Preprint

OpenBioLink: A resource and benchmarking framework for large-scale biomedical link prediction

Anna Breit 1, Asan Agibetov 1 and Matthias Samwald 1,∗

1 Section for Artificial Intelligence and Decision Support, Medical University of Vienna, Vienna, 1090, Austria
∗ To whom correspondence should be addressed.

Abstract

Summary: Recently, novel machine-learning algorithms have shown potential for predicting undiscovered links in biomedical knowledge networks. However, dedicated benchmarks for measuring algorithmic progress have not yet emerged. With OpenBioLink, we introduce a large-scale, high-quality and highly challenging biomedical link prediction benchmark to transparently and reproducibly evaluate such algorithms. Furthermore, we present preliminary baseline evaluation results.

Availability and Implementation: Source code, data and supplementary files are openly available at https://github.com/OpenBioLink/OpenBioLink

Contact: matthias.samwald@meduniwien.ac.at

1 Introduction

Advances in deep learning and vector-space embedding models have enabled the creation of a sizeable array of novel methodologies for link prediction, the task of predicting missing links in knowledge graphs. As many fundamental biomedical problems can be formulated as link prediction problems, there is growing interest in the application of these algorithms in the domain of biomedicine. Advances in methodology are both measured and steered by established general-domain benchmarks, such as the FB15K benchmark (Bordes et al. [2013]). Unfortunately, despite their wide usage, these benchmarks are often found to have flaws such as information leakage via between train- and test-set (Toutanova and Chen [2015]) and do not reflect the domain-specific properties of biomedical knowledge graphs. A large-scale, high-quality and highly challenging benchmark optimized for the task of evaluating link prediction methods in the biomedical area has not yet been established. Ideally, such a benchmark would have the following properties:

• Openly available
• Large-scale
• Wide coverage of current biomedical knowledge and entity types
• Standardized, balanced train-test split
• Open-source code for benchmark dataset generation
• Open-source code for evaluation (independent of model)
• Integrating and differentiating multiple types of biological entities and relations (i.e., formalized as a heterogeneous graph)
• Minimized information leakage between train and test sets (e.g., avoid inclusion of trivially inferable relations in the test set)

• Coverage of true negative relations, where available
• Differentiating high-quality data from noisy, low-quality data
• Differentiating benchmarks for directed and undirected graphs in order to be applicable to a wide variety of link prediction methods
• Clearly defined release cycle with versions of the benchmark and public leaderboard

In this paper, we introduce the OpenBioLink suite of software, datasets and benchmarks to create a resource that fulfills all of these desired properties.

2 Related Work

The first major work on link prediction in the biomedical domain was published by Alshahrani et al. [2017], who evaluated a modified version of the DeepWalk algorithm adapted to heterogeneous graphs on a large-scale biomedical graph, containing Linked Data, biomedical ontologies and ontology-based annotations. Crichton et al. [2017] and Yue et al. [2019] performed multiple evaluations on different graph embedding methods for link prediction, including different data sets and comparing different train-test-set splitting techniques. This work did not focus on evaluation of multi-relational graph data and corresponding algorithms. Recently PyKEEN (Ali et al. [2019]), a python library for training and evaluation of link prediction methods, was introduced. It offers an excellent unified interface for various graph embedding models, but no dedicated benchmark dataset was established.
on confidence scores. These confidence scores are data source specific, relation type pairs (e.g., for gene-anatomy relationships, over-expression either extracted directly from the data source or inferred from disjoint and has_part) were included to describe hierarchical relationships of (Fig. 1). Where applicable, ontological relationship types (i.e., is_a types, covering a wide range of biomedical entities and relationships as hits@k, mean reciprocal rank (MRR), area under the receiver operator

[2019] is available. For evaluation, a wide range of metrics is offered, such as graph embedding libraries. Currently, an interface for PyKEEN (Ali et al. 2019) defines an interface through which models can be trained with external training data and afterwards evaluated on the test set. The training model contains only entities that are also present in the training set and does not contain relations that can be trivially inferred from the training set (such as reverse edges of symmetric relations, inverse relations or super-relations). Negative samples are produced using the negative edges present in the benchmark dataset and - where needed - by applying typed negative sampling. In the third module, the desired model is first trained on the training data and afterwards evaluated on the test set. The training model defines an interface through which models can be trained with external graph embedding libraries. Currently, an interface for PyKEEN (Ali et al. [2019]) is available. For evaluation, a wide range of metrics is offered, such as hits@k, mean reciprocal rank (MRR), area under the receiver operator characteristic curve (ROC AUC) and area under the precision-recall curve (PR AUC).

The OpenBioLink benchmark dataset consists of 7 node and 30 edge types, covering a wide range of biomedical entities and relationships (Fig. 1). Where applicable, ontological relationship types (i.e., is_a and has_part) were included to describe hierarchical relationships of entities. Corresponding true negative edge types used in the data set were either extracted directly from the data source or inferred from disjoint relation type pairs (e.g., for gene-anatomy relationships, over-expression and under-expression data). Statistics about the dataset are available in the supplementary material. The benchmark dataset is available in four different quality filter settings (high, medium, low and all) which are based on confidence scores. These confidence scores are data source specific, corresponding thresholds for the different quality settings are taken from the documentation of the data sources. The high-quality version should be the primary target of system evaluations. To be applicable to a wider variety of link prediction methods, the OpenBioLink benchmark graph is available in both a directed as well as undirected version. In the undirected version, each relationship is present only once in the data set, while in the directed version additional explicit reverse edges for symmetric relations (e.g., "interaction") are added.

4 Discussion and Future Work

A preliminary baseline evaluation with the graph embedding methods TransE Bordes et al. [2013] and TransR Lin et al. [2015] was performed. Hyperparameter optimization was performed for each model and the best model configuration was trained and tested against the OpenBioLink benchmark dataset. Details on hyperparameter estimation are available in supplementary table S4. The best results with hits@10 of 7.5% was achieved by a TransE model with an embedding dimensionality of 100. This result reflects that established, simple graph embedding models can make some useful predictions on this benchmark, but there is still ample room for algorithmic improvement.

To further establish the OpenBioLink framework, we will host annual, public OpenBioLink benchmarking events so that a wide range of current and upcoming link prediction models can be evaluated, and the resources of the broader research community around link prediction can be better utilized for biomedical use-cases. Furthermore, future iterations of the benchmark dataset will be extended with additional types of biomedical knowledge.

Eventually, the connections predicted by sophisticated models should be verified in cooperation with domain experts, human curators and experimentalists. Ultimately, they might help improve the generation of novel research hypotheses and become an important tool for driving the advancement of biomedical research.

Funding

This project has received funding from the European Union’s Horizon 2020 research and Innovation programme under grant agreement No 668353.

References

Ali, M., Hoyt, C. T., Domingo-Fernández, D., Lehmann, J., and Jabben, H. (2019). BiKEEN : A library for learning and evaluating biological knowledge graph embeddings. Bioinformatics, 35(18), 3538–3540.

Aliuloeami, M., Khan, M. A., Maddour, O., Kajjo, A. R., Qurabi-Rosich, N., and Hoehndorf, R. (2017). Neuro-symbolic representation learning on biological knowledge graphs. Bioinformatics, 33(17), 2723–2730.

Bordes, A., Usunier, N., Garcia-Duran, A., Weston, J., and Yakhnenko, O. (2013). Translating Embeddings for Modeling Multi-relational Data. In Advances in Neural Information Processing Systems 26 (NIPS 2013), pages 2787–2795.

Crichton, G., Gao, Y., Pysadko, S., and Korhonen, A. (2017). Neural Networks for Link Prediction in Realistic Biomedical Graphs : A Multidimensional Evaluation of Graph Embedding-based Approaches . BMC Bioinformatics, 19(176), 1–11.

Lin, Y., Liu, Z., Sun, M., Liu, Y., and Zhu, X. (2015). Learning Entity and Relation Embeddings for Knowledge Graph Completion. Proceedings of the Twenty-Ninth AAAI Conference on Artificial Intelligence Learning, pages 2181–2187.

Toutanova, K. and Chen, D. (2015). Observed versus latent features for knowledge base and text inference. In Proceedings of the 3rd Workshop on Continuous Vector Space Models and their Compositionality (CVSC), pages 57–66.

Yue, X., Wang, Z., Huang, J., Parthasarathy, S., Mozafari, S., Huang, Y., Liu, S. M., Zhang, W., Zhang, P., and Sun, H. (2019). Graph embedding on biomedical networks: methods, applications and evaluations. Bioinformatics. btz718.