Development of Biomedical Knowledge Graphs and their application to drug discovery

Alexander TROPSHA

Laboratory for Molecular Modeling, UNC Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC, 27599, USA.

The volume of biomedical research data stored in various databases has grown immensely in recent years due to the proliferation of high-throughput biomedical '-omics' technologies. Nearly all of respective databases, or 'knowledge sources' (KSs), address a particular area of biomedical research, leading to natural diversity but also growing disintegration between individual KSs, which generates downstream inefficiencies when mining diverse databases for knowledge discovery. Expanding efforts, both in academia and industry, are focused on the development of methods and tools to enable semantic integration and concurrent exploration of disparate biomedical KSs, using specially constructed biomedical 'graph knowledgebases' (GKBs) that support the generation of new knowledge through the application of reasoning tools and algorithms. Our group has contributed to these efforts by initiating the development of a GKB-based question-answering system termed Reasoning Over Biomedical Objects linked in Knowledge-Oriented Pathways (ROBOKOP) [1], [2]. ROBOKOP's publicly accessible user interface (UI) [3] allows users to address both relatively simple questions such as "what genes are associated with drug-induced liver injury?" and more complex ones such as "what drugs could be used to treat airborne pollutant–induced asthma exacerbations in patients who are non-responsive to traditional medications?" I will discuss the development of ROBOKOP and provide examples of applications including the elucidation of Clinical Outcome Pathways of drug action and drug repurposing including methodologies relying on knowledge graph embedding [4].

Bibliography:

[1]   K. Morton et al., "ROBOKOP: An abstraction layer and user interface for knowledge graphs to support question answering," Bioinformatics, vol. 35, no. 24, pp. 5382–5384, Dec. 2019, doi: 10.1093/bioinformatics/btz604.
[2]   C. Bizon et al., "ROBOKOP KG and KGB: Integrated Knowledge Graphs from Federated Sources.," J. Chem. Inf. Model., vol. 59, no. 12, pp. 4968–4973, Dec. 2019, doi: 10.1021/acs.jcim.9b00683.
[3]   "ROBOKOP." https://robokop.renci.org/.
[4]   C. Moon et al., "Learning Drug-Disease-Target Embedding (DDTE) from knowledge graphs to inform drug repurposing hypotheses," J. Biomed. Inform., vol. 119, p. 103838, Jul. 2021, doi: 10.1016/J.JBI.2021.103838.