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Journal Title: AMIA Annu Symp Proc
Volume: Volume 2022, Number
Publisher: (publisher) | 2022, Pages 962-971
Type of Work: Article
Publisher DOI:
Permanent URL: https://pid.emory.edu/ark:/25593/w6dzd

Accessed October 20, 2023 10:37 AM EDT
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Abstract Pathology text mining is a challenging task given the reporting variability and constant new findings in cancer sub-type definitions. However, successful text mining of a large pathology database can play a critical role to advance ‘big data’ cancer research like similarity-based treatment selection, case identification, prognostication, surveillance, clinical trial screening, risk stratification, and many others. While there is a growing interest in developing language models for more specific clinical domains, no pathology-specific language space exist to support the rapid data-mining development in pathology space. In literature, a few approaches fine-tuned general transformer models on specialized corpora while maintaining the original tokenizer, but in fields requiring specialized terminology, these models often fail to perform adequately. We propose PathologyBERT - a pre-trained masked language model which was trained on 347,173 histopathology specimen reports and publicly released in the Huggingface1 repository2.

Our comprehensive experiments demonstrate that pre-training of transformer model on pathology corpora yields performance improvements on Natural Language Understanding (NLU) and Breast Cancer Diagnose Classification when compared to nonspecific language models.

1 Introduction

Pathology reports document specific observations of tissue specimens which can play a critical role to advance ‘big data’ cancer research like similarity-based treatment selection, case identification, prognostication, surveillance, clinical trial screening, risk stratification, and many others3-5. However, due to the high variability in language and documentation templates, the content of pathology reports can be difficult to mine automatically. The complexity of pathology ontology structuring, clinical diagnoses interspersed with complex explanations, different terminology to label the same cancer, synonymous and ambiguous terms, and multiple diagnoses in a single report are just a few of such challenges. Recent advances in Natural Language Processing (NLP) techniques can be leveraged for better understanding of contextual relations in pathology text mining by exploiting attention based Encoder-Decoder6 architectures. The Bidirectional Encoder Representations from Transformers (BERT)7 is a contextualized language representation model based on a multilayer bi-directional encoder, where the transformer neural network uses parallel attention layers rather than sequential recurrence. Therefore, BERT model can represent words or sequences in a way that captures the contextual information, causing the same sequence of words to have different representations when they appear in different contexts. As a result, previous state-of-the-art language models such as Word2Vec8,9, fastText10, ELMo11, and ULMFiT12 were outperformed by BERT7 in several targeted NLP tasks.

Recently, several studies have explored the utility and efficacy of contextual models in the biomedical domains13-16. Lee et al.13 trained a BERT model using a corpus of biomedical research articles derived from PubMed abstracts and PubMed Central full texts to achieve new state-of-the-art performance on several text mining tasks, including named entity recognition, relation extraction, question answering. In order to provide a standardized benchmark for comparison of different models, Peng et al.16 created the Biomedical Language Understanding Evaluation (BLUE), a benchmark consisting of five tasks (i.e., sentence similarity, named entity recognition, relation extraction, document multi-label classification and inference). In addition, the authors released BlueBERT, a BERT model trained using PubMed abstracts and MIMIC III17 (Medical Information Mart for Intensive Care III) clinical notes. Alsentzer et al.14 released a clinical BERT base model trained on the MIMIC III17 database. Beltagy et al.15 released SciBERT which is trained on a random sample of 1.14M full-text scientific papers from Semantic Scholar (18% computer science papers,
82% biomedical papers).

While there is a growing interest in developing language models for more specific clinical domains, the current trend appears to prefer fine-tuning general transformer models on specialized corpora rather than developing models from the ground up with specialized vocabulary. However, in fields requiring specialized terminology, such as pathology, these models often fail to perform adequately. One of the major reasons for this limitation is because often transformer-based models employ WordPiece for unsupervised input tokenization, a technique that relies on a predetermined set of Word-Pieces. The word-piece vocabulary is built such that it contains the most commonly used words or sub-word units and any new words (out-of-vocabulary) can be represented by frequent subwords. Although WordPiece was built to handle suffixes and complex compound words, it often fails with domain-specific longer terms. As example, while ClinicalBERT successfully tokenizes the word “endpoint” as ['end', '#point'], it tokenize the word “carcinoma” as ['car', '#cin', '#oma'] in which the word lost its actual meaning and replaced by some non-relevant junk words, such as ‘car’. The words which was replaced by the junk pieces, may not play the original role in deriving the contextual representation of the sentence or the paragraph, even when analyzed by the powerful transformer models. In summary, word-Piece tokenizer have three major drawbacks: (1) they do not retain the the full word representation of every word in the vocabulary, (2) they often fail to tokenize domain-specific compound words, and (3) they are brittle to noise, meaning that even minor typos may affect the representation of a word. Training a domain specific transformer model is often challenging as it requires a large amount of domain specific training data. Lack of availability of the biomedical domain specific data is a constraint for training the BERT model for many biomedical NLP tasks.

In this work, we propose PathologyBERT - a pre-trained masked language model which was trained on 347,173 histopathology specimen reports. As far as we know, we are the first authors to propose and publicly release a pre-trained masked language model for pathology domain. The contributions of the study can be summarized as following:

i) We train and publicly release PathologyBERT - a transformer-based model trained on Histopathology specimens text; ii) We perform extensive experimentation and comparison between PathologyBERT and other publicly available BERT models to investigate the performance of masked word prediction; and iii) finally, compared a targeted task performance between PathologyBERT and other publicly available BERT models to show the utility of the language space.

The rest of this paper is organized as follows. Section 2 presents the details of the methodology, including the proposed BERT model architecture, the training processes, and detailed analysis of the dataset. Section 3 describes the experiment design and analyzes the results of experiments. Section 4 concludes the paper by describing the limitations and setting forth future work.

2 Methods

Figure 1 presents the core steps of the proposed pipeline by highlighting different training steps. First, we employed experts to generate an annotated dataset with diagnosis labels from randomly selected samples. Second, we used the unsupervised dataset to train and evaluate the masked language model. Finally, both supervised and unsupervised datasets are used to assess the masked language prediction and classification performance on the annotated data. Each processing block (gray background) is described in the following section.

2.1 Dataset

In order to train the model and validate the language space, we collected the following two non-overlapping corpora of histopathology reports from Emory University Hospital (EUH).

**Corpus I. Unlabeled pathology reports from EUH** - With the approval of Emory University Institutional Review Board(IRB), a total of 340,492 unstructured Histopathology specimens from 67,136 patients were extracted from the clinical data warehouse of Emory University Hospital (EUH) between the years of 1981 and 2021. These reports are written following a semi-structured template, and contain standard sections such as: "HISTORY", "DIAGNOSIS", "GROSS DESCRIPTION", "MICROSCOPY EXAMINATION", and "COMMENTS". Although all sections may contain relevant pathology information, due to the size constraint of the BERT input sequence, we only incorporated the "DIAGNOSIS" section in this study. Using simple regex, we divided each part from a single specimen into an
individual diagnosis element. The average report length is $42 \pm 26$ tokens resulting in a corpus size of approximately $7.2M$ tokens. The reports may contain varying year-wise templates which makes the language space generation very challenging. The quality of extracted text features has been demonstrated to be improved by data pre-processing\(^9\). When building the language model vocabulary, we employ pre-processing to minimize the feature space and improve data generalization. In this work, we transformed the segmented data through a series of standard pre-processing techniques. This was accomplished by applying a conversion to lowercase and removal of numbers. In addition, we discarded identifying details of pathologist, clinicians, and patients from the reports. A descriptive statistics across years are illustrated on Table 1. We train the masked language PathologyBERT model using only Corpus I. We leveraged corpus I to train, test and validate the masked language model by randomly splitting the corpus into 238,342 ($70\%$) for training, 34,050 ($10\%$) for validation, and 68,100 ($20\%$) for testing purpose.

**Corpus II. Manually labeled pathology reports from EUH** - In order to evaluate the influence of vocabulary coverage on the common masked language model prediction and domain-specific breast cancer diagnose task, we have collected a total of 6,681 unstructured histopathology specimens from 3,155 patients from the EUH clinical data warehouse between the years of 2010 and 2021. This corpus does not overlap with corpus I as there is no intersection of patients between corpus. Each part was classified into fifty eight benign and malignant pathologic diagnoses (invasive ductal carcinoma, lobular carcinoma in situ, radial scar, fibroadenoma, etc.) and grouped into six categories (invasive breast cancer, in situ breast cancer, high risk lesion, non-breast cancer, benign, and negative.). Each part was labeled with at least one label but no upper limit on the number of possible labels. The whole corpus was used in our study to evaluate the model performance.

### 2.2 Pathology Language Space Training

We trained the traditional 12-layers transformer block architecture of BERT starting from random weights at each block. Rather than demonstrating technical novelty in the model design, the focus of this research is to generate a
Figure 2: WordPiece tokenizer full word coverage over Corpus I for: (a) All unique tokens; (b) Only tokens with minimal frequency of 10.

Table 1: Descriptive statistics from corpus 1 across years.

| Year of reporting | Dataset Statistics |
|-------------------|--------------------|
|                   | No. of patients    | Number of reports | Mean report size | No. of words | No. of tokens |
| 1981-1984         | 70                 | 112               | 10 ± 2         | 837         | 139          |
| 1985-1988         | 300                | 1,020             | 30 ± 21        | 20,381      | 1,386        |
| 1989-1992         | 227                | 1,247             | 40 ± 50        | 31,691      | 2,067        |
| 1993-1996         | 1,507              | 7,920             | 45 ± 36        | 111,651     | 3,231        |
| 1997-2000         | 5,716              | 26,386            | 45 ± 36        | 319,387     | 4,093        |
| 2001-2004         | 8,150              | 88,771            | 48 ± 22        | 950,367     | 7,068        |
| 2005-2008         | 20,061             | 268,922           | 39 ± 20        | 1,253,935   | 7,586        |
| 2009-2012         | 10,189             | 428,312           | 32 ± 23        | 1,263,248   | 7,396        |
| 2013-2015         | 11,789             | 397,210           | 42 ± 26        | 1,024,134   | 7,396        |
| 2016-2019         | 18,584             | 1,017,185         | 42 ± 26        | 1,884,896   | 9,529        |
| 2020-2021         | 2,303              | 365,445           | 39 ± 20        | 365,445     | 5,618        |
| Overall           | 67,136             | 22,125            | 42 ± 26        | 7,225,972   | 18,355       |

Vocabulary - BERT uses WordPiece\textsuperscript{18} for unsupervised input tokenization. The vocabulary is built such that it contains the most commonly used words or sub-words. As a result, any new words can be represented by frequent sub-words (e.g. BERT tokenizes dysplasia as d ##ys ##p ##lasia). We trained a new WordPiece vocabulary on our pathology Corpus I in order to create a new PathologyBERT vocabulary. In this study, we only produced uncased vocabularies, and the vocabulary size was set to 13K after an extensive hyperparameter search. The resulting token coverage comparison between ClinicalBERT\textsuperscript{14}, BlueBERT\textsuperscript{16}, and PathologyBERT is illustrated in Fig 2. The findings show a substantial difference in frequently used words between pathology and other medical domain texts.

Pre-training - We explored the following hyperparameters: learning rate $\in \{2e^{-4}, 2e^{-5}\}$, batch size $\in \{32, 64\}$, word minimal frequency $\in \{2, 4\}$, and vocabulary size $\in \{10k, 13k, 15k\}$. The best model was trained with a batch size of 32, a maximum sequence length of 64 (mean size of report is 42 ± 26), a learning rate of 2e-5, and masked language model probability of 0.15. Models were trained for 300,000 steps. All other BERT default parameters were used. We used a GeForce Quadro RTX 6000 24 GB GPUs. The extensive hyperparameter searching on our corpus I takes approximately 5 days when using multiple available GPUs. Finally, training the PathologyBERT model with optimal hyperparameter from scratch on our corpus I takes 36 hours.

2.3 Targeted tasks

With minimal architectural modification, PathologyBERT can be applied to various downstream text mining tasks. Within the scope of this study, we applied the learnt language space for two targeted tasks - (i) masked language prediction with different thresholds to show the semantic understanding of the model; and (ii) classification of reports according to cancer severity.
Table 2: Inference table results across diagnosis from masked language prediction over corpus II. We randomly mask 15% of tokens per diagnose report, resulting in a total of 111,524 samples. In addition to Accuracy, we also report the Top 5 Accuracy, which takes the top five predictions into account. We consider a prediction correct if it matches one of the top five predictions.
Table 3: Masked language prediction results over Corpus I holdout test set with varying thresholds. We also report the Top 5 Accuracy, which takes the top five predictions into account. We consider a prediction correct if it matches one of the top five predictions.

We fine-tune PathologyBERT on Corpus II to predict 6 breast cancer diagnose severity (invasive breast cancer, high risk lesion, borderline lesion, non-breast cancer, benign, and negative). Note that each specimen has at least one label but no upper limit on the number of possible labels, making the task a multi-label prediction problem. To overcome this challenge, we reformulated each label learning as a binary classification task and transformed the multilabel learning into multiple binary classification tasks.

The architecture, optimization, and hyperparameters are essentially the same as that of presented on BERT. During the fine-tuning process, we feed the final BERT vector for the [CLS] token into a linear classification layer to predict multi-labels for each specimen report. We optimize binary cross entropy loss using Adam and applied a dropout of 0.2. We fine-tune for 6 epochs using a batch size of 16, 32, or 64 and a learning rate of 5e-6, 1e-5, 2e-5, or 5e-5 with early stopping on the development set (patience of 10). The best model was trained with a batch size of 32 and a learning rate of 2e-5.

3 Experiments and Results
3.1 Vocabulary coverage and masked language prediction

Our experiments are focused on two aspects; 1) pathology-specific vocabulary coverage, 2) performance of masked language model. We report results on both Corpus I and Corpus II. As described in the dataset section, reports in Corpus II are labelled by diagnoses. Hence, this corpus allowed us to judge the performance of PathologyBERT stratified by the diagnosis label.

Major advantage of training a tokenizer and a transformer based language model for pathology reports is coverage of pathology-specific terminology. Figure 2 shows the overall coverage of pathology vocabulary by the proposed PathologyBERT compared to pre-trained models like ClinicalBERT and BlueBERT. It is clear that PathologyBERT provides far better coverage than pre-trained models. Pathology-BERT nearly covers all terms with a frequency of at least 10. This is intuitive as PathologyBERT has specifically been designed and trained on pathology reports while none of the pre-trained BERT models had this opportunity.

On the unseen cohort II, we also validated the coverage of the ClinicalBERT, BlueBERT and PathologyBERT for both common and extremely rare diagnosis classes. Figure 3 shows the coverage ratio of models on the unseen cohort II along with number of representative class samples. Coverage ratio is defined as \( N(w_p)/N(w_n) \) where \( N(w_p) \) is the number of unique words within the class member present in vocabulary and \( N(w_n) \) is the total number of unique words within the class member. As seen from the figure, PathologyBERT achieved good coverage (> 0.75) for extremely rare classes, such as Apocrine Carcinoma (3 samples), Atypical Phyllodes (3 samples). Other transformers vocabulary coverage have only been limited to 0.5 range.

Given better vocabulary coverage, we expect to see better masked language prediction accuracy from the masked language model built on top of PathologyBERT. Results in Table 3 confirm this expectation on the hold-out validation data. We report both the accuracy and the ‘Top 5 Accuracy’ which counts occurrence of the masked token in the top-5 predicted tokens as a correct prediction. PathologyBERT outperforms both BlueBERT and ClinicalBERT by a large margin, i.e., accuracy of 0.73 achieved by PathologyBERT compared against 0.37 for BlueBERT and 0.26 for ClinicalBERT at conventional 15% masking rate. We extended these experiments across a wide range of masking rate, i.e., from 15% to 75%. It is interesting to note that performance remains stable, especially in terms of accuracy values, across such a wide range of masking rate for PathologyBERT. ClinicalBERT and BlueBERT drop their performances by 3 and 6 percentage points, respectively. We attribute this phenomenon to narrow frequency range of unique tokens. Only about 6000 tokens have frequency 10 or more. We believe smaller token set size results in more frequent
repetition of tokens, and hence more predictable token patterns resulting in stable prediction performance even with very high masking rate. ClinicalBERT and BlueBERT fail to predict even this smaller variety of tokens because their tokenizers do not properly cover tokens included in this small but specialized token set containing pathology-specific terminology.

Table 2 presents the masked language prediction results (masked 15%) for each class present in the unseen Corpus II. Similar test observation (Table 3) holds for the unseen dataset - PathologyBERT provides better coverage than pre-trained BERT models on all diagnoses. Overall prediction accuracy is much higher in PathologBERT (71% accuracy) compared to ClinicalBERT (27%) and BlueBERT (38%). Interestingly, even for the rare classes with <20 occurrences, PathologyBERT obtained decent accuracy while other models achieved very low performance with both strict and relaxed metrics.

In order to present the concept more intuitively, we show in Table 4 a few randomly chosen examples of prediction by masked language models. It is interesting to note that PathologyBERT not only makes more accurate predictions, its top few suggestions consist of words pointing to similar concept or synonyms. This indicates model’s ability in understanding the context of the word and its suggesting potential tokens suitable to the same context. When PathologyBERT predicts ‘mastectomy’ as top candidate, it also predicts ‘resection’ and ‘excision’ as second and third choices. All of these words point to the idea of tissue removal. Similarly, when ‘calcification’ is predicted as the top word, the second choice is ‘micro-calcification’.

3.2 Breast Cancer Diagnose Severity Classification

Language models are widely used for generating semantically rich embeddings for words or word sequences that can be further used for downstream prediction tasks. Performance of downstream predictor is another indicator of
In this article, we introduced PathologyBERT, which is a pre-trained language representation model for pathology text mining. In our comprehensive experimental setting, we showed that pre-training transformer model on pathology corpora is crucial in applying it to Pathology Natural Language Understanding (NLU), information extraction, text classification, and several other text mining tasks. Further, with minimal task-specific architectural modification and with a multi-label unbalanced dataset, PathologyBERT outperforms previous models on breast cancer severity classification task. To support pathology informatics development, we released the model with open-source license in the HuggingFace model repository. While PathologyBERT shows significant promises in regards to pathology text mining, it faces several limitations. One major limitation is that it has been trained on pathology reports collected from a single institute. Only the DIAGNOSIS section of each report was included in the training process. Different institute may use somewhat different vocabulary as well as report structure. However, given the semi-structured nature of re-

| Sentence | PathologyBERT | Masked Language Model |
|----------|---------------|-----------------------|
| right breast, non palpable | invasive vs non-invasive cancers, necrotizing granulomas, with a nodular growth pattern | BlueBERT | 0.99 vs 0.89 | 0.99 vs 0.89 | 0.99 vs 0.89 | 0.99 vs 0.89 |
| usual ductal epithelial hyperplasia, specific [atypia], calcifications associated with benign | usual ductal epithelial hyperplasia, specific [atypia], calcifications associated with benign | ClinicalBERT | 0.99 vs 0.89 | 0.99 vs 0.89 | 0.99 vs 0.89 | 0.99 vs 0.89 |
| chronic [atypia] with regenerative changes, no keratinizing pilaris | chronic [atypia] with regenerative changes, no keratinizing pilaris | BlueBERT | 0.99 vs 0.89 | 0.99 vs 0.89 | 0.99 vs 0.89 | 0.99 vs 0.89 |
| invasive breast tissue including malignant nodular fibroepithelial lesion, nodular [atypia] vs fibroepithelial lesion | invasive breast tissue including malignant nodular fibroepithelial lesion, nodular [atypia] vs fibroepithelial lesion | ClinicalBERT | 0.99 vs 0.89 | 0.99 vs 0.89 | 0.99 vs 0.89 | 0.99 vs 0.89 |

Table 4: Inference examples from masked language model. Samples are selected from holdout test set and a random token is masked. The sentence is then fed into the model for mask prediction.

It is important to note that the largest performance improvement is achieved for Non-breast cancer (NBC) label (0.59 f1-score of BlueBERT to 0.70 f1-score of PathologyBERT). This label has the lowest support value, indicating it to be the rarest of all considered labels. It is an intuitive assumption that tokens indicative of a rare label are also rare and are not covered by BlueBERT and ClinicalBERT, but are covered by the tokenizer of PathologyBERT. Thus PathologyBERT outperforms other BERT based predictors by a significant margin for this label.

| Severity category | BlueBERT | ClinicalBERT | PathologyBERT | Support |
|------------------|----------|--------------|----------------|--------|
| Invasive breast cancer-NBC | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 |
| Non-invasive breast cancer-NBC | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 |
| In situ breast cancer-ISC | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 |
| High-risk lesion-HRL | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 |
| Negative | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 |
| Accuracy | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 | 0.99 ± 0.002 |

Table 5: Inference table performances of BERT, BioBERT, ClinicalBERT, BlueBERT, and PathologyBERT on predicting Breast Cancer Diagnoses. Bold indicates the state-of-the-art results with 95% bootstrap confidence interval.

4 Conclusion
In this article, we introduced PathologyBERT, which is a pre-trained language representation model for pathology text mining. In our comprehensive experimental setting, we showed that pre-training transformer model on pathology corpora is crucial in applying it to Pathology Natural Language Understanding (NLU), information extraction, text classification, and several other text mining tasks. Further, with minimal task-specific architectural modification and with a multi-label unbalanced dataset, PathologyBERT outperforms previous models on breast cancer severity classification task. To support pathology informatics development, we released the model with open-source license in the HuggingFace model repository. While PathologyBERT shows significant promises in regards to pathology text mining, it faces several limitations. One major limitation is that it has been trained on pathology reports collected from a single institute. Only the DIAGNOSIS section of each report was included in the training process. Different institute may use somewhat different vocabulary as well as report structure. However, given the semi-structured nature of re-
porting, template structure may not pose significant generalizability challenge for our model and can be fixed easily by pre-processing and section segmentation. Another limitation is that although the model uses a range of data from 1981 to 2021, it is uncertain how historical data may affect the behavior and generalizability of the language model. Another limitation is smaller input size of 64 tokens as compared to 512 for BERT and 128 for ClinicalBERT. This parameter value works well with our current training corpus where we can easily extract DIAGNOSIS section with mean size of 42 tokens. However, this may pose problems when applying our model to a longer pathology reports coming from other institutions. In future, we intend to alleviate above-mentioned limitations by employing multi-institutional data for fine-tuning of our model. The scope of this work is limited to quality evaluation of the language model for its inherent task of masked token prediction and breast cancer diagnosis classification. In future, we intend to experiment with a wider variety of downstream prediction labels including named-entity recognition and hierarchical modeling for subcategories of diagnoses.

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