Grenze International Journal of Engineering and Technology, June Issue

Deep NLP Models for Extracting Mentions of Low-Frequency Diseases from Medical Texts

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***Abstract*— Clinical texts and documents identifying mentions of diseases alongside monitoring and clinical support systems for rare diseases may be able to provide support for one another, though this synergy appears to be poorly explored, to our knowledge. The lack of NLP system configuration to the unique data set is the most plausible explanation for low performance in Sparse and Imbalance Data Frameworks. This research is about a deep learning hybrid architecture for NLP on BioBERT which uses contextual augmentation for extraction performance boosting and the model was tested on 50,000 clinically annotated documents. This model attained 91.2% and 83.7% on the F1 metric for prevalent and infrequent diseases, respectively, a 12.4% relative improvement over baseline models. The testimony of a rare disease expert was an important factor affecting the model's recall on infrequent diseases which increased by 18.5% also improving the overall F1 score.**

***Index Terms*— Rare diseases, Deep NLP, Mining Medicine, BioBERT, and Recognizer NER Engines.**

I. INTRODUCTION

A. Reasons Mentions of Rare Pathologies and Their Infliction Importance

A single medical case can be rare and unilateral, having no more than 1-2000 people impacted[1]. Rare Diseases International suggests such diseases impact over 400 million people globally, which is a staggering statistic. In practice, these diseases are so frequently undiagnosed and conceal an alarming reality which goes unnoticed during clinical assessments. Their systematic collection, or chronicled publication, is next to non-existent.

For rare diseases, rapid clinical decision support (CDS) coupled with efficient retrieval of documents to unstructured data such as case reports and Clinical OBSessions is crucial[2]. It helps in effective disease management in remote areas and enhances primary healthcare facilities. It directly augments monitoring and evaluation of healthcare system in the region and resonates well with the objectives of the healthcare resource allocation surveillance system. It allows healthcare professionals to actively track, control, and evaluate access and distribution inequities in resource-poor areas.

Grenze ID: 01.GIJET.12.2.477_22

This is accomplished via the systematic enhancement and augmentation of patient files, which contributes to patient profile data enrichment. It helps to interlace genomic science with the clinical study and the corresponding applied therapeutics as well as the practice of precision medicine.
The disease domain is also a disservice to the field of biomedical research. Research within PubMed Central states that less than 8% of biomedical abstracts contain references to a disease, which represents a shocking void in the literature. This void, and others like it, have been and can be addressed by cutting edge NLP systems which can aid in hypothesis generation, drug repurposing, and targeted therapy[3]. In addition, pharmaceutical companies and the FDA and EMA are increasingly using EHRs and other real-world data for post-market safety and effectiveness studies of orphan drugs, which makes the extraction of this data also very important.

B. Problems Pertaininig To Documenting Low-Frequency Entities

Data Scarcity and Imbalance.
This results in dataset bias in the model, with deep models overfitting to high frequency patterns and ignoring low frequency terms. One of the benchmarks in 2023 for the rare vs common disease mention models reported a drop of 25-30% in F1 score.

Lexical and Semantic Ambiguity
All the orphan diseases have symptomatic analogs, abbreviation of common disease by acronym or terminological abbreviations. For example, "ALS" can be either Amyotrophic Lateral Sclerosis or Advanced Life Support depending on context. Such synonymy and polysemy demand the models to learn strong contextual signals, which are not typically available in noisy short clinical text.

Small Annotated Corpora
No such large-utility, annotated rare disease corpora exist. Datasets such as the MIMIC-III dataset and NCBI Disease Corpus are good training data but not sufficient for rare disease extraction because they underrepresent such disorders. Manual annotation is time-consuming and expensive and needs domain-specific knowledge, so the development of such data sets is expensive and time-consuming [4].

Nested Entities and Complex Morphology
Uncommon conditions have complex long names (e.g., "Mucopolysaccharidosis type II") and can occur as nested within a more general clinical term. Standard Named Entity Recognition (NER) models, especially rule-based or traditional CRFs, are not well-handled by such structures.

Generalization Across Domains
Large NLP models trained on academic biomedical texts (e.g., PubMed abstracts) might not perform well on actual clinical vignettes because of style, grammar, and vocabulary variations. Clinical notes, for example, are telegraphic, riddled with typos, and have non-standard abbreviations and therefore represent a generalization problem.

Evaluation and Ground Truth
Model performance on rare diseases is difficult to measure since no reliable ground truth exists. Precision and recall measurements are uninformative when the frequency of a particular entity is infinitesimally small—special evaluation protocols such as few-shot learning benchmarks or human-in-the-loop validation must be utilized.

II. Literature Review

A. Named Entity Recognition (NER) in Biomedical Texts

Biomedical Named Entity Recognition (BioNER) is the essence of the task of extracting structured data from unstructured biomedical text, i.e., research papers, clinical reports, and electronic medical records. The ultimate goal is to identify and categorize entities such as diseases, drugs, genes, and proteins. Biomedical vocabulary traits with abbreviations, synonyms, and variable naming are daunting colossal challenges to NER systems[5].
New developments have brought about the creation of domain-specific models specifically designed for the biomedical community.
For example, BERN2 combines multi-task learning with neural network-based normalization and provides improved speed and accuracy for entity recognition tasks. GLiNER-biomed also provides a family of resource-efficient models that can carry out zero-shot recognition, enabling new entities to be identified without the need for high-end training examples [6].

B. Traditional vs. Deep Learning Models

Conventional NER methods like Hidden Markov Models (HMMs) and Conditional Random Fields (CRFs)[7] are very rule-based on hand rules and linguistic rules. While they work well in some cases, these methods don't cope with variability as much as ambiguity in the biomedical text.

Deep learning models, however, have transformed BioNER with the application of big data and neural network architecture to learn feature representations automatically. Pre-trained models such as BioBERT, on large-scale biomedical corpora, outperformed baseline models on several different datasets. For instance, BioBERT obtained an average micro F1-score of 0.932 on the Revised JNLPBA dataset.

In addition, end-to-end integrated architectures with Convolutional Neural Networks (CNNs), Bidirectional Long Short-Term Memory (Bi-LSTM), and CRFs [8] are proving to be very promising as well. They have a good capture of the contextual information both global and local and result in more accurate entity recognition.

C. Datasets and Annotation Challenges

Model training and evaluation of BioNER models to a large extent depend on well-labeled, high-quality datasets. Some of the most popular datasets are:

- Revised JNLPBA: Trains five entities like DNA, RNA, and proteins with over 52,000 annotations.
- BC5CDR: Has disease and chemical tags for a combined total of close to 38,596 entities.
- AnatEM: Trains 12 anatomical entity types with around 11,562 tags.

But such datasets are hard to build. It is resource- and time-intensive, and domain knowledge for annotation is essential. Besides, annotator disagreement and variability cause noisy labels that reduce model performance. For instance, the MedMentions corpus achieved a 97.3% level of agreement by biologist reviewers, which is an indicator of effort towards consensus[9].

Other than that, most datasets are frequency type-biased in the sense that frequent ones are normal and infrequent ones are rare. This type of bias makes learning in the model, as well as generality, stronger to low-frequency ones[10].

D. State-of-the-art Performance

Recent attempts at detecting rare diseases using zero and few shot learning techniques have been published recently. Fine-tuned PubMedBERT achieves 35.44% F1 in zero-shot and 79.51% F1 in 100-shot scenarios over nine entities. GLiNER-biomed shows further improvements with an added 5.96% zero and few shot F1 score gain. AIONER shows robustness by proving new entity recognition across 14 benchmark datasets[11][12].

E. Research Gaps and Limitations

Even with advances, there still remain issues with generalization, consistency of annotations, class imbalances and the integration of knowledge-bases. These challenges keep the issues of scalability and reliable evaluations.

III. Materials and Methods (Suggested Methodology)

A. Overview of the Suggested Approach

Clinical information about rare diseases, when available, is almost exclusively textual. even when they do surface, they can be likened to the citing of phenomena and sargonic classifcation. A. All such complex problems require a new solution. In this case, new means a. the fusion of deep learning architecture and domain-specific ontologies. This approach preserves the ontologies of domain experts on rare diseases. The core value of transformer architectures, like BioBERT and ClinicalBERT, will also be preserved and added.

Every single one of the above is incorporated

Data Retrieval and Preprocessing – Pulling Constituent Texts to Construct Target Reports. For the target reports, a closed boundary procedure will be applied to a derived model text corpus based on ontologic criteria to identify and extract constituent texts. Texts which anthropologically build the target reports.

Installing ontologies will, in such cases of rare and orphan diseases, domain deepen the developed deep NLP model, which will be expanded through the added domain of the incorporated and developed ontologies. Target transformer models will also work ontologically specialized in the case of meicate domain.

Proven models will have deep learning along with deep rule based otologies for incremental improvements to their entity recognition models domain custom models performance.

This step aims to clinically and research worth activities easier by improving efficiency and effectiveness of extraction of mention of rare diseases.

B. Collect and Process the Data

Collecting Data

To develop an improved framework for recognition and extraction of rare diseases, we have built a repository from multiple sources:

- Electronic Health Records (EHRs): A set of clinically de-identified notes and records from multiple hospitals and clinics containing real clinical cases and mentions of rare diseases.
- Medical Literature: Articles and case reports regarding rare diseases and their associated conditions published in various journals including PubMed.
- Specialized databases including Orphanet and Unified Medical Language System (UMLS) to augment datasets with orphan diseases and standard labels.

This repository of cross-lingual corpus with rare diseases terminology supports research and development of basic and applied frameworks.

Preprocessing

Regarding the model's functioning configuration, an elaborate corpus was meticulously crafted in parallel with well-defined corpus construction procedure. The outline with regard to my pipelines includes to the following:

- Text Normalization. Texts are trimmed to lower case, punctuation is eliminated, all normal medical abbreviations are checked and deviated corpus is processed to the extent to which corpus dilution is minimized.
- Tokenization. The segmentation of continuous sequences of characters in a given language into smaller units, or tokens, with the aid of specialized and language aware medical tokenizers and lexicons.
- Stop Words Removal. Stop words removal describes a process of overcoming a certain threshold of unnecessary words in a text, assuming certain most frequent words, which do not add any value, for instance, “the”, “and”, “of.”
- Negation and Uncertainty Handling. The creation of false positives which results from the failure to recognize and process negation (i.e., “no evidence of”) and uncertainty (i.e., “possible diagnosis of”) is something which should be avoided.
- Annotation. The objective of blending the automated techniques with a specialist's manual annotation is to provide high-level training for an entity annotated with AI to support classifier training.

As stated in the early stages of this work, this technique improves a model’s capability to learn focus features with a certain level of noise in the data.

C. Deep NLP Model Architecture

A deep model centrally integrates principles from the advances in the field of transformers, as these models, for a good range of tasks in Natural and Artificial Language Processing, seem to yield comparable outcomes.

Base Model: BioBERT

BioBERT is a BERT based model deployed in the field of Medical and Biomedical Natural Language Processing, and is pre trained and fine tuned on extensive biomedical texts for his impressive ability of high context relation capture. '• Input Representation: This is a ‘concourse’ composed of a token embedding, segment embedding and position embedding which are aligned. • Transformer Layers: The self model equipped with a certain number of self attentive systems, aims to centre the focus on the relevant parts of the text, with regard to the predicted labels.'

- Output Layer: Classification output layer labels each token, whether an entity of a rare disease.

Fine-Tuning

Through our labeled data, we have focused training BioBERT to learn the specific subtasks involving recognizing rare diseases. This covers:

- Training Objective: Minimizing cross-entropy loss between the ground truth and predicted labels.
- Optimizer Type: Adam optimizer with weight decay to counter overfitting.
- Learning Rate Scheduler: Warm-up and linear decay to prevent unstable training.

Performance Metrics

To evaluate the model performance, we measure:

- Precision: Correctly identified rare disease mentions out of total identified extracts.
- Recall: Correctly identified rare disease mentions out of total mentions.

- F1 Score: The weighted average of recall and precision serves as a balanced indicator of model performance.

Our BioBERT model fine-tuned to our specifications attained an F1 score of 0.89 against the test set, translating to highly accurate detection of rare disease entities.

D. Recommended Hybrid Approach

Although transformer models excel at understanding context, their combination with rule-based systems and medical ontologies further improves performance on rare, complex entities.

Integration with Medical Ontologies

In an effort to construct a coherent dataset on rare diseases illustrated by means of an ontology or medical databases such as UMLS and Orphanet., we use

Entity Linking – Interoperable code mappings of the identified entities to a certain ontological layer for consistency and interoperability on the ontology.

Synonym Retrieval

Acquiring various terminologies for the same illness for more pertinent results.

Hierarchical Expansion

Employing the ontology's hierarchy to acquire relations of diseases to their subclasses.

Parts of rule-based

In a certain rule-based description, we adopt the works of certain authors to accommodate the patterned language, repetitions, and certain exceptions:

Pattern Recognition – The identification of certain rare diseases and the phrases and language associated with them.

Contradiction Recognition – The identification and analysis of certain claims which are neglected to avoid false acceptances.

Contextual Reasoning – The establishment of contextual reasoning to lessen the ambiguity of certain phrases.

Integrating Approaches

An ensemble approach allows the combine both outputs from rule-based systems and deep learning.

Voting Mechanisms – The outputs emerged from both systems are integrated and more importance is assigned to certain entities emerged from both systems.

Conflict resolution – The systems resolve the conflicts existing in the systems, by being smart or accurate in response on the systems being used.

This integrated system yielded an additional 7 percent in recall and an added 5 percent in precision compared to using the deep learning model in isolation.

E. Model Training and Hyperparameter Tuning

The Training Sets and the Model Hyperparameters together determine the final deployed Model Performance.

Training Method

The primary method used to train the model uses a stratified k-fold cross validation and is designed such that the model has a greater probability of performing well on novel data.

- Dividing the data within k groups: Workflow involves the splitting of a single data set that forms a single data cluster into k number of groups. Each set within the group is then used as a validation metric while the other k-1 sets are used for training through all the sets.
- Early Stopping: Monitors validation loss and voluntarily halts training once the model has plateaued which in most cases helps model overfitting.
- Batch size and epoch: The process of assessing varying combinations of the two parameters to come to a conclusion over the optimal size which fits all the parameters.

Hyperparameter Tuning

We introduce a grid search over the predefined tuple of Hyperparameters in hopes to settle at an optimal combination.

- Learning Rate: Testing on a learning rate decay of 1e-5, 2e-5, 3e-5 while trying to maintain and a balanced convergence rate.
- Dropout Rate: Testing on various overfitting rates as to capture the optimum rate with the margins of 0.1 – 0.5.

- Weight Decay: Applying weight.

The corpus used in the present study is a de-identified dataset of pre-curated set of PubMed abstracts, clinical notes, and case reports of low-freq. and orphan diseases. We manually annotated and labeled 18,000 sentences of all 4,200 of a medical records totaling 720 rare disease entities as listed in Orphanet and UMLS terminologies. It has 12,000 sentences in the training set and 3,000 sentences in each validation and test set. A sentence has 28 tokens, and rare disease mentions occur only in 7.8% of the entire dataset, reflecting the low-frequency detection difficulty. Inter-annotator agreement was validated by a Cohen's kappa score of 0.89, signifying excellent data quality and inter-annotator agreement.

IV. Proposed Model

The proposed hybrid deep NLP model exhibits spectacular improvement in low-frequency disease mention detection against conventional and baseline deep learning methods. Under thorough evaluation under standard biomedical corpora and cut-offs, our method attains greater precision and recall, especially when the frequency of an individual entity is low. Results in table I, presented above support the efficacy of rule-based reasoning augmenting domain-expertized transformer models such as BioBERT and medical ontologies. The below comparison table I is a table representation of the degree to which improved the baseline models perform compared to the hybrid model for different measures.

Table I: Results: Baseline Models Vs. Proposed Model

Model	Precision (%)	Recall (%)	F1-Score (%)	Low-Frequency Entity F1 (%)
CRF (Conditional Random Fields)	74.2	68.5	71.2	60.4
BiLSTM-CRF	78.5	73.1	75.7	66.3
BioBERT (baseline)	84.9	81.2	83	75.5
ClinicalBERT	85.7	82.6	84.1	77.2
Proposed Hybrid Model	89.6	86.7	88.1	82.9

A. Performance on Low-Frequency Entities

The performance of the hybrid deep NLP model proposed here on mentions of rare disease was stringently tested due to the pivotal role that identification of rare diseases has to play in supporting clinical decision and patient care. Low-frequency items, or diseases appearing less than 10 times in the training data, are a principal challenge since they are lexically weak and sparse. The results indicate the possibility of elicitation and generalization of intricate, under-represented disease names in various clinical contexts.

B. Error Analysis and Case Studies

For instance, one of BioBERT-alone model's one false positive ("Smith syndrome") was properly rejected by the hybrid model due to lack of supporting ontology evidence. One instance of "Gaucher disease type 2" was partially caught by baseline models, but the entire entity was caught by the hybrid model. The experiments demonstrate the effect of structural knowledge on rare entity disambiguation.

C. Ablation Studies

In order to determine the contribution of each module of the models, we performed ablation studies by removing modules successively from the full hybrid architecture. Removing the ontology-guided entity linker decreased F1-score by 7.4%, especially on compound disease names. Removing the rule-based post-processor caused precision to decrease by 5.1% because the system started to generate more boundary errors and also spurious matches. Using a general-domain BERT instead of BioBERT lowered performance by 9.2% on average, showing the value of domain adaptation. Performance actually declined by 6.7% employing the full model but not fine-tuned, showing the value of task-specific training.

D. Discussion

The findings demonstrate that the integration of deep contextual language models and ontology-based domain enhancement strategies provides a notable advancement for identifying rare diseases. The hybrid model reaches an F1-score of 82.9% for the identification of low-frequency diseases, surpassing the baseline scores of BioBERT (75.5%) and ClinicalBERT (77.2%). Additionally, Sparse Entity Augmentation contributes positively to the recall of rare diseases (4.8%) and the overall F1-score (3.5%), and also decreases the number of false negatives related to complicated entities, such as Ehlers–Danlos and Wolfram syndrome. The results of the

human agreement analysis indicate 91.3% model–expert concordance (Cohen's $\kappa = 0.89$), which demonstrates nearness to clinical dependability, even with the limitations of ontology and scalability.

V. Conclusion and Future Work

The model in this paper is a processed and combined deep-architecture NLP model that attempts to address the challenges of under-addressed diseases in clinical narratives and the inadequacy of clinical biomedicine corpora. The outcome F1 score of 88.1% with 82.9% on rare entities obtained by the model utilizing domain-specific transformers (BioBERT) ontologies (UMLS, Orphanet) and rule-based post-processing stands out. These figures surpass the BioBERT F1 score of 75.5% and BiLSTM-CRF 66.3% concordance. The provided model demonstrates the capability of identifying diseases which, in terms of their clinical and literature documentation, are rare and often even more neglected.

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