given event. In this case, the modification

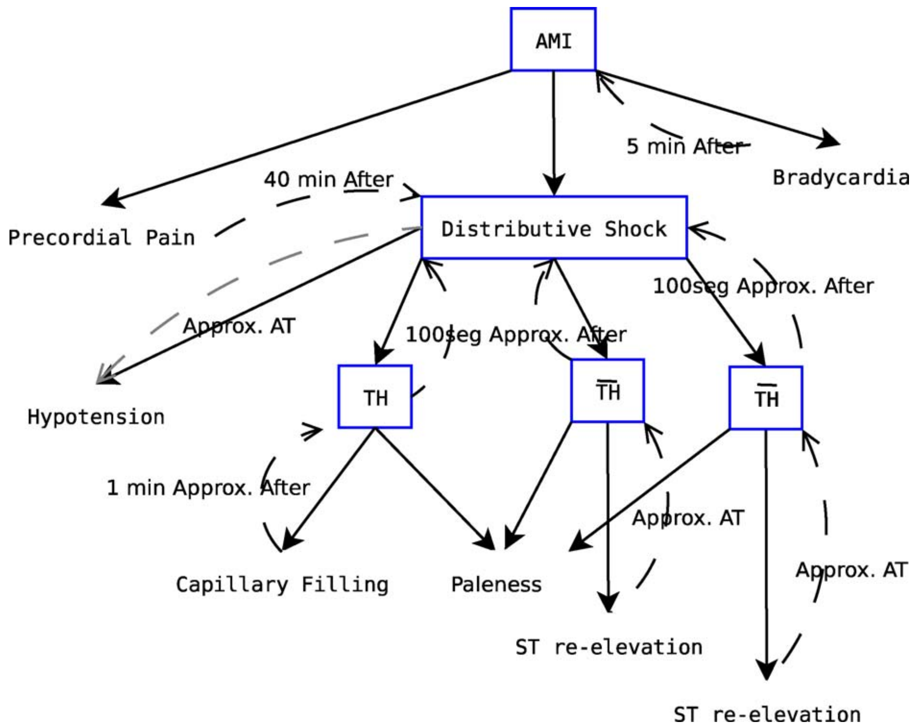

Figure 7 Diagnostic explanation for the example clinical case.

functions defined in the TC are applied to the temporal pattern definition. The process to check whether a given TC, $\mathrm{TC}_i = \langle A_i, T_i, R_i^{ct}, MF_i \rangle$, can be applied to its associated temporal pattern, $\mathrm{DFTP} = \langle \mathrm{H}, \mathrm{IM}, \mathrm{IH}, R^{\mathrm{DFTP}}, S_1, S_2, \mathrm{TC} \rangle$, is as follows:

1. First, the process tries to check that the atemporal concepts, A_i, with their corresponding attribute-value pair, are present in EVT.
2. Second, the process tries to check that the temporal concepts, T_i, are present in EVT, and their temporal constraints, R^{tc}, are consistent with those defined in R^{in}.
3. Finally, if the previous steps are verified, the process applies the modifications defined in MF_i to the temporal pattern definition.

In the example under consideration, a contextualization is produced on instantiating the temporal pattern, AMI. According to its definition (Section 3), a possible contextualization of the pattern exists if there is *dehydration* and *Solinitrine* has been administrated, and if these events fulfill a set of temporal constraints. As has been seen in the clinical case, these events are present, thus allowing the contextualization of the pattern, which in the particular case of AMI is reduced to add a new implied manifestation, *bradycardia*, with its respective S_1 and S_2 values, and the temporal constraint to the main hypothesis of the pattern.

Once the pattern is contextualized, the contextualization process checks that the pattern still explains the event, because we must take into account that some modification functions (such as *remove_implication*) could modify the causal link between the pattern and the event. Once a temporal pattern has been contextualized and instantiated to explain a certain event, no subsumption is attempted, since we assume that a contextualized pattern is the best possible explanation for a given event. Fig. 7 summarizes the causal network generated by the TCP for the clinical case used as the example.

6. Hypothesis discrimination

TCP (see Section 5) could generate hypotheses which are not sufficiently supported by the observed evidence or which may be inconsistent with some of the observations not explained by TCP. In order to eliminate such hypotheses, it is necessary to establish some measure that will indicate the degree of credibility associated to a hypothesis. The approach we propose is based on possibility theory [14], which allows us to calculate the degree of possibility and of necessity associated to each hypothesis. Such degrees allow HDP to eliminate from the final explanation all those hypotheses, which should not be included therein.

HDP (Algorithm 3) starts with the evaluation of the possibility, $\Pi(\hbar)$, and necessity, $N(\hbar)$, degrees of the abducibles generated by TCP (*abducibles*(EXP)). This evaluation triggers the evaluation downwards through the causal network of all the hypotheses (recursive function *Calculate*Π*N*). The possibility degree for each hypothesis is compared to the given threshold, Π_{th}. If $\Pi(\hbar)$ is less than Π_{th}, there is not enough evidence to confirm the hypothesis, so it is removed from explanation causal network. This hypothesis pruning is propagated downwards the causal network through implied hypotheses by applying the *conservative pruning* process (line 5 in Algorithm 3). *Conservative pruning* only removes from the explanation those elements with no alternative explanation (an alternative path to another abducible exists). In the case that an alternative explanation exists, the pruning process is stopped and the link with the explanation path pruned is removed. As indicated in Section 4, the final solution includes multiple subordinate hypotheses since it is an instantiation of the causal network.

Algorithm 3. The hypotheses discrimination function.

Function $Hypotheses\_Discrimination(EXP)$ **return** EXP

```
1: for each ab ∈ abducibles(EXP) do
2:     Π(ħ_ab), N(ħ_ab) = CalculateΠN(ab, EXP)
3: end for
4: if Π(ħ_ab) < Π_th then
5:     Conservative_pruning(ab, EXP)
6: end if
```

6.1. Hypothesis evaluation

In order to analyse the process for obtaining the degrees of necessity, N, and possibility, Π, associated to a hypothesis, we need to resort to a logic approach to TBM. A DFTP with several manifestations and implied hypotheses can be rewritten as:

$$(\hbar, t^{\hbar}) \to (m_1, t_{m_1}) \wedge \ldots \wedge (m_n, t_{m_n}) \wedge (h_1, t_{h_1}) \wedge \ldots \wedge (h_r, t_{h_r}) \wedge C(t^{\hbar}, t_{m_1}, \cdots, t_{m_n}, t_{h_1}, \cdots, t_{h_n}) \quad (8)$$

As can be deduced from temporal formula (8), TCP seeks to construct an explanation which satisfies the backward meaning of the temporal formula (abductive reasoning). Based on the evaluation of the hypotheses necessity and possibility degrees, HDP will be in charge of satisfying the forward meaning of the temporal formula (deductive reasoning).

For the sake of simplicity, let us suppose that we have a DFTP which only associates one hypothesis, $\hbar$, with one manifestation, m. In such a case, temporal formula (8) reduces to

$$\hbar \to m \wedge C(t^{\hbar}, t_m) \quad (9)$$

The degrees of necessity and possibility associated to $\hbar$, $N(\hbar)$ and $\Pi(\hbar)$, can be calculated by a combined form of *Modus Tollens* and *Modus Ponens* used in the possibility theory [14], and which in our case is reduced to expression (10). (See [24] for a complete discussion on the deduction of this expression.)

$$\begin{array}{ll} N(\hbar \to m) = S_1(m) & \\ N(m \to \hbar) = S_2(m) & \\ N(m) = b & \Pi(m) = c \\ N(\hbar) = \max(S_2, b) & \Pi(\hbar) = \max(1 - S_1, c) \end{array} \quad (10)$$

In the calculus of $N(m)$ and $\Pi(m)$, it has to be taken into account that for an implied manifestation to be considered as a necessary condition of $\hbar$, the estimated appearance time of the pattern must occur before τ_{now}, the time at which the diagnostic process began. This means that the absence of a manifestation — but one which according to the information in the temporal pattern may, nevertheless, still occur — may contribute positively to the consistency of the hypothesis. Hence, a new, disjunctive term in the consequent of equation (8) must be added:

$$\hbar \to (m \wedge C(t^{\hbar}, t_m)) \vee be\,fore(\tau_{\text{now}}, t_m) \quad (11)$$

Therefore, the possibility degree of a given manifestation can be formulated as follows:

$$\begin{aligned} \Pi(m) &= \Pi(m \wedge C(t^{\hbar}, t_m) \vee be\,fore(\tau_{\text{now}}, t_m)) \\ &= \max(\Pi(m \wedge C(t^{\hbar}, t_m)), \\ &\qquad \Pi(be\,fore(\tau_{\text{now}}, t_m))) \end{aligned} \quad (12)$$

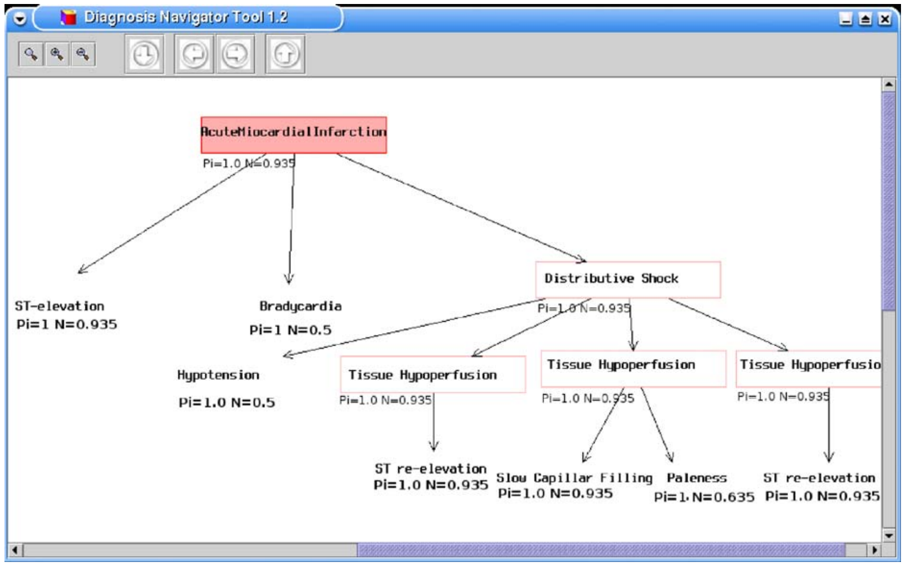

Figure 8 Diagnostic explanation for the clinical case used as example.

It needs to be taken into account that in temporal query $\Pi(m \wedge C(t^h, t_m))$ is implicit in the query on consistency. In the case of an event associated to the manifestation in the explanation, a high possibility value will be returned. If the associated event does not exist, or another event exists, the possibility value will be low, or even 0. In the same way, $N(im_i)$ can be defined as follows:

$$N(m) = \max\left(N(m \ \wedge \ C(t^h, t_m)) \vee N \times (before(\tau_{now,t_m}))\right) \quad (13)$$

For the evaluation of implied hypotheses we must take into account two different situations:

1. If the implied hypothesis has been explained by TCP, expression (10) is applied in a recursive way.
2. If the implied hypothesis has not been explained, nothing can be said about the hypothesis, and therefore it is completely possible that it occurs, $\Pi(ih_i) = 1$ (no evidence to refute it), although there is no certainty of its occurrence, $N(ih_i) = 0$.

Finally, it has to be taken into account that several implied hypotheses and manifestations can contribute to the evaluation of $\Pi(\hbar)$ and $N(\hbar)$. In this case, they can be combined by means of expressions (14) and (15)[14].

$$N(\hbar) = \max_k (N^h_{mh_k}) \quad (14)$$

$$\Pi(\hbar) = \min_k (\Pi^h_{mh_k}) \quad (15)$$

where mh stands for all the manifestations and implied hypotheses included in the temporal pattern; $N^h_{mh_k}$ and $\Pi^h_{mh_k}$ stands for the contribution to the global pattern's necessity and possibility degree due to implied manifestation or hypotheses mh_k.

The possibility and necessity degrees calculated for the causal network provided by HDP can be seen in Fig. 8. As can be seen, no conservative pruning is performed on the example. This is due to the selection of $\Pi_{th} = 0$. Other values could be considered for this threshold (always belonging to [0,1] interval) which could affect TCP, since conditions for subsumptions are more restrictive. Nevertheless, the selection of $\Pi_{th} = 0$ allow us to illustrate all the concepts introduced in this paper in a concise manner.

7. System implementation

Initially, the aim of this work was the development of a real-time diagnostic system to support the patient monitoring process. However, experts' suggestions, the nature of the work at an ICU and performance analysis (explained latter in this section) shifted the initial objective towards the development of an off-line diagnostic system to assist physicians in writing the different reports legally required (admission and discharge reports, as well as those related to daily evolution). Monitoring and therapy are important problems in contemporary medicine, but quality of care issues cannot be left aside. In this sense, this work was reoriented to the design of a diagnostic agent. This agent can be used

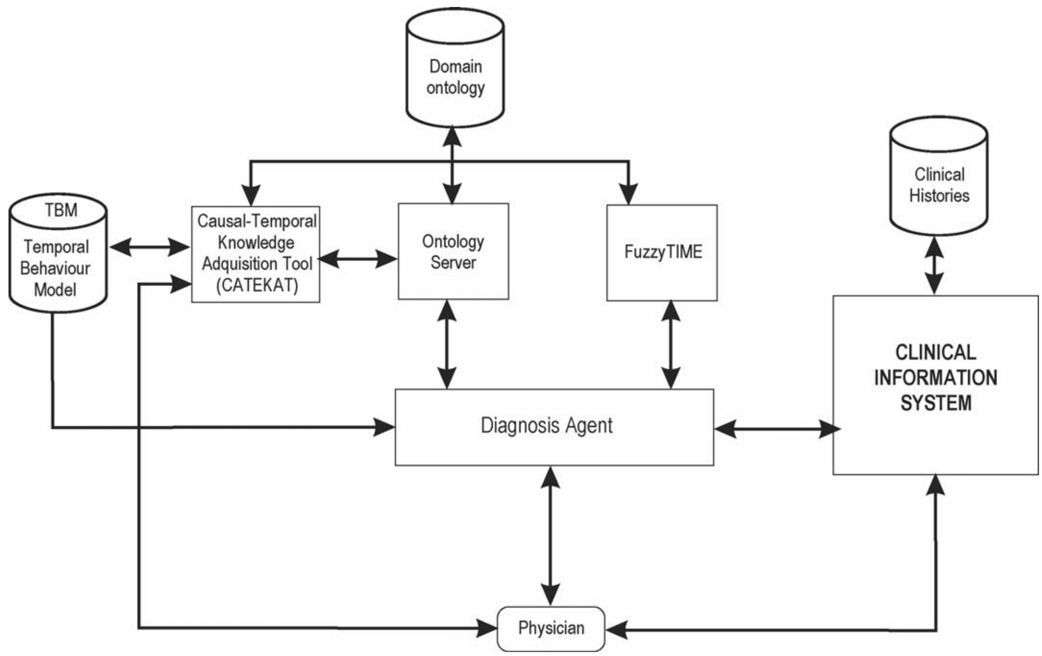

Figure 9 System architecture.

by physicians to check if what they write in a report is coherent with the explanations provided by the agent, which can be seen as a summary of the complete patient evolution.

A general modular description of our implemented system is shown in Fig. 9. The diagnostic agent is integrated with a clinical information system developed by our group with the suggestions of the medical staff. This information system provides capabilities for automatic generation of reports with the information stored about the patient. When a report is generated, the diagnostic agent tries to build an explanation of the patient evolution, and present it to the physician (see Fig. 8). This explanation can be used to verify the diagnosis and disorders provided in the report.

One of the main problems that the process of implementing this system must deal with is the acquisition of knowledge necessary for creating instances of the DFTP in the TBM. The complexity of the TBM presented forced us to design a set of components to reduce the knowledge acquisition bottleneck. The first component is CATEKAT which is a web-based collaborative knowledge-acquisition tool [28,29]. This tool allows us to acquire knowledge (including contextual temporal meta-knowledge described in Section 3.2) directly from an expert and to detect temporal inconsistencies, if any, in the temporal information provided. This is done by applying constraint propagation to the temporal relation provided by the medical expert, thus obtaining the equivalent minimal constraints and detecting inconsistences. CATEKAT is also in charge of automatically asserting what we call default temporal constraints; as mentioned in Section 3.1, this is necessary to avoid medical experts asserting temporal information that is inconsistent with the standard axiom which states that a disorder precedes the onset of its manifestations. Every task related to the temporal reasoning is delegated to FuzzyTIME, which has already been briefly described in Section 2.

The other component is the domain ontology, which represents the concepts that can be used in the description of diseases, in our case, it is restricted to diseases related to cardiac insufficiency. The use of the domain ontology restricts the user to those concepts that can be actually used for defining DFTP, thus reducing the experts' cognitive load in defining diseases.

The diagnostic agent has been evaluated through a process divided in two phases. In the first phase, we have focused our attention on verification issues and performance analysis. The verification process was made using artificially generated TBMs, and by changing some parameters, which allows us to accomplish the performance analysis under different assumptions. The objective of performance analysis was not only to obtain an absolute measure of execution time, but to assess scalability issues. The parameters used in the performance analysis are [30]:

- *The number of inputs events*. It is obvious that the more evidences to be explained, the more time is required to obtain a solution, i.e., time

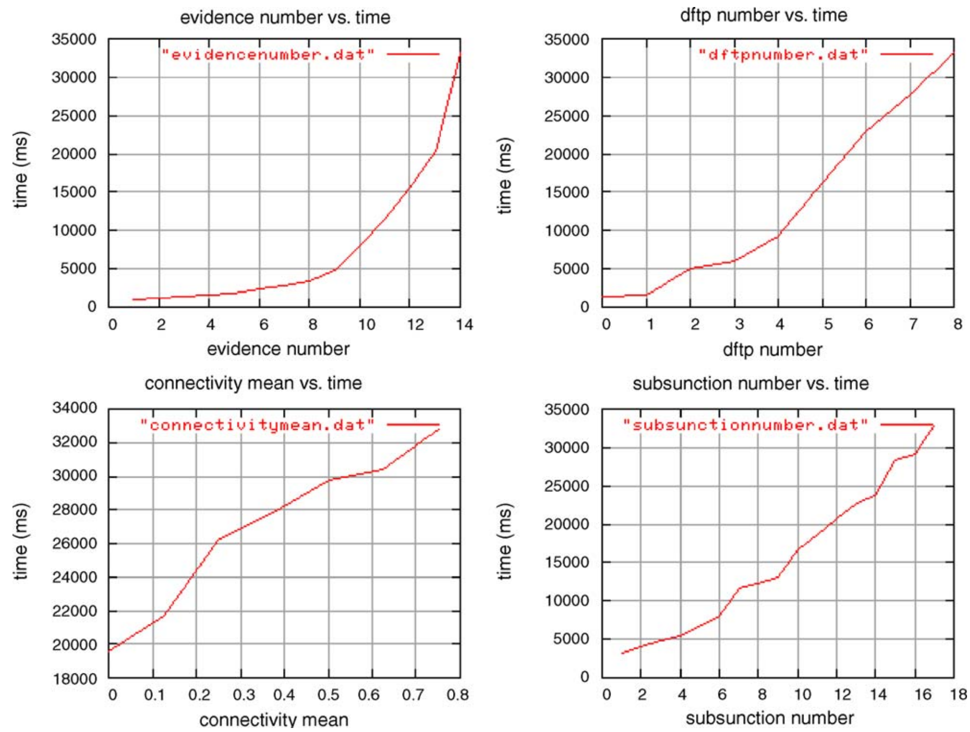

Figure 10 Experimental results of the algorithm. Prototype: Java; processor: AMD Athlon XP; frequency: 1.53 GHz; RAM: 256MB.

necessary to find patterns in TBM, testing if subsumptions are possible and temporal constraints propagation in new hypotheses generation, subsumption and temporal shifting. As is shown in Fig. 10(top left), the execution time presents an exponential behaviour over time.

- *The number of patterns* required to find a solution (Fig. 10(top right)). This parameter shows how the number of DFTPs in the solution affects the performance, and it shows a linear behaviour.
- *Mean pattern connectivity degree* (K_m). Let us define connectivity (K) of a pattern (DFTP) in the TBM as follows: $K_{\mathrm{DFTP}} = |\mathrm{IH}|$, i.e., the number of patterns' implied hypotheses. Then, K_m can be defined as:

$$K_m = \frac{\sum_{\mathrm{DFTP} \in \mathrm{TBM}} K_{\mathrm{DFTP}}}{|\mathrm{TBM}|} \tag{16}$$

where $|\mathrm{TBM}|$ is the number of DFTPs in the TBM. K_m can be considered as a mesure of the TBM complexity and is associated to the complexity in building $\mathrm{CN}_{\mathrm{exp}}$ upwards from the first implied hypothesis to abducibles (Fig. 10(bottom right)).
- *Number of subsumptions* performed. As can be seen in Fig. 10(bottam right)), execution time depends linearly on the number of subsumptions. This is due to the use of local propagation in the constraints propagation process.

The aim of the second phase of the evaluation process is to test if the system produces the correct solutions. To this end, a complete TBM and real patient data are required. The specification of the TBM restricted to disorder related to cardiac insufficiency is currently under development. The use of CATEKAT by physicians required some sessions in order to demonstrate how diseases can be defined. And, regarding to the data, the information system is being deployed in an ICU. The final objective is to perform, in the near future, a complete clinical evaluation with the system integrated into the hospital infrastructure and in real conditions.

8. Conclusions

This paper describes a general framework for TMBD which can deal with the time varying behaviour found in the medical domain. The proposed model provides solutions to the problems of modelling complex interaction between deep causal models and context knowledge, evaluation of hypotheses possibility degree, and the structure and the expressiveness of the solution. Time is modelled by means of a metric time-ontology, in which temporal information is represented by FTCN [15,16], although qualitative temporal constraints are allowed for knowledge acquisition purposes.

Different interpretations of temporal diagnosis explanation have been proposed by MBD community, ranging from totally consistency-based diagnosis [2,31], in which the explanation provided should be consistent with all the observations, to totally abduction-based diagnosis [5,32], in which the explanation should logically entail all the observations. The same considerations can be made for temporal dimension. Brusoni et al. [3] present a generic knowledge level model for TMBD in which the definition of explanation has been parameterized. This parameterization allows the definition of explanation to be moved along the continuous line defined between totally consistent diagnosis and totally abductive diagnosis. In our proposal, we choose an intermediate model in which an abductive component is applied to explain a subset of the inputs events, those considered as abnormal by the TBM, i.e. EVT^{-}. A consistency component is applied for the remaining of events, EVT^{+} (events not explained by the TBM), and the temporal dimension.

The concept of temporal pattern has been used by various authors in the medical domain. In [33,34] diseases are described using a graph in which the temporal constraints of the associated manifestations are specified. The temporal constraints are expressed through qualitative temporal relations, although these are stored as metric point to point relations in an FTCN. The distinction between necessary and possible manifestations makes partial graph recognition possible (necessary manifestations must be present). Hypotheses evaluation requires information about the intensity of the causal links and manifestations, given by a possibility distribution. Our proposal presents a more general model, since it allows causal relations between diseases, thus conforming a causal network. Furthermore, our method for hypotheses evaluation is based on inference mechanisms based on possibility theory [14]. Finally, another advantage of our model lies in the knowledge acquisition process, since our equivalent to the information on intensity of causal links (functions S_1 and S_2 in the definition of temporal patterns) is specified in terms used in evidence-based medicine, thus facilitating the model building process.

In the ATD system [6], used for the diagnosis of hepatitis B, diseases are described as processes, segmented in states in which temporal constraints are described using Allen's interval algebra. The causal relations included in the processes are used to evoke those processes, which explain the observations, and temporal constraints are used to force temporal consistency between the constraints defined in the process and those defined in the observations. However, causal relations between diseases are not allowed. Neither are there mechanisms for the evaluation of hypotheses, nor for differentiation of simultaneous processes. In the Déjà Vu system [10,35], the scenario concept is used to describe the physiological evolution of the diseases. In the same paper a disease is described through a sequence of events and a temporal network to represent constraints between the elements. Partial recognitions of scenarios are allowed, as in our proposal. The evaluation of recognized scenarios is made with an index which only takes into account those aspects related to the temporal proximity between the scenario and the constraints network representing the real case. However, the case in which the same scenario can appear in different time instants is not taken into account, and nor is the causal relation between diseases. A similar model to that used in the Déjà Vu system is presented in [36—38], with the difference that only the scenarios are modelled as constraints networks, with the input events being indicated by absolute dates.

One of the main contributions of our proposal is related to the possibility of modelling complex contextual interactions, such as hose found in medical domains. In classical TMBD models contextual knowledge is modelled as atoms, which are not included n the observations sets and can be added in the antecedent of diagnostic rules [3,5,12]. Our model allows elements from the observation set to be included in the description of diagnostic rules modifications, making it possible to capture complex contextual situations in a more compact way. This is possible since contextual knowledge is orthogonal to the temporal behaviour model.

Another contribution of our work is that different instances of the same diagnostic hypothesis, but located at different time instants, can be found in the same diagnostic solution. Finally, regarding the expressivity of the solution, as in other approaches, the solution conforms a causal network entailing the abnormal observations, including pathophysiological and etiological states. However, in our causal network, different instances of the same temporal pattern can exist in a given solution, since patterns are dynamically instantiated and linked to build the final solutions. Other approaches [5,9—11,34] only provide portions of a single tightly linked causal network. Nevertheless, providing the complete causal network facilitates integration with medical decision-making processes. To this extent, we have tried, as far as possible, to adapt the description of the behavioural model to the medical domain in order to facilitate knowledge acquisition.

There is a number of limitations in our proposed model. Despite the advantages of modelling temporal imprecision using a fuzzy approach, some works [39] argue that non-probabilistic methods, such as fuzzy logic, are often difficult to understand, and they propose simpler strategies in medical decision support systems. However, the use of adequate knowledge acquisition tools, like CATEKAT [28,29], provides a suitable way of solving this problem by isolating medical staff from internal representation of knowledge. As in most fuzzy systems, the selection of possibility distributions parameters is subjective, but these parameters are fixed in FuzzyTIME. However, and thanks to CATEKAT, it is possible to check if the constraints provided by experts are mutually consistent.

The use of TCs allow us to take into account that, for example, a patient evolution can be modified by a given therapy. However, a cost must be paid, since it is necessary to describe contextual knowledge explicitly. This is possible in our case since our domain is restricted to Cardiac Insufficiency, including the most common contexts such us anamnestic information, demographic and therapy information. Furthermore, the use of CATEKAT makes the specification of TCs from expert a simple task and facilitates the detection of redundancies and inconsistencies.

Some of these limitations have been addressed in an ongoing work on the optimization of the diagnosis process, especially in reducing the amount of computation in the temporal constraints propagation process. Other improvements are focused on extending the model to cope with time intervals to model observation and disorder persistency. Among future works, we will try to integrate the diagnostic agent in a Case-Based Reasoning system, in order to improve the quality of the diagnosis reached and to provide users with retrospective clinical histories similar to the one being analysed. Finally, temporal data mining techniques based in the DFTP model proposed in this paper are being developed.

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