

Interval-Valued Inference in Medical Knowledge-Based System CLINAID

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In a series of papers and a monograph [21], we have described the conceptual structures as well as the basic architecture of the knowledge-based system CLINAID. Its generic architecture is aimed at support of knowledge-based decision making with risk and under uncertainty.

The majority of extant medical expert systems deal with a limited medical context, the largest domain of knowledge being just a single medical field. The inherent limitation of such medical expert systems is in its essence conceptual and logical: their knowledge bases and inference engines cannot mix easily the knowledge from several fields without some adverse effects. CLINAID deals with this problem by introducing a multi-centre architecture in the Diagnostic Unit. The medical data and knowledge of each medical specialist field exhibit different logical properties. This in turn leads to the several kinds of many-valued logics on which the relational inference and data manipulation is based. Semantic and epistemological justification of the use of these logics for the *interval-valued inference* is provided by a theoretical device called the *checklist paradigm* [25].

The Diagnostic unit of CLINAID deals with a number of body systems [21]. In this paper we shall use several body systems to demonstrate the *interaction across* the body systems during the inferential process and to show how interval based methods of inference help in dealing with the problems induced by this phenomenon.

Интервальнозначный вывод в медицинской базе знаний CLINAID

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В ряде работ и монографии [21] нами описаны принципиальные структуры и базовая архитектура базы знаний CLINAID. Архитектура системы CLINAID ориентирована на основанную на базе знаний поддержку принятия решений в условиях риска и неопределенности.

Большинство существующих медицинских экспертных систем имеют дело с ограниченным медицинским контекстом, их объем знаний покрывает лишь одну область медицины. Неизбежная ограниченность подобных систем носит принципиальный логический характер: их базы знаний и средства вывода не могут легко сочетать знания из разных областей, не вызывая при этом нежелательных последствий. Система CLINAID решает эту проблему использованием многоцентральной архитектуры в диагностической подсистеме. Медицинские данные и знания из каждой специальной области обладают различными логическими свойствами. Это, в свою очередь, приводит к нескольким типам многозначных логик, на которых основаны относительный вывод и работа с данными. Семантическое и эпистемологическое обоснование использования этих логик для интервальнозначного вывода обеспечивается теоретической схемой, носящей название <парадигма проверки списка> (checklist paradigm) [25].

Поскольку CLINAID призвана стать удобной медицинской консультационной системой, ее база содержит большое число медицинских экспертных данных. Диагностическая подсистема системы CLINAID работает с несколькими системами тела [21]. В данной статье рассматриваются некоторые из них, чтобы продемонстрировать взаимодействие во время процесса вывода и показать, как интервальные методы вывода помогают справляться с возникающими проблемами.

1 The basic knowledge handling mechanisms of CLINAID

1.1 Dynamics of medical diagnostic process

The clinician's activity while treating a patient consists of the following *processes*: **1.** Observation and acquisition of relevant patient data. **2.** Conceptual classification and filtration of relevant observational data for process (3). **3.** Clinical decision and patient management [22]. All these components interact strongly with one another. This interaction of clinical activities manifests itself in the properties of the dynamic process of clinical inference. *Incompleteness, locality of inference* and *directed complexity reduction* play a substantial role here. In order to deal successfully with these factors, triangle and square relational products of relations [10, 7] were used to represent inference structures in CLINAID [20].

All the above activities have to be represented in CLINAID and this diversity is reflected in the virtual architecture of the system. The basic architecture consists of the following cooperating units (basic shell substra-

tum):

1. Diagnostic Unit (comprised of several parallel cooperating centres).
2. Treatment Recommendation Unit.
3. Patient Clinical Record Unit.
4. Co-ordination and Planning Unit.

A fully comprehensive medical system has to have the capability of dealing with a number of diverse body systems. The multiplicity of body systems in which the given signs and symptoms of a particular patient are interpreted, defines logically a multiplicity of contexts. It requires special precautions for the inferential system to deal with this multiplicity of contexts correctly, as will be seen later.

1.2 Use of triangle and square relational products in interval reasoning

There are two different facets of the problem. The first is specifying relational inference structures in the form where connectives are specified only as generic logic types: AND, OR, PLY etc. The second is the choice of specific valuation (many-valued logic algebra operations) for the generic logic connective-types, e.g. usual fuzzy AND: $\text{val}(A \text{ AND } B) = \min(a, b)$ or what is called fuzzy bold AND: $\text{val}(A \text{ AND } B) = \max(0, a + b - 1)$, etc. Thus the *generic* relational knowledge representation and inferential structures (with generic logic types of connectives) are *instantiated* by the choice of a specific many-valued system of connectives. Then the system becomes a specific relational inference system in which, however, this instantiation can be changed according to different circumstances during the run time. The generic framework can be instantiated either to an *interval system*, such as the pair of AND in the example above, or to a usual many-valued *system with point valuation* e.g. $\text{val}(A \text{ AND } B) = a + b - ab$. The generic relational framework for inference is provided by relational products. The choice of the specific logics is guided by the checklist paradigm.

1.2.1 Triangle and square types of relational products

Triangular and square products play a pivotal role not only in medical applications but also in other fields. See [24] for a recent survey and selected

bibliography. The triangle *subproduct* $R \triangleleft S$, the triangle *superproduct* $R \triangleright S$, and *square product* $R \square S$ were introduced in their general form defined below by Bandler and Kohout in 1977. The square product, however, stems from Riguet (1948) [37], needing only to be made explicit [10]. Independently of Bandler and Kohout, Sanchez defined an “ α -composition” which is a special form of the triangle product using implication operator of Breuwerian logic, and is used in the theory of relational equations. The products were more recently rediscovered and described in 1986 by J. P. Diognon, M. Monjardet, B. Roubens, and P. Vincke [12, 13]. Aubin and Frankowska in their book of 1990 [1] use a triangle product, which they, however, call “square”.

Let us look now at the definitions and meaning of the products. Where R is a relation from X to Y , and S a relation from Y to Z , a *product relation* $R * S$ is a relation from X to Z , determined by R and S . There are several types of product used to produce product-relations [10, 24]. Each product type performs a **different logical action** on the intermediate sets, as *each logical type* of the product enforces a *distinct specific meaning* on the resulting product-relation $R * S$. When the relations are fuzzy, there is a further wide choice of realization for each of the four product kinds defined below, because several many-valued logics provide *implication operator* and other connectives suitable for interval computation. In order to explain clearly the need for, and the significance of, different logical types of relational products, we begin with crisp relations, and then extend these to fuzzy.

Definition

Circle product:	$x(R \circ S)z \Leftrightarrow xR \text{ intersects } Sz$
Triangle Subproduct:	$x(R \triangleleft S)z \Leftrightarrow xR \subseteq Sz$
Triangle Superproduct:	$x(R \triangleright S)z \Leftrightarrow xR \supseteq Sz$
Square product:	$x(R \square S)z \Leftrightarrow xR = Sz$

Before the relational products can be of real service in interval computing, they must be fuzzified. For their fuzzification, the many-valued logic based (fuzzy) *power set theories* are essential [3, 4]. Once the concept of the fuzzy power set is clearly understood, the way of fuzzifying formulas defining relational compositions becomes obvious. In order to switch over to the matrix notation that is more convenient computationally because of its explicit handling of logic values, we express the relational products in their pure logical form. In the logic formulas, R_{ij} will represent the fuzzy degree

to which the statement $x_i R y_j$ is true.

$$\begin{aligned} (R \circ S)_{ik} &= \bigvee_j (R_{ij} \wedge S_{jk}) \\ (R \triangleleft S)_{ik} &= \bigwedge_j (R_{ij} \rightarrow S_{jk}) \\ (R \triangleright S)_{ik} &= \bigwedge_j (R_{ij} \leftarrow S_{jk}) \\ (R \square S)_{ik} &= \bigwedge_j (R_{ij} \equiv S_{jk}) \end{aligned}$$

The customary logical symbols for the logic connectives *AND*, *OR*, both *implications* and the *equivalence* in the above formulas represent the connectives of some many-valued logic, **chosen** according to the properties of the products required. The details of choice of the appropriate many-valued connectives are discussed in [5, 7, 9].

It is important to distinguish what we call *harsh* fuzzy products (defined above) from a different family, the family of *mean* products. Given the general formula $(R@S)_{ik} ::= \#(R_{ij} * S_{jk})$, a mean product is obtained by replacing the outer connective $\#$ by \sum and normalizing the resulting product appropriately. The mean products are very effective in medical applications, although their mathematical theory does not take such a neat form as that of harsh products.

The mean products provide an effective inference mechanism in CLINAID applications. Their superiority has been shown empirically, for most recent extensive experiments see [38]. In some non-medical applications, such as urban studies [40], harsh products, however, work equally well. See [24] for further references.

In representing clinical knowledge structures not only quantitative but also qualitative notions are involved. Product-relations formed by the relational products represent new entities composed from the original data. Their specific semantics defines the conceptual meaning which is partially dependent on the conceptual meaning of the original data-relations. If R is the relation between *patients* and *individual symptoms*, and S a relation between *symptoms* and *diseases*, $R * S$ will be a relation between *patients and diseases*. The diagnostic clinical interpretation of each distinct logical type (e.g. the triangular square product types) of these product-relations has a **distinct clinical meaning**:

- $x(R \circ S)z$: x has at least one symptom of illness z .
 $x(R \triangleleft S)z$: x 's symptoms are among those which characterize z .
 $x(R \triangleright S)z$: x 's symptoms include all those which characterize z .
 $x(R \square S)z$: x 's symptoms are exactly those of illness z .

1.3 Choice of appropriate many-valued logics

1.3.1 Empirical criteria

The triangle and square products may be based on a large variety of many-valued logic implication operators; a practical question then arises, as to which many-valued set or relational theory is the best for a particular application and/or knowledge domain, or inference task. Evaluation experiments performed in various applications [11, 28] conclusively show how essential it is to select the fuzzy knowledge representation structure or inference/decision making method that would appropriately match the data / knowledge structures dictated by a particular application. The most important point that emerges from empirical studies is that the technique that should be employed in a specific application will crucially depend on the nature of data and knowledge involved. For an extensive recent survey with selected bibliography that addresses both the theoretical and empirical criteria for the choice of logic see [24].

1.3.2 Theoretical criteria: the checklist paradigm in interval inference

The interval inference in CLINAID is theoretically justified by the checklist paradigm. The checklist paradigm generates *pairs* of distinct connectives of the same logical type that determine the end points of intervals, thus providing formally and epistemologically justified systems of *interval-valued* approximate inference. The most relevant further references are [5, 6, 8, 9, 32], each addressing a different aspect of the problem. Two recent surveys [25, 24] list further theoretical papers as well as applications and also link the checklist paradigm to the computational aspects and to Bandler and Kohout's papers on "fast fuzzy relational algorithms". A brief explanation of the mechanism of the checklist paradigm and of its link to interval logic based inference is given in this section.

Let O be a set of concrete or abstract objects, C a set of abstract constructs and P a set of items that may be associated with O or C . Let Q, R be two crisp relations from the lattice of all relations from O to P , and from C to P , respectively; in symbols: $Q \in \mathcal{R}(O \rightsquigarrow P)$ and $R \in \mathcal{R}(C \rightsquigarrow P)$. Then xQy reads: ‘object x is associated with item y ’, and zRy reads ‘construct z is associated with item y ’. zR is the *afterset* of z , i.e. the set of all y in the range of R that are related to z .

A *checklist* is a tuple (x, xR) such that $x \in C$, where xR is the afterset of x .

An *object-description* is a tuple (y, yQ) such that $y \in O$, where yQ is the afterset of y .

Notational convention. The value of $x_i R y_j$ is written as R_{ij} .

Given a fixed object $x_k \in O$ and a fixed construct $x_i \in C$, a *checklist valuation* is a triple $(\mathcal{V} = x_i, y_j, D)$ such that $D \subseteq P$. This triple will also be called ‘fine valuation structure’, or briefly ‘fine structure’. The value D_j of the element $d_j \in D$ is given by the formula $D_j := Q_{ij} \equiv R_{jk}^T$, where \equiv is the two-valued equivalence connective. The *coarse checklist valuation structure* \mathcal{W} associated with \mathcal{V} is the triple $(\mathcal{W} = x_i, y_j, \underline{d})$, where \underline{d} is computed from D of the given \mathcal{V} by the formula $\underline{d} := \sigma(D_i) = 1/n \sum_{i=1}^n D_i$. $\sigma(\dots)$ is called sigma count in fuzzy set theory.

Given two checklist valuation structures, one may ask about more complex fine structures that can be formed by logic operations over their values. For example given $\mathcal{V}^a = (a, y, D^a)$ and $\mathcal{V}^b = (b, y, D^b)$, can one construct $\mathcal{V}^{a\text{AND}b} = (a\text{AND}b, y, D^a)$? Obviously, $D_i^{a\text{AND}b} := D_i^a \& D_i^b$. The value of the corresponding coarse structure can be computed the obvious way as the sigma count $\sigma(D_i^{a\text{AND}b})$.

If the fine structures \mathcal{V}^a and \mathcal{V}^b are not available, the question arises, whether there exists a many-valued connective AND_{MVL} by which the exact value of $\mathcal{W}^{a\text{AND}b}$ can be computed from \mathcal{W}^a and \mathcal{W}^b .

To obtain the exact value for the composed coarse structure is unfortunately impossible in general, as the truth-functionality is lost in transition from the fine to the coarse structure. The rule of compositionality of Fregean logic does not hold in this case. We can, however find a pair of many-valued logic (MVL) connectives, AND_{TOP} and AND_{BOT} that give the upper and the lower bound, thus forming an interval in which all the *unknown* exact values of the coarse structure *must* be contained.

Let us introduce the following convenient notational conventions for future use. For 2-valued crisp fine structure components let us define: $\underline{a}_i := D_i^a$ etc. For the many-valued coarse structures introduce \underline{a} by the definition $\underline{a} := \underline{d}^a = \sigma(D_i^a) = 1/n \sum_{i=1}^n D_i^a$, etc.

Let us look now at other remaining cases. For any of 16 two-valued connectives [35, 18], say F , the exact value of the coarse structure $\underline{a} \text{ CON } \underline{b}$ can be computed from the fine structure by the formula $\underline{a} F \underline{b} := \sigma(\underline{a}_i F \underline{b}_i)$. If only \underline{a} and \underline{b} are available, it is not always possible to find a many-valued connective CON such that $\underline{a} \text{ CON } \underline{b} = \underline{a} F \underline{b}$ would hold in general.

Fuzzy logics in general deal with uncertainty, imprecision and incompleteness of data. The transition from the fine to the coarse structure is usually accompanied by loss of information, or what can be called “loss of variety” in Ashby’s sense. Hence, the coarse structure *approximates* the fine structure in such cases. One must specify in a more precise way, what kind of information loss is expected in order to derive a pair of interval many-valued logic connectives, *CONTOP* and *CONBOT* that give the bounds within which the exact value must fall. This specification determines the character of approximation and the exact meaning of the phrase “ \mathcal{W} is associated with \mathcal{V} ”.

Above, the fine structure \mathcal{V} and the coarse structure \mathcal{W} associated with it were defined. The coarse structure was “associated” with the fine structure by the formula for computation of its exact values from the fine structure. In general, the form of this association of structures, and hence the formula yielding the values of \mathcal{W} , is determined by a measure. In the case of association presented above, measure $m_1 = 1 - u_{10}$ was used [5], which yields $\text{TOP}(\underline{d}) = \max(0, \underline{a} + \underline{b} - 1)$, $\text{BOT}(\underline{d}) = \min(\underline{a}, \underline{b})$. To understand the meaning of this measure, the meaning of u_{lm} has to be clarified first.

Pairs of binary values of two fine structure composed by F , yielding the composed binary values ν_{lm}^k can be combined in four distinct ways:

$$\nu_{00}^k = \neg \underline{a}_k \& \neg \underline{b}_k; \quad \nu_{01}^k = \neg \underline{a}_k \& \underline{b}_k; \quad \nu_{10}^k = \underline{a}_k \& \neg \underline{b}_k; \quad \nu_{11}^k = \underline{a}_k \& \underline{b}_k.$$

From these four types of components, u_{lm} with $l, m \in 0, 1$ is computed by the formula $u_{lm} := \sigma(\nu_{lm}^k) = 1/n \sum_{k=1}^n \nu_{lm}^k$.

Using the measures $m_1 - m_5$ of [5] leads to interval logics of various kinds. For each measure, a pair of connectives (*conbot*, *contop*) were derived (cf. [5], Theorem 6.3), giving the upper bound $\text{TOP}(\underline{d})$ and the lower bound

$\text{BOT}(\underline{d})$ of the value \underline{d} for the composite structure.

In general, $m_i = m(F; G(u_{lm}))$ is a function of two parameters, F and $G(u_{lm})$, where u_{lm} is parametrised by $l, m \in 0, 1$ as seen from the formulas above. Relation $G(u_{lm})$, the so-called *constraint table* can be found e.g. in [19] and is explained in detail in [5]. The constraint table has two distinct forms, one for the object language connectives, the other for the rules of inference that belong to the metalanguage [19].

The inequality restricting the possible values of measure $m(F; G(u_{lm}))$, expressing the logical values that fall within the interval, is written in its general form as: $\text{contop} \geq m(F; G(u_{lm})) \geq \text{conbot}$. In this paper we employ $m(F) = m_1(F) = 1 - u_{10}$. When the type *PLY* (implication operator) is chosen for F , this choice yields the bounds [5]:

$$\min(1, 1 - a + b) \geq m_1(\text{PLY}) \geq \max(1 - a, b)$$

where the Lukasiewicz implication represents one bound while the other bound (plybot) is the Kleene-Dienes implication operator. Other measures give other bounds, as listed in Appendix 2. Inequalities for all 16 possible logic types of connectives F and measure m_1 appeared e.g. in [6, 8]. As far as we are aware, the papers of Bandler and Kohout [5] and [6] appear to be the first in the literature on the topic of checklist paradigm.

Choosing for F the connective type **AND** Bandler and Kohout [6, 8] obtained for the same measure the bounds $\min(a, b) \geq m_1(\text{AND}) \geq \max(0, a + b - 1)$. The last two inequalities are formally identical with those of Schweitzer and Sklar [39] giving the bounds on *copulas* which play an important role in their theory of *norms* and *conorms*. Surprisingly, these checklist paradigm bounds also coincide with Novák's recent derivation of bounds on fuzzy sets approximating classes of Vopěnka's Alternative Set Theory [34]. Hisdal derives the same inequalities as the bounds on some connectives of her TEE model and comments on a possible link (cf. Appendix A2 "The TEE model and Bandler and Kohout's checklist paradigm" in [15]). In the context of modalities in fuzzy logics, checklist paradigm-like inequalities for $F = \{\text{AND}, \text{OR}\}$ were recently also independently discovered by Resconi, Klir, and St.Clair [36]. Yet all these models are neither formally nor epistemologically identical. This indicates the need for a more precise meta- and metametalogical formulation of many-valued based mathematical systems, that would include in their full definition a part formulating their "mathematical epistemology".

Crispness and its dual fuzziness, two important characteristics of fuzzy sets, were introduced by Bandler and Kohout in their 1978 paper [2, 3]. Later, independently, fuzziness was also introduced and investigated in detail by Yager [42] and further studied in a more abstract setting by Higashi and Klir [14]. Bandler and Kohout's paper [3] motivated further abstract generalizations of Weber [41]. Weber's paper contains many important theoretical results that are also useful in applications.

In the context of interval logics, crispness and fuzziness provide important characteristic of fuzzy propositions, predicates and power sets. The higher the degree of fuzziness of a proposition is, the wider is the margin of its imprecision. Interval connectives-pairs generated by the measure m_1 are of theoretical and practical interest, because of the theorem of Bandler and Kohout (cf. [8], 'Gap Theorem' in Sec. 5, p. 108) concerning the fuzziness of the logics generated by m_1 . This theorem links the *width of the interval* that the values of two many-valued (fuzzy) logic propositions composed by a connective of logical type F attain, with the imprecision of that proposition, measured by the degree of unnormalized *fuzziness*. The theorem holds for all non-trivially 2 argument logic types of connectives. We quote a useful result that holds for the connectives used in the present paper:

$$a\text{ANDTOP}b - a\text{ANDBOT}b = a\text{PLYDTOP}b - a\text{PLYBOT}b = \min(\phi a, \phi b)$$

where $\phi x = \min(x, 1 - x)$ is *unnormalized fuzziness* of x . This gives us an epistemological justification for giving preference to m_1 generated connectives in context of the present application.

If additional statistical assumption are used for characterizing the unknown fine structure together with the approximation measures $m_1 - m_5$, a many-valued connective can be derived for each measure which is optimal with respect to these assumption. This "optimal" connective is a point (non-interval) many-valued logic. Hence, under these additional statistical assumptions, the interval logics *collapses* into point logics. A different logic will result for each different approximation measure — see e.g. the results for measures $m_1 - m_5$ in Theorem 7.1 in [5]. For use of these so-called "expected measures" in CLINAID see [33].

1.4 Dealing with the inferential context in CLINAID

Knowledge-based system architectures of CLINAID type can deal with a *multiplicity* of contexts provided by the multiplicity of the body systems and other factors. Deep knowledge concerning *individual contexts*, takes into account cross-contextual similarities and differences. We distinguish: a) the *context of different body systems*; b) the *context of different diagnostic levels* within the super-context of a specific body system. The multiple context of clinical inference, when a clinician interacts with the system is reflected in the diagnostic hierarchy, which uses *syndromes* in a substantial way.

The strategy of clinical inference used over this diagnostic hierarchy which includes syndromes, is realized in CLINAID by means of fuzzy triangle products [10]. Within each specific body system of CLINAID, (e.g. cardiac or respiratory, etc.) the inferential levels have to be related appropriately. Each body system has specific conceptual semantics that assign the clinical meaning to the relational compositions.

The inferential process is performed in a hierarchical or heterarchical manner, involving the following levels:

1. Symptoms and Sign Level
2. Risk Factors Level
3. Body System Level
4. Syndrome Level
5. General Disease Level
6. Specific Disease Level
7. Aetiological Level

Experience shows that the dynamic paths of inference in diagnosis performed by an inexperienced medical student (in spite of her/his textbook knowledge) are *different* than those performed by an experienced clinician. This is due to the fact that an experienced clinician utilizes the above hierarchies in a more efficient manner than a novice. This reflects also in the way the essential input information (patient's signs and symptoms) is utilized within the context of additional knowledge.

Let us look at a concrete example: *sore throat* may point to diseases in many body systems. The most likely of these will include:

- 1) an upper respiratory tract infection
- 2) rheumatic fever
- 3) collagen diseases (a large group)
- 4) leukemia
- 5) immune deficiency syndrome (a large group)

To decide which body system is affected we need to obtain a ranking order of likelihoods (plausibilities, possibilities and such like) of body system candidates. This is obtained by asking *questions* about the presence of other symptoms. It is a *constellation of symptoms* that makes one or other disease more likely.

Let us take *sore throat*, together with *running nose, eyes; headache, fever/chills*. If one or more of these are positive, this makes the *upper respiratory infection URI* most likely. Even if the answer is *no* to some questions this does not exclude the URI diagnosis.

We have, however to distinguish the context in which the answers appear: e.g. if the patient is a child with *aching in the joints*, another diagnosis, namely, *rheumatic fever* is more likely.

In order to include context, it is not sufficient to present just symptoms, in many instances *risk factors* are also needed. These are obtained from *patient history*. Patient history includes such items as past history, alcohol, drugs, diseases appearing in patient's family, relations, etc. So, the context also comes from the patient history.

The likelihoods (plausibilities, possibilities) of this example are reinterpreted with respect to the context that is embedded within the structure containing *signs/symptoms, risk factors* and *body system* levels. The intervals come with this reinterpretation.

The expertise lies in utilizing this additional knowledge consisting of:

- knowing which question to ask next;
- the ability to interpret the answers in the right context;

- the competence in deciding which is the next body system to consider when the likelihood of the first candidate body system becomes less and less likely with the new questions presented.

Superficially it would appear that the relation between signs, symptoms and illnesses is sufficient for performing adequate diagnostic inference in the broad medical context of multiple body systems. It is also sometime erroneously assumed that this inference can be performed in a way similar to that used in the rule-based medical expert systems concerned with a narrow medical specialty. Investigation of the logical structure of broader categories of medical knowledge, however, shows that this would not be an adequate way of dealing with this problem.

Indeed, the multiplicity of contexts which causes that the same sign/symptom may acquire a different meaning in a different context (as shown by the example) leads to a number of problems. These problems cannot be dealt with correctly in all situations by classical rule-based systems or Prolog systems using logic without types, despite the popular belief perpetuated amongst others, by the providers of rule-based expert system shells. Briefly summarizing [21], three problems have to be dealt with. One faces:

- *The Problem of INCOMPLETENESS:*
Not all signs and symptoms characterizing the disease are always observable or present.
- *The Problem of LOCALITY OF INFERENCE:*
Not all signs and symptoms are relevant in a particular given diagnostic context.
- *The Problem OF COMPLEXITY OF INFERENCE:*
The complexity of exhaustive matching of all disease descriptors and indicators (e.g. signs, symptoms, tests, etc.) may be forbiddingly high.

The multiple context dilemma of clinical inference is resolved by the diagnostic hierarchy which uses *syndromes* as the main instrument. Syndromes are essential when dealing with a multiplicity of body systems of general medicine, a matter that narrowly specialist medical expert systems

have failed to handle adequately. A syndrome is defined as a cluster of signs and symptoms that appear together and characterize a specific group of diseases. This cluster consists of signs and symptoms that, when viewed in probabilistic/statistical terms, are mutually dependent. When handled by relational methods, however, the additional knowledge contained in syndromes and similar semantic constraints, vastly reduces complexity of the inferential task as well as increasing its reliability.

Computational aspects of this complexity reduction follow from the detailed functional arrangement of inferential processes in the diagnostic unit of CLINAID (see [21], Sec. 10.4 and Fig. 10.5 referring to ‘activity graph of the dynamics of a body system on CLINAID’). This is a typical “divide and conquer strategy” as often used in construction of algorithms. Instead of dealing with hundreds of signs and symptoms pointing directly to the hundreds of diseases within a body system, the signs and symptoms point to the syndromes, typically 5–15 in a body system. The syndromes that are found to be relevant will point directly to a much smaller number of candidate diseases. Their number is further reduced by introducing further signs and symptoms into the inferential process. Without the application of such constructs as syndromes, the inferential process might have difficulty in reaching the final conclusion. For discussion of clinical evidence of this phenomenon comparing the inferential process of a medical expert with that of a novice see [26], quoting findings of Anderson.

Although syndromes carry important medical information and are instrumental in reducing complexity of inference, they are usually neglected by the designers of medical ESs. There are several reasons for this. One of these is the fact that when the Bayesian inference is used, the *dependency* of the syndrome’s components substantially increases the complexity of Bayesian inference. This has the consequence that the resulting expert system cannot deal with the multiple contexts and works satisfactorily only within the narrow context of one body system. If, on the other hand, the designer opts for the inclusion of syndromes, it has the following serious consequences when Bayesian inference is used. Given m diseases and n signs & symptoms that are independent, one requires $P_{ind} = m \cdot n + m + n$ probabilities. Without the assumption of independence, and given k dependent signs & symptoms simultaneously, one requires $P_{dep} = (m \cdot n)^k + m + n^k$ probabilities. Taking for example one body system which contains for the purpose of this example 200 diseases and 200 signs & symptoms, $P_{ind} = 40,400$. Taking

10 dependent signs & symptoms that enter into 1 syndrome, $P_{dep} = 4 \cdot 10^{40}$. This explains why excluding syndromes and/or using Bayesian inference is an inadequate, albeit common, approach. We believe that our CLINAID approach avoids this pitfall as described below.

Contribution of interval logics of appropriate kind to improvement of inferential process when dependent entities (such as signs and symptoms related to a syndrome) are involved stems from their mathematical properties. Some logics, such as Kleene-Dienes introduced below are optimal for dealing with dependent data, while the other pole of the interval bound, Lukasiewicz is optimal for data with independent properties. This follows from the theory of the checklist paradigm introduced in Section 1.3. When the fuzziness of data is small, the interval is narrow. With increasing fuzziness, the interval widens (see the formulas relating the fuzziness to the width of the interval in Section 1.3 above). When the width of the interval becomes unacceptably large, the inferential process is stopped, or maybe returned to the point where a request for further data can be made. For point-based inference this option of eliminating the danger of instability does not exist as there is no acceptable criterion for judging the quality of inference, the grade of the point premiss or conclusion refers only to the uncertainty inherent in data itself.

We have discussed the limitation of the conventional systems that are due to the mismatch of the properties of the data with the properties of the Bayesian statistics. The next issue is the multiplicity of contexts in which a given item of input data (patient's signs and symptoms) have to be interpreted, in order to reach the conclusion — by deciding which of the competing hypotheses is the most plausible one.

2 Multi-context inference in CLINAID involving interval-valued inference

In this section we present a clinical example clearly demonstrating how the use of interval logics can improve the quality of reasoning of a medical knowledge based system. The main contribution of interval reasoning is to provide the limits by which the degrees of validity of logical conclusion must be bound. After outlining the necessary prerequisites in terms of the relational structures involved, we present the actual computations that clearly

demonstrate the merit of our method. The computations outlined below use both triangle and square products. Unlike the usual “circle” product which is used for conventional composition of relations and functions, these other products are second order constructs, involving the power sets of ranges and domains of relations. The triangle products are concerned with inclusion of structures, while the square products with symmetrical matching and equality of structures. Unlike the usual circle product, these products are *not associative* even in their crisp Boolean form. The basic intuition for the choice of products can be obtained by re-reading section 1.2.1 above and looking at other applications such as [7, 29, 30, 16].

2.1 Relationships over the basic relational structures of CLINAID

Let us list now the medical meaning (semiotic descriptors) of all the sets entering into the relations of individual levels used in the sequel.

Name:	A set of:
A attributes.
B body systems.
D specific diseases.
O observation events.
P of patients.
S symptoms and physical signs.

Name:	Definition:	Relation
AB $\mathcal{R}(A \rightsquigarrow B)$	from <i>attributes</i> to <i>body systems</i> .
OA $\mathcal{R}(O \rightsquigarrow A)$	from <i>observation events</i> to <i>attributes</i> .
OB $\mathcal{R}(O \rightsquigarrow B)$	from <i>observation events</i> to <i>body systems</i> .
POA $\mathcal{R}(P \times O \times A)$	between <i>patients</i> , <i>observation events</i> and <i>attributes</i>
PS $\mathcal{R}(P \rightsquigarrow S)$	from <i>patients</i> to <i>symptoms and physical signs</i> .
PD $\mathcal{R}(P \rightsquigarrow D)$	from <i>patients</i> to <i>specific diseases</i> .
SB $\mathcal{R}(S \rightsquigarrow B)$	from <i>symptoms and physical signs</i> to <i>body systems</i> .
SD $\mathcal{R}(S \rightsquigarrow D)$	from <i>symptoms and physical signs</i> to <i>specific diseases</i> .

Now, we shall briefly explain the meaning and purpose of the relations employed in the inference.

Definition of the relation from *observation events* to *body systems*:

$$OB_{ik} = (OA \square AB)_{ik} = 1/n \sum_j (OA_{ij} \equiv AB_{jk}).$$

This computes the degree of involvement of each body system relative to available symptoms and signs (and generally other observables) and may involve the time dimension. The set of attributes over which the two relational components are matched is formed by logic formulas over the elementary attributes, such as signs and symptoms.

The relation *involvement of a body system* RI is defined as a fuzzy identity relation, specifying to what degree the body systems are involved with respect to a given OB relation. It is computed by the formula:

$$BI_{ik} = ((OB)^T \square OB)_{ik} = 1/n \sum_j ((OB)^T_{ij} \equiv OB_{jk}).$$

As we are concerned only with the degree of identity of individual elements, not with its violations, only the diagonal of the matrix containing *locally reflexive* [24] elements is used in further inference. Mathematically, the

degree of identity of an element in the sense used here the degree of it being a singleton in its fuzzy power set [3].

Definition of the relation from ‘symptoms and signs to body systems’

$$SB \in \mathcal{R}(S \rightsquigarrow B).$$

The relation SB is an element of the lattice \mathcal{R} of all fuzzy relations from the set S of symptoms and physical signs to the set of individual body systems B . The aim of this relation is to select the body systems relevant to presented patient information.

The relation PA relates the set P of patients to the sets of attributes. It is computed from the ternary relation POA by the relational composition (square product) over the set O of observation events.

$$PA_{ik} = (POA \square POA)_{ik} = 1/n \sum_{j=l} (POA_{ijk} \equiv POA_{ilk}).$$

This is special case of a product of two 3-ary (3 dimensional) relations. In general, given an r -ary and an s -ary relation, the dimension of the product is $(r + s - 2)$ -ary [10]. Here, however, we deal with a special case, as the same variable ranges over the first and the third index of both relations. Hence, the result is a 2-ary relation. The first argument of the product, say, (p_i, o_j, a_k) is matched with the second argument (p_i, o_l, a_k) by \equiv for $j = l$ and summed.

The relation $HPD \in \mathcal{R}(P \rightsquigarrow D)$, expresses a hypothetical relationship between *patients* to *specific diseases*, the hypothesis being based on the data contained in PS :

$$HPD_{ik} = (PS \triangleleft SD)_{ik} = 1/n \sum_j (PS_{ij} \rightarrow SD_{jk}).$$

This relation is computed directly from individual (observed) signs and symptoms PS and the knowledge of SD . The alternative is to involve the syndromes as well.

It can be combined with the BI to form the *working diagnoses* relation $WD \in \mathcal{R}(P \rightsquigarrow D)$ by the formula:

$$WD = HPD \square BI.$$

This formula computes the intersection of the relations *HPD* and *BI*. The connectives *ANDTOP* and *ANDBOT* used to compute this intersection are $\min(x, y)$ and $\max(0, x + y - 1)$, respectively.

Let us take a concrete example, a fragment of the knowledge structure dealing with the relationship of signs/symptoms to several body systems. This example will be used in the sequel to demonstrate how the interval based inference is performed in CLINAID.

Signs/symptoms	Diseases			
	RI	RF	St	Le
fever	.8	.8	.8	.8
sore throat	.8	.2	.2	.8
running eyes	.4	.1	.1	.4
headaches	.2	.2	.2	.2
rash	.1	.3	.6	.7
red nasal mucosa	.6	.1	.1	.6
red pharynx	.6	.1	.1	.6
enlarged tonsils	.8	.1	.1	.8
pus on tonsils	.9	.1	.1	.9
child with aching joints	.3	.9	.9	.2
PH chloramphenicol	.1	.1	.1	.9
child in day care	.7	.1	.1	.2

Table 1. Relation of Signs/symptoms to Diseases

Attributes	Body systems									
	RS	CVS	GIS	US	NS	ES	MS	GS	Skin	HEM
F	.7	.2	.3	.3	.2	.2	.2	.3	.1	.3
Ch	.1	.6	.2	.1	.2	.1	.9	.1	.1	.1
F & Ch	.4	.9	.2	.1	.2	.1	.6	.1	.1	.3

Table 2. Relation from Attributes to Body Systems

Let us assume that our clinical case is a child with aching joints that also has fever with chills. The set *S* is a crisp set consisting of $s_1 = Ch$ (Child with aching joints) and $s_2 = F$ (Fever with chills). From this set, and using

the clinical knowledge structure of Table 1, one computes the relation HPD that suggests the diseases that the patient may be suffering from. The result of this computation is listed in the column HPD_1 of Table 3. The diagnosis based on the set $S = \{F, CH\}$ cannot distinguish between RF (rheumatic fever) and St (Still's disease), both are suggested to the degree 0.85. Other two diseases respiratory infection (RI/0.55) and leukemia (Le/0.5) are very close. The implication operators used in the computations were Lukasiewicz and Kleene-Dienes operators, for the TOP and BOT values of the intervals entering HPD_1 . As the values of S are crisp, the TOP and BOT values are identical. For fuzzy values of S , one obtains a true interval.

In the above computation, no information about the interaction of F and Ch was used. The suggested working diagnosis can be refined using this available information, that is used to compute the candidate body systems, using additional clinical knowledge contained in Table 2. It will be seen that in this refinement the interval logics play useful role. Let us compute the first refinement. To obtain WD we have to compute BI first.

The patient's signs and symptoms are not oscillating, that is, the relational matrix POA has all the rows of the same values. The set S yields the following attributes: $A = \{F\&\overline{Ch}/0, \overline{F}\&Ch/0, F\&Ch/1\}$. This is also the set of all attributes (afterset) o_iOA of the relation OA (i.e. the i -th column of the relational matrix OA). From OA and AB (given in Table 2) the relation OB is computed using $S\#$ based equivalence. Only four the most significant body systems are used in this example. These are: *Respiratory (RS)*, *Cardio-vascular (CVS)*, *Muscular (MS)*, and *Hematological (Hem)* body systems. The intervals enter into the computations first while computing the relation $BI = OB^T \square OB$. The TOP and BOT values of the intervals are computed by the equivalences based on Lukasiewicz and Kleene-Dienes implication operators, respectively. The diagonal of BI determines the involvement of individual body systems. We obtain: $BI_{ii} = \{RI/[.6, 1], CVS/[.9, 1], MS/[.6, 1], HEM/[.7, 1]\}$. The resulting *working diagnoses* computed by the formula $WD_1 = BI \sqcap HPD_1$ are listed in Table 3.

We can see now that after adding the information about the interaction of F and Ch and the clinical knowledge about the plausible involvement of the body systems, rheumatic fever R in CVS is very close to Still's disease St in MS and both more plausible than other two diseases. This suggests a strategy for further refinement: try to find the signs/symptoms that push

RI and *Le* to the top. If this fails, the previous diagnosis stands.

To demonstrate the dynamics of the changes, let us introduce other three elements of S , *rash (R)*, *enlarged tonsils (Et)*, *pus on tonsils (Pt)* and assume that all have degree 1, i.e. are crisp elements of S . Table 3 shows also these further refinements. HPD_1 is computed from F, Ch , HPD_2 is computed from F, Ch, R, Et , HPD_3 is computed from F, Ch, R, Et, Pt .

Body Systems	Diseases	BI_{ii}	HPD_1	WD_1	HPD_2	WD_2	HPD_3	WD_3
RS	RO	[.6, 1]	.55	[.15, .6]	.5	[.1, .5]	.58	[.48, .58]
CVS	RF	[.9, 1]	.85	[.75, .9]	.525	[.42, .52]	.44	[.34, .44]
MS	St	[.6, 1]	.85	[.45, .85]	.387	[0, .39]	.5	[.1, .5]
HEM	Le	[.7, 1]	.5	[.2, .5]	.62	[.32, .62]	.84	[.54, .84]

Table 3. Interval-Based Diagnoses

	[TOP - 30%, TOP]	[BOT, BOT + 30%]
WD_1	{ RF, St }	{ RI, Le }
WD_2	{ RI, RF, Le }	{ RI, St }
WD_3	{ RI, Le }	{ St }

Table 4. Plausibility Partitions of Working Diagnoses

Each collection of diseases that forms a WD_i contains the most plausible disease, having the degree of plausibility TOP and the least plausible, having the degree BOT. Table 4 show the top and bottom band of diseases. The remaining diseases are placed in the third band, in between the other two. This kind of partition is used with advantage to generate interval based questioning strategies that extend and improve the previously developed non-interval based questioning strategies of CLINAID [27]. The width of the bands that is set in the example to 30% is usually variable, regulated by the required size of the working hypotheses set. This is similar to the way the dynamic tuning is done in information retrieval algorithms [23].

In the early information retrieval applications, the size of the set of retrieved objects was regulated by a point threshold [17, 31, 23], α -cut of a fuzzy set. Here, the regulating mechanism comes from the interval logic of the checklist paradigm. Practical interest in checklist paradigm intervals stems in this context from the following consideration. Let the *toler-*

ance of imprecision of a many-valued (fuzzy) be $\tau \in [0, 1]$. An interval fuzzy proposition A is τ -acceptable, if its value interval satisfies the constraint $a_{top} - a_{bot} \leq \tau$). Any proposition that does not satisfy the constraint is called τ -unacceptable. Epistemologically, the concept of τ -acceptability means that only the propositions with the degree of fuzziness smaller than τ will be used as the logic premisses in further inference. If during the inference process a τ -unacceptable proposition is derived, two actions can be taken: (1) adding more information by using the premisses that are less fuzzy but carry the same conceptual information and recomputing the logical interval proof again; or (2) abandoning the inference process because of lack of precise enough information.

3 Conclusion

The generic architecture of CLINAID is designed to operate in a multi-environmental situation and make decisions within a multiplicity of contexts. In this paper we have used several body systems to demonstrate interaction across body systems during the inferential process and have shown how interval massed methods of inference help in dealing with large amounts of medical expert knowledge across a number of body systems. Interval reasoning provides the limits by which the degrees of plausibility of a logical conclusion must be bound.

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