Using Bottleneck Adapters to Identify Cancer in Clinical Notes under Low-Resource Constraints

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Abstract

Processing information locked within clinical health records is a challenging task that remains an active area of research in biomedical NLP. In this work, we evaluate a broad set of machine learning techniques ranging from simple RNNs to specialised transformers such as BioBERT on a dataset containing clinical notes along with a set of annotations indicating whether a sample is cancer-related or not.

Furthermore, we specifically employ efficient fine-tuning methods from NLP, namely, bottleneck adapters and prompt tuning, to adapt the models to our specialised task. Our evaluations suggest that fine-tuning a frozen BERT model pre-trained on natural language and with bottleneck adapters outperforms all other strategies, including full fine-tuning of the specialised BioBERT model. Based on our findings, we suggest that using bottleneck adapters in low-resource situations with limited access to labelled data or processing capacity could be a viable strategy in biomedical text mining. The code used in the experiments are going to be made available at [LINK ANONYMIZED].

1 Introduction

Clinical notes involve important information about patients and their current state and medical history. Automatic processing of these notes and the terms that appear in them would help researchers classify them into standard conditions that can also be looked up in medical knowledge-bases. In combination with other medical signals, this information has been shown to be useful in predicting in-hospital mortality rate (Deznabi et al., 2021), prolonged mechanical ventilation (Huang et al., 2020), or clinical outcome (van Aken et al., 2021), among others.

In this work, we looked at a real clinical notes database and designed a pilot experiment in which a set of different ML models were used to predict whether a clinical note is cancer-related or not. The incentive behind this experiment is to help clinicians and data curators to automatically search for and identify notes that signal a particular medical condition, instead of solely relying on laborious human annotation and keyword-based search.

The promise of ML is in automating this task reasonably close to human-level performance and ultimately expanding this work to include other conditions in a multi-class scenario. Ideally a model would be able to identify cancer types that are not seen during training and would be able to have some understanding of context and grammar to be sensitive to negation.

Contributions

In this work, we targeted the task of disease identification within a clinical notes dataset. We tested a range of different models including RNN-based and transformer-based architectures to tackle this problem. We particularly focused on efficient fine-tuning approaches to adapt our pre-trained models to the biomedical task. The novelty of this work is

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in the successful application of bottleneck adapters to the cancer identification task which to the best of our knowledge has not been explored before. We compare this method with multiple other strong baselines and conduct experiments and analyses to evaluate these different approaches. The systems developed in this study and those that will follow in related future work will be added to the data curation system of a biomedical database with the aim to enable automatic processing of clinical notes in real EHR data.

2 Pre-Trained Transformers and Fine-Tuning

In recent years, the Transformers architecture (Vaswani et al., 2017) and large language models (LMs) have become the staple baseline for many NLP tasks. The conventional paradigm is to first pre-train an LM on a large corpus of general text (e.g. Wikipedia) with a pre-training objective such as masked or causal language modeling and then fine-tune the LM on downstream tasks.

In our task, we focus on transformers pre-trained with the Masked Language Modeling (MLM) objective. In MLM, a portion of the text is masked out and the objective of the model is to learn to reconstruct the masked portion based on the available context. The most commonly used model pre-trained with MLM is named BERT (Devlin et al., 2019).

Despite BERT's promising results on many downstream NLP tasks, it has been shown that large LMs pre-trained on generic text do not always perform well on specialised domains like biomedical tasks (Lee et al., 2020; Gururangan et al., 2020). The standard approach, therefore, is to pre-train models on corpora that are related to the target domain. BioBERT (Lee et al., 2020) is an example of an LM trained on specialized data. It is trained on a large corpus of general and biomedical texts making it a strong model for biomedical text mining.

2.1 Efficient Fine-Tuning Methods

The benefits of fine-tuning large LMs for downstream applications are offset by a significant computational cost. Some LMs, for example, include more than 100 billion parameters, making their fine-tuning costly. Furthermore, complete fine-tuning may be ineffective when the amount of training data is small or different from the initial domain that the model was trained on, which might result in catastrophic forgetting.

As a response to these limitations, more efficient fine-tuning approaches have been developed, among which prompt tuning (2.3) and bottleneck adapters (2.2) are two of the most effective and well-known.

2.2 Bottleneck Adapters

Bottleneck Adapters (BAs) (Houlsby et al., 2019; Pfeiffer et al., 2021; Rücklé et al., 2020; Pfeiffer et al., 2020) are Multi-layer Perceptron (MLP) blocks that are made up of a down-projection dense layer, an activation function, and an up-projection dense layer with a residual connection. These blocks are inserted between the frozen attention and feed-forward blocks of a pre-trained LM, and only these modules will be updated during fine-tuning. This method has proven to be effective in terms of both computational and parameter efficiency.

Houlsby et al. (2019) showed that by training only around 3% of the parameters, BERT trained with adapters can get competitive results compared to complete fine-tuning. Adapter tuning can be expressed in the below equation where X_i is the output of the frozen attention or MLP component of the i_{th} layer of the pre-trained LM.

$$O_i = f_{up}(Activation(f_{down}(X_i))) + X_i \quad (1)$$

2.3 Prompt Tuning

Another efficient method of fine-tuning is called Prompt Tuning (PT) (Li and Liang, 2021; Lester et al., 2021). PT is mostly used for autoregressive LMs such as GPT (Brown et al., 2020). In this approach, a set of learnable vectors (prompt) are concatenated with the original input and passed to the LM. During fine-tuning, the objective is to learn a prompt which is intended to encode task-specific knowledge for the downstream task while the original model parameters are kept frozen. In some variations of PT, instead of concatenating a set of learnable vectors with the input before passing it to the model once, a set of prompts are learned for each individual attention layer of the pre-trained LM (Li and Liang, 2021). The PT approach used in this study can be expressed in the below equation where $Attention_i$ is the attention block of the i_{th} layer of the pre-trained transformer and P_i^k and P_i^v denote the learnable prompts for keys and values respectively.

$$O_i = Attention_i(Q_i, [P_i^k, K_i], [P_i^v, V_i]) \quad (2)$$

2.4 Bottleneck Adapters in Biomedical Domain

BAs are increasingly used for efficient knowledge extraction and domain adaptation due to their parameter efficiency and low computational cost. Following this trend, there are some works in the biomedical domain that have used adapters to insert task-specific knowledge via pre-training into the LMs (Grover, 2021; Lu et al., 2021), or employed them in layer adaptation for developing compact biomedical models (Nouriborji et al., 2022).

3 Challenges of Identifying Cancer-Related Records

Clinical notes usually involve abbreviated and non-standard language. A single concept like cancer is mentioned in different ways depending on cancer subtype. The same subtype might have a scientific and a commonly known variant and both can appear in the text. Grammar is sometimes broken and language can appear cryptic. Another issue is the prevalence of misspellings which further complicates this task.

There are also words that co-occur with a condition and can easily confound the model. For instance, words like 'breast' and 'lung' which are not specific to cancer appear a lot in cancer-related samples and the model can mistake them for a cancer signal. Another important issue is negation. If a condition is ruled out, ideally a model should not return positive. However since most rows that are classed as positive in the dataset include the token 'cancer', an example like 'not cancer' could be mistaken as positive. Encoding awareness of negation into the model is a challenge since it is known that pre-trained LMs lack an innate ability to handle negation (Hosseini et al., 2021).

4 Dataset and Annotation

The dataset in this pilot experiment was provided by ISARIC, a global initiative that, among other things, provides tools and resources to facilitate clinical research[1]. The larger dataset contains
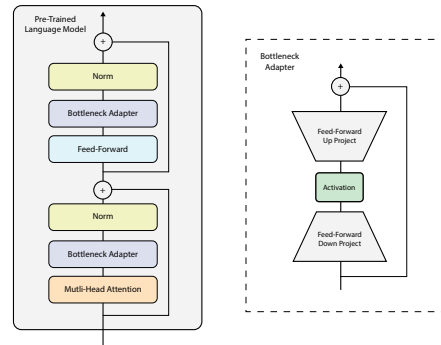
Figure 1: The overall architecture of Adapter Tuning, Note that the original parameters of the pre-trained model are kept frozen for the fine-tuning of the model and only the Bottleneck Adapters in between attention and feed-forward layers will be updated.

125381 rows corresponding to clinical notes related to different conditions and patients. For the purposes of this experiment a portion of this data was annotated for presence of cancer. The annotated subset contains 2563 rows that include cancer labels, out of which 343 are repeated notes where the doctors have written the same cancer-related note for a different patient. The human experts who tagged the data for cancer, had access to a set of cancer-related terms to guide them in the annotation. The negative cohort of 3K rows was generated by filtering out the larger data by any row that contained keywords that could potentially signal cancer definitively or with a very high possibility. The details of the lists and more information on the annotation scheme are included in the appendix (A.1).

5 Experiments

The experiments in this work are divided into two categories, namely, attention-based and RNN-based methods. We conducted all our experiments on an internal cancer detection dataset with ~$6k$ labeled samples with roughly equal instances in each classes and evaluated them on a gold standard consisting of 1k samples, 31 of which were positive and the rest negative. Note the distributional shift between training and test sets which reflect the real clinical setting under which the models are expected to perform.

5.1 Baselines

We used three baselines in this work all of which are RNN-based. The initial weights in embedding

layer of all the baselines comes from Chen et al. (2019) which is a `word2vec` model pre-trained on medical data. The first model is a simple Bi-LSTM, the second uses a 1D-convolution before the Bi-LSTM (CNN-Bi-LSTM), and the final model adds a multi-head self-attention layer after the CNN-Bi-LSTM model (CNN-Bi-LSTM-Att). All models are trained for 24 epochs with a batch size of 64.

5.2 Approach

Our aim was to improve upon the strong RNN baselines by the use of efficient fine-tuning of pre-trained transformers, namely, BERT (Devlin et al., 2019) and BioBERT (Lee et al., 2020). Three fine-tuning approaches were tried: full fine-tuning, tuning with BAs (Sec. 2.2), and PT (Sec. 2.3).

5.2.1 Tuning with Adapters

The BA used in this work is from Houlsby et al. (2019) and implemented using Adapter Hub (Pfeiffer et al., 2020). The reduction factor of the adapter is set to 16 and its activation function is ReLU. The adapters are used after attention layers and feed-forward layers of each transformer block while the parameters of the model are kept frozen. The overall architecture of the model used in this work is depicted in Figure 1.

5.2.2 Tuning with Prompts

For the PT, the approach from (Li and Liang, 2021) with a prompt size of 30 is used and implemented with the Adapter Hub library (Pfeiffer et al., 2020). In this approach, a set of prompts are learned for each attention layer of the frozen language model.

5.2.3 Encoding knowledge of Negation and Uncertainty

Negation is not by default understood by any of the models we have explored in this work. For instance, the phrases 'Evidence of lung cancer' and 'No Evidence of lung cancer' are both predicted as cancer-related by a model as the negative samples in the training set do not include negation patterns for cancer. To encode some understanding of negation into the model, we analysed the larger dataset and identified a number of different ways a condition can be ruled out with varying degrees of certainty (full list available at A.2). We used these examples to generate synthetic negative samples that include a cancer-related term (e.g. 'not lymphoma' or 'Melanoma not formally diagnosed').

6 Results

Reported results in Table 1 are best out of three subsequent runs. For each approach, the hyperparameters that seemed to work best during training were kept fixed for all the runs. Full fine-tuning was done with 5 epochs and a learning rate of $2e-5$. Tuning with BAs was done with 10 epochs and a learning rate of $1e-3$. PT was used with 10 epochs and a learning rate of $1e-4$. All approaches used a batch size of 64, AdamW Optimizer, Weight Decay of 0.01, and a cosine scheduler. As can be seen, the best performing model is the BERT trained with Adapters (including variants which are equipped with some notion of negation as explained in 5.2.3).

Analysing the outputs of individual models, we found that the majority of positive labels in the test set are correctly identified by most models. The bottleneck, however, is the false positives that happen due to the presence of certain words (e.g. 'diagnosed with', 'lung', 'breast' etc) that co-occur with cancer and can cause models to incorrectly label an instance as positive. The best model had only 4 false positives and no false negatives. The values for the confusion matrices of all the models are provided in A.3.

To alleviate the false positive issue, using the method explained in 5.2.3, we trained our best model (BERT with adapter-tuning) with additional 250 and 500 generated negative samples. The model was subsequently able to predict cases such as 'neither cancer nor covid', 'lung infection but no cancer', and 'diagnosed with covid but not cancer' correctly with only minor performance drops.

A point of strength in all the models was their ability to correctly identify cancer, given rare cancer types that had not occurred in the training set. This generalisation to unseen cancer types indicates that the models can effectively use information from the pre-trained resources they rely upon.

7 Conclusion

In this work, we trained and tested a number of classification approaches as part of a preliminary experiment on a dataset of clinical notes annotated for presence of cancer. We compared a number of RNN models utilising pre-trained biomedical embeddings with two different pre-trained transformer-based models that were fine-tuned in separate ways. We also addressed the issue of negation by integrating negation patterns into the negative training samples. Our find-

Model Architecture	Approach	Precision	Recall	F-Score
RNN	Bi-LSTM	0.98	0.75	0.83
	CNN-Bi-LSTM	0.96	0.70	0.77
	CNN-Bi-LSTM-Att	0.96	0.72	0.79
BERT	Complete Fine-Tuning	0.97	0.77	0.84
	Adapter-Tuning	**1.00**	0.94	**0.97**
	Prompt-Tuning	0.97	0.79	0.86
BioBERT	Complete Fine-Tuning	0.99	0.84	0.90
	Adapter-Tuning	0.98	0.85	0.90
	Prompt-Tuning	0.98	0.87	0.92
BERT + Negation	Adapter-Tuning-500	0.98	**0.95**	**0.97**
	Adapter-Tuning-250	0.98	0.93	0.95

Table 1: Results obtained on the gold standard dataset with 1k annotated samples. Note that the Adapter-Tuning-500 and Adapter-Tuning-250 denote models trained with 500 and 250 artificially generated negative samples, respectively.

ings suggest that efficient fine-tuning of transformers using adapters resulted in the best performance among all the tested approaches. The codes for the experiments conducted in this project are publicly available at `https://github.com/omidrohanian/bottleneck-adapters`.

Limitations

This work has certain limitations in terms of the scope of the experiments and what can be reliably inferred from them. Our dataset contains notes that are predominantly from anglophone countries. However, there are less than 20% of the rows that originate from non-English speaking regions. They might contain words in other languages (e.g. Italian), and although the disease names are usually rendered similarly as English, our models are pretrained on English and their ability to process other languages is therefore limited.

Another issue is the relatively short length of these notes. While some notes span a few sentences, most are very short and no more than $4-5$ tokens in length. This hampers the ability of a contextualised model to derive meaning from the context around each word and limits the power of attention-based architectures that are well-suited for larger contexts.

In this preliminary study we only targeted one condition and looked at binary classification. The natural step towards a more inclusive experiment would be to consider other conditions and also use multi-class classification setups where a more fine-grained scheme is used to classify a condition. Creating a sizable multi-class and multi-label corpus is a labour-intensive endeavor that requires more time and effort and would be a goal for a future work.

We did have access to multi-class annotations for our current training set, however, one major issue is that the cancer-positive cases are a small percentage of the entire rows and among the cancer types themselves, there are types that occur only once or twice and the rest belong to more frequent classes. This would make it harder for the model to learn infrequent classes. We plan to augment the annotations over time to be able to conduct experiments in scenarios beyond binary classification and cancer alone.

The issue of negation was further complicated in this work by a few cases where the note had been classified as cancer positive because the doctor had identified a history of this condition in the patient but had ruled out or downplayed the possibility of cancer at the present time. Distinguishing a current co-morbidity of cancer from a past history of cancer would introduce further complexity and this work does not attempt to address that.

Ethics Statement

Ethics Committee approval for the data collection and analysis for this work was given by the World Health Organisation Ethics Review Committee (RPC571 and RPC572 on 25 April 2013). National and/or institutional ethics committee approval was additionally obtained by participating sites according to local requirements.

This work is a part of a global effort to accelerate and improve the collection and analysis of data in the context of infectious disease outbreaks. Rapid characterisation of novel infections is critical to an effective public health response. The model developed will be implemented in data aggregation and curation platforms for outbreak response –

supporting the understanding of the variety of data collected by frontline responders. The challenges of implementing robust data collection efforts in a health emergency often result in non-standard data using a wide range of terms. This is especially the case in lower-resourced settings where data infrastructure is lacking. This work aims to improve data processing, and will especially contribute to lower-resource settings to improve health equity.

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A Appendix

A.1 ISARIC Dataset and the Annotation Procedure

As of January 2022, the ISARIC COVID-19 Clinical Database comprises of standardised data from over 800,601 hospitalised COVID-19 patients, collated during the pandemic to facilitate high quality and timely research (Group, 2021). The database contains demographic and clinical data, including hospital admission and discharge records, signs and symptoms, comorbidities, vital signs, treatments, and outcomes. Cancer is one of many comorbidities that has been found to be relevant to patient outcomes and was therefore chosen as the focus of this work (Palmieri et al., 2020). For initial model development in this experiment, a stratified sample of non-prespecified (free text) medical terms from the ISARIC COVID-19 Clinical Database was extracted. The sample was searched by a data manger (HJ, with previous clinical medicine experience) for the following cancer-related terms [2]:

- Adenocarcinoma
- Adeno-carcinoma
- Adeno CA
- Adenocarcinome
- ALL
- AML
- Astrocytoma*
- BCC
- Blastoma
- CA
- Cancer
- Carcinoma
- Carcinosarcoma

[2]* Denotes terms for which there was uncertainty as to the nature of the neoplasm/diagnosis; these terms were labelled as cancer-related during this process.

- Carcinoid*
- Cholangiocarcinoma
- CLL
- CML
- DLBCL
- Ependymoma*
- Ewing
- Gastrointestinal stromal tumour*
- Gestational trophoblastic disease*
- GBM (Glioblastoma multiforme)
- Glioblastoma
- GIST*
- HCC
- Hodgkin
- Hepatoblastoma
- Kaposi
- Leukaemia
- Leukemia
- Lymphoma
- Malignancy
- Malignant
- MDS
- Melanoma
- Meningioma*
- Mesothelioma
- Met
- Metastases
- Metastatic
- Mets
- Mycosis fungoides
- Myelodysplasia
- MDS

- Myelodysplastic syndrome
- Myeloma
- NHL
- NSCLC
- Neuroblastoma
- Neuroendocrine cancer
- Neuroendocrine neoplasm*
- Neuroendocrine tumour*
- Non-Hodgkin
- Osteosarcoma
- Pancoast
- Retinoblastoma
- Sarcoma
- SCC
- SCLC
- Sezary
- TCC
- Tumor*
- Tumour*
- Wilms

A.2 Negation Patterns

Having observed general patterns of negation in the larger dataset, we used the following 12 templates to generate negated cases of cancer:

1. Most likely not CONDITION.

2. Not CONDITION.

3. CONDITION is ruled out.

4. No CONDITION was observed

5. Unlikely to be CONDITION.

6. Not suggestive of CONDITION.

7. No indication of CONDITION.

8. No CONDITION detected

9. CONDITION not diagnosed.

10. `CONDITION` not confirmed.

11. No evidence of `CONDITION`.

12. No `CONDITION` found.

Below are some generated examples:

- Lung cancer is ruled out.

- No Gastrointestinal Stromal tumour was observed.

- Unlikely to be malignant.

- Not suggestive of CA.

- No malignancy detected.

- CA not diagnosed.

- Cancer not formally diagnosed by a doctor.

A.3 Confusion Matrices of Tested Models

Table 2 contains the confusion matrices for all the classification models that are compared in this work.

A.4 ISARIC Clinical Characterisation Group

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Model Architecture	Approach	TN	FP	FN	TP
RNN	Bi-LSTM	939	30	0	31
	CNN-Bi-LSTM	925	44	1	30
	CNN-Bi-LSTM-Att	931	38	1	30
BERT	Complete Fine-Tuning	944	25	1	30
	Adapter-Tuning	965	4	0	31
	Prompt-Tuning	947	22	1	30
BioBERT	Complete Fine-Tuning	954	15	0	31
	Adapter-Tuning	956	13	1	30
	Prompt-Tuning	959	10	1	30
BERT + Negation	Adapter-Tuning-500	966	3	1	30
	Adapter-Tuning-250	964	5	1	30

Table 2: Confusion matrices obtained from the gold standard dataset with 1k annotated samples. Adapter-Tuning-500 and Adapter-Tuning-250 denote models trained with 500 and 250 artificially generated negative samples, respectively.

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