Relationship Extraction based on Category of Medical Concepts from Lexical Contexts

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Abstract

Medical information extraction is an emerging task in healthcare services aim to acquire crucial information of the concepts like diseases, symptoms, and drugs and also to identify their relations from corpora. In the present article, we have proposed a relationship extraction system based on such categories of medical concepts. We have employed rule-based as well as Support Vector Machine (SVM) based feature-oriented approach along with a domain-specific lexicon viz WordNet of Medical Event (WME 2.0). The lexicon assists in recognizing medical concepts and their related features like Parts-Of-Speech (POS), categories, and Similar Sentiment Words (SSW). We have opted only four fundamental categories diseases, drugs, symptoms, and human_anatomy of medical concepts as provided in WME lexicon. Such categories play a crucial role in identifying eight types of different semantic relations viz. drug-drug, disease-drug, and human_anatomy-symptom from the medical context. Thereafter, we have validated both rules and features-oriented approaches and offers an average F-Measures of 0.79 and 0.86 individually.

1 Introduction

The availability of medical documents such as reports, discharge summaries, and prescriptions and their related information are growing quickly. In order to extract critical and crucial information, the researchers have applied various statistical and ontology-based approaches with well-known machine learning classifiers (Mondal et al., 2016b; Uzuner et al., 2011). The extracted informations are medical concepts (terms), categories (classes), and their relations, which assist the experts such as doctors and other medical practitioners as well as the non-experts as patients in understanding the problems (e.g. diseases, symptoms) and their related remedies (e.g. drugs).

The medical concepts are presented by the key terms like words or phrases of the corpus whereas the category refers to the fundamental classes of medical concepts such as diseases and symptoms. The assigned categories of medical concepts and their in-between relations help to build a medical annotation system. Besides, each sentence of the corpus is presented as a medical context in this paper. For an example, “abdominal pain” denotes the medical concept and its category is denoted by “symptom” in the following medical context.

“Abdominal pain is a sign of early pregnancy.”

In order to design our category based relationship extraction system, we observed the following major challenges:

A. The first challenge was how to identify the medical concepts and their textual spans from unstructured or semi-structured medical corpora. To address this challenge, we have used WordNet of Medical Events (WME), a domain-specific lexicon (Mondal et al., 2016a, 2015). The lexicon provides a good coverage while extracting medical concepts from our experimental dataset viz. SemEval-2015 Task-61 and MedicineNet2.

B. The second challenge was how to decide the set of categories for the medical concepts and assign them. To overcome the first sub-challenge, we adopted the help of a group of medical practitioners and to cope-up with the second sub-challenge

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1http://alt.qcri.org/semeval2015/task6/
2http://www.medicinenet.com/script/main/hp.asp
challenge, we used the categorization system of medical concepts (Mondal et al., 2017, 2016a). The categorization system assists in assigning one of the four medical categories such as diseases, symptoms, drugs, and human anatomy to the concepts.

C. The third and final challenge of the present work was how to identify the relations between a pair of medical concepts in a context and evaluate the relations. To address this issue, we have built a rule-based and a feature-based relationship extraction systems, which help to predict the type of relations between a pair of medical concepts. Table 1 shows the proposed eight types of relations with illustrative examples. Besides, we have manually prepared a labeled dataset, which contains 2000 medical contexts and their tagged medical concepts, categories, and relations as shown in Figure 1.

In the present research, our primary motivation was to build an annotation system which helps to assign all four types of medical categories such as diseases, symptoms, drugs, and human anatomy and their related relations in a context. According to the best of our knowledge, we are unable to find any medical corpora which contain all the mentioned categories at a time. Afterwards, we have discussed the contribution of the paper as follows.

I. A labeled dataset preparation by a group of medical practitioners. The dataset has been labeled with medical concepts and their categories and proposed eight types of category-based relations in a context. We have acquired the dataset from SemEval-2015 Task-6 and MedicineNet resources which contain around 2000 number of medical contexts. The dataset helps to design and validate the relationship extraction system.

II. Relationship extraction plays a key role in identifying the semantic information from the corpus. To extract these relations, we have proposed a linguistic rule-based (Abacha and Zweigenbaum, 2011a; Hearst, 1992) and a feature-oriented machine learning (Rink et al., 2011; Zhu et al., 2009) approach. The rule-based patterns help to identify the specific relations from the dataset, whereas machine learning approach assists in extracting generalize relations with promising accuracy. For an example, the following medical context is able to extract disease - symptom (illustration, inflammation symptom for the adnexitis disease) and symptom - human anatomy (illustration, inflammation affect the uterus) relations.

"The adnexitis disease characterizes inflammation symptom of attachments of the uterus human anatomy."

The proposed relation extraction system assists in understanding the subjective information of the corpus. Besides, these systems guide to build various applications namely, annotation and recommendation system in healthcare services.

The overall structure of the paper is as follows. Section 2 presents the related work carried out in this field. Section 3 describes the dataset preparation and brat representation technique. Section 4 and Section 5 present the proposed relation extraction system and its evaluation approach. Finally, Section 6 presents the concluding remarks related to our study.

2 Related Work

2.1 Medical Ontologies and Lexicons

Biomedical information extraction research is challenging due to the availability of a large number of daily produced unstructured and semistructured medical corpus. To represent the structured corpus and extracting the subjective and conceptual information from the corpus, a domain-specific lexicon is essential (Borthwick et al., 1998). To this end, the standard vocabularies and ontologies such as UMLS (Unified Medical Language System) and SNOMED-CT (Systematized Nomenclature of Medicine-Clinical Terms), and lexicons like MEN (Medical WordNet) and WME (WordNet of Medical Event) have used by the researchers (Smith and Fellbaum, 2004; Kilgarriff and Fellbaum, 2000; Mondal et al., 2016a).

2.2 Medical Category and Relation Extraction

These ontologies and lexicons assist in extracting the relevant information from the corpus such as medical concept categories and relations between medical concepts.
| Relation   | Explanation and Example                                                                                                                                                                                                                                                                                                                                                     |
|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Dr-SyDi    | A drug how helps to improve or cure or side effects the diseases or symptoms.                                                                                                                                                                                                                                                                                                   |
|            | *Warfarin* is also used to reduce the risk of clots causing strokes or heart attacks.                                                                                                                                                                                                                                                                                     |
| Ha-SyDi    | A disease or symptom which effects a part of the body.                                                                                                                                                                                                                                                                                                                   |
|            | A painful inflammation of the big toe and foot.                                                                                                                                                                                                                                                                                                                     |
| Di-Sy      | The symptoms which reflect a disease.                                                                                                                                                                                                                                                                                                                                  |
|            | Anal fissures typically cause pain and bleeding with bowel movements.                                                                                                                                                                                                                                                                                                    |
| Dr-Dr      | How the drugs are related each other.                                                                                                                                                                                                                                                                                                                                 |
|            | An oral lipid-lowering medicine (*trade name* Zocor) administered to reduce blood cholesterol levels; recommended after heart attacks.                                                                                                                                                                                                                                                                                         |
| Sy-Sy      | How the symptoms are related each other.                                                                                                                                                                                                                                                                                                                               |
|            | A rhythmic tightening in labor of the upper uterine musculature that contracts the size of the uterus and pushes the fetus toward the birth canal.                                                                                                                                                                                                                       |
| Di-Di      | How the diseases are related each other.                                                                                                                                                                                                                                                                                                                               |
|            | Kaposi's sarcoma is a form of skin cancer that can involve internal organs.                                                                                                                                                                                                                                                                                                |
| MMT-SyDi   | The medical terms such as process and chemical components etc. how helps to refer the diseases or symptoms.                                                                                                                                                                                                                                                                 |
|            | When you swallow or inhale these highly toxic products, you can experience life-threatening symptoms.                                                                                                                                                                                                                                                                     |
| Ha-Ha      | How various body parts are related or effected each other under a situation.                                                                                                                                                                                                                                                                                               |
|            | Nodding movement of the head or body.                                                                                                                                                                                                                                                                                                                                  |

Note: Di− > Disease, Dr− > Drug, Sy− > Symptom, Ha− > Human anatomy, and MMT− > Miscellaneous Medical Term

Eklund (Eklund, 2011) developed an annotation system to extract the relations as diseases for treatments from the scientific medical corpus. Yao et al. (Yao et al., 2010) extracted category relations as cures, prevents, and side effects, which describe the distinctive nature for the biomedical text (medical papers) (Abacha and Zweigenbaum, 2011b; Frunza and Inkpen, 2010). Franzen et al. (Franzén et al., 2002) have annotated Yapex corpus with 200 medical abstracts to extract the category as proteins. These ontologies are fundamentally looking for extracting protein-protein interaction and disease-treatment relations from corpora under a BioText project (Rosario and Hearst, 2005).

Khoo et al. (Khoo et al., 2000) developed a causal relations extraction system from abstracts of biomedical articles by aligning manually constructed graph patterns with syntactic dependency trees. Lee et al. (Lee et al., 2003) applied UMLS to identify semantic relations between medical entities. Their first method was able to extract 68% of the semantic relations in their test corpus but if many relations were possible between the relation arguments no disambiguation performed. Their second method (Lee et al., 2004) targeted the precise extraction of "treatment" relations between drugs and diseases. Manually written linguistic patterns were constructed from medical abstracts talking about cancer. Their system reached 84% recall but an overall 48.14% precision. Embarek and Ferret (Embarek and Ferret, 2008) developed an approach to extract four kinds of relations (Detect, Treat, Sign, and Cure) between five kinds of medical entities. The employed patterns were constructed automatically using an alignment algorithm which maps sentence parts using an edit distance (defined between two sentences) and different word-level clues.

### 3 Dataset Preparation

The present section describes how we employed a domain-specific lexicon namely WME 2.0 and prepared an annotated dataset for relation extraction system. Also, discussed the brat environment to visualize the tagged concepts, categories and relations of our medical corpora.

**Evaluation Data:** We initially acquired corpora from SemEval-2015 Task-6 and MedicineNet resources. Thereafter, the corpora have been converted into medical contexts in the form of single sentences according to the presence of medical concepts for our experiment. Table 2 shows the distributions of medical concepts and contexts from SemEval, MedicineNet as well as WME 2.0 resources.

We randomly collected 2000 medical contexts from the acquired corpora and manually labeled
by a group of medical practitioners in the brat environment. Table 3 shows the distributions of manually labeled category-based relations. In order to label the corpus, the medical practitioners have used WME 2.0 lexicon, which assists in understanding medical concepts and their categories based on their glosses and semantics.

Table 3: A statistics of manually labeled various relations

**WME Lexicon:** In healthcare, a lexicon from the medical domain is demanding to identify the conceptual information such as category or sentiment from the corpus (Cambria, 2016). To this end, we borrow the knowledge from WordNet of Medical Event (WME 2.0), a domain-specific lexicon (Mondal et al., 2016a, 2015).

However, the current version of WME namely WME 2.0 was enhanced with more sentiment and semantic features for 10186 number of medical concepts (Mondal et al., 2017, 2016a). WME 2.0 was added with affinity score, gravity score, Similar Sentiment Words (SSW), and category feature along with the existing features of WME 1.0, e.g., gloss (descriptive explanation), Parts-Of-Speech (POS), polarity score, and sentiment.

The conventional WordNet, a preprocessed medical dictionary, and SenticNet were applied to prepare our present resource for extracting semantic relations of concepts. Affinity score indicates what extend two concepts are close to each other by measuring the number of common sentiment words (SSW) appeared for a pair of concepts within the range of 0 to 1. On the other hand, gravity score identifies sentiment-oriented relevance between medical concepts and their various glosses (descriptive explanations) and ranges from -1 to 1. While -1 suggests no relation and 1 indicates strong relations either positive or negative, which helps to identify a proper gloss for concepts. Besides, the assigned categories such as *diseases, drugs, treatments, human_anatomy, and MMT* assist in extracting the subjective information of the concepts.

For example, WME 2.0 lexicon presents the properties of a concept say *amnesia* as of category (disease), POS (noun), gloss (“loss of memory sometimes including the memory of personal identity due to brain injury, shock, fatigue, repression, or illness or sometimes induced by anesthesia.”), SSW (memory_loss, blackout, fugue, stupor), polarity score (-0.375), affinity score (0.429), gravity score (0.170), and sentiment (negative).

**Brat Annotation:** We have used an annotation tool namely brat to manually label the relations between a pair of medical concepts within their contexts. The tool helps to easily label the contexts, which generate an annotation (.ann) file for each input text (.txt) file. The .ann file has labeled medical concepts along with their IDs (Ti), categories (Disease, Drugs etc.), textual spans and concepts and relations with IDs, categories and arguments. Thereafter, we have written a python script to convert the manually tagged annotation file into the format according to our proposed system output. The script assists in evaluating the proposed extracted relations.

For example, the following medical context denotes an annotated output as

"T1 Disease 1 39 Giant cell interstitial pneumonia (GIP)"

"T2 Disease 59 77 pulmonary_fibrosis"

"R1 Di-Di Arg1:T1 Arg2:T2":

"**Giant_cell_interstitial_pneumonia** (GIP) _disease is a rare form of pulmonary_fibrosis_disease.""

### 4 Relationship Extraction

Biomedical texts are primarily rich with subjective information such as *problems and treatments* and they are represented as medical concepts, category and their relations in case of ours. Recognition of important relations between medical concepts is a challenging task due to lack of involvement of domain-experts. Thus, to overcome the challenge, we have proposed a relation extraction system by utilizing the categories of medical concepts. To
develop the category-based relation extraction system, we have considered the following hypothesis and proposed methodology viz. rule-based and feature-oriented approach.

4.1 Hypothesis:
In the present research, we have considered four primary categories of medical concepts, \textit{diseases, drugs, human anatomy, and symptoms} and a combined category \textit{MMT} that refers to unrecognized categories of medical concepts. To identify the relationship between these categories, we have adopted eight types of relations after close observations done by experts. Figure 2 shows the overall presentation i.e. how we proposed eight relations based on various concepts and their categories in a context. Finally, we have classified these relations into two major groups as combined and direct. The combined relations are \textit{Ha-SyDi}, \textit{Dr-SyDi}, and \textit{MMT-SyDi} and rest of the five relations are presented as direct relation as mentioned in Table 1.

We have also observed that two of the categories (e.g., Disease and Symptom) are very close to each other in their context level appearances and therefore we merged them to make a single category (e.g., SyDi) instead of making the individual pair of relation with other categories.

4.2 Proposed Methodology:
\textbf{Rule-based Approach} In case of relation extraction, rule-based approach adopts various linguistic textual patterns between the pair of medical concepts. To identify these patterns, we have collected the promising pairs of the medical category that are semantically or subjectively related each other as shown in Figure 2. The consecutive appearance of concepts has not been taken into account in case of identifying rules because such concepts are ambiguous in nature and conflicting in their medical senses.

These identified patterns converted to Static Surface Patterns (SSP) using various regular expressions and are labeled by our proposed relations. An example, the linguistic textual pattern "<Drug> used to combat <Disease>" is converted to static surface pattern as "<Drug>(.*)<Disease>" with \textit{Dr-SyDi} relation label.

The linguistic patterns help to reduce the manual effort and enhance the list of patterns with new relations where SSP assists in designing an automated relationship extraction system. Table 4 presents the number of extracted SSPs for eight relations with the specific example.

Therefore, the following algorithm has been applied to extract the category-based relations between the pair of medical concepts in a context. The output of the proposed system is shown in Figure 3.

\textbf{Algorithm:}
1. Identify the category of annotated medical concepts in a context and present them as \(C = \{MC1, MC2, \ldots, MCn\}\), where MCn is nth identified medical concept with category in a context.
2. Compare the Static Surface Patterns (SSP) with the pair of medical concepts from C.
   
   2.1. If SSP matches with the pair of concepts in C, then assigned the corresponding relation.
   
   2.2. Else look for the next pair of concepts in C as mentioned in Step 2.
3. If not found any relation in C then label "No relation" and move to next context (C).
4. Else combine the assigned relations with labeled concepts for the context (C) and move to next context (C).

\textbf{Feature-oriented Approach} Relation extraction is presented as a multi-label classification problem due to the presence of various types of semantic relations between medical concepts. To address this problem, we have considered feature-oriented machine learning approach over rule-based approach. The concerned features are category, intermediate word sequence, POS, and SSW of the pair of medical concepts in a context for our experiment.
Table 4: A statistics and examples of relation patterns in the contexts.

| Relation | Patterns | Example                                                                                     |
|----------|----------|----------------------------------------------------------------------------------------------|
| Dr-SyDi  | 12       | .... <Warfarin/Drug> is also used to reduce the risk of <clots/Symptom> ....                 |
| Ha-SyDi  | 14       | .... <coronary artery/Human anatomy> by a <thrombus/Disease> ....                             |
| Di-Sy    | 24       | .... <halitosis/Disease>, is an <unpleasant odor/Symptom> ....                               |
| Dr-Dr    | 6        | .... <oral lipid-lowering medicine/Drag> trade name <Zocor/Drug> ....                        |
| Sy-Sy    | 10       | .... <Frozen shoulder/Symptom>, also known as <adhesive capsulitis/Symptom> ....             |
| Di-Di    | 18       | .... <Kaposi’s sarcoma/Disease> is a form of <skin cancer/Disease> ....                      |
| MMT-SyDi | 27       | .... <toxic products/MMT>, you can experience <life-threatening symptoms/Symptom> ....       |
| Ha-Ha    | 6        | .... <vagus nerve/Human anatomy> included, emerge from or enter the <skull/Human anatomy> .... |

Figure 3: Output of the extracted relation using rule-based approach.

To identify the mentioned features, we have also employed WordNet and WME 2.0 lexicons. These lexicons help to assign the category, POS, and Similar Sentiment Words (SSW) for the medical concepts. Besides, we have written a python script to recognize the intermediate word sequence between the pair of the concepts.

For example, the following medical context identifies the features say 1. annotated medical concepts (“degenerative brain disorder” and “dementia”) 2. POS labels (noun and verb) 3. intermediate word sequence (“(.*) that leads to (.*)”) 4. categories of medical concepts (disease and disease), and 5. SSW (“Alzheimer’s disease, Huntington’s disease, and Parkinson’s disease” and “mental illness, madness, and insanity”), respectively.

“Degenerative brain disorder that leads to dementia.”

Figure 4 illustrates the steps to extract the relations between a pair of medical concepts using proposed feature-oriented approach along with machine learning classifier. Besides, we have extracted these features from the evaluation dataset and processed through the linear Support Vector Machine (SVM) classifier to predict the relations. The following section discusses the evaluation process for both of the proposed approaches.

5 Evaluation

We have used the state-of-the-art evaluation metrics such as precision, recall, and F-Measure to validate the proposed relation extraction approaches.

Rule-based Relation Extraction In order to reduce the ambiguity of the extracted relations,
we have employed the same annotated medical concepts and their categories in both rule-based as well as feature-oriented approaches. Table 5 presents the distribution of manual and system tagged category-based relations and their related precision, recall, and F-Measure.

| Relation | Manually labeled | Extracted/Correct/Incorrect | Precision | Recall | F-Measure |
|----------|-----------------|-----------------------------|------------|--------|-----------|
| All relations | 2071 | 2681/1881 / 780 | 0.70 | 0.91 | 0.79 |
| Dr-SyDi | 52 | 102 / 46 / 56 | 0.45 | 0.88 | 0.59 |
| Hu-SyDi | 198 | 223 / 178 / 35 | 0.76 | 0.90 | 0.82 |
| Di-Sy | 312 | 386 / 282 / 104 | 0.73 | 0.90 | 0.81 |
| Dr-Di | 15 | 22 / 13 / 9 | 0.59 | 0.87 | 0.70 |
| Sy-Sy | 132 | 193 / 155 / 76 | 0.60 | 0.90 | 0.71 |
| Di-Di | 282 | 341 / 294 / 87 | 0.74 | 0.90 | 0.81 |
| MMT-SyDi | 927 | 1227 / 871 / 356 | 0.71 | 0.94 | 0.81 |
| Hu-Hu | 153 | 177 / 112 / 55 | 0.69 | 0.80 | 0.74 |

Table 5: A statistics of various relation identification between the pair of medical concepts in context using rule-based approach.

Feature-oriented Relationship Extraction Besides, to validate the feature-oriented system, we additionally prepared a test dataset along with our built-in evaluation dataset. The test dataset contains rest of 11816 medical contexts as referred in Table 2.

Thereafter, the features have been extracted from the evaluation dataset and processed through linear Support Vector Machine (SVM) classifier to learn the proposed relation extraction model. Hence, the test dataset has been applied to the learned model for predicting and validating the extracted relations. Table 6 summarizes the result as precision, recall, and F-Measure.

| Relation | Precision | Recall | F-Measure |
|----------|-----------|--------|-----------|
| All relations | 0.92 | 0.81 | 0.86 |
| Dr-SyDi | 0.90 | 0.72 | 0.80 |
| Hu-SyDi | 0.91 | 0.80 | 0.85 |
| Di-Sy | 0.90 | 0.79 | 0.84 |
| Dr-Di | 0.88 | 0.76 | 0.82 |
| Sy-Sy | 0.89 | 0.78 | 0.83 |
| Di-Di | 0.91 | 0.80 | 0.85 |
| MMT-SyDi | 0.93 | 0.82 | 0.87 |
| Hu-Hu | 0.88 | 0.72 | 0.79 |

Table 6: A statistics of various relation identification between the pair of medical concepts in context using feature-oriented approach.

Finally, we have observed that the feature-oriented approach provides a better F-Measure (0.86) over the rule-based approach (0.79) for extracting relations. So, we conclude that both approaches are important to extract the mentioned eight relations from the unstructured corpus.

6 Conclusion and Future Scope

In this article, we have focused on extracting eight types of category-based relations of medical concepts from the context. The relation extraction system facilitates to design various domain-specific applications. We have employed two well-known approaches such as rule-based and feature-oriented. Also, we have manually prepared an evaluation dataset to design and validate the relation extraction system. The rule-based approach helps to understand the semantic knowledge where linguistic features assist in improving the accuracy of the system. Finally, the evaluation section shows the effectiveness of the proposed relation extraction approaches by offering the average F-Measures of 0.79 and 0.86 for the rules and features-oriented techniques, respectively in healthcare. In future, we will try to introduce new relations for the medical concepts to build a relation database, which helps to design a medical recommendation system.

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