Ontologies and Bayesian Networks in Medical Diagnosis

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Abstract

The amount of information that must be taken into account in medical diagnosis is huge and subject to evolution. Ontologies are a means for formalizing the concepts of the domain of interest. Open, interoperable ontologies already exist for the biomedical field, enabling scientists to communicate with minimum ambiguity. Unfortunately, reasoners acting upon ontologies operate in a deterministic manner, which is unsuitable for the medical domain, where uncertainty must also be taken into account. Bayesian networks (BNs) offer a coherent and intuitive representation of uncertain domain knowledge. This paper presents an approach to the use of ontologies and BNs in medical diagnosis. The approach is based on the adoption of predefined structures for the BNs. These lead to reduced extensions to the domain ontology, yet allowing probabilistic analysis.

1 Introduction

Medical diagnosis is the process of attempting to identify the diseases underlying patients' complaints based on signs, symptoms and medical history of the patient. Usually, the physician makes a first evaluation of patient's clinical situation by considering the pathologies that are compatible with symptoms and signs, then he can proceed with differential diagnosis, i.e. a systematic, iterative method of weighing the probability of one disease versus that of other diseases possibly accounting for a patient's illness, until the most likely diagnosis matching the symptoms is deduced. In this process the physician may require execution of additional tests.

Unfortunately, the amount of information that must be taken into account in medical diagnosis is huge and thus hardly manageable by human minds [24]. To assist the physician, a number of systems have been introduced based on computational intelligence [18, 20]. Expert systems make deductions by referring to the knowledge (even incomplete) provided by domain experts. Validating and keeping up to date that knowledge may result in a heavy burden, since, the medical domain is practically infinite and in continuous evolution. Therefore, it does not make sense to group a number of experts hoping that they will produce a complete, definite set of data; thus, a different approach must be taken, that is we must build systems that allow qualified user to contribute their knowledge in the course of system life, without the intervention of system developers. Knowledge contribution must take place with respect to the intensional and the extensional aspect, that is with respect to the schema of the domain model and to the actual data. This is made possible through the use of ontologies.

An ontology is a formal representation of a set of concepts related to the domain of interest. Ontologies aim at capturing domain knowledge, providing a commonly agreed understanding that can be reused and shared across applications, enabling interoperability and knowledge reuse but also machine-readability and reasoning about information through inferencing [13, 16, 19]. They natively allow representation of semantic models combining non ambiguity of technical specification with the understandability needed to fill the gap between technicians and stakeholders. Ontologies naturally fit into a distributed context, enabling creation of reusable models, composition and reconciliation of fragments developed in a concurrent and distributed manner [27, 28]. For instance, an OWL ontology is an RDF graph, which in turn is a set of RDF triples that can actually be expressed in XML, according to RDF/XML syntax [29, 30]. Each element of a triple has an unique identifier, given by its URI, and thus there is no limitation to distribution and reconciliation of triples over the network. Last, but not least, ontologies are inherently extensible and thus they can model evolving domains, encouraging an incremental approach that can accompany the evolution towards shared models, meeting the increasing needs of data and information integration in the biomedical field. A number of open, interoperable ontologies are available for the biomedical field [23], which aim at "enabling scientists and their instruments to communicate with minimum ambiguity", so that "the data generated in the course of biomedical research will form a single, consistent, cumulatively expanding, and

algorithmically tractable whole" [23]. Off-the-shelf tools supporting methods for information search, model validation, inference and deduction of new knowledge are also available [1, 3, 15, 21, 26, 12].

First order logic provides the theoretical foundation for inferential analysis, but, unfortunately, this leads to resolution algorithms which are deterministic in nature. The limit of ontologies is actually their inability to deal with uncertainty, a typical aspect of diagnostic processes. On the other hand, BNs offer a coherent and intuitive representation of uncertain domain knowledge [31]

A BN consists of a graphical structure, encoding statistical variables from the domain of application along with the influential relationships between them, and an associated numerical part, encoding a joint probability distribution over these variables.

Building a BN involves three basic tasks [9]. The first is to identify the variables that are important in the domain, along with their possible values. The second is to identify the relationships between these variables and to express them in a graphical structure. The last task is to obtain the probabilities that are required for the network's quantitative part. These tasks are typically performed with the help of domain experts.

As discussed in section 2, a number of papers addressing the use of BNs in conjunction with ontologies have been published. Schematically, they tend to follow the approach of interpreting ontological constructs in a probabilistic manner, so as to express uncertainty about the knowledge contained in the model. BN are usually generated in a semi-automatic manner from the ontological model [10, 14]. Several authors [5, 7] propose extensions to the language used for describing the ontology (e.g. OWL, the ontology language recommended by the World Wide Web Consortium, W3C), thus loosing standardization.

This paper deals with the application of ontologies and BN to medical diagnosis, following a somewhat different approach which was shaped after the consideration that a domain-specific algorithm for generation of BNs leads to a simpler ontological model and to BNs exactly tailored to applicative targets. Besides defining the ontological model for the specific domain, we also defined a template of form of BNs required in the diagnostic process. The implemented algorithm is illustrated in section 4.

In so doing, BNs are generated in a completely automatic way, while the ontology is dealt by in the usual manner, adopting standard OWL.

We have developed a prototype system in which the knowledge base can be progressively extended by accredited users (i.e. specialists) contributing additional knowledge. Since BNs are produced in a predefined form, the ontology is not required to model those aspects that are needed for building the graph. The algorithm is able to estimate the probability that a patient is affected by a given pathology and is also capable of suggesting possible additional tests, as well as to compute their usefulness (for this part, we generate *decision network* an extended form of BNs).

The rest of this paper is organized as follows. The next section discusses related work, while section 3 introduces the defined ontological model for medical diagnosis; section 4 describes the kind of BNs that are needed to perform medical diagnoses; section 5 introduce decision networks as a means for evaluating the usefulness medical tests; section 6 extends the ontological model of section 3 with correlations between pathologies and observations; conclusions are drawn in section 7.

2 Related work

In [14] a knowledge-engineering methodology is proposed for constructing and maintaining BNs. The methodology builds upon an ontology which constitutes the repository of shared and agreed domain knowledge and is used to derive, in a sequence of steps, the graphical structure of a BN. The fashion in which the graphical structure is derived from the ontology provides for explicit management of modeling decisions. Due to the complexity of the domain and the high impact of misclassification, the derivation of the graph structure is done manually by expert analysis. Phase-specific guidelines support the knowledge engineer in taking the decisions required. The method is applied to the domain of oesophageal cancer.

The automatic construction of a BN has been addressed in [6] referring to the domain of telecommunication. The construction of the network comprises essentially the same tasks outlined in [9]. The paper relies on knowledge representation and inference capabilities of ontologies to build automatically a BN that can be used to support machine decision-making processes. The ontology which models the domain knowledge is augmented with concepts related to BNs. To create the BN, an instance of each leaf class that inherits from the <BayesianNetworkNode> concept is created. Properties and relations of nodes are set out using the constraints offered by ontology restrictions.

In [34], an ontology representing Clinical Practice Guidelines is developed. The ontology includes uncertainty features that permit the construction of conditional probability tables and the automatic generation of the corresponding BNs. The approach is not meant to address the generation of BNs in a general manner, but rather to address the generation of networks in the forms implied by the specific application.

Fenz et al. [10] follow essentially the same approach of [6], but they construct the BN directly from existing/public domain ontologies, avoiding the development of a a specific ontology with Bayesian extensions. However, since

the functions for calculating conditional probability tables are not provided by the ontology, these must be modeled externally; furthermore, human intervention is still necessary if the ontology does not provide a knowledge model which exactly fits the domain of interest.

In [4] and [5], extensions to OWL are proposed aimed at providing the ability to express probabilistic knowledge. Though this research is focused in the Semantic Web, the idea is to establish a framework aimed at providing full support for uncertainty in the field of ontology engineering. The new language, called PR-OWL, extends both syntax an semantics of OWL, so as to make possible to express uncertainty about the all forms of knowledge contained in the ontological model. The proposed extensions will allow legacy ontologies to interoperate with newly developed probabilistic ontologies. In the authors' view, the proposed extensions should become part of future version of OWL. Of course, this would imply improvements of current tools, from editors to reasoners.

Extensions to OWL so as to incorporate BNs are proposed in [7] [8]. To this end probabilistic markups for attaching probability information, are introduced. The probabilistically annotated OWL ontology is converted into a BN by a set of structural translation rules, The translated network can support accurate ontology reasoning under uncertainty as Bayesian inferences.

A similar, though less impacting proposal is in [33] and [32], where annotation are used to specify probabilities associated to classes and properties. Dependency relations between random variables are explicitly specified via the property element <dependsON> specifically introduced to markup dependency information in an OWL ontology.

3   The ontological model

Let us start with the model of Figure 1, which represents the part of the ontology relevant for the discussion that follows. The schematization of Figure 1 closely corresponds to the Analysis Pattern "Observation" of [11]. This pattern has an important feature: it separates the operational from the knowledge part, thus providing the paradigm for implementing an ontology in which observations represent the extensional part, while observation types represent the intensional part of the ontology itself. Analysis Patterns provide ready-to-use solutions to many medeling problems and thus reference to these patterns was very useful in smoothing the inherent complexity of building an ontology for the medical domain.

In Figure 1 class `PMR` stands for the Personal Medical Record, while `Observation` is the generic concept for representing symptoms, signs and other medical fact/factors related to patient's health, including past treatments and/or predispositions. The two actors, physician and the specialist, interacting with the knowledge base have been added.

The specialist is responsible for contributing new knowledge, that is for extending the scope of the intensional part of the ontology. For instance, he can add new observation types as well as new pathologies as a consequence of the growth of the body of medical knowledge. Furthermore, he can define rules for inference analysis so as to allow use of a reasoner. For example, a rule concerning the fact that "if the patient has a temperature greater than 39°C then he has high fever" could be expressed (in a pseudo formal language) as:

Patient(?p) $\wedge$ hasObservation(?p,?t)

$\wedge$ TemperatureObservation(?t) $\wedge$?t.value $> 39°$C

$\rightarrow$ hasObservation(?p,?f) $\wedge$ FeverObservation(?f)

$\wedge$?f.value $=$ "HIGH"

The physician is responsible for diagnosis execution, an activity which naturally leads to augmenting the extensional part of the ontology with new facts (i.e. observations). Of course, the physician can interrogate the knowledge base to gather those data that he considers useful to help him formulating his own personal diagnosis.

Note that the inference rules of Figure 1, can be used by the reasoner to: (a) validate the consistency of the observations introduced by the physician; (b) infer new facts (observations) which will go to extend the knowledge base; and (c) automatically perform a diagnosis relying on the content of the knowledge base itself. An off-the-shelf reasoner (such as [21] or [12]) is actually a convenient way to address the previous points.

However, referring to point c), the kinds diagnoses that are made possible by the ontology outlined so far are those that derive from deterministic reasoning [25] . This is certainly valuable in situations whereby, given certain symptoms, the presence/absence of a pathology is directly deductable. But this is not always the case in medicine. Quoting from [25]: "Trying to use first-order logic to cope with a domain like medical diagnosis fails for three main reasons: (a) Laziness: it is to much work to list the complete set of antecedents or consequents needed to ensure an exceptionless rule, and too hard to use the enormous rules that result; (b) Theoretical ignorance: medical science has no complete theory of the domain; and (c) Practical ignorance: even if we know all the rules, we may be uncertain about a particular patient because all the necessary test have not or cannot be run".

To summarize, ontologies are excellent to represent large complex domains as that of medicine, but they fail when probabilistic reasoning is needed [25]. In other words, a system addressing medical diagnosis must be capable of dealing with uncertainty. BNs are used for this purpose.
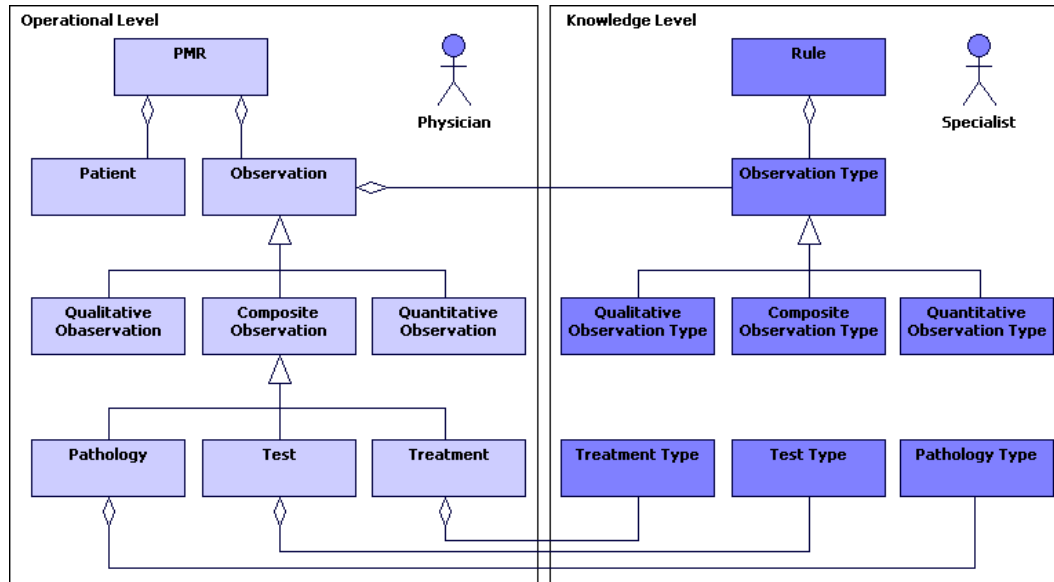
Figure 1. The ontology for medical diagnosis

4 Bayesian networks for medical diagnosis

Referring to the model of Figure 1, the question is: what is the information that must be included into the knowledge base to permit generation and use of BNs for medical diagnosis? To answer this question, two aspects must be considered:

  a) the the structure of the network, i.e. the topology of the graphical representation of the network;

  b) the parameters characterizing the entities that can be comprised in a network.

Concerning point a), we propose the use of a simple two-level network, as that of Figure 2 (from symptoms to pathologies). In this network the probability that a given pathology is present is conditioned by the probability of observations (symptoms). Observations can represent other factors that are relevant in the diagnostic process, including: disease proneness, results of medical tests, effects of treatments, multi-pathology conditions and phenomena that evolve over time. Representation of these factors was actually a major requirement set forth by clinical specialists. Consequently, we assumed that the structure of BNs for medical diagnosis had to be always that Figure 2.

The important consequence of choosing a predefined network structure is that, in our system, the generation of BNs is left to the simple algorithm described below, avoiding the representation of any structural aspect in the ontology.

Concerning point b), since the structure of the network is left to the predefined algorithm, what is needed for augmenting the ontology of Figure 1 to allow the production of BNs reduces to the correlations between pathologies and observations. As will be shown in section 6, correlations are given through conditioned or a-priori probabilities.

The algorithm works as follows:

  1. Add asserted observations relative to the patient to the knowledge base and then run the reasoner to discover further possible observations, according to inference rules.

  2. For all observation types corresponding to the set of asserted and inferred observations, extract all the compatible pathology types, so as to build the BN as in Figure 2. Then add to the nodes of the generated net the a-priori probabilities contained in the knowledge base.

  3. Change nodes' probability in accordance to the findings (i.e. asserted and inferred observations) and then compute a-posteriori probabilities.

In our system, the algorithm for generating and computing Bayesian networks takes advantage of an existing off-the-shelf library [2]. As a result, it reduces to a sequence of invocations to library's interface.

The network of Figure 2 shows the causal relationship between observations and pathologies and thus it is intuitively the most appropriate for diagnosis, since it corresponds to how the physician proceeds in performing the diagnosis. However, it has some drawbacks as regards the population of the knowledge base. In fact, it requires
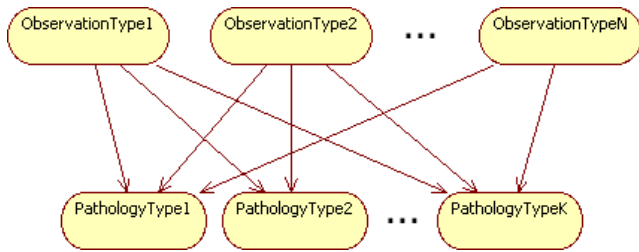
Figure 2. The topology of a Bayesian network for medical diagnosis.

the a-priori probabilities of observations, which, unfortunately, are hardly available as published data. Use of the net of Figure 2 would force the specialist to guess these probabilities from his experience and/or from his understanding of the given situation. Furthermore, the structure of the network easily leads to a large Conditional Probability Table (CPT), which can result hardly manageable by the human. To circumvent this difficulties, a system should provide a friendly user interface, through which the specialist can rather input a-priori probabilities of pathology types and conditional probabilities of observation types given the pathologies. Formally, P(Pathology Type) and P(Observation Type|Pathology Type). In practice, the specialist as to contribute CTPs as in the following example

PatholoyType: Flu

P(Flu)	
value	probability
present	0.00027
absent	99.99973

ObservationType: Cough

P(Cough $\mid$ Flu)		
value	prob. flu present	prob. flu absent
absent	51	77
dry cough	46	13
not dry cough	3	10

Due to the properties of BNs, it is always possible to transform these probabilities and to derive the CPTs for the network in the form of Figure 2. Furthermore, a learning algorithm [22] [17] can be used afterwards to refine both CPTs and a-priority probabilities.

5 Decision networks

In performing the diagnosis the physician may require that the patient undergoes to additional medical tests. This poses the problem of evaluating which is the most useful test to be done.

The search for the most useful medical test is done via "decision networks" [25], an extension of BNs that adds decision and utility nodes. Graphically, decision nodes are in the form of rectangles, while utility nodes are in the form of diamonds.

Usefulness of a medical test can be evaluated with respect to:

a) utility indexes that can be computed through a simple cost function, depending only on the type of test; these include cost and invasiveness of the tests. The corresponding utility node is labeled as C in Figure 3;

b) utility indexes that are computed taking into account both the pathology and the type of test; these include the ability to identify the most serious pathologies among those taken into consideration and the time for getting test results. The corresponding utility nodes are labeled as T_i in Figure 3;

c) utility indexes related to sensitivity and specificity of a test with respect to a given pathology. The corresponding utility nodes are labeled as U_i in Figure 3.

In Figure 3, pathology types represent the probability that the given patient has those pathologies. This probabilities result from the probabilistic inference done through a BN as discussed in section 4. Box `Which Test?` is the decision node for medical tests; in practice, this is a variable which takes values identifying the tests that are related to the considered pathologies; the set of admitted values are obtained querying the ontological model. Nodes `PathologyType-Tests Correlation` depend on the type of pathology and the type of test; it either models: (i) test sensitivity, i.e. the probability that a test produces a positive result (when performed on patients affected by the pathology); or (ii) test specificity, i.e. the probability that a test produces a negative result (when performed on patients not affected by the pathology).

Note that, in Figure 3, tests have an associated utility functional that solely depends on them (i.e., diamond C); utility nodes labeled T_i quantify the usefulness of tests relative to their urgency with respect to the given pathology; finally, diamonds labeled U_i, which depend on the presence/absence of the pathology as well as on specificity and sensitivity of the test, provide a measure the test effectiveness for the various pathologies.

In our system, the structure of decision networks is predefined as being that of Figure 3 (the only possible variation is the absence of one or more utility nodes if the related utility index is not considered of interest). To construct a net, the physician interacts with the system specifying which are the utility indexes he wants to compute. This leads to querying the knowledge base for the elements that are passed to the library (that actually builds the network and computes
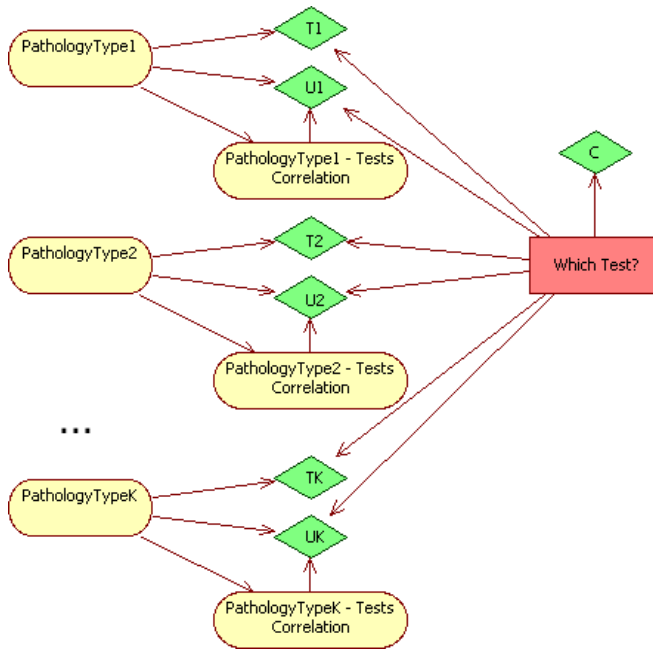
Figure 3. Decision network for a (single) pathology.

come qualitative observations. This is why in the model of Figure 4 there are only qualitative observations.

In accordance with [11], in drawing Figure 4, the concept of phenomenon has been introduced. `Phenomenon` actually represents the set of discrete values (viz, absence, low, medium, high) that a qualitative observation (viz, fever) can take. The correlation is thus between `Pathology Type` (viz, flu) and `Phenomenon`; and this is nothing but a CPT.
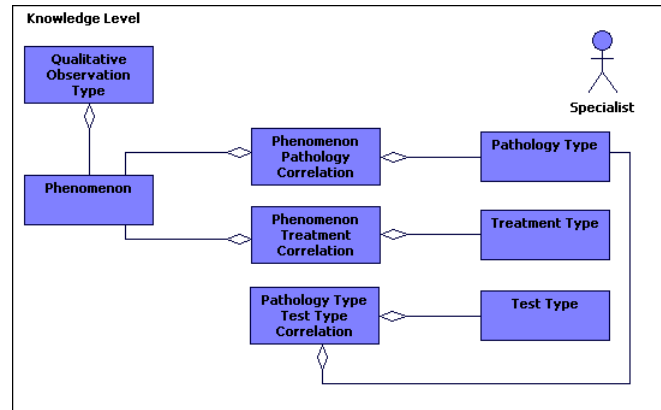

Figure 4. Correlations to perform Bayesian analysis.

the quantities of interest). The algorithm for generating decision networks is similar to that for generating BNs.

6   Model for medical diagnosis

As anticipated in section 4, in order to construct BNs, the ontology must comprehend correlations between pathologies and observation (which are missing in Figure 1). Before introducing these correlation we must spend a few words on qualitative and quantitative observations (composite are a mix of them).

In Fig 1 observations are classified as being qualitative or quantitative. A quantitative observation could be "patient's body temperature is 37.5C", while a qualitative observation could be "patient has fever" or, better "patient has low fever". In the clinical practice, the exact value of an observed parameter has often less significance that the range in which the parameter value falls. This considerations, and the fact that the treatment of quantitative observations would require the introduction of probability distributions (instead of discrete probabilities), are the motivations for discretizing quantitative observations. This is done through the inference rules defined by the specialist so as to perform discretization based on correlations with pathologies. For instance a measured temperature of 37.5C can be classified as being low or medium depending on the pathology. In other words, interpretations of quantitative observations be-

Figure 4 shows also the correlation between `Treatment Type` and `Phenomenon` which has not been discussed here due to space limitations. Furthermore, the figure models also the correlation between pathologies and tests, which are used to measure test sensitivity and specificity (section 5).

7   Conclusions and future work

We discussed the construction of a system for medical diagnosis. The systems uses an ontology as a repository of the medical knowledge relative to the medical field. The ontology can be extended by the specialist in the course of system usage. To this end, the accredited user is presented with a graphical interface trough which possible new pathologies and symptoms are introduced, along with the probabilities that characterize their dependencies. A reasoner provides support for validating the consistency of any introduced data, as well as to infer implicit properties ad relations among them, thus providing a means for further knowledge expansion. The ontology is treated in a most conventional manner, using well established standards as OWL.

In order to perform the Bayesian analysis, probabilistic correlations among observations and pathologies have been introduced. We decided to use always a two-level BN and a

predefined structure for decision networks. This simplifies network generation and lowers the amount of information to be stored in the knowledge base. To generate and evaluate bayesian and decision networks we resorted to an off-the-shelf library, whose functionalities are called on the basis of the kind of network the physician may want to use. This is specified through a friendly system interface that assist the operator in formulating the diagnosis and thus the implied network.

A prototype of the system is currently in use by a the specialists who contributed in defining system requirements, which, as described in section 4, have a strong impact on the structure of the BN. The experimentation is mainly aimed at verifying whether this adopted network structure satisfies any diagnostic need. A future line of investigation will consist in trying to formalize the relationship between the algorithm and both ontologies and BNs, so as to abstract the algorithm's properties that are independent of the specific properties of the latter. The target will be to make possible the specialization of the algorithm to different applicative fields at minimal cost.

Acknowledgements

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