Data and text mining

BERN2: an advanced neural biomedical named entity recognition and normalization tool

Mujeen Sung 1,†, Minbyul Jeong 1,†, Yonghwa Choi 1, Donghyeon Kim 2, Jinhyuk Lee 1,* and Jaewoo Kang 1,3,*

1 Department of Computer Science and Engineering, Korea University, Seoul, 02841, Republic of Korea
2 AIRS Company, Hyundai Motor Group, Seoul, 08620, Republic of Korea
3 AIGEN Sciences, Seoul, 04778, Republic of Korea
† These authors wish it to be known that they should be regarded as joint first authors.
* To whom correspondence should be addressed. These authors wish it to be known that they should be regarded as joint last authors.

Abstract

Summary: In biomedical natural language processing, named entity recognition (NER) and named entity normalization (NEN) are key tasks that enable the automatic extraction of biomedical entities (e.g., diseases and chemicals) from the ever-growing biomedical literature. In this paper, we present BERN2 (Advanced Biomedical Entity Recognition and Normalization), a tool that improves the previous neural network-based NER tool (Kim et al., 2019) by employing a multi-task NER model and neural network-based NEN models to achieve much faster and more accurate inference. We hope that our tool can help annotate large-scale biomedical texts more accurately for various tasks such as biomedical knowledge graph construction.

Availability and implementation: A web service of BERN2 is publicly available at http://bern2.korea.ac.kr. We also release the source code of BERN2 at https://github.com/dmis-lab/BERN2.

Contact: jinhyuk_lee@korea.ac.kr, kangj@korea.ac.kr

Supplementary information: Supplementary data are available at Bioinformatics online.

1 Introduction

Biomedical text mining is becoming increasingly important due to the constantly increasing volume of biomedical texts. From these texts, biomedical entities of different types such as genes (e.g., Atg7) or chemical compounds (e.g., arginine) can be automatically annotated using a named entity recognition (NER) tool and linked to a unique concept using a named entity normalization (NEN) tool. One popular example is PubMed Central (PTC) (Wei et al., 2019), which combines NER and NEN in the pipeline while recent progress in biomedical NLP (Lee et al., 2020) has produced stronger tools such as BERN (Kim et al., 2019) for NER and NEN.

However, existing NER tools that support NEN as well have several limitations. First, despite the diversity of biomedical entity types, existing tools support a limited number of entity types (e.g., HunFlair by Weber et al. [2021]). Second, they often use multiple single-task NER models to annotate different entity types, which result in slow inference time and require a large amount of computational resources. Finally, their NEN models rely on a dictionary or rule-based approach, which cannot cover variations in biomedical entity mentions. For instance, ‘metabolic defect’ and ‘metabolic disease’ should be linked to the same concept.

As shown in Table 1, our proposed tool called BERN2 (Advanced Biomedical Entity Recognition and Normalization) tackles these challenges by: 1) supporting the largest number of biomedical entity types, 2) dramatically reducing the latency by using a multi-task NER approach, and 3) combining both neural network-based and rule-based NEN models (Hybrid) to increase the coverage of entity normalization.

Table 1. Comparison between off-the-shelf NER tools and BERN2. Supporting types are denoted as: gene (Ge), disease (Di), chemical (Ch), species (Sp), mutation (Mu), cell line (CL), and cell type (CT). ML: Machine Learning. Latency measures the average time to annotate one abstract (sec/abstract).

| Tool       | Supporting Types | Latency (PMID) | Latency (Plain) | NER   | NEN   |
|------------|------------------|----------------|----------------|-------|-------|
| HunFlair   | Ge, Ch, Di, Sp   | N/A            | 0.54           | Neural| N/A   |
| PTC        | Ge, Di, Ch, Sp, Mu, CL | 0.78       | N/A            | ML    | Rule  |
| BERN       | Ge, Di, Ch, Sp, Mu | 1.47          | 1.12           | Neural| Rule  |
| BERN2      | Ge, Di, Ch, Sp, Mu, CL, CT, DNA, RNA | 0.03  | 0.33           | Hybrid|       |

© The Author 2022. Published by Oxford University Press. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com
2 Description of BERN2

Figure 1 shows the overview of BERN2, which is designed to annotate nine types of biomedical entities (Gene, Disease, Chemical, Species, Mutation, Cell Line, Cell Type, DNA, and RNA) and link them to their Concept Unique Identifiers (CUIs). We support two input formats: PMID and plain text. Note that PTC (Wei et al., 2019) does not support plain text inputs.

When a PMID is given, BERN2 returns a cached annotation from its database if possible. Otherwise, BERN2 takes the plain text of the PMID from PubMed and annotates it. When a plain text is given, NER models first detect the exact locations and types of entities in the text. For example, for a plain text input such as ‘tumour growth through arginine’, our NER models annotate ‘tumour’ as a disease entity and ‘arginine’ as a chemical entity. We mainly use a multi-task neural network model trained on multiple NER datasets of different types. Using a multi-task model has many advantages over using multiple single-task models such as faster inference time, performance improvement, and more efficient GPU usage.

As shown in Supplementary data, our multi-task NER model outperforms previous NER models on most NER benchmarks.

After the entities in the plain text have been tagged by the NER models, NEN models link (i.e., normalize) each entity to its corresponding CUI specified in existing knowledge bases. For example, the NEN models will normalize a recognized chemical name ‘arginine’ into ‘MeSH: D001120’. For diseases and chemicals, we use hybrid NEN models, which are a combination of both rule-based and neural network-based models. Specifically, an entity that is not normalized by the rule-based model is then normalized by a neural network-based model (Sung et al., 2020), which increases the coverage of normalized entities. See Supplementary data for the performance of our hybrid NEN models.

3 Use Cases of BERN2

We introduce two use cases in which BERN (Kim et al., 2019) was used in the field of biomedical information extraction. For these cases, BERN2 can directly replace BERN with faster and more accurate inference.

Biomedical knowledge graph construction

Biomedical literature contains considerable amount of expert knowledge. Constructing biomedical knowledge graphs from the biomedical literature can help researchers navigate this information more easily. Biomedical entities extracted by BERN2 can be used as essential components (e.g., nodes in the graphs) when building biomedical knowledge graphs. For example, Xu et al. (2020) use BERN to automatically extract biomedical entities from 29 million PubMed abstracts and build a PubMed knowledge graph, utilizing the extracted entities as nodes.

Biomedical entity-based search engine

As biomedical documents are rich in domain-specific terminology, extracting named entities can enhance search engines to find documents related to the entities in queries. Vapur (Koksal et al., 2020), which is a search engine for finding protein compounds in COVID-19 literature, pre-process a document into a set of triples (Entity1, Relation, Entity2). They adopt BERN to recognize and normalize the named entities in a document so that relevant documents that contain the same concepts can be retrieved. For example, if ‘IL1B’ is given as a query, Vapur retrieves documents that not only contain ‘IL1B’ but also ‘Interleukin1β’, since they are normalized to the same concept (EntrezGene:3553) by BERN.

4 Conclusion

We introduce BERN2, an off-the-shelf tool for fast and accurate biomedical entity recognition and normalization. Using multi-task NER models and neural network-based NEN models, BERN2 outperforms existing tools for biomedical NER and NEN. We also provide web interfaces for researchers to make use of BERN2 in various downstream tasks.

Funding

This work was supported in part by National Research Foundation of Korea (NRF-2020R1A2C3010638, NRF-2014M3C9A3063541), the Ministry of Health & Welfare, Republic of Korea (HR20C0021), the ICT Creative Consilience program (IITP-2021-0-01819) supervised by the ITP (Institute for Information & Communications Technology Planning & Evaluation), and Hyundai Motor Chung Mong-Koo Foundation.

Conflict of Interest: none declared.

References

Kim, D. et al. (2019). A neural named entity recognition and multi-type normalization tool for biomedical text mining. IEEE Access, 7.
Koksal, A. et al. (2020). Vapur: A search engine to find related protein-compound pairs in covid-19 literature. In Workshop on NLP for COVID-19 at EMNLP.
Lee, J. et al. (2020). BioBERT: a pre-trained biomedical language representation model for biomedical text mining. Bioinformatics.
Sung, M. et al. (2020). Biomedical entity representations with synonym marginalization. ACL.
Weber, L. et al. (2021). Hunflair: an easy-to-use tool for state-of-the-art biomedical named entity recognition. Bioinformatics, 37(17).
Wei, C.-H. et al. (2019). Publisher central: automated concept annotation for biomedical full text articles. Nucleic acids research, 47(W1).
Xu, J. et al. (2020). Building a pubmed knowledge graph. Scientific data, 7(1).
Supplementary Data

A. Usage

A.1 Web Demo
We provide a BERN2 web demo to allow users to easily experience our tool. Figure 2 shows an example of a webpage in our demo. When a user types in a plain text or a PubMed ID (PMID) in the input box and presses the submit button (Figure 2-A), annotated results are shown (Figure 2-B) and results in the JSON format are also provided (Figure 2-C). For annotation results, recognized entity spans are colored with their entity types and the CUI of each entity can be seen when a mouse hovers the entity.

![Interactive web demo of BERN2](http://bern2.korea.ac.kr). (A) Input box and submit button. (B) Annotation results. (C) Annotation results in the JSON format.

A.2 RESTful API
As shown in Table 2, BERN2 offers RESTful APIs to allow users to get annotation results for plain texts or PMIDs in a programmable way. The URL format for a single or multiple PubMed articles is http://bern2.korea.ac.kr/pubmed/PMID using the HTTP GET method. For a plain text, the format of the URL is http://bern2.korea.ac.kr/plain using the HTTP POST method. Listing 1 shows an example of the JSON annotations from BERN2.

| API       | HTTP Method | URL example                     | Data                                      |
|-----------|-------------|---------------------------------|-------------------------------------------|
| Single PMID | GET         | http://bern2.korea.ac.kr/pubmed/29446767 | -                                         |
| PMIDs      | GET         | http://bern2.korea.ac.kr/pubmed/29446767,2568119 | -                                         |
| Plain text | POST        | http://bern2.korea.ac.kr/plain |{"text":"tumour growth through arginine"} |
B. Multi-task Named Entity Recognition

According to Wang et al. (2019), multi-task learning (MTL) often performs better than single-task learning (STL) on biomedical named entity recognition (NER). It is because MTL allows the model to share information such as word semantics across different tasks. MTL is also advantageous in that it uses less memory size and has faster inference speed than STL for multi-type NER. In this section, we describe the design of our multi-task named entity recognition (MT-NER) model and demonstrate its performance compared to a single-task named entity recognition (ST-NER) model.

B.1 Module Description

Following Wang et al. (2019), our MT-NER model consists of a shared backbone language model (LM) and separate task-specific layers per entity type as shown in Figure 3. Specifically, we select Bio-LM (Lewis et al., 2020) as our backbone LM and two layers with ReLU activation as a task-specific layer. The output of each task specific layer is the logits for three classes (i.e., B, I, and O classes following the BIO scheme). At training time, we merge all train sets across different types and use cross entropy objectives to fine-tune the shared language model and the task-specific layers. At inference time, the model takes a input text and each task-specific layer produces its predictions all at once. This parallel inference across types allows a faster and more memory-efficient way than using multiple ST-NER models independently. Due to the lack of a public training set for mutations, both BERN (Kim et al., 2019) and BERN2 uses tmVar2.0 (Wei et al., 2018) as a mutation NER model.

B.2 Evaluation

To validate the effectiveness of MT-NER over ST-NER, we compare their performance on eight types of biomedical NER benchmarks in Table 3. We also compare Bio-LM with BioBERT (Lee et al., 2020). The result shows that MT-NER with Bio-LM outperforms the other NER models. Compared to ST-NER with BioBERT that is used in BERN, our NER model can obtain 1.44 F1 performance gain (macro-averaged). MT-NER is also superior to ST-NER in terms of the inference speed and model size (i.e., the number of parameters) as shown in Table 4. Therefore, we select MT-NER with Bio-LM because it performs the best on benchmarks with much faster inference time (0.22 sec/abstract) and more efficient model size (365M parameters) than ST-NER.

---

2 We use ‘RoBERTa-large-PM-M3-Voc’ released in https://github.com/facebookresearch/bio-lm.
BERN2

![Diagram of MT-NER model]

**Fig. 3**: The overview of MT-NER model. It shares the language model as a backbone model and uses additional task-specific layers for each task.

**Table 3**: The comparison of the performances of the named entity recognition models on eight entity types. The highest scores are boldfaced.

| Type         | Dataset                  | ST-NER | MT-NER |
|--------------|--------------------------|--------|--------|
| Disease      | NCBI-disease (Dogan et al., 2014) | 89.41  | 89.73  |
|              | BioBERT                  | 89.42  | 88.64  |
| Chemical     | BC4CHEMD                 | 91.42  | 92.30  |
|              | BioBERT                  | 91.62  | 92.30  |
| Gene         | BioBERT                  | 90.41  | 92.30  |
|              | Bio-LM                   | 90.41  | 92.30  |
| Species      | Linsaæus (Gerner et al., 2010) | 84.40  | 83.63  |
|              | BioBERT                  | 83.52  | 83.65  |
| Cell Line    | JNLPBA (Kim et al., 2004) | 76.44  | 76.56  |
| Cell Type    | JNLPBA (Kim et al., 2004) | 78.58  | 80.73  |
| DNA          | JNLPBA (Kim et al., 2004) | 75.72  | 77.78  |
| RNA          | JNLPBA (Kim et al., 2004) | 73.98  | 76.47  |
| Average      |                          | 82.47  | 82.94  |

*F1-scores are used for all entity types*

**Table 4**: The comparison of the inference time and the number of parameters on eight entity types. The best and second-best results are boldfaced and underlined, respectively.

|               | ST-NER  | MT-NER |
|---------------|---------|--------|
| Inference Time (sec/abstract) | 1.21    | 0.15   |
| # Parameters  | 864M    | 117M   |

C. Hybrid Named Entity Normalization

A named entity normalization (LEN) module aims to find the concept unique ID (CUI) of a mention recognized by the NER module. Compared to BERN that relies only on rule-based LEN modules, BERN2 additionally applies neural network-based LEN modules introduced by Sung et al. (2020) to cover ‘CUI-less’ entities that were not normalized by the rule-based approaches. We call this two-stage approach as hybrid LEN. In this section, we focus on describing how the neural network-based LEN works, and then present the performance of the hybrid LEN compared to the single-stage approaches (i.e., rule-based LEN or neural network-based LEN). We focus on drug/chemical and disease types since they have public datasets to train on (Li et al., 2016) and we still use rule-based approaches for other types (e.g., gene/protein, mutation, and etc.).

C.1 Module description

Given an input mention, the neural network-based LEN module is designed to retrieve an entity from a dictionary with the highest similarity score and return its CUI. Specifically, we perform maximum inner product search (MIPS) from a dictionary embedding matrix given an input mention representation.

---

1 We use the same rule-based normalization tools as described in BERN (Kim et al., 2019) for five types (chemical, disease, gene, mutation, species). We additionally adopt dictionary-lookup normalization for newly added types (cell line, cell type). When the public datasets for normalization of other types are released, we can extend our hybrid approach to those types as well and leave it as future work.
Table 5. The comparison of normalization accuracy. We denote using only rule-based NEN as ‘Rule-only’ and neural network-based NEN as ‘Neural-only’.

| Type     | Dataset       | Rule-only | Neural-only | Hybrid |
|----------|---------------|-----------|-------------|--------|
| Disease  | BC5CDR (Li et al., 2016) | 90.8      | 93.5        | 93.6   |
| Chemical | BC5CDR (Li et al., 2016) | 92.8      | 96.6        | 96.7   |

The dictionary embedding matrix and the input mention representation are built by biomedical entity encoder BioSyn (Sung et al., 2020). To improve latency, we pre-index the dictionary embedding matrix using Faiss (Johnson et al., 2017) (IndexFlatIP) and perform approximate nearest neighbor search to retrieve the normalized entity.

C.2 Evaluation

Table 5 shows the normalization accuracy on the BC5CDR (Li et al., 2016) test set with two entity types comparing rule-based, neural network-based, and hybrid normalization approaches. We observe that neural network-based NEN outperforms the rule-based approaches by 2.7% and 3.8% accuracy score in each entity type. We also observe that the hybrid approach can further boost the performance over using only neural network-based NEN. While this performance gain seems marginal, we choose the hybrid NEN model because the rule-based NEN model is normally more robust to false positives than the neural network-based NEN model. We finally inform users whether the entity is normalized by rule-based NEN or neural network-based NEN (i.e., is_neural_normalized).

D. Overlapping Entity Resolution

Task-specific layers for different entity types sometimes predict the overlapping results. According to BERN (Kim et al., 2019), 12.55% of mentions that are recognized as gene entities are also recognized as chemical entities. For example, in ‘the androgen is synthesized from ...’, a gene layer and a chemical layer can annotate ‘androgen’ as both a gene and a chemical because an androgen is a natural or synthetic steroid hormone. Instead of providing all overlapping entities, it is more desirable to annotate proper entities based on the context. BERN proposed the decision rules for resolving overlapping entities based on the probability of each prediction. As BERN2 supports much more entity types than BERN (5 vs. 9 types), overlapping entities appear more frequently. Based on the motivation that entities with CUIs are more informative than those without CUI (i.e., CUI-less), we add another decision rule where entities that are normalized is preferred than entities that are not normalized. Annotation results always include mutation entities recognized by TmVar2.0 (Wei et al., 2018).

References

Doğan, R. I. et al. (2014). Ncbi disease corpus: a resource for disease name recognition and concept normalization. *Journal of biomedical informatics*.

Gerner, M. et al. (2010). Linnaeus: a species name identification system for biomedical literature. *BMC bioinformatics*.

Johnson, J. et al. (2017). Billion-scale similarity search with gpus. *arXiv preprint arXiv:1702.08734*.

Kim, D. et al. (2019). A neutral named entity recognition and multi-type normalization tool for biomedical text mining. *IEEE Access*, 7.

Kim, J.-D. et al. (2004). Introduction to the bio-entity recognition task at jnlpba. In *Proceedings of the international joint workshop on natural language processing in biomedicine and its applications*.

Krallinger, M. et al. (2015). The chemdner corpus of chemicals and drugs and its annotation principles. *Journal of cheminformatics*.

Lee, J. et al. (2020). BioSBERT: a pre-trained biomedical language representation model for biomedical text mining. *Bioinformatics*.

Lewis, P. et al. (2020). Pre-trained language models for biomedical and clinical tasks: Understanding and extending the state-of-the-art. In *Proceedings of the 3rd Clinical Natural Language Processing Workshop*, pages 146–157, Online. Association for Computational Linguistics.

Li, J. et al. (2016). Biocreative v cdr task corpus: a resource for chemical disease relation extraction. *Database*, 2016.

Smith, L. et al. (2008). Overview of biocreative ii gene mention recognition. *Genome biology*.

Sung, M. et al. (2020). Biomedical entity representations with synonym marginalization. *ACL*.

Wang, X. et al. (2019). Cross-type biomedical named entity recognition with deep multi-task learning. *Bioinformatics*, 35(10), 1745–1752.

Wei, C.-H. et al. (2018). Tmvar 2.0: integrating genomic variant information from literature with dbnsnp and clinvar for precision medicine. *Bioinformatics*, 34(1).

---

4 We use the fine-tuned entity encoders ‘biosyn-sapbert-bc5cdr-disease’ for disease type and ‘biosyn-sapbert-bc5cdr-chemical’ for chemical type from https://github.com/dmis-lab/BioSyn.