# A Sui Generis QA Approach using RoBERTa for Adverse Drug Event Identification

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## Abstract

Extraction of adverse drug events from biomedical literature and other textual data is an important component to monitor drug-safety and this has attracted attention of many researchers in healthcare. Existing works are more pivoted around entity-relation extraction using bidirectional long short term memory networks (Bi-LSTM) which does not attain the best feature representations. In this paper, we introduce a question answering framework that exploits the robustness, masking and dynamic attention capabilities of RoBERTa by a technique of domain adaptation and attempt to overcome the aforementioned limitations. Our model outperforms the prior work by 9.53% F1-Score.

**Keywords:** adverse drug event, RoBERTa, question-answering, entity-relation extraction, healthcare

## 1 Introduction

Recent advancements in drug development and approval have bolstered our healthcare ecosystem. However, this rapid paced development is accompanied by an increase in associated risks. Adverse Drug Events (ADEs) form an integral component of those risks. An ADE is defined as "an injury resulting from a medical intervention related to a drug" [1].

These events create an economic burden over the system. A study by Rocchiccioli et al. showed "a statistically significant increase in all direct costs (inpatient, outpatient, therapy) during post-ADE period (+US$1310 for all ADEs and +US$1983 for preventable ADEs, versus the pre-event period)" [3, 20, 23]. Further, national estimates are indicative of the fact that ADEs contribute at least an additional US$ 30 billion to US healthcare costs [8, 9]. Thus, it becomes an utmost requirement to identify these ADEs at an early stage from biomedical literatures, EHR data and other sources in order to avoid additional costs incurred in patient management while improving pharmacovigilence practices at the same time.

Several Adverse Drug Events have been reported to U.S. Food & Drug Administration (FDA) through Federal Adverse Event Reporting System (FAERS). These reports submissions are voluntary and hence they may suffer from cases of massive under-reporting [6]. Hence, researchers have started moving towards more automated approaches in machine learning. There has been a gradual shift towards using natural language processing (NLP) based methods. Early attempts have incorporated the use of resources like NLM’s MetaMap, Unified Medical Language System (UMLS) etc. [24] to extract drugs for ADE identification tasks. However, a major limitation of these approaches is that they are not able to capture the causal relationships between drug and ADE properly.

Another popular approach in the community has been to treat this problem as entity recognition and relation identification task. This approach has further been tackled using either a 1. pipeline method where entity recognition tasks are done first followed by relation identification or 2. a joint training method where training weights are shared between these two sub-tasks so that errors don’t accumulate [12, 15, 17]. Most of these works have utilized different variants of long short term memory (LSTM) networks for both entity recognition and relation identification tasks. Though these networks have shown promising results, they fail to capture best feature representations.

There have been ground-breaking developments in NLP with the advent of transformer architectures like BERT [4], GPT [19], RoBERTa [16] etc. Transformer networks utilize the power of multi-head self-attention mechanism to capture context-sensitive embeddings and interactions between tokens. Since they have been pre-trained on extremely large documents for language modeling task, they have shown state of the art results with downstream tasks like sentiment analysis, question answering, machine translation etc.

Our work exploits the use of "RoBERTa" architecture for ADE task using a question-answering(QA) framework. There are three components that lead to the final identification of ADE: NER module, Classification module to identify relevant texts and most important component i.e. a Query module fine-tuned for establishing relation between drug and the ADE. There has been very limited work in this direction that leverages the transformer architecture in QA setup to extract entity-relation especially in context of ADE identification using a drug.

Rest of our work is organized as follows. Section 2 contains related work. In Section 3, we discuss our approach in detail.
i.e. system architecture, dataset, experimental setup, training and evaluation metrics. Section 4 discusses the experimental results which is followed by a conclusion in Section 5.

2 Related Work

Initial works in NLP focussed on the use of statistical features or kernel-based methods for relation extraction or classification related tasks [2, 24]. These research works focus on a pipeline approach where entities are identified first using a NER module and then a relationship is identified between those entities. Explicitly computing these statistical features poses a requirement for a large amount of annotated documents for training purposes and they are also associated with risk of errors propagating to different steps.

Li & Ji [14] tackled the joint entity relation extraction problem as a single transition based model using integer linear programming method to draw inferences. Deep Learning methods have recently picked up a lot of pace and contributed a lot in field of NLP. In biomedical domain, the task of NER to identify drug, disease, dosages etc. has been worked out as a sequence labelling problem where tokens are tagged according to BILOU/BIO scheme. Miwa & Bansal [17] proposed an end-to-end joint relation extraction model where they stacked bidirectional tree-structured LSTMs on bidirectional sequential LSTMs. Their work inspired many researchers to take this knowledge to biomedical entity and relation extraction tasks.

Li et. al [12] proposed a neural joint model for ADE relation extraction from biomedical texts. They utilized Bi-LSTM architecture for biomedical entity recognition using concatenation of character representation, POS embedding and word embedding as input features. This layer shared partial parameters with another Bi-LSTM layer which was tuned during a joint training process. These works using Bi-LSTMs helped to make a significant progress in entity-relation extraction tasks. However, the multi-head self attention capabilities allowed transformers to capture long range dependencies efficiently. This along with contextual dense representations from pre-training using a very large corpus allowed a better feature extraction capability.

Li et. al [15] in their work formalize a QA framework using BERT architecture. Their research emphasizes how question based queries can encode the important information for entity-relation class identification in the question and at the same time provide a natural way of jointly modeling entity and relation. Eberts and Ulges [5] present a span-based joint entity and relation extraction model with transformer pre-training. They add a span classification layer that filters entities from non-entities. The filtered entities are then used for relation identification purposes. We build upon the learnings of these research endeavours to devise a new QA framework for ADE identification task using a more powerful transformer architecture RoBERTa that we describe in the next section.

3 Approach

In this section, we introduce our system architecture (Figure 1) and explain different modules it invokes.

3.1 Entity Recognition Module

Name entity recognition has been identified as a pivotal task in NLP. Classification of words from biomedical text into predefined categories like drug, disease, dosage etc. is a challenging problem. Many researchers have faced an issue of unavailability of annotated medical corpus due to which model generalization becomes difficult.

In our system, to identify the drug names in a given phrase, we leveraged recently developed Med7 [11] NER module which is trained on a collection of 2 million free-text patients’ record from MIMIC-III corpus followed by fine-tuning on the NER task. 'It has attained a lenient micro-average F1 of 0.957 across seven different categories (Dosage, Drug, Duration, Form, Frequency, Route, Strength)'.

3.2 Classification Module

Denoising and extraction of relevant information in textual data is a crucial step as it improves the learning mechanism and generalizing capability of any model. After recognizing the drug entities (section 3.1), to identify the phrases where at least one drug and adverse event pair coexists at stage 2, we trained a Bi-LSTM [21] based binary classifier on ADE sentences (section 4.1) and cross-validated it in K-Fold setting.
This model aims to filter out phrases with no presence of drug and adverse event pair and helps in improving the performance of our Q&A module and thereby making it more robust.

3.3 Q&A Module
Given a passage of text with a user query, a question-answering system discovers the span of text in the passage that best describes answer to the question being asked.

BERT [4] based pre-trained language models have achieved state-of-the-art performances on multiple tasks like semantic role labeling, question answering, machine translation, etc as it has been trained on large scale corpora and generalizes the downstream task very well. It can learn the extremely complex representation in text with a transformer-based [22] self-attention mechanism and play a crucial role in improving varieties of NLP systems.

Liu et. al [16] in their paper that introduces RoBERTa, observed BERT to be "significantly undertrained" and also found out that with a better selection of hyperparameters and training size, its performance could be considerably improved. RoBERTa, a re-implemented version of BERT in FAIRSEQ [18], has been trained with different learning rate, number of warm-up steps, batch size and out-performs state-of-the-art results on GLUE, RACE and SQuAD dataset. We use a pre-trained RoBERTa base model and fine-tune it on drug-related adverse effects corpus (section 4.1) to identify the adverse event corresponding to a drug by adding a Q&A head (Figure 2). First we process the data in desired input format for RoBERTa into 2 segments A and B. Segment A consists an encoded vector of drug treated as a question followed by segment B that consists another encoded vector of context/sentence where adverse event is mentioned. Then we pass this processed data into a 12-layered transformer network of RoBERTa and use its output that represents the 768 dimensional learnt embeddings of encoded input for further processing. After this, we apply a one dimensional CNN layer with a (1 x 1) convolution filter that creates a feature map of these embeddings followed by a softmax activation layer to predict the probability of start/end tokens of the adverse event present in a span of the given text.

4 Experimental Studies
4.1 Dataset and Evaluation Metrics
We use drug-related adverse effects corpus [7] containing sentences from 1644 PubMed abstracts. These sentences are divided into 2 categories (i) ADE (ii) Non-ADE. Former consists of sentences where at least one pair of drug and its adverse effect is present while latter consists of sentences with no such pair.

| Category | Number of Unique Sentences |
|----------|----------------------------|
| ADE      | 6617                       |
| Non-ADE  | 16688                      |

Examples for ADE and Non-ADE instances are:
- **ADE:** 14-year-old girl with newly diagnosed sle developed a pruritic bullous eruption while on prednisone
- **Non-ADE:** This patient did not have any predisposing factors for the development of an aortic thrombus before the chemotherapy was initiated.

To gauge the performance of our system, we use common performance metrics such as Precision, Recall and F1.

\[
P = \frac{TP}{TP + FP},\quad R = \frac{TP}{TP + FN},\quad F1 = \frac{2 \times P \times R}{P + R}
\]

4.2 Training
We perform training for 2 different modules involved in our system i.e. Classification and Q&A.

(i) For classification module, we construct a train and test dataset by selecting randomly sampled 9931 training and 1272 testing instances. We train a Bi-LSTM with Adam optimizer [10] minimizing binary-crossentropy loss in stratified K-Fold (k=10) setting to ensure consistency in our model performance. For final prediction on hold out dataset, we use an ensemble of these 10 Bi-LSTMs. Below appears the distribution of target variable in train and test sets:

| Positive (ADE) | Negative (Non-ADE ) | Dataset |
|----------------|----------------------|---------|
| 3976           | 5955                 | Train   |
| 610            | 662                  | Test    |

(ii) To predict ADE corresponding to a drug, we create the train & test data by determining 5955 training and 662 testing instances from ADE sentences (section 4.1) with random sampling.

We use pre-trained RoBERTa base model and fine-tune it on these 5955 sentences with a 1D CNN head (Figure 2) followed by a softmax activation layer to generate probability corresponding to start and end token of adverse event present in a context.

We train this entire architecture in K-Fold setting (k=5) with 3 epochs each on 12GB Nvidia P100 GPU. We use an ensemble of prediction probabilities for start & end tokens generated by models trained on each of the 5 folds. We set

\[
P = \frac{TP}{TP + FP},\quad R = \frac{TP}{TP + FN},\quad F1 = \frac{2 \times P \times R}{P + R}
\]
Figure 2. Q&A Module for Adverse Drug Event Identification. Input segment A consists of a drug acting as an alias for question and segment B consists of context where an ADE is mentioned. Encoded representation of segments passed as an input through 12-layered transformer network. 1-D convolutional layer is applied on top of 768 dimensional embedded representations followed by a softmax activation to identify the ADE.

5 Results

Our RoBERTa based QA approach utilizes drug entity passed as a question to determine answer i.e. adverse drug event in the given context. We determine the performance at two levels: (i) Performance of individual modules (ii) Performance of entire architecture (system).

Previous works [5, 12, 15] in the field focus on approaches that leverage either a joint training approach or a cascading pipeline approach to identify entities and then classify those extracted entities to ascertain existence of any relationship. However, our approach as described in previous section is not tailored similar to these settings. Hence, a direct comparison of individual modules is difficult. We elucidate our approach for calculation of system’s performance using these three modules together.

5.1 Performance of Individual Modules

Table 3 below details the performance of Classification and QA module corresponding to their selected training and validation set as described in the previous section. The results for classification module are reported based on mean results from 10-Fold validation sets. The presence of Non-ADE sentences (Section 4.1) where drug is either not known or wrongly identified is expected to create a bias in understanding of effectiveness of RoBERTa QA module for ADE identification tasks. Hence, we use only ADE sentences where drug
is known beforehand for determining the performance of Roberta QA framework. In this scenario, the precision would equal to 1 and hence we use recall to gauge the true efficacy of QA module.

| Table 3. Performance Evaluation of Classification & QA Modules |
|---------------------------------------------------------------|
| Metrics                  | Classification Module | QA Module |
|--------------------------|------------------------|-----------|
| Precision                | 82.74                  | -         |
| Recall                   | 81.44                  | 87.37     |
| F1                       | 82.06                  | -         |

5.2 Performance of End-to-End Architecture

Errors generated by different components in a system create a cascading effect and this aggregation of errors might render the system to a practically futile state.

In real-world applications, the overall task comprises of drug identification, noise removal and then drug-ADE relationship identification. In that process, obliteration of noisy textual information should also be accounted into the success criteria for smooth functioning of a NLP pipeline. We describe our approach to calculate the efficacy of entire system through Figure 3 below.

Figure 3. End-to-End System Architecture’s Overall Performance Calculation. Sentences in two sets (S\textsubscript{pos} & S\textsubscript{neg}) are passed into the system with an objective to identify drug-ADE relationship from S\textsubscript{pos} and removal of all the S\textsubscript{neg} instances. Classification matrix generated at each stage is leveraged for final calculation of precision, recall and F1 metrics.

At each stage either a sentence is eliminated from system or it moves to next module for operation. S\textsubscript{pos} [+D,+C,+A] denotes that among the positive sentences passed as input, these sentences had drug and were sent to QA module by classification module where ADE was accurately identified by RoBERTa QA architecture. S\textsubscript{neg}[-D], S\textsubscript{neg} [+D,-C] contribute to correctly removed instances from system. Similar analogy for their S\textsubscript{pos} counterparts identifies misclassified samples from the system. Equations for calculation of Precision, Recall and F1 scores for the entire architecture can be calculated using (1) and the modified definitions below:

\[
TP = S\textsubscript{neg}[-D] + S\textsubscript{neg} [+D,-C] + S\textsubscript{pos} [+D,+C,+A]
\]

\[
FN = S\textsubscript{pos}[-D] + S\textsubscript{pos} [+D,-C]
\]

\[
FP = S\textsubscript{pos} [+D,+C,+A] + S\textsubscript{neg} [+D,+C,+A]
\]

We detail the final performance metrics for the end-to-end system architecture in Table 4. We also visit the effectiveness of prominent approaches for ADE identification task in Table 5 below. After a thorough study of the relevant literature for ADE identification tasks, we observed that in joint training approaches, reporting of results is done in a way that the relation classification task also incorporates effects due to errors generated by entity recognition modules. Hence, we compare the results of relation classification task to the effectiveness of our entire end-to-end architecture.

| Table 4. End-to-End System Performance |
|----------------------------------------|
| P         | R         | F1 |
|-----------|-----------|----|
| 88.37     | 84.44     | 86.36 |

| Table 5. Comparison with different methods |
|--------------------------------------------|
| Methods                                | P    | R    | F1  |
|------------------------------------------|------|------|-----|
| CNN + Global features [13]              | 64.00| 62.90| 63.40|
| BiLSTM + SDP [12]                       | 67.50| 75.80| 71.40|
| SpERT [5]                               | 77.77| 79.96| 78.84|
| Our Model (End-to-End)                  | 88.37| 84.44| 86.36|

With a closer and detailed inspection, we observe that even after error propagation effect, the overall effectiveness of our system is better than existing approaches for ADE identification.

6 Conclusion

In this paper, we propose a novel approach for ADE identification tasks in biomedical texts. The experimental results highlight the effectiveness of using an end-to-end pipeline comprising of NER, classification and RoBERTa based QA modules where it achieves competitive performances in comparison to the existing best systems. We hope that our work would open up a new dimension in ADE identification and entity-relation tasks in general.

Although our end-to-end architecture achieves promising results, we plan to improve on the NER component in the architecture by building a transformer based biomedical NER. We also plan to extend this pipeline to social media platforms like twitter for pharmacovigilance based studies.
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