Hypothyroid Disease Diagnosis with Causal Explanation using Case-based Reasoning and Domain-specific Ontology

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Abstract. Explainability of intelligent systems in health-care domain is still in its initial state. Recently, more efforts are made to leverage machine learning in solving causal inference problems of disease diagnosis, prediction and treatments. This research work presents an ontology based causal inference model for hypothyroid disease diagnosis using case-based reasoning. The effectiveness of the proposed method is demonstrated with an example from hypothyroid disease domain. Here, the domain knowledge is mapped into an expert defined ontology and causal inference is performed based on this domain-specific ontology. The goal is to incorporate this causal inference model in traditional case-based reasoning cycle enabling explanation for each solved problem. Finally, a mechanism is defined to deduce explanation for a solution to a problem case from the combined causal statements of similar cases. The initial result shows that case-based reasoning can retrieve relevant cases with 95% accuracy.

Keywords: Case-based Reasoning · Causal Model · Explainability · Explainable Artificial Intelligence · Hypothyroid · Diagnosis · Ontology.

1 Introduction

With the outburst of AI applications, expectations have been increased for intelligent systems in all domains including the health-care domain. The growing capabilities of AI, especially the applications of Machine Learning (ML) leverage new requirements to be fulfilled such as human-level intelligence. According to Pearl, at present three prime obstacles in AI and/or ML applications are there to achieve human-level intelligence, which are; i) adaptability or robustness, ii) explainability and iii) understanding of cause-effect connections. Explainability is one of the major characteristics of human-level intelligence. In recent years, a good number of works have been done to equip systems with causal models in disease diagnosis. Incorporating causal model would facilitate explainability of the prevailing systems [18]. State-of-the-art techniques to develop AI applications are gaining more accuracy gradually but lack of proper explanation with the solution inhibits the reliability of those techniques. Another significant issue is to include causality in the explanation to a solution. If these issues can be solved, most of the challenges to produce AI/ML applications with human-level intelligence will be conquered. Causality in intelligent health-care applications is still in an immature state and there are rooms for further research and improvement. According to Sene, medical information is doubling every 5 years but only 20% of the evidence based knowledge is used by medical practitioners [22]. Several research works have been carried out to make evident based knowledge useful to clinicians as well as intelligent health-care systems. Case-based reasoning (CBR) has been being used for health systems due to its close characteristics to human behaviour, intimidating previous experience as the medical practitioners do. In CBR, only the solution is produced for a new problem case with responsible features only. In this paper, we have adapted the traditional structure of the CBR cycle and introduce causal inference using domain ontology. This research work is aimed at making CBR systems more explainable for health-care services with the support of domain knowledge from an ontology. The objective of this work is further elaborated by considering the following example scenario.

Problem scenario: A patient is reported to be diagnosed for having thyroid diseases provided he/she has taken several tests and recorded his/her history of medication, treatment and symptoms. For this scenario, a physician with access to machines that are capable of classifying based on historical data, can diagnose the patient primarily. From state-of-the-art techniques, for example rough sets learning [19], the physician could get the final verdict of the diagnosis. The verdict may provide that due to having Thyroid Stimulating Hormone (TSH) test value less than or equal to 6 mU/L, the patient may have negative hypothyroid. But for $TSH > 6$ mU/L, the patient might be diagnosed for negative, primary hypothyroid and compensated hypothyroid with 40%, 30% and 30% possibilities respectively. In this uncertain scenario, some causal statements in support of each verdict along with the contribution of other features from the diagnosis would facilitate the decision making for a physician. To overcome these uncertainties and obstacle for explainable AI applications, this research work is destined to produce human understandable explanation in natural language with the label or verdict generated by a classification mechanism from predefined causal statements.

The remaining parts of this paper is divided into several sections. Section 2 describes the background of the concerned topics with several related works. Detailed description of the proposed causal model with formal definitions and brief descriptions of developed components are discussed in Section 3. Section 4 presents a brief evaluation on case retrieval model and the description of extracting explanation for extracted solution. Finally, Section 5 states some of the future possibilities of this research work and conclusive statements respectively.

2 Background and State-of-the-Art

This section contains a short description of the methods used to achieve the goal of this work followed by a brief discussion on recent research works.

CBR is an AI approach that uses previous experiences to solve a current problem which perfectly aligns with the characteristics of physicians in case of patient for diseases. According to Kolodner [13], CBR is a reasoner that solves a new problem by remembering and using past situations similar to the current. CBR is an instance-based lazy learning method, i.e., it does not try to reason until it has to [15]. The term "case" represents an experience achieved from a previously solved problem. The term "based" means in CBR cases are the source of reasoning. Finally, the term "reasoning" means the approach of problem-solving, i.e., solving a problem by concluding using previously solved cases [21]. Based on implementation techniques, CBR can be distinguished into four main types: i) CBR using nearest neighbour, ii) CBR using induction, iii) CBR using fuzzy logic and iv) CBR using database technologies [22]. In addition to the basic implementation methodologies, Barua et al. have shown a distributed architecture of CBR using XML files containing individual cases [1].

Ontology structures the concepts with definition and relations. The term ontology has been evolved from philosophy which means a systematic account of existence [9]. A number of definitions exist about ontology in terms of computer science. Gruber has defined, "Ontology is an explicit specification of a conceptualization" [9]. The previous definition rises another fundamental question, what is conceptualisation? According to Gruber, "A conceptualisation is an abstract, simplified view of the world that we wish to represent for some purpose." [9]. There are other definitions of ontology. Ontology is defined as a formal, explicit specification of a shared conceptualisation [7]. A number of domain independent ontologies are developed for knowledge representation. For instance, BioPortal[1] is a collection of ontologies in biomedical domain.

Various forms of causal models are being investigated for long to be used in disease diagnosis. Mostly causal models are comprised of mathematical models that represent the causal relationships in a system [10]. Pearl introduced causal models based on the Bayesian Network (BN) [17], a commonly used methodology for prediction and classification tasks in different domains. Basically, a BN consists of a directed acyclic graph (DAG) and a set of conditional probability tables such that each node of the graph represents a variable and it is associated with a conditional probability table that contains probability of each form of the variable with every possible state of its parent states. Causal Bayesian Network (CBN) [16] is upgraded from BN with autonomous causal relations with the *do* operator by Pearl [25]. Several works have been done to learn and adopt the CBN for developing causal models. A theoretical study has been carried out by Eberhardth et al. on lower bound of worst case for the number of experiments to be done to recover causal structures [6]. Tong and Daphne have developed a score-based technique to learn CBN from experimental data [24].

Recent works have been done to incorporate ontologies in systems to achieve explainability. Besnard et al. have proposed ontology-based inference rules for causal explanation [3]. In order to facilitate causal models, researchers have also worked on fusing ontology to BN [5][2]. Ishak et al. have proposed Object-

[1] `http://bioportal.bioontology.org/`

Oriented Bayesian Networks based on Ontologies [12]. CBR and ontologies have often be used collaboratively by researchers to facilitate the works of physicians [23][22]. These methodologies achieve the primary goal but lack in overcoming the challenges of modern AI applications. In recent years, there have been some researches on disease diagnosis using causal models. Raghu et al. have proposed a probabilistic causal model for lung cancer prediction [20]. In another research work, Huang et al. have developed a causal discovery of autism based on constrained functional causal models [11]. Wang and Tansel have proposed an ontology based decision support system for medical diagnosis where case retrieval has been done on the basis of semantic similarity [26]. Lamy et al. have proposed an approach to detect breast cancer with explanation using CBR and visual reasoning [14].

3 Proposed Casual Inference Model

The proposed model is an accumulation of several components from different concepts i.e., CBR, ontology and causal inference model. The formal definitions followed by the description of each of the components and their overall collaboration are stated in the following subsections.

3.1 Formal Definition

An ontology is a representation of a domain with respect to its entities, relationship among entities and their attributes which is known as DERA knowledge representation framework [8]. Formally, $D = < E, R, A >$, where, D represents the domain of interest, E is the set of all the entities i.e. concepts and individuals, R is the set of relations among the entities or object properties and A is the set of data properties or attributes. In ontology, classes are arranged in hierarchy which is reflected in statements as *is_a* i.e., *Sub-class is_a Class*. ABox is a fact used in description logic (DL) to define an individual with respect to its respective class in the form of *Class*(`Individual`). It is used to represent the causal statements associated with each of the cases in case base. For example, to express this statement; "`I131` is a specific *Therapy* that is a type of *Treatment*", we use the propositional statements: *Therapy* is_a *Treatment* and *Therapy*(`I131`).

To facilitate causation in the system, we propose to define causal statement C comprised of two atomic statements, α and β as ABox connected with the keyword "*causes*" in the form of "$C : \alpha$ *causes* β". Causal statements will be associated with cases as individual or in a set. For example, a possible causal statement is "C : *TT4*(`Abnormal`) *causes* *Hypothyroid*(`Primary`)" which summarises "*Primary hypothyroid is caused by abnormal free thyroxine level (TT4)*"

Explanation for the solution case will be generated by translating causal statements associated with the similar cases – γ *because_of* Φ, where γ is the solution and Φ is the set of probable explanations to the solution. "*because_of*" is used to make statements shorter which can be translated in natural language as "the probable solution is given because of the facts".

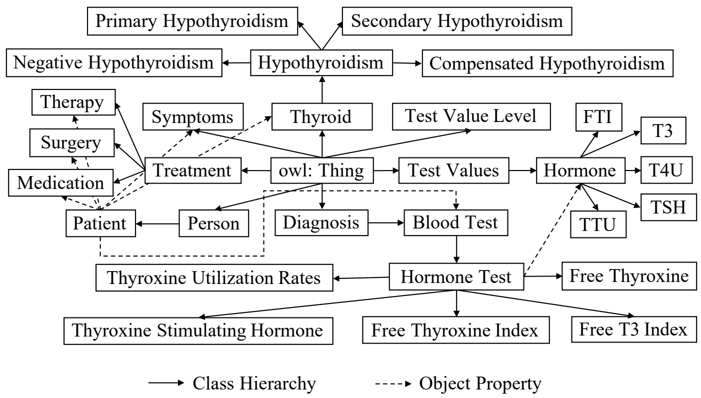

Fig. 1. Class hierarchy and object properties of hypothyroid ontology. Class hierarchy is built on `is_a` relation and object properties among different classes differ on the basis of their characteristics.

3.2 Building Hypothyroid Ontology

An ontology was built to facilitate explanations of solutions produced using CBR. Thyroid disease dataset [19] was used to build the concepts of the ontology. This dataset was created by the Garvan Institute, Sydney, Australia which is now available at UCI Machine Learning Repository[2]. The thyroid disease dataset contains 3772 instances with 26 attributes each. The attributes represent information of diagnosed patients for hypothyroid i.e. age, sex, ongoing medications, disease history, values for different diagnosis tests for determining levels of hormones – TSH, triiodothyronine (T3), thyroxine (TT4), thyroxine utilization rates (T4U) and free thyroxine index (FTI). Instances of the dataset are labelled with four classes: primary hypothyroid, compensated hypothyroid, secondary hypothyroid and negative. Concepts and relations in the ontology were developed and validated in respect of two expert curated medical ontologies built by Shen et al. [23] and Can et al. [4]. Ontology building tool Protégé[3] was used to define the entities, relations and attributes in the ontology. Figure 1 illustrates the classes of hypothyroid ontology which is a subset of E from the equation of DERA given in section 3.1. In the figure, the solid arrows represent the `is_a` relation and dotted arrows shows the object properties of the concepts. At first the concept hierarchy was built. Afterwards, object properties were defined to create relation among the concepts. The object properties from the set R of the equation defined in section 3.1 for the developed hypothyroid ontology are given below:

- `defines`: Represents the relation between *Diagnosis* class and *Thyroid* class.

[2] `http://archive.ics.uci.edu/ml/datasets/thyroid+disease`
[3] `https://protege.stanford.edu/`

- `hasDisease`: Represents the relationship between *Thyroid* class and *Patient* class.
- `hasReceived`: Represents the relationship between *Patient* class and *Treatment* class.
- `hasSymptoms`: Represents the relationship between *Patient* class and *Symptoms* class.
- `hasTestDone`: Represents the relationship between *Patient* class and *HormoneTest* class.
- `hasValueType`: Represents the relationship between *HormoneTest* class and *Hormone* class.
- `hasValueLevel`: Represents the relationship between *HormoneTest* class and *TestValueLevel* class.

Data properties of the developed ontology were defined afterwards which represent values for various entities in the ontology. Set A holds these data properties in equation defined for DERA in section 3.1. The data properties of the hypothyroid ontology are described briefly below.

- `hasAge`: Represents the age of a patient.
- `hasGender`: Represents the gender of a patient.
- `hasTestDefinition`: Represents the information of a diagnostic test.
- `hasTestName`: Represents the name of a diagnostic test.
- `hasTestValue`: Represents the value of a diagnostic test.
- `hasValue`: Represents the reference values of a diagnostic test.
- `lowerLimit`: Represents the regular lower limit of a diagnostic test.
- `upperLimit`: Represents the regular upper limit of a diagnostic test.

Finally, the individuals were added to the ontology based on the experimental data from Thyroid Disease dataset. Most prominent way to store an ontology is to use web ontology language (OWL) or resource description format (RDF). In this work, the built ontology is stored using RDF since it facilitates to hold the inferred axioms of the ontology whereas OWL holds the defined axioms only.

3.3 Case Representation

Cases in the case base are stored in the form of XML files. This method is adopted from the work of Barua et al. [1] to facilitate inclusion of the causal statements to the case representation. In each of the files, there will be a case id, list of features, tested solution, causal statements and index to similar cases to reduce the computation for retrieving similar cases in distributed architecture. Graphical representation of a sample case from the case base of our proposed model is shown in Figure 2. During the preparation of cases, causal statements were added according to the relations among the attributes defined in the domain ontology and their contributions to the final solution. In our concerned scenario, attributes are the levels of various hormone tests and other clinical issues of the patient.

```
<case>
        <case_id>id</case_id>
        <features>
                <feature id=1>true</feature>
                <feature id=2>21.41</feature>
                :
        </features>
        <solution>
                :
        </solution>
        <causations>
                <causation id=1>
                        <cause>Instance_1</cause>
                        <effect>Instance_2</effect>
                </causation>
                :
        </causations>
        <similar_cases>
                <similar_case>case_id_1</similar_case>
                <similar_case>case_id_2</similar_case>
                :
        </similar_cases>
</case>
```

Fig. 2. Sample case representation.

3.4 CBR with Causal Model

The proposed causal model is incorporated within the naive CBR architecture. Figure 3 illustrates the working mechanism of the model. This model is described based on the basic four steps of a CBR system: i) retrieve, ii) reuse, iii) revise and iv) retain [21]. The first step of the mechanism is to represent the new problem into defined format of the old cases. After the new case is built, following steps are followed to generate solution with probable explanations.

Retrieve: Similar cases were retrieved from the case base using similarity function developed based on k-nearest neighbour (k-NN) algorithm associated with voting from the most similar cases. Detailed evaluation of the accuracy of retrieval model is discussed in section 4.

Reuse: In this step, the new solution was formed from the similar cases. To represent the causal statement associated with the solution, the inference engine combined all the relevant statements to the new case and prepared for the translation into explanations. For example, if three similar cases were found with two different solutions α and β. According to the definition in section 3.1, the representation of the causal statements – $C_{\alpha,1} : \gamma$ *causes* α, $C_{\alpha,2} : \delta$ *causes* α and $C_{\beta,1} : \eta$ *causes* β.

Causal inference engine combines these causal statements into a single statement with union operator – $C : \ \alpha \ because\_of \ \{\gamma, \delta\} \ \sqcup \ \beta \ because\_of \ \{\eta\}$.

Revise: The solved case from the previous step containing a solution with explanation translated from the associated causal statements by the explanation

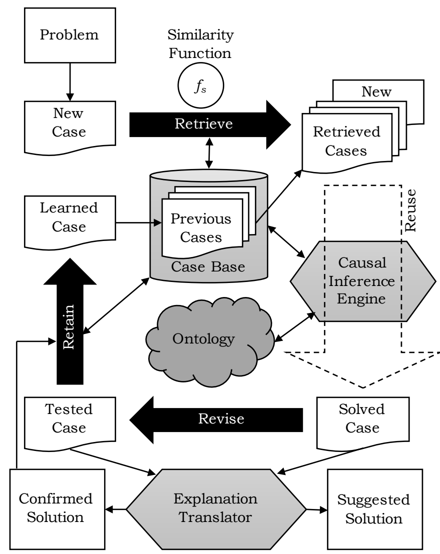

Fig. 3. Overview of proposed CBR architecture with Causal Model.

translator. Brief discussion on the explanation translator is discussed in the section 4. Finally, the suggested solution was manually curated by an expert on the basis of domain expertise to produce tested case.

Retain: By further generating explanation from modified suggested solution, confirmed solution was developed. This solution was inserted in the case base for future reference. In some cases, there were requirements to modify facts in the ontology, this was also done in this step.

4 Evaluation

To retrieve similar cases from the case base, k-NN was used. The value of k was determined after tuning the model parameters using grid search over different values of k. Moreover, 5-fold cross validation for all the values were done and $k = 3$ produced the highest mean cross-validation accuracy. Table 1 shows the accuracy for 5-fold cross validation with different values of k.

After retrieving similar cases from case base, explanation for the solution case was deduced by inferring associated causal statements of the solved cases. For better understanding of the mechanism, consider the following example demonstrating a translation mechanism to generate explanation from causal statements.

Table 1. Accuracy (%) for 5-fold cross validation of k-NN with different values of k.

k-NN	**Iterations**					**Mean**
	1	**2**	**3**	**4**	**5**	
$k = 1$	94.70	94.04	94.56	94.83	94.95	94.62
$k = 3$	94.57	94.17	95.36	96.02	95.61	95.15
$k = 5$	94.44	94.17	94.43	95.76	95.74	94.91
$k = 7$	94.04	94.17	94.56	95.62	95.74	94.83

Example 1. Let us consider the causal statements associated with a solved case:

$$\begin{aligned} &C_1 : TSH(\texttt{Low})\ \ because\_of\ \ Symptom(\texttt{Pregnancy}) \\ &C_2 : Hypothyroidism(\texttt{Secondary})\ \ because\_of \\ &\qquad\qquad\qquad \{TSH(\texttt{Low}),\ TT4(\texttt{Low})\} \end{aligned} \tag{1}$$

For generalisation, these statements can be represented with symbols –

$$\begin{aligned} &C_1 : A(\alpha)\ \ because\_of\ \ B(\beta) \\ &C_2 : \varGamma(\gamma)\ \ because\_of\ \ \{A(\alpha),\ \varDelta(\delta)\} \end{aligned} \tag{2}$$

Splitting the previous statements into atomic ones, we get –

$$\begin{aligned} &C_{1,1} : B(\beta)\ \ causes\ \ A(\alpha) \\ &C_{2,1} : A(\alpha)\ \ causes\ \ \varGamma(\gamma) \\ &C_{2,2} : \varDelta(\delta)\ \ causes\ \ \varGamma(\gamma) \end{aligned} \tag{3}$$

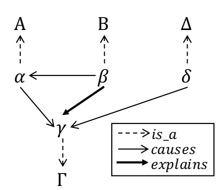

Fig. 4. Generic diagram for deducing explanation.

Figure 4 illustrates the hierarchy and causation of the concerned entities in this example. The path from the nodes representing individual causes to the verdict node leads to an explanation for the predicted verdict produced from CBR. From the generic statements $C_{1,1}$, $C_{2,1}$ and $C_{2,2}$ it is found that, *Pregnancy causes low TSH*, *Low TSH causes secondary hypothyroidism* and *Low TT4 causes hypothyroidism* respectively. Finally, the probable explanation is extracted with predefined natural language for each of the object properties as, "*Pregnancy causes low TSH. Low TSH with low TT4 causes secondary hypothyroidism. Therefore, Pregnancy can be an explanation of secondary hypothyroidism.* "

5 Conclusion

The rapidly growing nature of AI applications in the aspects of capabilities and performance leverages the need of upgrading the intelligence. People seek more humanly intelligence from the machines. To be specific, explanations are expected more often in addition to the result of any task. This work represents a framework for adding causation to CBR architecture using domain specific ontology on hypothyroid disease diagnosis. Thyroid disease dataset was used to develop the ontology and causal model. The outcome of this work would have been more credible if there were instances of all types of hypothyroidism in the selected dataset though some evaluation method was applied to justify the use of k-NN in case retrieval step. Progressive works are still on to make this system more robust and test with more feasible datasets. However, this causal model was developed in a generalised fashion that can be adopted to any domain by using a domain specific ontology and tuning several parameters in explanation translator which enables the model with adaptability. Moreover, representing cases in XML files can make provision to use this type of case-bases in distributed architecture which would contribute to overcoming challenges of being scalable.

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