MEDNARODNA PODIPLOMSKA ŠOLA JOŽEFA STEFANA

JOŽEF STEFAN INTERNATIONAL POSTGRADUATE SCHOOL

Community-based semantic subgroup discovery (CBSSD)

Blaž Škrlj, Anže Vavpetič, Jan Kralj, Nada Lavrač

September 16, 2017

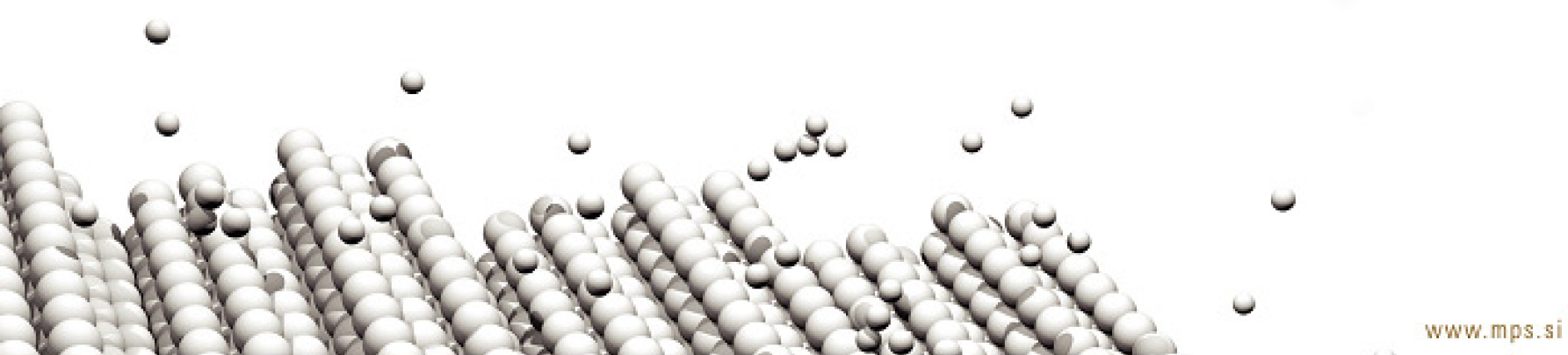


Table of contents

General overview

Problem definition

Proposed approach

Use case

Introduction

Properties of biological networks

- Multiple types of nodes and edges $\rightarrow$ heterogenous networks
- Possible connections between distinct entities
- Large in some sub-domains
- Not trivial to interpret

How can an algorithm learn from a complex network?

Network representation

Important network features can be encaptured via community detection, graphlets, semantic clustering and other methods..

Example use

Such methodology is used to infer protein-RNA interactions, identify expression patterns, compare protein structures, fuse systems-level data etc.

Problem definition

Term-subset enrichment

Let $t_1, t_2, .., t_n$ represent individual terms of interest from the whole term set ψ. Identify subsets $\Lambda_1, \Lambda_2, .., \Lambda_n \subseteq \psi$, which represent interpretable patterns, previously unknown to a human observer.

Example situation

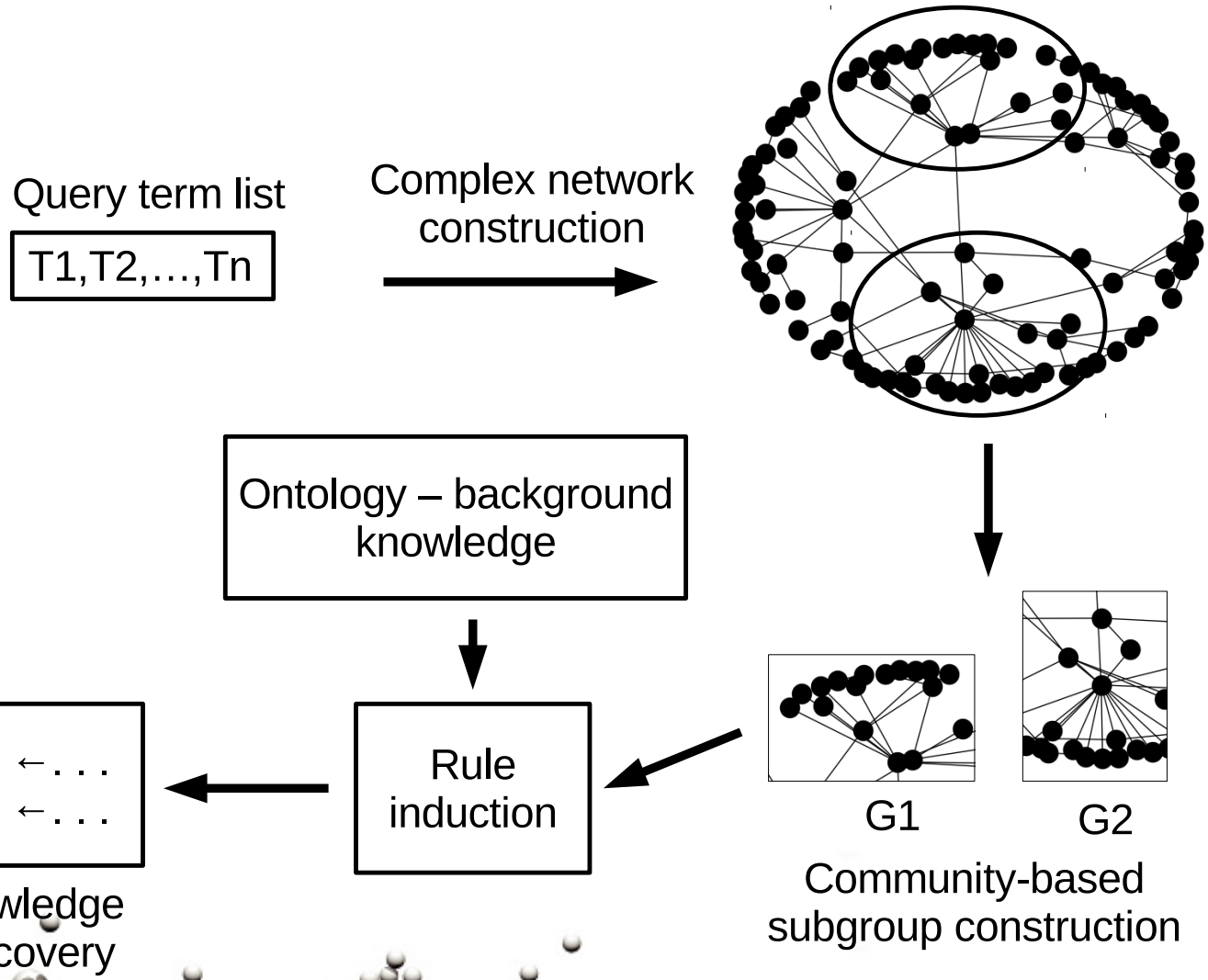
Let $G_1, G_2, .., G_n$ be n distinct genes we are interested in. Although individual genes, or the whole group of genes doesn't return any interesting results, we can further explore the subspace of n genes.

Problem

Exploring all possible combinations can be computationally expensive procedure, as there are $\sum_{i=2}^{n} \frac{n!}{(n-i)!i!}$ possible options.

Fighting the combinatorial explosion

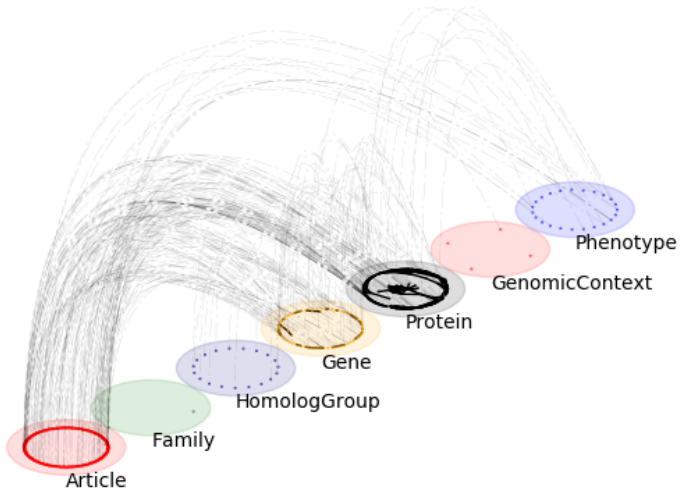
We argue there exists an efficient heuristic-based approach.



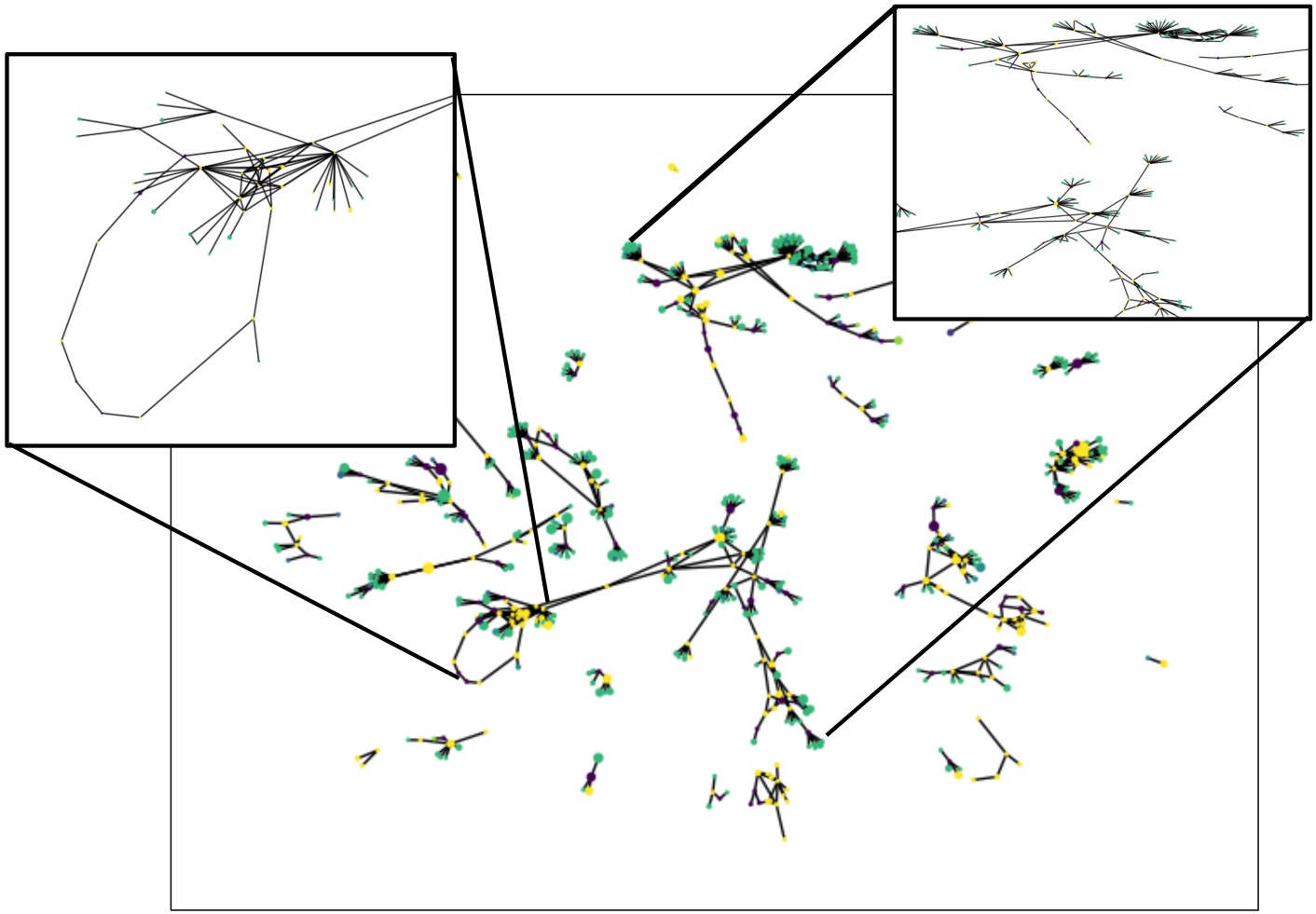
Fighting the combinatorial explosion - network construction

Basic procedure

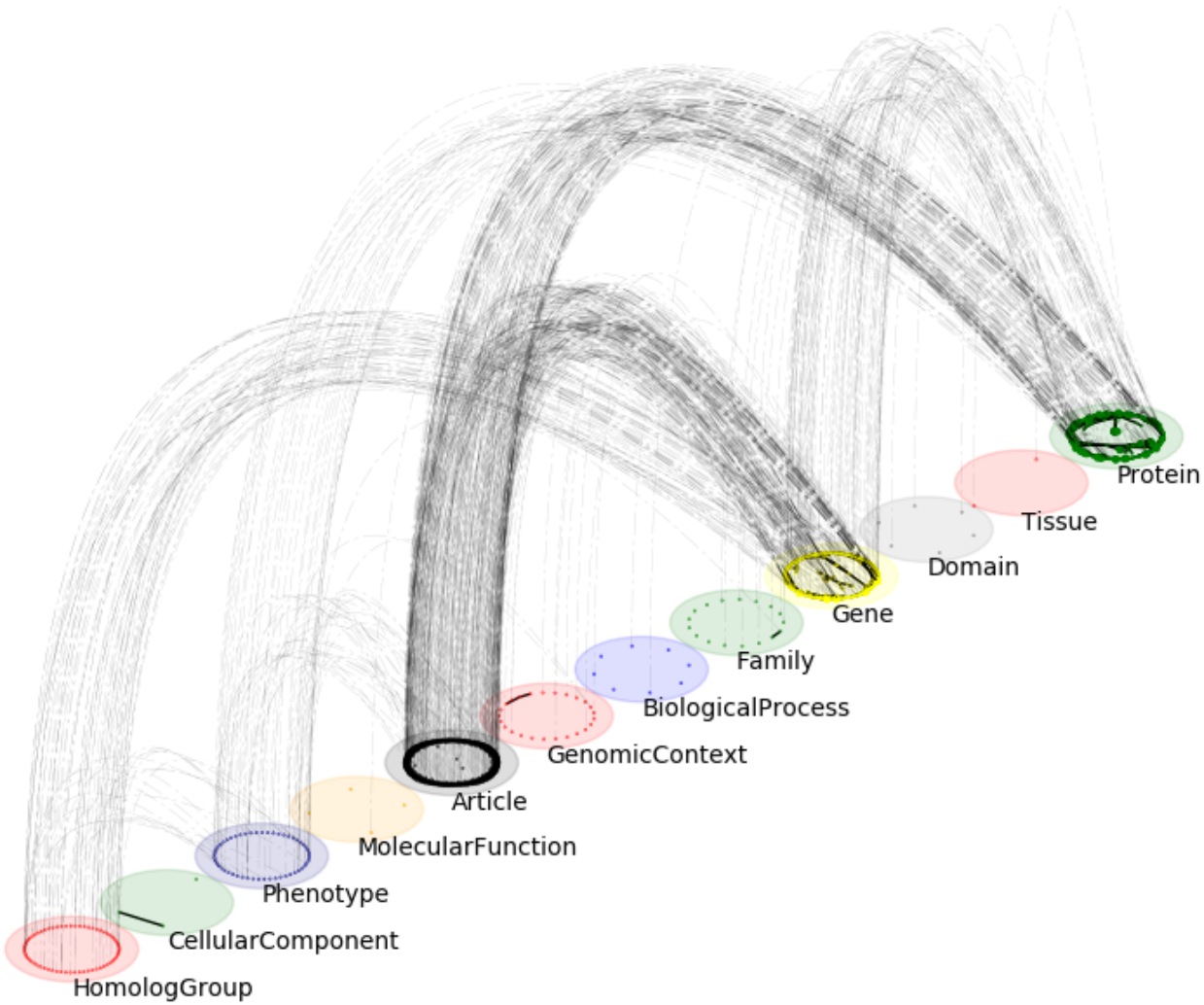
- collect network data on the studied phenomenon
- merge the data into a single heterogeneous network
- simplify the obtained network, or learn directly from it



Example BioMine network



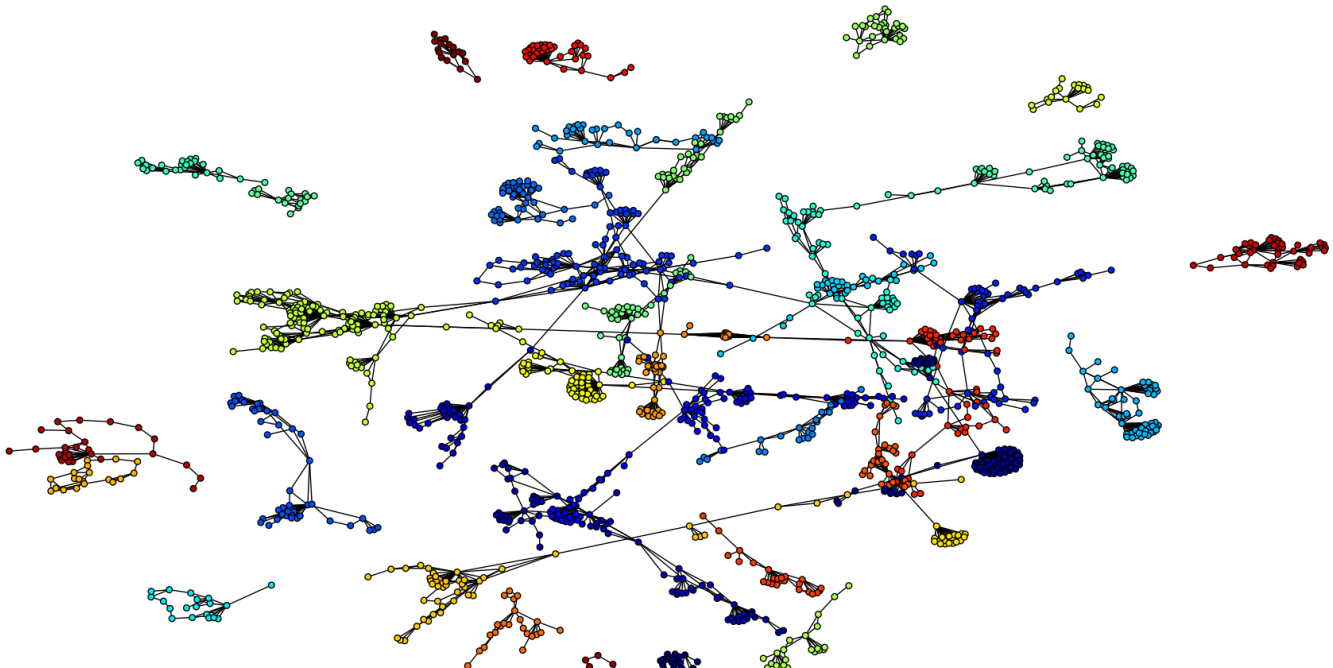
Up to 12 layers of interconnected information



Subset extraction

Extraction algorithm

A multiplex network Ψ is decomposed into individual communities via the use of *Louvain* algorithm. Initial term list ψ is then splitted according to community presence, such that initial terms $t_1, .., t_n$ are assigned to a subset $\zeta_{x,..,y} \in \psi$ *iff* $\exists t_{x,..,y} \in \Psi_{x,..,y}$.



Intermediary result

After community detection, the initial term list Ψ is splitted into n smaller subsets $\zeta_{1,..,n}$, which are interpreted as target classes for the semantic rule learning step. The objective function thus becomes:

Learning objective

Learn a rule set $\Delta_{1,..,n}$ for individual classes $\zeta_{1,..,n}$ using background knowledge (Ξ) in form of ontologies, such that the likelihood of individual class $\zeta_x; x \in \{1, .., n\}$ is maximized.

$$\Delta_{\zeta_1,..,\zeta_n} = \underset{i \in R_1,..,R_n}{argmax}\Big[P(R_i|\Xi)\Big] \tag{1}$$

Semantic rule learning

Background knowledge representation

- Individual term sets projected into $\Delta(BK)$ space
- Extensive knowledge from $GO, PFAM, KEGG, ..$ used
- Rules can be generalized according to BK
- Semi-supervised, multi-class learning problem

$$R_1 \rightarrow \bigwedge_i GO_i; i \in \{GO_{R_1}\}$$
$$R_2 \rightarrow \bigwedge_i GO_i; i \in \{GO_{R_2}\}$$
$$...$$
$$R_n \rightarrow \bigwedge_i GO_i; i \in \{GO_{R_n}\}$$

Practical example - SNPs

Description

SNPs within protein binding sites previously identified term set ψ indicates association with DNA-related processes, cancer development and membrane mechanisms. We were interested, whether there exist more detailed, yet generalized properties of the studied phenomenon. **Skrlj2017**

Practical example - SNPs (2)