Chapter 6: Time in Clinical Diagnosis

Carlo Combi\textsuperscript{1}  Elpida Keravnou-Papailiou\textsuperscript{2}  Yuval Shahar\textsuperscript{3}

Author of the slides: Elena Gaspari\textsuperscript{1}

\textsuperscript{1}Department of Computer Science, University of Verona
\textsuperscript{2}Department of Computer Science, University of Cyprus
\textsuperscript{3}Department of Information Systems Engineering, Ben Gurion University
Outline I

1. Introduction
   - A Historical Perspective

2. Diagnostic Notions
   - Consistency-Based versus Abductive Diagnosis
   - Diagnosing under the Assumption of Multiple Disorders
   - The Simplest Representation: Associational Disorder Models
   - The Causal-Temporal-Action Model
   - Deriving the ‘Best’ Diagnostic Solution
   - Illustrating some of the Temporal Requirements for Clinical Diagnosis
Outline III

- Case III: Occurrences with Duration and Relative Constraints
- Temporal Constraints in Causal Networks
Diagnostic problem solving has attracted and continues to attract considerable interest in the AI community simply because it is a difficult task to model.

- One such challenge is the modeling of time.
- The majority of diagnostic systems deal with clinical domains.
A Historical Perspective II

Pioneering diagnostic systems:

- MYCIN,
- INTERNIST-1,
- CASNET,
- ABEL.

These systems did have a number of shortcomings, some of which were attributed to their inability to model and reason with time.
In **MYCIN**, whose domain was antimicrobial infections, some of the contexts (objects of reference for the system’s rules) were distinguished into *past* and *current*, e.g. past cultures, current cultures, past organisms, current organisms, etc.
CASNET’s best known application was the domain of glaucoma. The central knowledge structure in this system was a causal network of pathophysiological states from causes to effects. CASNET’s inferencing comprised two main reasoning mechanisms:

- the assignment of confidence factors to simple hypotheses referring to pathophysiological states,
- the construction of complex hypotheses of causal chains of pathophysiological states.
The creators of **INTERNIST-1** for the broad domain of internal medicine, did acknowledge that the absence of time was a source of problems for the performance of the system.

The *presentation time* of disorders was implicitly included in the disorder models through attribute AGE.

For example, the frequency of occurrence of cardiac sarcoma primary amongst people between the ages of 16 and 25 is low and hence the hypothesis of this disorder would not be evoked for patients in this age group.
Causality was not a central relation in INTERNIST-1’s disorder models, although a number of complementary relations between disorders, such as predisposes, causes, caused-by, etc. were included in the system’s vocabulary. Such relations were used for promoting the consideration of some disorder hypothesis in light of the conclusion of one of its complementary disorders.
Temporal data abstraction appeared in the PATREC system that acted as an intelligent manager of patient data, in assistance to MDX, a diagnostic system for the syndrome of cholestasis.

- PATREC’s ‘intelligence’ was primarily drawn from hierarchical structures of medical concepts, that enabled the derivation of abstractions from raw data.
- The diagnostic rules used by MDX could make use of such notions and the patient data could make references to time.
PATREC was able to match the raw patient data against the more abstract expressions used in the diagnostic rules. This matching involved some kind of temporal reasoning.
Diagnostic Notions

Definition

A **diagnostic problem** with respect to some artificial or natural system, a person say, arises when at least one observation (of abnormality) is made suggesting that the particular individual is not functioning ‘normally’.

A solution to the problem, referred to as **diagnosis**, is an **explanation** of the abnormal functioning.
Generally there are two paradigms of diagnostic problem solving:

1. the *consistency-based* paradigm,

2. the *abductive* paradigm.
Consistency-based diagnosis advocates the use of models of normal behavior such as structure-and-function models describing the normal decomposition and functioning of natural organisms or artifacts.
A solution to a diagnostic problem is a set of abnormality assumptions:

- An abnormality assumption states that a (replaceable) component is abnormal.
- The behavior generated when the model of normal behaviour is perturbed under the given set of abnormality assumptions, must be consistent with the observed abnormalities.
- Consistency means that nothing is entailed which is in conflict with the observations to be explained.
A malfunctioning organism is treated by reverting the abnormal components back to normal behaviour.

- In the case of artifacts this is easily done, simply by replacing the abnormal primitive components with new ones.
- This course of treatment is not usually viable for natural organisms.

The malfunctioning ‘components’ need to be brought back to normality, or as close to normality as possible, by other means, such as the administration of drugs, operative actions, etc.
For these courses of action to be effective it is necessary to point out, at a sufficiently detailed level, the causes of the observations of abnormality.

This is the essence of abductive diagnostic problem solving.

Clinical diagnosis centers around disorders and as such the prevailing paradigm is that of abductive diagnosis. Disorder models are therefore a central knowledge structure. Models of normal behaviour are not excluded and in fact are often used as a special kind of model (background model) in conjunction with the disorder models.
Abductive diagnostic reasoning comprises the *generation* and *evaluation* of diagnostic hypotheses as two distinct but tightly coupled steps.

The reasoning is performed under the assumption of *single* or *multiple disorders*.

The assumption of multiple disorders is broader in scope, but the generation of possible combinations of disorders is often a computationally complex process.
The use of appropriate heuristics can make this process tractable by pruning the search space.

If the reasoning is atemporal, multiple disorders essentially means multiple *concurrent* disorders ⇒ *This is restrictive.*
Diagnosing under the Assumption of Multiple Disorders III

- **CASNET** had complex hypotheses, i.e. paths in the causal network.
  - Individual pathophysiological states on such paths constituted simple hypotheses.
  - Given the atemporal set up under which the system reasoned, one could say that:
    1. either it was assumed that once a state was brought into existence, it persisted indefinitely,
    2. or that when a state began to exist its causal predecessor(s) ceased to exist, thus giving rise to disjoint existences.
Diagnosing under the Assumption of Multiple Disorders IV

INTERNIST-1 also operated under the multiple disorders assumption.

- The conclusion of one disorder could promote the consideration of active hypotheses that were related with the concluded disorder.
- This way the system tried to piece together, in a sequential fashion, a complex hypothesis whose components exhibited some sort of coherence through some complementary relation.
When a diagnostic system deals with complex hypotheses (as it is the case when it operates under the multiple disorders assumption) a further consideration is whether a complex hypothesis is constructed in a parallel or sequential fashion.
Parallel fashion means that the entire complex hypothesis is fully constructed before it may be concluded in its entirety.

Parallel reasoning is often based on the requirement that a complex hypothesis should be as coherent as possible, i.e. its components should be related in some way.

Sequential fashion means that the individual components comprising the (as yet unknown) complex picture are separately selected and concluded and this progressive way of construction continues, possibly in a ‘blind’ fashion, until the picture is considered complete.
Sequential reasoning does not necessarily guarantee coherence and has the drawback of propagating erroneous conclusions. But obviously sequential reasoning is computationally more tractable than parallel reasoning.
Diagnosing under the Assumption of Multiple Disorders VIII

Consider the simple causal network given in Figure 1. Disorder $d_1$ can cause manifestations $m_1$ and $m_2$, while disorder $d_2$ can cause manifestations $m_3$ and $m_4$. These two disorders are related in a complementary fashion since $d_1$ can act as a predisposing factor for $d_2$. Finally, disorder $d_3$, which is unrelated to the other two, can cause manifestations $m_2$, $m_3$, and $m_4$.

Let us assume that the findings of the patient in question refer to the presence of all four manifestations. Applying sequential reasoning to this case would result in the conclusion of $d_3$ and $d_1$. Disorder $d_3$ is concluded first because it represents the 'best' single hypothesis, as it explains 3 out of the 4 findings. Reasoning by considering simple, single disorder hypotheses in sequence, has resulted in an incoherent complex conclusion since its two components, disorders $d_1$ and $d_3$, are unrelated.

Parallel reasoning, on the other hand, considers at once complex, multi-disorder hypotheses. The competing hypotheses are $\{d_1, d_2\}$ and $\{d_1, d_3\}$. The first one is concluded because of its coherence.

CASNET applied parallel reasoning at the level of complex hypotheses (causal chains of states). INTERNIST-1 used sequential reasoning, which was shown to be prone to erroneous conclusions.

**Figure:** Sequential vs Parallel Construction of Complex Hypotheses
The simplest kind of a disorder model is an *associational model*.

- A disorder is modeled in terms of its external, observable manifestations.
- Such a model is appropriately represented as a set of manifestations.
Diagnostic knowledge forms a bipolar structure, with the disorders residing on a higher (unobservable) plane and the manifestations on a lower (observable) plane. The associations from disorders to manifestations express causality at the highest level.
The Simplest Representation: Associational Disorder Models III

Example

Consider the following diagnostic problem, in connection with the disorder models of Figure below. The findings of the patient in question assert the presence of \( m_2, m_3 \) and \( m_4 \) and the absence of \( m_1 \). More specifically, \( m_2 \) appeared, then disappeared and then appeared again.
The Simplest Representation: Associational Disorder Models IV

Example

- The appearance of \( m_3 \) followed the start of the second appearance of \( m_2 \), the two overlapped and continued together.
- The appearance of \( m_4 \) preceded the first appearance of \( m_2 \).
- The contextual information that this person is currently undergoing treatment a is known.
The Simplest Representation: Associational Disorder Models V

Figure: Associational Disorder Models
The only information that can be considered is the presence of $m_2$, $m_3$ and $m_4$ and the absence of $m_1$.

There are three potential hypotheses:

- the two simple hypotheses, that either $d_1$ or $d_2$ is the cause of the patient’s situation;
- the complex hypothesis that both disorders are operative in the patient.
The Simplest Representation: Associational Disorder Models VII

- Disorder $d_1$ on its own explains the presence of $m_2$ and $m_3$ but is in conflict with the absence of $m_1$ and does not explain the presence of $m_4$.
- Disorder $d_2$ on its own explains the presence of $m_2$, $m_3$ and $m_4$ and is not in conflict with the absence of $m_1$. 
Given that the coverage of the hypothesis that $d_1$ is present is a subset of the coverage of the hypothesis that $d_2$ is present, there is no justification in pursuing the complex hypothesis since its explanatory power will not be any higher and what’s more it will inherit the conflict between $d_1$ and the absence of $m_1$. 
The Simplest Representation: Associational Disorder Models IX

Figure: Considering the Effects of Therapeutic Actions
The Simplest Representation: Associational Disorder Models X

Figure above extends the knowledge to include the effects of therapeutic action $a$.

- Action $a$ inhibits $m_1$ but gives rise to $m_4$.
- When the two hypotheses are now considered in conjunction with $a$, they appear equally favorable.
The Simplest Representation: Associational Disorder Models XI

By bringing action a into the scene, a dilemma is created, since the simple associational descriptions of the two disorders and the effects of the action do not provide any means for differentiating between the two competing hypotheses.

The next step is to take into account causality and time, thus enabling the modeling of disorders, therapeutic actions and patient states, as dynamic, evolving processes.
The Simplest Representation: Associational Disorder Models XII

**Figure:** Adding Internal States in Disorder Models and Considering the Effects of Therapeutic Actions
The Causal-Temporal-Action Model I

Definition

An associational disorder model can be extended into a causal model by adding some detail about the causal mechanisms underlying the given associations.

This can be done in a number of ways.

- A simple way is to intercept another (unobservable) plane of internal pathophysiological states between the disorder and manifestation planes.
  - The evolution of disorders is thus described in terms of intermediate states.
The Causal-Temporal-Action Model II

- Disorders point to their starting states, states point to states that form their direct consequents in the causal chains.

- Temporal constraints occupy a fourth plane, orthogonal to the tri-planar hierarchical structure, since they can refer to any entity or link, within or between planes.

- By definition temporal constraints, specify constrains on the existence of disorders, states and manifestations.
The Causal-Temporal-Action Model III

Temporal constraints in $d_1$

Temporal constraints in $d_2$

Figure: Extending Disorder Models with Temporal Constraints
The extended diagnostic knowledge model, **Causal-Temporal-Action model (C-T-A model)** is given in Figure below.
The Causal-Temporal-Action Model V

Figure: Causal-Temporal-Action Model
The patient findings are shown in next Figure and listed below. As can be seen the temporal information is no longer ignored.

- $f_1$: first appearance of $m_2$
- $f_2$: second appearance of $m_2$
- $f_3$: appearance of $m_3$
- $f_4$: appearance of $m_4$
- $f_5$: absence of $m_1$
- $f_6$: $f_2$ precedes $f_3$
- $f_7$: $f_4$ precedes $f_1$
The Causal-Temporal-Action Model VII

Figure: Patient Findings
The Causal-Temporal-Action Model VIII

Example

All patient data are considered, including the recurrence of $m_2$ and the temporal relations between manifestations. In addition the contextual finding about the ongoing execution of action $a$ is borne in mind:

$f_8$: therapeutic action $a$ is under execution, having started at a certain point in time prior to the appearance of $m_4$. 
The following hypotheses are considered:

- The first hypothesis says that disorder $d_1$ is present.
  - This would explain findings $f_1$, $f_2$, $f_3$ and $f_6$.
  - However it is in conflict with $f_5$ and it does not cover $f_4$ and $f_7$.
  - The absence of $m_1$, an expected manifestation of $d_1$, could be attributed to $f_8$ since $a$ is known to inhibit $m_1$.
  - Similarly the appearance of $m_4$ could be attributed to $f_8$.
  - Thus the hypothesis that $d_1$ is present in the context of $f_8$ explains all patient findings and there is no conflict.
The second hypothesis says that disorder $d_2$ is present.

- This would explain just one appearance of $m_2$, $f_3$ and $f_4$.
- This hypothesis is not in conflict with $f_5$ but it is in conflict with $f_6$ and $f_7$.
- As before, $f_8$ is called into play to see whether it would enhance the plausibility of the hypothesis.
- As a result, the first hypothesis wins hands down, whilst previously our ignorance of time (and the omission of contextual information) had given rise to an erroneous diagnosis.
The Causal-Temporal-Action Model XI

- The C-T-A model gives a very high view of diagnostic knowledge, that does not make any commitments as to the representation of causality, actions and time.

- For each approach discussed we examine which of the five planes comprising the C-T-A model are included and in the case of the temporal constraints plane in particular.

- Briefly, we can say that in almost every approach therapeutic interventions are ignored. A notable exception is the Heart Disease Program (HDP).
A diagnostic problem often has multiple potential solutions.

Generating such potential solutions is one challenge of diagnostic problem solving.

Another challenge is selecting the ‘best’ potential solution.

In clinical diagnosis different criteria may be used in combination for the evaluation of hypotheses.
In simple domains where the *closed world assumption* may be viably applied simple criteria such as minimality based on cardinality or entailment may be sufficient for selecting the best explanation. Clinical domains are rarely simple given the inherent uncertainty and incompleteness of clinical knowledge and patient data.

- To start with, the requirement for a diagnostic solution to be a cover (of observations of abnormality), often is not attained.
Observation

An evaluation mechanism would need to balance the observations of abnormality that are entailed by a diagnostic hypothesis against those that are not entailed, taking into consideration the significance of the various observations. Other criteria are also used, for example integrity and coherence are important for complex hypotheses.
Evaluation of hypotheses

The evaluation of hypotheses involves **deductive reasoning** in order to discover what is entailed by some hypothesis. Hence, the generation and evaluation of hypotheses (comprising the abductive paradigm) is also referred to as the **hypothetico-deductive** model of reasoning.
Illustrating some of the Temporal Requirements for Clinical Diagnosis

**Figure:** High Level Causal Network Illustrating the Action of Buphenine

- **Administration of buphenine (A)** causes
- **Release of buphenine in blood stream (R)** causes **Adverse side-effects (E)**, which includes **anxiety** and **insomnia**.
- **Prevention of premature labour (P)** causes **Relaxation of uteral muscles (U)**, which is part of **Bed rest (B)**.
Illustrating some of the Temporal Requirements for Clinical Diagnosis II

Example

Previous Figure gives a causal network illustrating, at a high level, the action of buphenine. This active ingredient is administered to pregnant women to reduce the chance of premature labor. Buphenine is released rapidly into the blood stream causing the relaxation of the uteral muscles. This reduces considerably the possibility of premature labour.
At this level we see that the administration of buphenine (process A) is a periodic process, involving a sequence of "instantaneous" events, "oral administration of a 15mg capsule of buphenine."

Next Figure analyses the relevant processes at a more detailed level.

Illustrating some of the Temporal Requirements for Clinical Diagnosis

Combi, Keravnou, and Shahar

Chapter 6: Time in Clinical Diagnosis

Consistency-Based versus Abductive Diagnosis

Diagnosing under the Assumption of Multiple Disorders

The Simplest Representation: Associational Disorder Models

The Causal-Temporal Action Model

Deriving the Best Diagnostic Solution

Illustrating some of the Temporal Requirements for Clinical Diagnosis
Illustrating some of the Temporal Requirements for Clinical Diagnosis IV

**Figure**: Temporal Analysis of Processes of previous Figure
The release of the active ingredient into the blood stream (process $R$) is a direct effect of process $A$.

Process $A$ is an intermittent process since there are gaps between its discrete components — the time interval spanning it is nonconvex.

Process $R$ starts 10 minutes after the initiation of process $A$ and terminates 8 hours and 10 minutes after the termination of process $A$. 
The relaxation of the uterine muscles (process $U$) is treated as a direct effect of process $R$.

The analysis of process $B$, ‘Bed rest’ is more qualitative. One extreme scenario is that it is also a continuous process, running concurrently with process $U$.

Processes $U$ and $B$ jointly cause process $P$, ‘prevention of premature labour’.

Process $P$ is a continuous process that hopefully lasts the duration of process $R$. 
Finally process $E$, ‘adverse side-effects’, can be analysed into the individual adverse side-effects. These represent its components.

The above description of the particular therapeutic process could be of relevance to a diagnostic system whose scope includes diagnostic problems relating to pregnancy.
Illustrating some of the Temporal Requirements for Clinical Diagnosis VIII

This example has illustrated a number of temporal requirements:

- **uncertainty**, expressed in a metric (ranges of intervals) or relative way (possible temporal relations),
- **convexity or non-convexity of processes** (continuous or non-continuous processes),
- **periodicity,**
- **temporal constraints of causal relations,**
compound processes with conditional components and multiple granularities (minutes, hours, weeks).

These requirements apply both to diagnostic knowledge and patient data. In addition, the need for temporal data abstraction with respect to patient data arises.
The Heart Disease Program I

Definition

The **Heart Disease Program (HDP)** diagnoses disorders of the cardiovascular system.

The diagnostic knowledge is modeled as a *Bayesian probabilistic network*.

- The nodes of the network represent pathological states, manifestations, or therapies.
The arcs represent causal relations, although an arc from a therapy to a pathological state represents a ‘correcting’ action (the therapy causes the ceasing of the pathological state).

As a result temporal constraints on the causal relations were then explicitly represented and the patient data became time-stamped entities.
The Heart Disease Program III

Figure: Temporal Model of a Causal Relation in HDP
The Heart Disease Program IV

- **Onset** is the range of time that can be assumed for the effect when it is observed.

- **Delay** is the range of time the cause must be true before the effect can start (this includes the onset time).

- **Persist** is the range of time that the effect will remain if the cause ceases to be true.

- **Max-exist** is the maximum time the cause will remain, even though the effect continues.

Onset, delay, etc., are **time intervals**. The possible durations of these intervals are expressed probabilistically.
A causal relation is classified as *self-limiting* if the abnormality ceases by max-exist without any rectification action while a state is classified as *intermittent* if it is absent over subintervals of the interval in which it is true.

The temporal constraints associated with causal relations are interpreted on the basis of the following rules:

1. When a node is observed, it is assumed to already be producing effects for onset time.

2. Effects are observable at a time after the cause given by the delay, if it exists, otherwise by the onset.
Effects are observable after the cause is observable and overlap the cause.

Effects continue until the cause ceases, unless the max-exist is exceeded or the effect is intermittent.

Effects continue after the cause ceases, in accordance with the persist.
The above temporal model of a causal relation enables the representation of different patterns of causality such as:

- **immediate**: the effect happens immediately,
- **progressive**: the effect, once it takes place, continues and often worsens,
- **accumulative**: when a cause is required to exist over a period of time,
- **corrective**: when a state causes another state to return to normality.
During a consultation with HDP, nodes in the Bayesian network are instantiated. This essentially means deriving their observable extents (earliest and latest, begin and end), relative to the current point in time.

The times are all temporal distances from the current time, so 1 day + 1 day is two days prior to the reference time. Since diagnostic reasoning is abductive reasoning the most common reasoning step is to infer a cause from an effect, starting from the effects matching patient findings.
The essential functions of the temporal reasoning performed by HDP are therefore to deduce and maintain the causal temporal constraints in hypotheses and to support the possibility of nodes having different values over different time intervals.

⇒ The issue of multiple granularities is very relevant to the domain of HDP since some processes take place over minutes while others take place over months or years.
Let us now analyze this system with respect to the C-T-A model.

- All five planes are included.
- The Bayesian probabilistic network is a causal network with probabilities, since the central relation is that of causality.
- Temporal constraints are expressed with respect to causal links.
- Onset, delay, max-exist, etc. are intervals of time whose durations are expressed as sets of possible values with corresponding probabilities.
Temporal uncertainty is expressed through ranges of absolute durations and probabilities.

During a consultation, nodes in the causal network are assigned earliest and latest begins and ends with respect to the reference time point, i.e. now.

There is a single causal network encompassing all relevant internal states, external manifestations and actions.
The parsimonious covering theory (PCT) of Peng and Reggia (1990) is a well known general theory of abductive diagnosis.

The basic version of the theory models diagnostic knowledge in terms of

- a set of causes (disorders), $D$,
- a set of manifestations, $M$,
- a causal relation, $C \subseteq D \times M$, relating each cause to its effects.
An efficient algorithm, BIPARTITE, is defined, which incrementally constructs, in generator-set format, all the explanations of a set of occurring manifestations, $M^+ \subseteq M$, for some case (patient).

There are three *parsimony criteria* which in ascending order of strictness are:

- **relevancy**: every disorder in the explanation is a cause of at least one element of $M^+$,
- **irredundancy**: no subset of the explanation is also a cover of $M^+$. 

Combi, Keravnou, and Shahar

Chapter 6: Time in Clinical Diagnosis
Wainer and Rezende (1997) have proposed a temporal extension to the basic version of PCT, referred to as t-PCT, which they have applied to the domain of food-borne diseases.

In PCT the diagnostic knowledge is a collection of causal associations between disorders and manifestations.

In t-PCT each disorder is modeled, separately, as a temporal graph.
This is a directed, acyclic, transitive, not necessarily connected, graph the nodes of which represent manifestations and the directed arcs represent *temporal precedence*.
Temporal Parsimonious Covering Theory V

Figure: Temporal Graphs of Disorders $d_1$ and $d_2$ in t-PCT
Figure above gives the temporal graphs of disorders $d_1$ and $d_2$.

- Here we assume that no quantitative information about the duration of manifestations or about the elapsed time between the starts of two manifestations is given.

- In the temporal graph of $d_1$, the first and second appearances of $m_2$ are denoted as $m_2^{(1)}$ and $m_2^{(2)}$ respectively.
Definition

An interval, \( I = [I^-, I^+] \), is defined to be a non-empty, convex, set of time points.

The time period modeled by the interval \( I \) is represented as a range of values between a min extent \( (I^-) \) and a max extent \( (I^+) \).
Definition

Two binary, arithmetic, operations are defined on intervals, intersection (\( \cap \)) and sum (\( + \)):

\[
I \cap J = [\max(I^-, J^-), \min(I^+, J^+)]
\]

\[
I + J = [I^- + J^-, I^+ + J^+]
\]

**Intersection** gives the common subrange, and hence the two intervals must denote the same temporal measure.
Example

Let the expected duration of manifestation $m_1$ under disorder $d_1$ be between 2 and 4 days, and let the actual duration of that manifestation in some patient be between 1 and 2 days.

$\text{dur}_{d_1}(m_1) = [2, 4]$

$\text{dur}^+(m_1) = [1, 2]$

The intersection of these two intervals is the interval $[2, 2]$. 
Sum propagates delays (between the begins of manifestations) along a chain of manifestations, or positions a manifestation on the time line.

Let’s say that in disorder $d_1$ the expected delay between the start of manifestation $m_1$ and the start of the first appearance of $m_2$ is between 2 and 3 days and the expected delay between the starts of the two appearances of $m_2$ is between 3 and 4 days.
The sum of the intervals 

\([2, 3]\) and \([3, 4]\)

gives the interval \([5, 7]\)

which is the expected delay between the start of \(m_1\) and the start of the second appearance of \(m_2\).
Let us further say that in the given patient, $m_1$ and (the first appearance of) $m_2$ started 5 and 2 days ago respectively. The actual begins of these manifestations are expressed as the intervals,

\[
\begin{align*}
  \text{begin}^+(m_1) &= [-5, -5] \\
  \text{begin}^+(m_2) &= [-2, -2]
\end{align*}
\]
Example

This inference is consistent with the actual begin of \( m_2 \), as can be shown through an intersection operation between the actual \((-2, -2]\) and the inferred \([-3, -2]\) that yields the consistent interval \([-2, -2]\). If \( m_2 \) had started 4 days ago, this would have generated an inconsistency with respect to the particular arc on the basis of the actual begin of \( m_1 \) since \([-3, -2]\) \( \cap \) \([-4, -4]\) would give the inconsistent interval \([-3, -4]\).
Temporal Parsimonious Covering Theory XIV

The operations of sum and intersection are therefore applied for deciding whether the model of some disorder (temporal graph) is temporally inconsistent with the patient information. Temporal inconsistency arises if

1. there is at least one arc inconsistency, or
2. the actual duration of a manifestation is different from its expected duration under the given disorder.
PCT is a well known theory of abductive diagnosis, although its basic version is only applicable to very simple medical diagnostic problems.

The temporal extensions of PCT discussed above, yielding t-PCT, certainly expand the application scope to more realistic medical diagnostic problems.

The principal objective is to use time for constraining the generation of diagnostic explanations beyond what is possible from the irredundancy parsimony criterion.
The work on t-PCT overviewed above has also been extended on a number of directions using fuzzy sets, namely:

- The crisp representation of a time interval as a range of values has been replaced with a fuzzy set giving ranges for typical as well as possible extents.

- The manifestations of a disorder are distinguished into necessary and possible. In addition, the intensity of manifestations, both in the disorder models and the patient information, is expressed in terms of fuzzy sets.
The speed of evolution of the ‘concluded’ disorder is computed on the basis of the patient data. This is used to make predictions about past and future events.

The diagnostic knowledge consists of models for the various disorders. Each disorder is modeled separately as a temporal graph.

- A single time scale, $\Theta$, is assumed. $D$ and $M$ are the sets of disorders and manifestations as before.
- Each disorder has a set of effects from $M$ (the causal relation used before).
The effects of a disorder are distinguished into necessary and possible.

In addition, a disorder is associated with a set of (instantaneous) events.
Figure: Temporal Graph of Disorder $d_1$ in Fuzzy t-PCT
Figure above gives the temporal graph of disorder $d_1$. The graph includes nodes for the begins and ends of all manifestations. In addition there is special node $m_0$ that represents the event signalling the start of the disorder.
A fuzzy temporal interval is a fuzzy interval. A fuzzy interval is a fuzzy set with a convex membership function.

A normalized fuzzy set is one for which at least one element belongs to it with certainty.
Definition

A **positive interval** is a fuzzy interval whose domain is the real line and every $x < 0$ does not belong to the interval, i.e. $\mu(x) = 0$ where $\mu(x)$ is the membership function.

An interval $A$ is **tighter** than an interval $B$, i.e. more constrained, if for every element from the relevant domain, its degree of membership in $A$ does not exceed its degree of membership in $B$. 
To perform the relevant temporal reasoning, a **minimal network** is computed from the temporal graph modeling a disorder.

A minimal network gives the most tight interval possible between any pair of events.

If nothing is known or can be derived for some pair of events, the default interval, ‘anytime’, is assumed.
Regarding patient information, the temporal distances, as fuzzy intervals, between all pairs of the relevant events are computed from the temporal distances between each event and the present moment of time.

A number of consistency measures between a disorder model and the patient information are defined. These are:
Temporal consistency, computed on the basis of the expected and actual temporal distances between pairs of events. More specifically, for each pair of events in the patient information that is also included in the minimal network of the disorder model, the height of the intersection of the given pair of intervals is computed (the height is the maximum value of the membership function).
Categorical consistency reflecting the fact that a necessary manifestation of a disorder must happen, assuming that there was enough time for it to happen. Categorical consistency is calculated as temporal consistency by assuming that all necessary manifestations that have not yet occurred will start sometime after the present moment of time.
Intensity consistency reflecting the match between the expected and actual intensities of the relevant manifestations in the disorder model and patient information. Intensity consistency is not a temporal measure.
Fuzzy Temporal/Categorical Diagnosis XIII

The analysis of t-PCT with respect to the C-T-A model given in the previous section applies to this approach as well.

- The internal states and actions planes are missing.
- The expression of temporal constraints has of course been usefully extended.
- A constraint is no longer confined to delays between begins of manifestations and durations of manifestations and expressed as a range of typical values.
- A constraint can now refer to any temporal distance between any pair of events.
In summary:

- This proposal, like its predecessor, t-PCT, and in turn its predecessor, PCT, is characterized by a rigorous set-theoretic exposition that makes the proposed notions clear and easy to reproduce.

- Although it improves t-PCT on a number of points, there are still a number of critical issues to be tackled, e.g. multiplicity of time scales, recurring manifestations, temporal data abstraction, etc.
Abstract Temporal Diagnosis I

Gamper and Nejdl (1997) have developed a logic-based framework for **Abstract Temporal Diagnosis (ATD)** that has been applied to the domain of hepatitis B with promising results.

This framework, in contrast with the previous approaches discussed, emphasizes the need to automatically derive abstract observations over time intervals from (direct) observations at time points.

- **ATD** is based on Allen’s (1984) time-interval logic.
- More specifically the temporal primitive used is the convex time-interval.
Abstract Temporal Diagnosis II

- A linear and dense time structure, called time line, is assumed which is unbound in both directions, past and future.

- The time line is represented by real numbers. So intervals have explicit Begins and Ends, \([B, E]\).

Temporal propositions are represented by introducing time as an additional argument to the relevant predicates, e.g., fever(high, \(i\)), meaning that fever is high during interval \(i\). Furthermore, this framework adopts Allen’s algebra of temporal relations between intervals.
The designers of ATD observe that a **process-oriented ontology** is more suitable for representing dynamic systems than a component-based ontology.

- The temporal evolution of a (normal or abnormal) process is expressed through a chaining sequence of states, described in terms of *process state assumptions, s(p, i)*.
- This says that process *p* assumes state *s* throughout interval *i*.
A process is non observable. There are, however, observable parameters (manifestations).

**Definition**

Manifestation propositions (or simply manifestations) are expressed as $m(v, i)$ which says that manifestation $m$ assumes value $v$ throughout interval $i$.

A manifestation can assume different values over different time intervals but only one value at a time.
Abstract Temporal Diagnosis V

Definition

The **State Description Model** (SDM) of a process \( p \) is a logical formula \( \alpha \land \tau_\alpha \supset \beta \land \tau_\beta \) where \( \alpha \) and \( \beta \) are conjunctions of temporal propositions (process state assumptions and/or manifestations) while \( \tau_\alpha \) and \( \tau_\beta \) are conjunctions of temporal relations between the implicated time intervals.

These temporal constraints denote the temporal behaviour of the given process.
Abstract Temporal Diagnosis VI

For illustration, the SDM of disorder $d_1$ is given below:

$$\forall I_{s_1} \forall I_{s_2} \exists I_{m_1} \exists I_{m_2(1)} \exists I_{m_2(2)} \exists I_{m_3}$$

$$s_1(d_1, I_{s_1}) \land s_2(d_1, I_{s_2}) \land I_{s_1} \{meets\} I_{s_2} \supset$$

$$m_1(\text{present}, I_{m_1}) \land m_2(\text{present}, I_{m_2(1)}) \land m_2(\text{present}, I_{m_2(2)}) \land$$

$$m_3(\text{present}, I_{m_3}) \land$$

$$I_{m_1} \{\text{finishes, during}\} I_{s_1} \land$$

$$I_{m_2(1)} \{\text{during, finishes, is\_met, after}\} I_{m_1} \land$$

$$I_{m_2(1)} \{\text{before}\} I_{m_2(2)} \land I_{m_2(2)} \{\text{during, finishes}\} I_{s_2} \land$$

$$I_{m_3} \{\text{finishes}\} I_{m_2(2)} \land I_{m_3} \{\text{during, finishes}\} I_{s_2}$$
Abstract Temporal Diagnosis VII

Figure: Constraint Network from the SDM of $d_1$
Abstract Temporal Diagnosis VIII

- An abstract observation is expressed as \( m(v, i) \wedge \tau \) where \( \tau \) gives the temporal constraints between interval \( i \) and the real time line and/or other abstract observations.
- The temporal constraints in the abstract patient information are also represented as a binary constraint network.
1. The ATD framework does not include the actions plane of the C-T-A model.
2. The constraints plane refers to the time intervals designating the period of occurrence, on the time line, of internal states and observable manifestations.
3. The constraints are expressed as relative temporal relations (using Allen’s set of relations) between intervals or between intervals and absolute periods of time.
Temporal uncertainty and incompleteness is supported since the relation between a pair of intervals can be expressed as a disjunction of possible relations and it is not necessary to specify the relation between any pair of intervals.
Console and Torasso’s Temporal Abductive Diagnostic Architecture I

Console and Torasso propose a logic-based, temporal abductive architecture for medical diagnosis.

This architecture is an extension of the causal component of CHECK, an atemporal diagnostic system which was applied to the domains of cirrhosis and leprosis.
Console and Torasso’s Temporal Abductive Diagnostic Architecture II

Definition

**Diagnostic knowledge** is represented as a single, acyclic, causal network where the arcs are associated with temporal information denoting a range (minimum and maximum) for the delay between the start of the cause and the start of the effect.

- The temporal primitive of the proposal is the time point.
- A time interval is a convex set of time points.
Console and Torasso’s Temporal Abductive Diagnostic Architecture III

- In order to allow uncertainty with respect to temporal existences, *variable intervals* are used which are expressed as quadruples of time points where the first pair of time points gives the range for the begin and the second pair the range for the end of the interval.

- A variable interval encompasses a set of precise intervals.

The nodes of the causal network define findings (*manifestations*), pathophysiological states (*initial and intermediary*), and contextual information (*c-nodes*).
Manifestations and contextual information are directly obtainable (observable entities) while pathophysiological states (p-states) are non observable, possibly with the exception of some initial states, and therefore need to be inferred.
Console and Torasso’s Temporal Abductive Diagnostic Architecture V

**Figure:** Types of Causal Links in Console and Torasso Architecture
Console and Torasso’s Temporal Abductive Diagnostic Architecture VI

- A causal arc in the network relates an antecedent to a consequent where a consequent is either a p-state or a manifestation.
- In the simplest form, an antecedent is a single p-state, but it can also be a conjunction of p-states and c-nodes involving at least one p-state.
A causal arc can be associated with an arbitrary logical expression the validity of which in a given diagnostic situation is a necessary condition for assuming the presence of the causal arc.

The nodes in the causal network are characterized by a set of attributes. A causal arc in fact encompasses a set of associations relating combinations of node-attribute-value triplets (for nodes of the antecedent) to combinations of attribute-value pairs for the consequent.
Finally there can be multiple causal arcs (either with simple or complex antecedents) sharing the same consequent.

A difference between this approach and the previous approaches discussed is that in this architecture no general duration information for the nodes in the causal network is given.
Console and Torasso’s Temporal Abductive Diagnostic Architecture IX

Figure: Causal Network. Annotated with Delay Information
Console and Torasso’s Temporal Abductive Diagnostic Architecture X

As can be seen there is a single causal network encompassing all disorders, just like in HDP, not separate networks for each disorder, as in the other approaches. Internal states $s_1$ and $s_3$ respectively denote the initial states for $d_1$ and $d_2$. Such states do not have causal antecedents.

- The authors view temporal reasoning in medical diagnosis as a **temporal constraint satisfaction problem**.
The patient information consists of a collection of manifestation instances (findings), and their (possibly variable) temporal extents. The objective is to determine the path in the network, whose delays are temporally consistent with the extents of the findings, and which accounts for the findings.
The representation of patient information in this approach, in the authors’ own admission, is rather restrictive; more specifically an observable parameter can attain an abnormality value during a single interval only and throughout the rest of the period of relevance to the diagnostic activity, this parameter is assumed to be normal.
From the discussion so far on the various proposals, two broad categories can be identified.

- In one category diagnostic knowledge is represented as a single causal network and as such the temporal constraints refer to delays between causes and effects and the persistence of states.
  - The HDP system and Console & Torasso’s architecture belong to this category.
In the other category each disorder is modeled separately, but in associational rather than causal terms, i.e., in terms of external manifestations.

- In these approaches, the temporal constraints refer to temporal relations between events marking begins and ends of manifestations.
- The ATD system, and the t-PCT and its fuzzy extensions, belong to this category.
The approach to be discussed in this section is based on a time ontology the central primitives of which are the **time-axis**, enabling a multidimensional and multigranular model of time, and the **time-object**, a dynamic entity embodying time as an integral aspect, and bringing together temporal, structural and causal knowledge.

- **A time-axis**, $\alpha$, represents a period of valid time from a given conceptual perspective. It is expressed discretely as a sequence of time-values, $\text{Times}(\alpha) = \{t_1, t_2, \ldots, t_n\}$, relative to some origin.
A *time-object* is a dynamic entity that has time as an integral aspect. It is an association between a *property* and an *existence*. The existence of abstract/concrete time-objects is given with respect to abstract/concrete time-axes. Formally a time-object, \( \tau \), is defined as a pair \( \langle \pi_\tau, \varepsilon_\tau \rangle \) where \( \pi_\tau \) is its property and \( \varepsilon_\tau \) its existence function.
Causality is a central relation in this ontology. More specifically, the ontology includes relations *causes*, *causality-link* and *cause-spec*, that are defined at the level of abstract time-objects, concrete time-objects and abstract properties, respectively.

**Axiom 1:**

\[
\text{causality-link}(\tau_i, \tau_j, cf) \iff \text{causes}(\tau_i, \tau_j, cs, cf) \land \text{conds-hold}(cs) \land \sim \text{starts-before}(\tau_j, \tau_i).
\]

Predicate *starts-before*(\(\tau_j, \tau_i\)) expresses that \(\tau_j\) starts before \(\tau_i\).
Relation *cause-spec* between properties has six arguments, where the first two are properties, the third is a granularity, the fourth and fifth are sets of relative (*TRel*) and absolute (*TAbs*) temporal constraints respectively and the last one is a certainty factor.
Axiom 2:

\[
\text{causality-link}(\tau_i, \tau_j, cf) \\
\iff \text{cause-spec}(\rho_i, \rho_j, \mu, TRel, TAbs, cf) \land \\
\pi(\tau_i) = \rho_i \land \pi(\tau_j) = \rho_j \land \\
r\text{-satisfied}(\tau_i, \tau_j, \mu, TRel) \land a\text{-satisfied}(\tau_i, \tau_j, \mu, TAbs) \land \\
\sim\text{starts\-before}(\tau_j, \tau_i).
\]
Abductive Diagnosis Using Time-Objects VIII

**Figure:** Modeling $d_1$ as a Causal-Temporal Structure of Atomic and Compound Time-Objects
Previous Figure gives the model of disorder \( d_1 \) as a causal-temporal structure of (abstract) time-objects.

In this model the expression of temporal constraints, both absolute and relative (see below), assumes a granularity of days.

The model involves two compound time-objects, the disorder per se, the evolution of which is analyzed in terms of a chaining sequence of the states \( s_1 \) and \( s_2 \) (its components) and the recurrence of manifestation \( m_2 \).
Abductive Diagnosis Using Time-Objects X

- The other time-objects \((s_1, s_2, m_1, m_2^{(1)}, m_2^{(2)} \text{ and } m_3)\) are atomic, although some, say \(s_1\) and \(s_2\), could also be decomposed into finer components.

- The compound time-object representing the recurrence of \(m_2\) has the complex property \(r(m_2, 2, \text{del} = \langle 3, 4 \rangle)\).

*It is important to note that temporal relations between time-objects are granularity-sensitive, meaning that the relation between a given pair of time-objects can be viewed differently under a finer granularity than under a grosser granularity.*
Formally the instance of relation `causes` from $s_1$ to $m_1$ can be expressed as the following ground atom:

```
causes
(s₁, m₁, 
{dur(s₁, days) = ⟨5, 5⟩, dur(m₁, days) = ⟨2, 4⟩, 
delay(days) = ⟨1, 1⟩, 

temp-rels
(days) = \{finished, contains\}, 1.0)
```
As another example, let us give the formal expression of relation *causes* from $s_1$ to $s_2$:

\[
\text{causes} \\
(s_1, s_2, \\
\{ \text{dur}(s_1, \text{days}) = \langle 5, 5 \rangle, \text{dur}(s_2, \text{days}) = \langle 6, 9 \rangle, \\
\text{delay}(\text{days}) = \langle 5, 5 \rangle, \\
\text{temp-rels} \\
(\text{days} = \{ \text{meets} \}, 1.0)
\]
As already explained, in a diagnostic context the most frequent, and critical, reasoning step is to hypothesize a cause from an established effect. **This is an abductive step.**

While exploring a hypothesized cause, a frequent reasoning step is to hypothesize further observable, but as yet unknown, effects of the cause. **This is a deductive step.**

- Relation *causes* is defined at the level of abstract time-objects and as such it is used in the definition of disorder models.
Relation *cause-spec* is similar to *causes* but as it is defined at the level of properties its use is independent of disorder models.
Example

An example of relation \textit{cause-spec} is the following:

\textit{cause-spec(bacteria(present), throat(sore), days, }\{\textit{finished}\}, \{\textit{dur(bacteria(present))} = \langle 7, 10 \rangle, \textit{delay} = \langle 1, 3 \rangle\}, 0.9\)

This instance of the relation specifies a general causal association between bacteria and soreness of throat, i.e. properties \textit{bacteria (present)} and \textit{throat (sore)}. 
Similarly to *causes*, *cause-spec* can be used both for deriving (hypothesizing) causal links or for hypothesizing causes from effects or vice versa.

**Figure**: Existences of Time-Objects Comprising the Model of $d_1$ (relative to the start of the disorder and at the granularity of days)
The existences, at the granularity of days, of the time-objects comprising the model of $d_1$, relative to the start of the disorder, are given in Figure above.

The models of disorders that belong to the category of infinitely persistent disorders (see below) can be given absolute existences with respect to the relevant abstract time-axes. This is illustrated by the model of disorder *spondyloepiphyseal dysplasia congenita (SEDC)*, a skeletal dysplasia.
The (spanning) abstract time-axis, \textit{lifetime} that begins at birth and terminates at death, and involves mixed granularities, is assumed in this model.
Abstract Temporal Diagnosis

Temporal Abductive Diagnostic Architecture

Abductive Diagnosis Using Time-Objects

Temporal Constraints

Introduction
Diagnostic Notions
The Heart Disease Program
Temporal Parsimonious Covering Theory
Fuzzy Temporal/Categorical Diagnosis
Abstract Temporal Diagnosis
Temporal Abductive Diagnostic Architecture
Abductive Diagnosis Using Time-Objects

Figure: Model of Skeletal Dysplasia SEDC

Combi, Keravnou, and Shahar

Chapter 6: Time in Clinical Diagnosis
The early roots of the time-object based framework for abductive diagnosis are found in the temporal reasoning framework of the Skeletal Dysplasias Diagnostician (SDD) system.

In this ontology, disorders and their manifestations are classified as follows from the temporal perspective:

- Infinitely persistent, either with a fixed or a variable initiation margin (e.g. SEDC);
Finitely persistent, but not recurring, again either with a fixed or a variable initiation margin (e.g. chicken pox);

Finitely persistent which can recur (here the initiation margin is variable), e.g. flu.
Temporal Constraints I

We examine further the temporal constraints encountered in clinical diagnosis.

- we consider a number of instantiations of the Abstract Temporal Graph (ATG), emanating from the proposals discussed above.

- The particular cases of the ATG structure considered are:
  a) the temporal entities are instantaneous events and the constraints are relative (case I) or absolute (case II);
  b) the temporal entities have duration and the constraints are relative (case III).
Temporal Constraints II

**Figure:** Transitivity Table for Relative Temporal Relations between Instantaneous Events
Case I: Instantaneous Events and Relative Constraints

Here the temporal entities are instantaneous events and $C = \{<, =, >\}$ or \{\textit{before}, \textit{equal}, \textit{after}\}, i.e. the domain of relative temporal relations.

Special constant \texttt{self_ref} is set to $=$, while relations $<$, $\neq$, and $\neq$ are respectively denoted by the disjunctive constraints $\{=, >\}$, $\{<, >\}$ and $\{<, =\}$.

The inverses of $<$, $\neq$, and $>$ are respectively $>$, $\neq$, and $<$. Finally function \textit{transit} is given by the transitivity table.
As an illustration, Figure below gives the case I ATG corresponding to disorder $d_1$. The nodes represent instantaneous events marking the begin or end of the disorder per se, its internal states and its external manifestations.
Case I: Instantaneous Events and Relative Constraints

Figure: Case I ATG for disorder $d_1$
Case II: Instantaneous Events and Absolute Constraints I

The temporal entities are again instantaneous events, but the domain of constraints is expressed in a metric way, in terms of temporal distances. Such distances could be expressed discretely with respect to a particular granularity, say *days*, i.e.
Case II: Instantaneous Events and Absolute Constraints II

\[ C = \{-\infty, \ldots, -4, -3, -2, -1, 0, 1, 2, 3, 4, \ldots, +\infty\}, \]

where a negative number means “days after”, a positive number means “days before” and 0 means “equal”. Hence \( C \) is an infinite set.

Special constant \( \text{self\_ref} \) is set to 0,

\[ \text{inverse}(c) = -c \] and

\[ \text{transit}(c_{ik}, c_{kj}) = \{c_{ik} + c_{kj}\}. \]
Case II: Instantaneous Events and Absolute Constraints III

Metric or absolute constraints can be expressed in various ways. What is described above is just one way.

- An arc in an ATG whose label is a disjunctive constraint, entails uncertainty since the temporal relationship between the existences of the particular pair of temporal entities cannot be given “precisely”, where the precision is always relative to the domain of constraints $\mathcal{C}$. 
The semantics of a pair, \( \langle c, u \rangle \), would depend on the semantics of the particular uncertainty measure used, which in turn would depend on whether the ATG in reference models diagnostic knowledge or patient data.

If the constraints are associated with uncertainty, complete temporal knowledge is denoted by a single pair \( \langle c, u \rangle \) where \( u \) represents absolute certainty.
Case III: Occurrences with Duration and Relative Constraints I

This is the generalization of case I.

- The temporal entities represent any occurrence and not just instantaneous events.
- The domain of constraints is Allen’s set of relative relations, namely $\mathcal{C} = \{\text{before, after, meets, is\_met, overlaps, overlapped, starts, started, during, contains, finishes, finished, equal}\}$, where after is the inverse of before and vice versa, etc. Special constant self\_ref is set to equal.
Case III: Occurrences with Duration and Relative Constraints II

- Function *transit* is defined in terms of Allen’s transitivity table. The constraint networks of ATD are covered by this case.
Case III: Occurrences with Duration and Relative Constraints III

Figure: Case III ATG for disorder $d_1$
The temporal constraints associated with causal relations can be represented in terms of an ATG. Causal links are not explicitly represented in an ATG; hence an ATG is not a causal graph.

In Console and Torasso’s proposal the temporal constraints of causal relations are expressed in a metric way as ranges for the delay between a cause and an effect.
In addition there are two general constraints, namely that a cause cannot ‘outlive’ its effect and that there cannot be a gap between the two.

The two general constraints refer to the end of a cause and the end of its effect or the end of a cause and the start of its effect. These constraints can be instantiated with respect to every specific cause and its (direct) effect.

Metric constraints are more precise than relative constraints, even if, in the case of discrete metric constraints, the abstraction of a single granularity is imposed.
The other option is to handle each type of constraint separately and then to perform the relevant matches across the same arcs. Let $C_m$ and $C_r$ be respectively the domains of metric and relative constraints. There is one ATG, but each arc has both a metric and a relative label.
As a case III ATG (relative constraints on occurrences with duration) can be converted to a case I ATG (relative constraints on instantaneous events), a single ATG whose nodes are instantaneous events, suffices for the representation of a mixed set of relative constraints between occurrences with duration and metric constraints between the starts and ends of such occurrences.
Temporal Constraints in Causal Networks

Figure: A Case III ATG for the Relative Temporal Constraints of HDP
In HDP the temporal constraints of causal relations are more complicated than simple delays between the starts of causes and effects.

- Here the existence of some occurrence is refined into interval *onset* and interval *observable*; possible durations for these intervals are expressed probabilistically.

- *Delay* is the period from the start of the onset of a cause to the start of the observability of its effect.

- *Persist* is the period from the end of the observability of a cause to the end of the observability of its effect.
Let us now return to the problem of deciding whether some constraint is satisfied by a given set of mutually consistent constraints.

*The solution to this problem is based on the assumption that all constraints, queried and given, are of the same form. Here we relax this assumption and say that the queried constraint $qc$ could be of a different form to the ATG representing the given constraints, e.g. the $qc$ could be $n_i \{\text{before}, \text{meets}\} n_j$ while the given constraints form a case II ATG.*
Such a heterogeneous situation could be handled by converting \(qc\) to the form of the ATG and proceeding in the same manner as before.
Example

In this example the translation of the $qc$ proceeds as follows:

$$n_i\{\text{before, meets}\}n_j \rightarrow$$

$$n_i\{\text{before}\}n_j \vee n_j\{\text{meets}\}n_j \rightarrow$$

$$n_i^e\{+\infty,\ldots,1\}n_j^s \vee n_i^e\{0\}n_j^s \rightarrow$$

$$n_i^e\{+\infty,\ldots,1,0\}n_j^s$$

where $n^s / n^e$ denotes the start/end of $n$. 
Finally, a minimal ATG representing the model of some disorder encompasses all feasible temporal scenarios about the evolution of the disorder. The specific scenarios can be obtained by a topological sorting of the ATG.