# ReOnto: A Neuro-Symbolic Approach for Biomedical Relation Extraction

**Monika Jain**[1] , **Kuldeep Singh**[2] , **Raghava Mutharaju**[1]
[1]Knowledgeable Computing and Reasoning (KRaCR) Lab, IIIT-Delhi, India
[2]Cerence GmbH and Zerotha Research, Germany
{monikaja, raghava.mutharaju}@iiitd.ac.in
kuldeep.singh1@cerence.com

## Abstract

Relation Extraction (RE) is the task of extracting semantic relationships between entities in a sentence and aligning them to relations defined in a vocabulary, which is generally in the form of a Knowledge Graph (KG) or an ontology. Various approaches have been proposed so far to address this task. However, applying these techniques to biomedical text often yields unsatisfactory results because it is hard to infer relations directly from sentences due to the nature of the biomedical relations. To address these issues, we present a novel technique called ReOnto, that makes use of neuro symbolic knowledge for the RE task. ReOnto employs a graph neural network to acquire the sentence representation and leverages publicly accessible ontologies as prior knowledge to identify the sentential relation between two entities. The approach involves extracting the relation path between the two entities from the ontology. We evaluate the effect of using symbolic knowledge from ontologies with graph neural networks. Experimental results on two public biomedical datasets, BioRel and ADE, show that our method outperforms all the baselines (approximately by 3%).

## 1 Introduction

In recent times, due to the exponential increase in data, knowledge bases have gained popularity as a means to efficiently store and organize information [Fensel *et al.*, 2020]. Although considerable efforts are invested in updating and maintaining knowledge bases, their incompleteness persists due to the dynamic nature of facts, which constantly evolve over the Web and other sources. Hence, there is a need to automate the process of extracting knowledge from text. Relation Extraction (RE) is task of predicting the relation given a sentence and an entity pair [Bastos *et al.*, 2021]. In domains such as biomedicine, relation extraction task poses a few critical domain-specific challenges. Consider a sentence, *atrio ventricular (C0018827) conduction defects and arrhythmias by selective perfusion of a-v conduction system in the canine heart (C0018787)*, with entities C0018827 (ventricular) and C0018787 (heart) linked to UMLS [Bodenreider, 2004]. Here target relation is *hasPhysicalPartOfAnatomicStructure*. The RE task aims to infer the semantic relationships. As demonstrated in the example, working with biomedical corpora poses several challenges. These include: complex input sentences that may require extensive parsing and interpretation to extract relevant information. Indirectly inferred relations between entities in the text, which may require sophisticated natural language processing techniques. Difficulty obtaining domain knowledge of the specific entities mentioned in the text, which may require specialized expertise and additional research. Moreover, in the biomedical domain, entities are intricately interlinked, resulting in numerous densely linked entities with high degrees and multiple paths connecting them [Angell *et al.*, 2021]. Hence, inferring the correct relation from a given sentence may require reasoning about the potential path.

**Limitation of Existing Works and Hypothesis**. The existing approaches employ various techniques for relation extraction such as multi-task learning [Crone, 2020], transformers [Eberts and Ulges, 2020], Graph Neural Network (GNN) models [Bastos *et al.*, 2021; Zhu *et al.*, 2019] have been used to process complex relationships between entities. While deep learning models [Nadgeri *et al.*, 2021; T.Y.S.S *et al.*, 2021] can incorporate semantic information of entities. Albeit effective, these models employ standard message-passing or attention-based approaches (transformers, GNNs) which are inherently focused on homophilic signals [Balcilar *et al.*, 2020; Bastos *et al.*, 2022] (i.e., only on neighborhood interactions) and ignore long-range interactions that may be required to infer the semantic relationship between two biomedical entities. Furthermore, sufficient domain-specific knowledge is available in various biomedical ontologies to be used as background knowledge for relation extraction. It is also evident in the literature that reasoning over ontologies [Bona *et al.*, 2019; Winnenburg *et al.*, 2015] allow capturing long-range dependencies between two entities [Pan *et al.*, 2019; Zhang *et al.*, 2022], which further helps in making predictions. For instance, in [Hong *et al.*, 2004], ontology information was utilized as a tuple and transformed into a 3-D vector for predicting compound relations. Hence, it remains an open **research question**: for biomedical relation extraction, can we combine reasoning ability over publicly available biomedical ontologies to enrich an underlying deep learning model which is inherently homophilic?

**Contributions:** To tackle this research question, to our knowledge our approach represents the first neuro-symbolic method for extracting relations in the biomedical domain. Our method is two-fold. Firstly, we aim to aggregate the symbolic knowledge in the form of axioms (facts) consisting of logical constructs and quantifiers such as *there exist*, *for all*, *union* and *intersection* between entities present in various public ontologies and build background knowledge. In the second step, we incorporate background knowledge into a Graph Neural Network (GNN) to enhance its capabilities to capture long-range dependencies. The rationale behind using a GNN is to exploit the correlations between entities and predicates due to its message-passing ability between the nodes. Inducing external symbolic knowledge makes our approach transparent as we can backtrack the paths used for inducing long-range dependencies between entities. Hence, we empower the GNN by externally induced symbolic knowledge to capture long-range interactions needed to infer biomedical relations between two given entities and a sentence. We name our approach as "ReOnto" containing following key contributions.

- Our novel relation extraction method, ReOnto, utilizes an ontology model to learn subgraphs containing expressive axioms connecting the given entities. It consists of a symbolic module incorporating domain-specific knowledge into a GNN, enabling the prediction of required relations between two entities within a biomedical knowledge graph.
- We study the effect of symbolic knowledge on the performance of the underlying deep learning model by considering several key characteristics such as 1) entity coverage from ontology, 2) the number of hops, etc. We provide conclusive evidence that aggregating knowledge from various sources to build the symbolic component (instead of using just one ontology for background knowledge) has a positive impact on the overall performance.
- We provide an exhaustive evaluation on two standard datasets, and our proposed method outperforms all baselines for biomedical relation extraction.

## 2 Related work

**Muti-instance RE**: Multi-instance relation extraction aims to utilize previous mentions of entities in a given document to infer the semantic relationship between them. Some approaches leverage attention-based convolution neural network [Shen and Huang, 2016], multi-level CNN attention [Wang *et al.*, 2016] and by ranking with CNN to classify relation [Santos *et al.*, 2015]. In contrast, alternative approaches employ recurrent neural networks for relation classification [Zhang and Wang, 2015] and hierarchical RNN with attention. Besides this, some works also use entity context information such as type and descriptions to improve the performance [Vashishth *et al.*, 2018]. To deal with the noise at the sentence-level and bag level, [Ye and Ling, 2019] proposed a distant supervision approach incorporating intra-bag and inter-bag attentions.

**Sentential and Biomedical RE**: GP-GNN [Zhu *et al.*, 2019] proposed a graph neural network with generated parameters which solves the relational message-passing task by encoding natural language as parameters and performing propagation from layer to layer. RECON [Bastos *et al.*, 2021] is an extended approach which uses the entity details like alias, labels, description and instance in an underlying GNN model for sentential RE. As discussed in [Nadgeri *et al.*, 2021], not all facts contribute to improved performance, and therefore, the context must be dynamically selected based on the given sentence. However, these works are limited to general domain and finds their limitation in the biomedical domain. In the biomedical domain, [Crone, 2020] introduced a multi-task learning approach that utilizes joint signals from entity extraction task to improve relation extraction. [T.Y.S.S *et al.*, 2021] enriched the performance of biomedical relation extraction by incorporating linguistic information and entity types into a BERT model. [Cabot and Navigli, 2021] employed an end-to-end seq2seq model for biomedical RE.

**Ontology based RE**: The authors of reference [Li and Huan, 2008] proposed using an ontology as a hyperlink structure for the web to facilitate relation extraction. Authors utilize the web structure using a breadth-first search for relation extraction. [Aghaebrahimian *et al.*, 2022] uses RNN with a convolutional neural network to process three features: tokens, types, and graphs. Work claim that entity type and ontology graph structure provide better representations than simple token-based representations for RE. We point readers to [Karkaletsis *et al.*, 2011] for details on ontology-powered information systems.

## 3 Problem Formulation and Approach

We define a KG as a tuple $KG = (\mathcal{E}, \mathcal{R}, \mathcal{T}^+)$ where $\mathcal{E}$ denotes the set of entities (vertices), $\mathcal{R}$ is the set of relations (edges), and $\mathcal{T}^+ \subseteq \mathcal{E} \times \mathcal{R} \times \mathcal{E}$ is a set of all triples. The *RE Task* aims to find the target relation $r^c \in \mathcal{R}$ for a given pair of entities $\langle e_i, e_j \rangle$ within the sentence $\mathcal{W}$. If no relation is inferred, it returns *NA* label. In this section, we first discuss the ReOnto framework, which integrates the power of the graph neural network (GNN) [Bastos *et al.*, 2021] with that of symbolic knowledge. A GNN primarily employs three modules, which are encoding, propagation, and classification. Symbolic knowledge is integrated with the GNN score in the aggregation module (Figure 1).

### 3.1 Symbolic Module

As a first step, we aggregate symbolic knowledge(SK), available in public ontologies for extracting long-range dependencies between entity pairs. We build a connected graph G of the symbolic knowledge derived from ontologies. We define G = (V, E, $T_+$) where V has a set of entities such that each edge ($v_s$, $v_o$) $\in$ E and $v_s$, $v_o \in$ V corresponds to a sequence s = $s_0^{s,o} s_1^{s,o} s_2^{s,o} \ \ldots \ s_{l-1}^{s,o}$ extracted from the text where s, o represent the source and destination entities. We also consider related SK of entity pair $SK^{s,o}$ which consist of path information ($\sum path_0^i$;$\sum axiom\_path_0^i$) $\in SK^{s,o}$ where i is the number of hops traversed to get the path. Path consists of multi hop details, each containing detailed information,

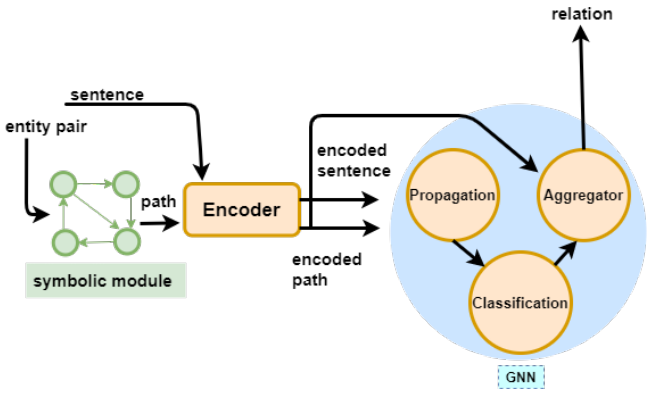


Figure 1: ReOnto Approach. The role of the symbolic module is to aggregate symbolic knowledge. It takes the entity pair and gives path information. 1) Encoding module accepts input vectors of sentence and path information to provide transition matrix. 2) Propagation module shares the hidden states of generated transition matrix with its neighbors 3) Classification module provides scores of prediction 4) Aggregator module integrates the score of the biased relation (from ontology reasoning) with that of the one from GNN to calculate loss.

while the axiom path contains path information enriched with expressive axioms. We identify the, directly and indirectly, connecting paths between the entities $v_s$ and $v_o$ (Algorithm 1).

**Single hop**. For retrieving the direct path, we query on the ontology using SPARQL to check if a path exists between entity pair ($e_s$, $e_o$). The study examined the potential interactions in a sentence *Sandimmun, a medication formulated as cyclosporin (cya) in cremophor and ethanol, and the muscle relaxants atracurium and vecuronium in anesthetized cats.* The correct relation label between sandimmun and cyclosporin is *hasTradename*. Upon querying this entity pair from the ontology, it was found that the direct path between given entity pairs is *synonymOf* relation which is similar to the correct relation label *hasTradename* present in the dataset. As depicted in Figure 2, the direct path between two given entities (if they exist) is extricated using $\text{path}(y;e) \rightarrow \text{cui}(x;y) \sqcap \text{edge}(x;z) \sqcap \text{cui}(z;e)$, where cui is concept unique identifier which uniquely identifies entity (assuming x is entity1, y is cui of entity1, z is entity2 and e is cui of entity2). It retrieves the connecting edge between two given entities. Once assimilating the path *synonymOf* between entity pairs, the aggregator module in ReOnto computes the similarity between the extracted path and all relations, assigning the correct label *hasTradename* as the similarity score reaches its maximum.

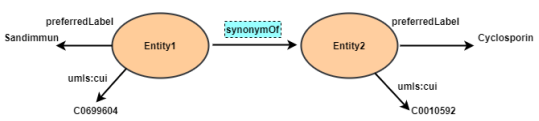


Figure 2: Subgraph of ontology illustrating direct connection between two entities

**Algorithm 1:** Path generation via ontology

**Input :** entity pair ($v_s$,$v_o$), Number of hops (N)
**Output:** finalpath
**Initialization:**
$i = 1$, source= $v_s$, $\text{path}_{i-1}$, $\text{axiom\_path}_{i-1}$, finalpath, adjacent node, hop_path$_i$, axiom_path$_i$ = {}
finalpath = PathGeneration($v_s$, $v_o$, N)
**Function** `PathGeneration` ($v_s$, $v_o$, $N$) **:**
  path, axiom_path, finalpath = {}
  **foreach** *entity pair* $v_s, v_o \in$ *ontology* **do**
    path.append(ExplorePath($v_s$, $v_o$, N))
    axiom_path.append(ExploreSymbolicPath($v_s$, $v_o$, N))
  **end**
  finalpath = path $\cup$ axiom_path
  **return** {finalpath}
**Function** `ExplorePath` ($v_s$, $v_o$, $N$) **:**
  hop_path$_i$, adjacent node= GetNHopFromSource($v_s$, 1) // calculates 1 hop distance from source
  $\text{path}_i$ = hop_path$_i$ $\cup$ $\text{path}_{i-1}$
  **if** $v_o \neq$ *adjacent node and* $i \neq N$ **then**
    path$_i$= ExplorePath(adjacent node, $v_o$, N)
    $i = i + 1$
  **end**
  **return** {$\text{path}_i$}
**Function** `ExploreSymbolicPath` ($v_s$, $v_o$, $N$) **:**
  axiom_path$_i$, adjacent node = GetNHopFromSource($v_s$, 2) // calculates 2 hop distance from source containing there exist and for all quantifier
  $\text{axiom\_path}_i$ = hop_path$_i$ $\cup$ $\text{axiom\_path}_{i-1}$
  **if** $v_o \neq$ *adjacent node and* $i \neq N$ **then**
    axiom_path$_i$= ExploreSymbolicPath(adjacent node, $v_o$, N)
    $i = i + 1$
  **end**
  **return** {$\text{axiom\_path}_i$}

**Multi hop**. Multi-hop path reasoning over the knowledge base aims at finding a relation path for an entity pair by traversing along a path of triples from graph structure data [Lv *et al.*, 2021]. For retrieving indirect path relation, we query on the ontology if a n-hop distance path exists between entity pair ($e_s$, $e_o$) starting from 1-hop distance path. Consider the sentence *Intravenous azithromycin-induced ototoxicity* with its relation label as *hasAdverseEffect*. From ontologies, we get the path as a concatenation of *causative agent of, has adverse reaction* using $\text{path(y;e)} \rightarrow \text{cui(x;y)} \sqcap \text{edge(x;z)} \sqcap \text{edge(z;a)} \sqcap \text{cui(a;e)}$. The aggregator module receives this path as input and using a similarity score, assigns the target relation label *adverseEffect*. Refer to Figure 3 for details.

**Using axioms**. So far, we have considered only shallow and transitive relationships among the concepts. However, the biomedical domain consists of several complex relations.

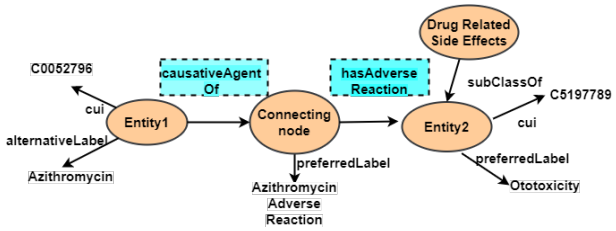


Figure 3: Subgraph of ontology depicting two hop distance between two entities

We argue that those relations can be captured using expressive axioms from ontology. Expressive axioms consist of logical quantifiers such as *there exist*($\exists$), *for all*($\forall$), *union*($\sqcup$), *intersection*($\sqcap$) which are part of popular biomedical ontologies. These expressive axioms enrich an ontology and play an essential role in the performance of downstream applications [Pan *et al.*, 2019]. Our objective is to determine the relation label between two entities by tracing the corresponding multi-hop triplet path that contains these axioms, starting from the first entity in the graph and continuing up to a specified distance until we reach the second entity. Note that when multiple paths are available between two entities, we have taken into account all the paths that are available which consist of unique keywords Consider the sentence, *A 73-year-old woman presented with fever and cough 2 weeks after completing the third cycle of fludarabine for chronic lymphocytic leukemia*. Here, correct relation label is *adverse effect*. From the ontology, we get following sub-graph enriched with axioms.

$$\textit{Fludaraline} \xrightarrow{\textit{causativeAgentOf}} \textit{Fludaraline Adverse Reaction}$$
$$\textit{Fludaraline Adverse Reaction} \sqsubseteq \exists \textit{hasFinding.Finding}$$
$$\textit{Cough} \sqsubseteq \textit{Finding}$$

From the above relations, one can see that Fludaraline and Fludaraline Adverse Reaction (FADR) has a relation *causativeAgentOf*. Moreover, there exists a *hasFinding* relation between FADR and Finding. Therefore, with ontology reasoning, we can interpret that Fludaraline has an axiom path consisting of *causativeAgentOf, hasSomeFinding*, which is closest to the relation label adverseEffect. Similarly, consider another sentence, *concentrations were significantly related to the degree of apocrine differentiation of the tumour and, in a subset of the cancers, capacity to release gcdfp-15 was positively correlated with incidence of progestogen and androgen receptors*. The labeled relation for this sentence is has *nichdParentOf* .

$$\textit{Tumor} \xrightarrow{\textit{qualifierBy}} \textit{Diagnostic Imaging}$$
$$\textit{Diagnostic Imaging} \xrightarrow{\textit{allowedQualifier}} \textit{Neoplasms}$$
$$\textit{Neoplasms} \sqsubseteq \exists \textit{parent.Post-Traumatic Cancer}$$
$$\textit{Post-Traumatic Cancer} \sqsubseteq \textit{Cancer}$$

For the above case, the derived path is *qualifierBy, allowedQualifier, subClass and there exist some parent and subClass*.

## 3.2 Encoding module

Entity pairs are encoded by concatenating the position embedding with the word embedding in the sentence (Equation 1), represented as $En(s_t^{s,o})$ where $s_t$ is the word embedding and $p_t^{s,o}$ is the position embedding at word position $t$ relative to the entity pair position $(s, o)$. Similarly, symbolic path information from the Symbolic Module ($SK$) is encoded by concatenating path ($path_0^i$) and axiom path details ($axiom\_path_0^i$) where $i$ represents the number of hops reaching destination.

$$En(s_t^{s,o}) = [s_t; p_t^{s,o}] \tag{1}$$

$$En(SK^{s,o}) = [\sum path_0^i; \sum axiom\_path_0^i]^{s,o} \tag{2}$$

The entity pairs representation and path information, after encoding with BioBERT are forwarded to a multi layer perceptron with non linear activation $\sigma$ (Equation 3 and 4). We concatenate them as a shown in Equation 5. Since our dataset are from biomedical domain, we have used BioBERT for encoding.

$$A_{s,o}^n = MLP_n(BioBERT(En(s_0^{s,o}), En(s_1^{s,o}), .., En(s_l{-}1^{s,o})) \tag{3}$$

$$SP_{s,o}^n = MLP_n(BioBERT(En(SK^{s,o}))) \tag{4}$$

$$M_{s,o}^n = SP_{s,o}^{(n)} + A_{s,o}^{(n)} \tag{5}$$

## 3.3 Graph Neural Network

**Propagation module**

In this module, we propagate information among graph nodes using equation 6, where given the representation of layer $n$ , representation of layer $n+1$ is calculated. Here $n$ represents the index, $B$ represents neighbors of $v_o$, and $\sigma$ is the nonlinear activation function.

$$h_s^{n+1} = \sum_{v_o \in B(v_o)} \sigma(M_{s,o}^{(n)} h_o^{(n)}) \tag{6}$$

**Classification module**

In the classification module, embeddings of entity pair are the input. Now, ReOnto performs element wise multiplication on input and then passed into multi layer perceptron using equation 7. Here $\cdot$ represent element wise multiplication.

$$MLP(v_s, v_o) = [h_{v_s}^{(1)} \cdot h_{v_o}^{(1)}]^T; [h_{v_s}^{(2)} \cdot h_{v_o}^{(2)}]^T; ...; [h_{v_s}^{(K)} \cdot h_{v_o}^{(K)}]^T \tag{7}$$

**Aggregator module**

Path information $(path_0^i; axiom\_path_0^i) \in SK^{s,o}$ from Symbolic Module is separately encoded using BioBERT[1] model, which is pretrained on biomedical text corpora. At first, we perform encoding of path information and total relation label $R_1^i$ where $i$ is the total number of potential relations (refer Equation 8 and 9). Then, we evaluate the semantic similarity between path information and complete labeled relation list. We get the relation label with the maximum similarity score and add it as a weighted bias as given in Equation 10. An important observation to make is that the weights generated by the GNN undergo modification by incorporating the knowledge of the Symbolic Module. This step is crucial as it

[1]https://www.sbert.net/

Table 1: Ontologies used for Symbolic Knowledge

| Ontology | Classes | Properties | Maximum depth |
|---|---|---|---|
| DINTO [Bona *et al.*, 2019] | 28,178 | 12 | 2 |
| OAE [He *et al.*, 2014] | 10,589 | 123 | 17 |
| NDF-RT [Winnenburg *et al.*, 2015] | 36,202 | 90 | 9 |
| MEDLINE [Yang, 2003] | 2,254 | 12 | 2 |
| NCIt [Kumar and Smith, 2005] | 177,762 | 97 | 21 |

involves combining the symbolic and sub-symbolic components. We employ the softmax function to obtain probabilities and compute the cross entropy loss (refer Equations 11 and 12), where S denotes whole corpus and n are total entity pairs such that s $\neq$ o. It is worth noting that if no path exists between two entities, the bias score is set to 0, and loss is computed accordingly.

$$Renc = enc(R_1^i) \tag{8}$$

$$Penc = enc(SK^{s,o}) \tag{9}$$

$$biasedscore_r = max(cosSim(Renc, Penc)) \tag{10}$$

$$P(v_s, v_o) = softmax((MLP(v_s, v_o) + biasedscore_r) \tag{11}$$

$$L = \sum_{t=0}^{S} \sum_{s,o=0}^{n} (logP(v_s, v_o))_t \tag{12}$$

## 4 Experimental Setup

We conduct our evaluation in response to following research questions.

**RQ1**: What is the effectiveness of ReOnto that combines symbolic knowledge with a neural model in solving biomedical relation extraction task?

**RQ2**: How does knowledge encoded in different ontologies impact performance of ReOnto?

**Datasets**. Our initial biomedical dataset is BioRel [Xing *et al.*, 2020], which includes a total of 533,560 sentences, 69,513 entities, and 125 relations. The second dataset we use is the Adverse Drug Effect (ADE) dataset [Gurulingappa *et al.*, 2012]. We treat the RE problem in this dataset as binary classification, where sentences are categorized as either positive adverse-related or negative adverse-related. Positive adverse relations are established when drug and reaction entities are associated in the given context, while negative relations involve drugs that are not accountable for a specific reaction. The ADE dataset comprises 6,821 labeled adverse sentences and 16,695 labeled negative adverse sentences, with a total of 5,063 entities. We consider two types of relations in this dataset: adverse-related and not adverse-related. The first entity is viewed as the drug, while the second entity is retrieved using named entity recognition. Table 1 provides details of the public ontologies utilized for constructing symbolic knowledge.

**Baseline Models for comparison**. We used several competitive baselines: 1) Multi-instance models such as [Nguyen and Grishman, 2015; Zeng *et al.*, 2014; Zeng *et al.*, 2015], 2) Sentential RE models such as [Bastos *et al.*, 2022; Zhu *et al.*, 2019; Sorokin and Gurevych, 2017]. For Recon [Bastos *et al.*, 2022], we used its EAC variant for fair comparison. Please note, we adapted these models to biomedical domain by retraining and inducing biomedical context needed for these models such as entity descriptions and types. 3) Biomedical relation extraction works such as [Huynh *et al.*, 2016; Rawat *et al.*, 2022; Haq *et al.*, 2022; Schlichtkrull *et al.*, 2017; Xing *et al.*, 2020]. For biomedical RE works, values are obtained from original papers, and for other works (sentential and multi-instance), if code is available, we executed them on both datasets.

| Hyper-parameters | Value |
|---|---|
| learning rate | 0.001 |
| batch size | 50 |
| dropout ratio | 0.5 |
| hidden state size | 256 |
| non linear activation | relu |

Table 2: Hyper parameter seetings

**Hyper-parameters and Metrics**. Table 2 outlines the best parameter setting. We employ GloVe embedding of dimension 50 for initialization. Since the datasets are from the biomedical domain for evaluating semantic similarity, we have used BioBERT model[2]. The size of position embedding is also kept at 50. We have used the open-source ontology (.owl) from BioPortal to extract the paths using the SPARQL query. We have followed [Zhu *et al.*, 2019] for experiment settings. We evaluated the accuracy (precision) and F1 score for both datasets.

Table 3: Biomedical Relation Extraction Results. ReOnto outperforms baselines on both datasets. We've left precision column blank for baselines that does not report it.

| Dataset | Model | Accuracy(in%) | F1 scores |
|---|---|---|---|
| ADE | CNN [Nguyen and Grishman, 2015] | 68 | 0.71 |
| | PCNN [Zeng *et al.*, 2015] | 76.9 | 0.73 |
| | ContextAware [Sorokin and Gurevych, 2017] | 93 | 0.93 |
| | RGCN [Schlichtkrull *et al.*, 2017] | 86 | 0.83 |
| | GPGNN [Zhu *et al.*, 2019] | 92.1 | 0.90 |
| | CRNN [Huynh *et al.*, 2016] | - | 0.87 |
| | CNN-Embedding [Rawat *et al.*, 2022] | - | 0.89 |
| | SparkNLP [Haq *et al.*, 2022] | - | 0.85 |
| | T5 [Raffel *et al.*, 2020] | 92 | 0.86 |
| | RECON [Bastos *et al.*, 2021] | 93.5 | 0.92 |
| | ReOnto **(Ours)** | **97** | **0.96** |

| Dataset | Model | Accuracy(in%) | F1 scores |
|---|---|---|---|
| BioRel | CNN [Nguyen and Grishman, 2015] | 48 | 0.47 |
| | PCNN [Zeng *et al.*, 2015] | 64.6 | 0.57 |
| | RGCN [Schlichtkrull *et al.*, 2017] | 72 | 0.78 |
| | GPGNN [Zhu *et al.*, 2019] | 85 | 0.84 |
| | CNN+ATT [Xing *et al.*, 2020] | - | 0.72 |
| | PCNN+AVG [Xing *et al.*, 2020] | - | 0.76 |
| | RNN+AVG [Xing *et al.*, 2020] | - | 0.74 |
| | ContextAware [Sorokin and Gurevych, 2017] | 89 | 0.87 |
| | T5 [Raffel *et al.*, 2020] | 88 | 0.86 |
| | RECON [Bastos *et al.*, 2021] | 89.6 | 0.86 |
| | ReOnto **(Ours)** | **92** | **0.90** |

[2]https://www.sbert.net/

# 5 Results

ReOnto outperforms all the baseline models on both datasets (From Table 3). These results indicate that our model could successfully conduct reasoning with a neuro-symbolic graph on the fully connected graph and combine it with the underlying deep learning model (GNN in our case). Observed results successfully answer **RQ1**. Methods such as [Bastos *et al.*, 2021; Sorokin and Gurevych, 2017] use contexts such as entity types and descriptions. Similarly, RECON and T5 include additional explicit information of long entity descriptions, its type that allows offline learning of entity context. However, in a real-world setting of the biomedical domain, it is viable that such context may not be present for each entity. In contrast, our model discards the necessity of available entity context and learns purely using reasoning over connected entity graphs. Furthermore, multi-instance baselines try to learn relations using previous occurrences of entities in the document. In both cases, missing reasoning to capture long-range dependencies of entities hampers their performance. One possible reason for CNN and PCNN not performing well is that the biomedical sentence is complex and direct adherence to relation is impossible in this type of text. We can also notice that the context-aware model is performing better than multi-instance on these datasets because entity contexts are helping up to an extent. Presently, we have added context information(symbolic knowledge) via ontology into the model. If enough context details are given our model can work on generalised datasets as well. Figure 4 presents plots a, b, c, d, which depict the training and validation F1 scores on both datasets, while plots e, f show the loss graph. Our observations indicate that ReOnto delivers consistent performance on these graphs within the considered timeframe.

# 6 Ablation study

## 6.1 Effectiveness of number of ontologies

To better understand the contribution of each ontology on ReOnto's performance, we conducted an ablation study. Table 4 presents a summary of our findings, which indicate a significant decrease in performance when considering individual ontologies. This validates our approach of merging knowledge from multiple ontologies to create symbolic knowledge.

For the ADE dataset, we have a lesser entity coverage of 22% using DRON ontology. However, we found that the performance significantly improves when we increase the entity coverage by incorporating the OAE and DINTO ontologies. This increase in entity coverage results in corresponding improvements in F1 scores. Similarly, for the BioRel dataset, we tested with MEDLINE ontology with entity coverage of 42% and then NCIt ontology with coverage of 34%, leading to corresponding improvements in F1 scores. Results also provide conclusive evidence that ReOnto's performance depends on the coverage of entities aligned with the dataset and combining encoded knowledge has positive impact on overall performance (answering **RQ2**).

## 6.2 Effectiveness of number of hops

We separately study the effect of the number of hops on the performance of ReOnto. Figure 5 shows the impact of the number of hops on the model. Increasing hops initially improve F1 scores until reaching a plateau. This is because additional hops don't provide new relevant information. Table 6 summarizes the extracted hops from the MEDLINE ontology, supporting our observation. Interestingly, increasing hops leads to redundant information that doesn't contribute to performance. To maintain context and meaningful connections, we preserved multi-hop information up to five hops in our experiment. Furthermore, Table 5 illustrates the relationship between ontology size, parsing time, and the number of hops, indicating an increase in time as hops increase.

Table 4: Effect of ontology on F1 scores

| Dataset | Ontology | Entity coverage(approx.) | F1 scores |
|---|---|---|---|
| ADE | DRON [Bona *et al.*, 2019] | 22% | 0.92 |
| | OAE [He *et al.*, 2014] | 34% | 0.93 |
| | DINTO [Herrero-Zazo *et al.*, 2015] | 41% | 0.95 |
| BioRel | MEDLINE [Yang, 2003] | 42% | 0.88 |
| | NCIt [Kumar and Smith, 2005] | 34% | 0.84 |

Table 5: Time taken to parse ontology and evaluate respective path. Parsing time increase w.r.t size of ontology

| Ontology | Size (in KB) | Time taken (in seconds) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Parsing | Direct hop | One hop | Two hop | Axiom path1 | Axiom path2 |
| OAE | 9286 | 6.75 | 0.11 | 2.73 | 7.47 | 2.19 | 5.92 |
| NDFRT | 69387 | 123.11 | 1.21 | 0.003 | 7.629 | 44.79 | 103.36 |
| DINTO | 1,10,865 | 137.4 | 1.6 | 3.8 | 8.54 | 5.67 | 11.32 |
| MEDLINE | 6975 | 2.19 | 0.002 | 0.0023 | 0.003 | 3.118 | 6.09 |
| NCI | 5,71,434 | 758.9 | 1034.5 | 1294.5 | 3454.1 | 2485 | 5569 |

Table 6: Derived path obtained by connecting "protein" and "dietary protein" entity

| Hops | Path |
|---|---|
| path1 | classifies |
| path2 | mapped from dietary proteins, classifies |
| path3 | classifies proteins, classifies dietary proteins, classifies |
| path4 | classifies proteins, classifies dietary proteins, mapped from dietary proteins, classifies |
| path5 | classifies proteins, classifies dietary proteins, related to carbs, related to dietary proteins, classifies |
| path6 | classifies Proteins, classifies dietary proteins, mapped from dietary proteins, related to carbs, related to dietary proteins, classifies |
| path7 | classifies Proteins, classifies dietary proteins, mapped from dietary proteins, related to carbs, related to dietary proteins classifies dietary proteins |

# 7 Case study

Table 7 shows qualitative results that compare the ReOnto model with the baseline models. We report a few results showing ReOnto can surmise the relationship with reasoning. ReOnto retrieved the relevant derived path from the ontology in the first case. ReOnto implicitly learns from the facts and captures the derived path to provide the correct relation label, even if it is not explicitly mentioned as *isPrimaryAnatomicSiteOfDisease*.

$$CUI{:}C0262950 \xrightarrow{preferredLabel} Bone$$
$$Bone \sqsubseteq \exists anatomicSiteOfDisease.Rickets$$
$$Rickets \xrightarrow{CUI} CUI{:}C0035579$$
$$Bone \xrightarrow{semanticType} Anatomic\ Structure$$

In the second case, ReOnto produces the following path by utilizing the expressive axiom of the ontology. ReOnto cap-

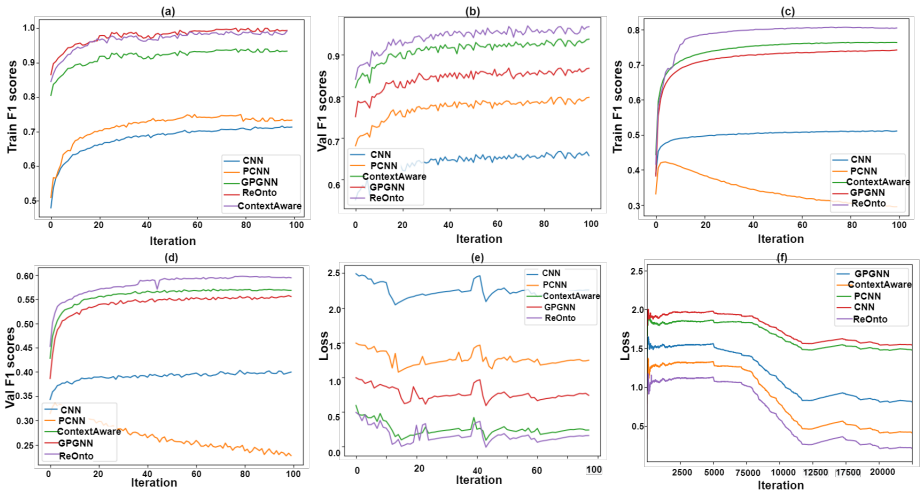


Figure 4: For the ADE dataset, Figures a) and b) show the training and validation F1 scores with baseline, respectively. Figure e) illustrates the cross-entropy loss for the iteration. For the BioRel dataset, Figures c) and d) show the training and validation F1 scores with baseline, respectively. Figure f) illustrates the cross-entropy loss concerning the iteration. ReOnto exhibits consistent and stable performance on both datasets, as indicated by the plotted F1 scores and loss.

Table 7: Sample sentences and predictions of various models. ReOnto using reasoning is able to predict the relations which are not explicitly observable from the sentence itself and requires long-range entity interactions.

| **Sentence** | **Relation** | **GPGNN** | **Context Aware** | **ReOnto** |
|---|---|---|---|---|
| Both compounds are equally potent in the stimulation of intestinal calcium transport , bone(C0262950) calcium mobilization , in the elevation of serum phosphorus , and in the healing of rickets(C0035579) in the rat | is primary anatomic site of disease | may be associated disease of disease | may be finding of disease | is primary anatomic site of disease |
| The ventricular effective refractory period, as well as the vt cycle length(C0042514), increased after propranolol(C0033497) and was further prolonged after the addition of a type i agent | may be treated by | may diagnose | may treat | may be treated by |
| dsip and clip [acth(18-39)] immunoreactive(ir) neurons and fibers were examined in the human(C0086418) hypophysis and pituitary stalk using immunmohistofluorescence and peroxidase(C4522012) antiperoxidase methods | is organism source of gene product | nichd parent of | organism has gene | is organism source of gene product |

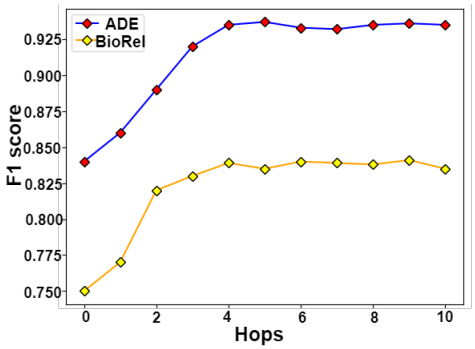


Figure 5: Effectiveness of hops on performance

$$CUI{:}C0042514 \xrightarrow{preferredLabel} Ventricular\ Tachycardia$$
$$Ventricular\ Tachycardia \equiv Techycardia$$
$$Techycardia \sqsubseteq \exists mayBeTreatedBy.Propranolol$$
$$Propranolol \xrightarrow{CUI} CUI{:}C0033497$$

tures the long-range dependencies between entities and provides the correct relation label.

In the last case study, several paths are derived from the ontology for the *Human* entity. It can be observed that ReOnto derives and asserts the dependency path between *Human* and *Peroxidase*, and concludes that the target relation label *isOrganismSourceOfGeneProduct* applies, as compared to other baseline models. Such complex ontology reasoning provides long-range interactions between entities, which is inherently not possible in baseline models.

$CUI{:}C0086418 \xrightarrow{preferredLabel} Human$
$\exists Human \sqsubseteq geneProductHasOrganismSource.Myeloperoxidase$
$Myeloperoxidase \xrightarrow{hasDisposition} Peroxidase(disposition)$
$Peroxidase(disposition) \xrightarrow{preferredName} Peroxidase$

$Peroxidase \xrightarrow{CUI} CUI{:}C4522012$

## 8 Conclusion and Future Work

We proposed a novel neuro-symbolic approach ReOnto that leverages path-based reasoning, including expressive axiom path with GNN. We apply our model to complex biomedical text and compare the approach with baselines. With empirical results, there are three key takeaways. Firstly, existing baseline models with any form of context only capture short-range dependencies of entities. In contrast, our model uses long-range entity dependencies derived from ontology reasoning to outperform all baselines on both biomedical datasets. Code is available at https://github.com/kracr/reonto-relation-extraction.

ReOnto provides effective reasoning on given text and entity pair, which can tackle the challenges of biomedical text. It also considers expressive axioms of ontology to reason on RE. The aggregation of these axioms outperformed the baselines. As a next step, we can consider using background knowlege on unsupervised data. An ontology reasoner can be used to infer more paths and perhaps these additional axioms can improve the performance further.

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