Relation Extraction Between Medical Entities Using Deep Learning Approach

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Medical discharge summaries or patient prescriptions contain a variety of medical terms. The semantic relation extraction between medical terms is essential for the discovery of significant medical knowledge. The relation classification is one of the imperative tasks of biomedical information extraction. The automatic identification of relations between medical diseases, tests, and treatments can improve the quality of patient care. This paper presents the deep learning based proposed system for relation extraction between medical entities. In this paper, a convolution neural network is used for relation classification. The system is divided into four modules: word embedding, feature extraction, convolution, and softmax classifier. The output contains classified relations between medical entities. In this work, data set provided by I2b2 2010 challenge is used for relation detection which consisted of total 9070 relations in test data and 5262 total relations in the train dataset. The performance evaluation of relation extraction task is done using precision and recall. The system achieved an average of 75% precision and 72% recall. The performance of the system is compared with the awarded i2b2 participated systems.

Povzetek: Metoda globokega učenja je uporabljena na iskanju relacij med zdravstvenimi entitetami.

1 Introduction

Relation extraction is an essential task of biomedical text mining. How any medical difficulty is related to symptoms, syndrome, and treatment, which tests will be required for disease diagnosis? These types of information are required in health care and clinical procedures. Relation extraction is the task of classification in which a pair of relations between medical entities can be identified. It is the core clinical information identification problem that identifies semantic relations between medical concepts problem, test, and treatment in discharge summaries [13]. It is one of the challenging tasks of i2b2 2010 NLP challenges. Relation extraction is divided into various types according to their usage such asTrIPindicates treatment improvement with problem, TrWP (treatment worsen the medical problem), TrCP (treatment causes the medical problem), TrAP (treatment is administered for the medical problem) and TrNAP(treatment is not administered because of the medical problem), other for test with problem TeRP (test shows the medical problem), TeCP (test conducted to investigate medical problem) and the problem with other problem indicates PIP (problem indicates problem) [1]. Examples of relations are: c="pacemaker" || r="TrAP"|| c="sinus node dysfunction", c="an angiography"|| r="TeRP"|| c="bleeding in two vessels" etc.Medical relations are classified into categories which shown in table I.

Remainder sections of this paper are organized as follows: Section 2 shows the review of papers related to medical relation extraction, Section 3 describes the proposed method and dataset, Section 4 gives experimental results and discussion and Section 5 conclude the results of proposed approach and give some novel directions for added research work.

Type of Relation	Categories of Relations
Medical Problem-Treatment	TrIP (Treatment improves medical problem)
	TrWP (Treatment worsens medical problem)
	TrCP (Treatment causes medical problem)
	TrAP (Treatment is Administered for medical problem)
	TrNAP (Treatment is not Administered because of medical problem)
	Relation between Treatment and Medical problem does not exist other than above types
Medical Problem-Test	TeRP (Treatment reveals medical problem)
	TeCP (Test conducted to investigate medical problem)
	Relation between Testand Medical problem does not exist other than above types
Medical Problem-Problem	PIP (Medical problem indicates medical problem)
	Relation between Medical problem and Medical problem does not exist other than PIP

Table 1: Relation categories provided in i2b2 2010 challenge [22].

2 Literature review

2.1 Review of i2b2 NLP challenge work

In 2010 i2b2 challenge, enormous work is done by authors in the field of relation extraction for medical text. In this NLP challenge several supervised and unsupervised machine learning classifiers are used. Various effective relation classification systems have been used such as CRF classifiers, Semi Markov models,SVM classifiers, Naive bayes classifier and SSVM (structural support vector machine)[2-5]. Some authors have used machine learning based modulesfor train data followed by post processing rules.

Maximum entropy (ME) classifier is trained using semantic and syntactic features in[6]. In this paper, results given by ME classifiers are relatively less memory demanding as compare to kernel based k-nearest neighbour (kNN) classifier and less computationally expensive than support vector machine (SVM) classifier. Other than these given reasons, did not detect a major difference in performance between these classifiers. This system attained top rank in the i2b2 NLP challenge. SVM classifier is used to train on dataset using word as features in [7], and classify the data into different relation types. Syntactic features are also taken as important

feature in the paper but recall can be improved using full parse tree implementation.

In [8], the system combines supervised classifier with rule based method. Entity and relation extraction in a joint framework is proposed using card pyramid parsing approach in [9]. Syntactic analysis of sentences is done by using the concept of bottom up parsing with SVM relation classification [10]. Few authors had used SVM classification algorithm with various features like syntactical, lexical, medical semantics and sentence level context information [11][12][13]. ConText algorithm is also designed for contextual feature creation [14], which recognizes context of patient's medical condition such as family history, previous record of disease or disease related treatment and symptoms etc. Relation extraction between treatment and problem concepts is explored in [15], and SemRep method is used for detection of semantic and lexical features associated with concepts [16]. But SemRep is trained for semantic representation of entities for general English text, so it is unable to extract treatment concepts in clinical domain precisely.

Semantic relation discovery on clinical records is presented in [17], in which SVM is used for classification of disease-test, disease–treatment, and symptom–treatmentrelation types. The performance of this work is dependent on semantic types of a particular domain.REMed is a learning-based approach which is introduced for automatic relation discovery in the work presented in paper [18]. Relation extraction from clinical notes is also given by the usage of parse tree enhancement with semantic features [19]. Performance of relation extraction system can be improved by the integration of semantic features into parse trees.

In [20], authors had used three different classifiers to classify problem-test, problem-treatment and problem-problem relations respectively. Maximum entropy framework is used as classifier and implemented in the maximum entropy OpenNLP toolkit. In the paper [1], Hybrid approach is explored which integrates the linguistic pattern matching with SVM classifier. SVM classifier is trained with libsvm tool and created linguistic patterns manually. It is found that, the usage of patterns with SVM classifier improves the relation extraction.

I2b2 challenge participants had used different set of features for relation classification. Features such as context features, semantic features, concepts co-occurrence, N-gram sequential feature and parser output are used for medical relation extraction in previous papers [4, 5,20,21]. Relationship between Coronary Obstructive Pulmonary Disease and cardiovascular diseases is detected through various machine learning classifiers in paper [22]. Diabetes complications are also detected by using various machine learning classifiers in paper [23].

2.2 Performance of Existing Systems

Performance evaluation of relation extraction for every relation category is done using recall, precision and F-score. Table II presents F-score of various relation

Relation Detection		
Authors of Systems	**Methods**	**F-Score (%)**
Roberts	Supervised method	73.7
DeBruijn	Semi Supervised method	73
Grouin	Hybrid method	71
Patrick	Supervised method	70.2
Jonnalagadda*and* Gonzalez	Supervised method	69.7
Divita	Supervised method	69.5
Solt	Supervised method	67
Demner-Fushman	Supervised method	66.6
Anik	Supervised method	66
Cohen	Supervised method	65.6

Table 2: Performance evaluation of Relation detection systemsin i2b2 challenge (2010) [24].

Relation Type	Training Data (figure)	Testing Data (figure)	Test data Recall, Train data Recall, In (%)	Test data Precision, Train data Precision, In (%)	Test data F-Score, Train data F-Score, In (%)
PIP Relation	1239	1986	62.5% 64%	67.7% 73%	65% 68%
TrWP Relation	56	143	2.8% 3.7%	80% 100%	5.4% 7%
TrAP Relation	1422	2487	72% 78%	70% 68.4%	71% 72.8%
TrNAP Relation	106	191	13% 26.4%	55.5% 70%	21% 38%
TrCP Relation	296	444	48% 44.9%	49.5% 63.6%	48% 52%
TrIP Relation	107	198	15.7% 23.3%	86% 69%	26.5% 35%
TeCP Relation	303	588	43% 47.8%	61% 77%	50% 59%
TeRP Relation	1733	3033	84% 87%	84% 82.3%	84% 84.6%
Overall Result	5262	9070	67.5% 70.9%	73% 74.5%	70% 72.6%

Table 3: Evaluation of Relation Extraction System [2].

extraction systems contributed in challenge 2010 [24]. Table 3 presents recall, precision and F-score for each relation class label shown by Patrick et al [4], in whichTeRP, TrAP and PIP relations got highest F-score; while TrWP relation got very low F-Score.

2.3   Summary and research gaps

Extensive review is done in the field of medical relation detection. In i2b2 challenge, participants have used

Relation Type	Training Data (figure)	Testing Data (figure)
PIP Relation	1239	1986
TrWP Relation	56	143
TrAP Relation	1422	2487
TrNAP Relation	106	191
TrCP Relation	296	444
TrIP Relation	107	198
TeCP Relation	303	588
TeRP Relation	1733	3033
Overall Result	**5262**	**9070**

Table 4: Summary of Relation Types of train and test data [1].

machine learning methods with feature of the engineering module. Machine learning methods performed well but feature engineering module is time taking and requires domain knowledge. The importance of feature design and usefulness of rich features influences the results. SVM classifier is used in relation extraction. It is observed that the use of patterns with SVM classifier improves the relation extraction. Medical relations in intra-sentences are extracted in existing systems accurately but relations in inter-sentences require more attention.

3   Proposed methodology

An extensive discussion on existing work in clinical relation extraction is done in related work. Different tools, techniques, and methods are discussed for the medical domain. The system is proposed for medical relation extraction which is based on the concept of deep learning.

3.1   Dataset

I2b2 2010 challenge organizers provided data set for relation classification which consisted of total 9070 relations in test data and 5262 total relations in the train dataset. The summary of each relation type for train and test data is shown in table 4. Example of annotated dataset for relation extraction is shown in table5.

3.2   Proposed deep learning based relation extraction system

The extraction of semantic relations is essential for the discovery of significant medical knowledge. Relation extraction is an important task in the field of biomedical text mining. For improving the relation between medical entities, Deep Learning based method CNN (convolution neural network) with word2vec is used [25]. The method is divided into four steps: word embedding, feature extraction, convolution, and softmax classifier. The word embedding model takes word tokens as input, so initially the sentences divided into word tokens. Then the word token are converted into vectors using word embedding. In this work, new word embedding model is trained

```
c="coronary   artery   bypass   graft"
115:4    115:7||r="TrAP"||c="coronary
artery disease" 115:0 115:2
c="a      amiodarone      gtt"      75:11
75:13||r="TrAP"||c="burst   of   atrial
fibrillation" 75:3 75:6
c="antibiotics"                     80:15
80:15||r="TrAP"||c="left          arm
phlebitis" 80:8 80:10
c="creams"                          124:1
124:1||r="TrNAP"||c="incisions"
124:10 124:10
c="cath"                            19:14
19:14||r="TeCP"||c="abnormal     ett"
19:9 19:10
c="powders"                         124:5
124:5||r="TrNAP"||c="incisions"
124:10 124:10
c="lotions"                         124:3
124:3||r="TrNAP"||c="incisions"
124:10 124:10
c="ointments"                       124:8
124:8||r="TrNAP"||c="incisions"
124:10 124:10
c="oxycodone - acetaminophen" 92:1
92:3||r="TrAP"||c="pain" 92:21 92:21
c="drugs"                           12:8
12:8||r="TrCP"||c="known   allergies"
12:5 12:6
c="cath"                            20:0
20:0||r="TeRP"||c="severe  3  vessel
disease" 20:2 20:5
c="cxr" 56:0 56:0||r="TeRP"||c="left
lower lobe atelectasis" 56:3 56:6
c="cabg" 28:8 28:8||r="TrAP"||c="mi"
28:2 28:2
c="po        amiodarone"        79:9
79:10||r="TrIP"||c="further  episodes
of afib" 79:3 79:6
c="overall left ventricular systolic
function"                           44:0
44:4||r="TeRP"||c="mildly depressed"
44:6 44:7
c="wounds"                          121:1
121:1||r="PIP"||c="infection"   121:3
121:3
c="wounds"                          121:1
121:1||r="PIP"||c="redness"     121:5
121:5
c="wounds"                          121:1
121:1||r="PIP"||c="drainage"    121:7
121:7
```

Table 5: Example of Annotated Relation Corpus.

using clinical 2010 i2b2 dataset. Then lexical and sentence level feature vectors are created separately and then concatenated into the final feature vector. In progression, the final feature vector is fed into the softmax classifier for the relation classification. The dimension of output vector is equal to number of predefined relation types. Figure 1 shows the architecture of deep learning based proposed relation extraction system. The description of each component is mentioned below.
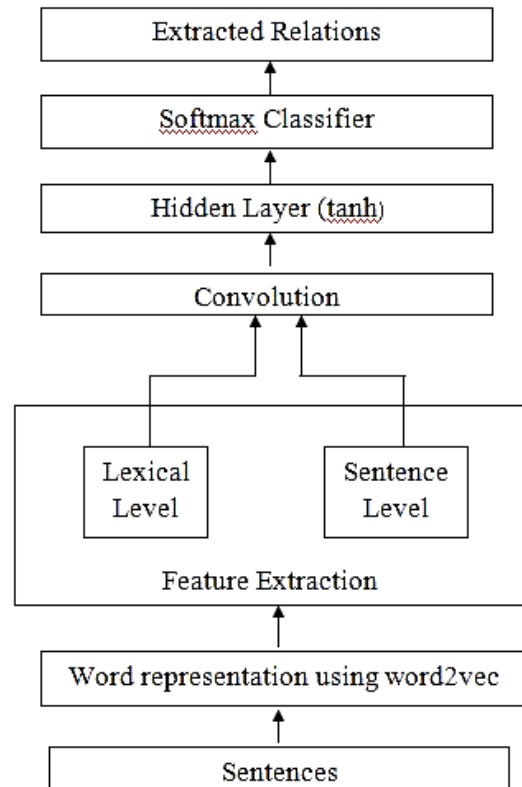

Figure 1: Architecture of proposed relation extraction system.

3.2.1 Word embedding

Word embedding is the word representation method which represents same context words in a similar representation [26]. Word2Vec is the technique to represent word embedding concept. In this component, Word2Vec takes word tokens as input and generates the vector of words as output. It constructs vocabulary from training text data and then creates vector of context similar words. However, there are many trained word embedding models are available which can directly used in the data set [27]. But these models are trained on general text. In the proposed work, new word embedding model is generated using clinical i2b2 data set. The size of vocabulary is 9060 of i2b2 test data set. Word2vec results are not entirely dependent on the corpus but also on the parameters used. Basic parameters for training the model are:

- CBOW (continuous bag of words) and SG (skip gram) vector model architectures
- Dimensionality of vector space such as 200, 300, 500 and 800
- Word windows size such as 5, 10 and 20

- min_count represents (Ignores all words with total frequency lower than this)

3.2.2   Feature extraction

In this component, lexical level and sentence level features are identified. Lexical level features are important indication for relation identification. In the proposed system, lexical features are identified by using word embedding method. For lexical features, clinical entities are also important, which identified by existing deep learning method proposed in [28]. Window and semantic features are identified by word2vec method. For medical semantic types mapping, UMLS (unified medical language system) is used [29]. These features are concatenated into lexical feature vector. Here lexical feature vector is denoted as:

L = {< l1, w1 >,< l2, w2 >, ..., <lk, wk>}

where li is a semantic concept in the UMLS, and wi is a weight to symbolize the importance of the clinical text associated with li. Lexical feature vector is obtained using the semantic types mapping with UMLS from given clinical text. This component has several layers: input layer, convolution layers, pooling layers and hidden layers.

Input Layer - The input layer converts the clinical text into a matrix of embedding, indicated as $W \in R^{(k+n) \times m}$, where k and n is the semantic types of word and maximum number of words respectively, and m is the dimension of word embedding. W is obtained by concatenating the embedding of words and semantic types together: W = Ww$\oplus$Wl. Here Wl and Ww are the embedding of the semantic types and words, respectively. And concatenation operation is denoted as $\oplus$.

Convolution Layer -In neural network model, the convolution approach is used to merge all the features. Convolution layer uses the filters to create features maps.

For predicting relation types, features are identified globally on complete data. The convolution layer is used to find out high level features from the input layer. To find different varieties of features, apply filters with different sizes. ReLU function is usedfor convolution layers asnon-linear function. The filter is applied to all possible windows of words and semantic types in W and produced a feature map $s \in R^{n+k-h+1}$.

Pooling Layer-Best feature can be extracted through max pooling operation of features. The pooling layer is used to further abstract the features by aggregating the score for each filter which produced from convolution layer. In this work, over each feature map, max-over-time pooling operation is applied. Important features are identified by selecting the uppermost value on each dimension of vector. Pooling layers are used to induce a fixed-length vector from feature maps.

Hidden Layer - Hidden layer is used to combine different features after getting from pooling layers.

In the present work, tanh is used as an activation function.

Sentence level feature vector is also generated like lexical level feature vector. It also consists of several layers: input layer, convolution layers, pooling layers and hidden layers. The input of this component is the word and its position in the sentence. Again W is obtained by concatenating the embedding of words and position together: W = Ww$\oplus$ Wp. Here, Ww and Wp are the embedding of the words and position of words, respectively. Finally, combine the output vectors of the lexical level features and sentence level features by concatenating them.

Softmax classifier – It is used as the final layer of neural network. It gives the confidence of each relation type. In the work, softmax classifier is used as multi class identification of relations.The output layer is applied on the combined vector to transform the output values into probabilities for relation detection.It returns the probabilities of each relation and target relation is having highest probability.

Training - In the present work, parameters are trained as a set Θ, in which the training data set is denoted as M and the class label as N. For each $m \in M$, the component computes a score s(n; m, Θ) for each class $n \in N$. The softmax operation is used to transform scores into a conditional probability distribution in the output layer which over the scores for all $n \in N$, Shown in Eq. (1).

$$p(n/m, \Theta) = \frac{\exp(s(n; m, \Theta))}{\sum_{\forall T \in N} (s(T; m, \Theta))} \qquad (1)$$

The training target of the model is to maximize the loglikelihood over the training set with respect to Θ. Shown in Eq. (2).

$$\Theta \mapsto \sum_{m \in M} \log p(n/m, \Theta) \qquad (2)$$

The architecture of sentence level feature generation is shown in fig 2. First component is feature extraction of word features and position features. Word features are representation of contextual similar words associated with the index of word in a sentence. Whole sentence is represented as list of word vectors with its ranking. Pair wise ranking is used to train word embedding model. Position features are relative distance (d1 and d2) of current word with left and right word, which is w1 and w2. Combination of word and position feature vector is fed into convolution component for extracting sentence level features. Table 6 shows different hyperparameters with its values which are tuned for convolutional neural network for relation extraction. The results are using 10 cross fold validation in which the model is trained for 10 times.
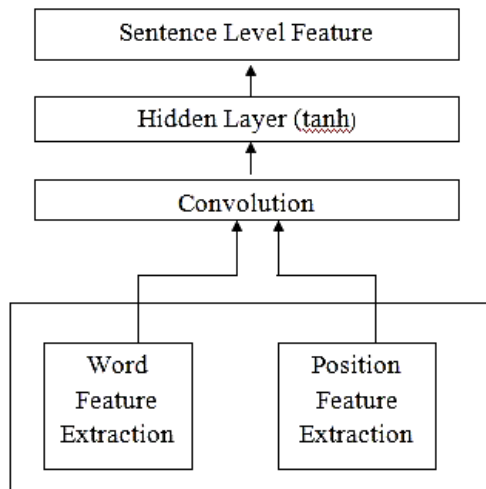
4   Results and discussions

Figure 2: Architecture of Sentence level feature component.

Description	Values
Activation Function	ReLU, Sigmoid, Softmax, Tanh
Feature Maps	50, 100, 128
Dropout rate	0.5, 0.7, 0.9
Pooling	1-Max

Table 6: Setup of Hyperparameters.

Relation Types	Precision (%)	Recall (%)
PIP	90	95
TrWP	10	5
TrAP	73	85
TrNAP	59	10
TrCP	60	30
TrIP	50	20
TeCP	70	35
TeRP	82	86
Overall Result	**75**	**72**

Table 7: Summary of result of medical relation types.

Authors of the Systems	Methods	F-Score (%)
Roberts *et al*[7]	Supervised method	73.7
DeBruijn*et al*[3]	Semi Supervised method	73.1
Grouin*et al*[8]	Hybrid method (Machine learning and linguistic pattern matching)	71
Proposed System	Convolution Neural Network	74

Table 8: Comparison of performance of proposed system with awarded i2b2 participated systems.

Performance evaluation of relation detection is done using recall and precision for every relation category. Table VII presents results of relation types in which TeRP, TrAP and PIP relations got highest precision and recall; while TrWP relation precision and recall is very low. Because training data contains less TrWP (treatment worsen problem) relations. Using convolution neural network, the performance of the system has improved for few relations. The F-score of PIP relation is increased from 68% to 92% and TrAP relation is increased from 73% to 79%. It is observed that relation types which are more presented in training data, gave best results. Table VIII shows the comparison of proposed system with existing i2b2 challenge systems.

5 Conclusion

Biomedical information is necessary for doctors, health care professionals, and clinical researchers. The information growing exponentially and scattered in published literatures and patient health records. The need is to identify appropriate tools and techniques for extracting knowledge from medical text. In this paper, medical relations are extracted between clinical concepts using word embedding and CNN based deep learning method. The system is trained using word embedding model with lexical and sentence level features. The performance of the system is compared with existing relation extraction systems. Medical relations in intra-sentences are extracted in existing systems accurately but relations extraction in inter-sentences has more scope for future work.

6 Acknowledgement

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