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Regulatory and signaling network assembly through Linked Open Data

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1 Introduction and problem statement

Nowadays, huge efforts address the organization of biological knowledge through linked open databases. These databases can be automatically queried to reconstruct a large variety of biological networks such as regulatory or signaling networks. Assembling networks still implies manual operations due to (i) source-specific identification of biological entities, (ii) source-specific semantics for entity-entity relationships, (iii) proliferating heterogeneous life-science databases with redundant information and (iv) the difficulty of recovering the logical flow of a biological pathway due to the bidirectionality of chemical reactions. Homogenization of biological networks is therefore costly and error-prone. Existing tools such as the ReactomeFIPlugIn of Cytoscape 3.0[1] or STRING[2] allow to link entities to each other or to identify an entity's membership to a single pathway. Nevertheless, they are still limited in the global modeling aspects (logical rules inferred from the knowledge representation). Here, we present a framework to automate the assembly of regulatory and signaling networks in the context of tumor cells modeling.

2 Approach

Our framework is based on Semantic Web technologies. It addresses (i) the uniform identification of multi-source biological entities, (ii) the description of labeled directed graphs through RDF, and (iii) the use of BioPAX [3] as a semantic reference. We consider a list of target gene names or IDs as entry points. The first step consists in retrieving transcription factors (TFs) controlling these target genes. Then, the second step consists in considering the TFs as new entry points for the reconstruction algorithm. The full regulatory network is finally assembled by iteratively applying the second step until no new TFs can be found.

3 Demonstration

To assemble networks our algorithm queries PathwayCommons[4] through its SPARQL endpoint and retrieves a graph of TFs associated to target genes. We developed a web tool that displays the biological network assembly step by step, allowing users to interact with the reconstruction process and to visually shape the network. Through this web tool, it is also possible to launch a command line tool (Java) to address larger scale input gene lists. These tools have been deployed on the BiRD Cloud infrastructure. From a list of 1800 targets genes, we were able to assemble in less than 3 minutes a graph of 1474 nodes and 12303 edges.

4 Discussion and Conclusion

As future works, we aim at integrating drug-target informations (e.g. KEGGdrug, DrugBank) through SPARQL federated queries to get insights on (i) tumor cells growth and (ii) drug response on patient and cell lines gene expression data. Our tool is freely available at <https://github.com/symetric-group/bionets-demo>

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