Graph Mining based clustering of PPI networks

Pallavi Gudipati Abhinav Garlapati

Computational Systems Biology

Outline

Objective

To cluster organisms based on the structure of their PPI networks.

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Usage

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- Basic information about the organism's PPI network can be derived from other members belonging to its cluster

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- Networks considered:

Strain	Phylo group	Pathogenecity
E.coli O6:K15:H31 536	Group B2	UPEC
E.coli O103:H2 12009	Group B1	EHEC
E.coli C ATCC 8739	Group A	-
E.coli O127:H6 E2348/69	Group B2	EPEC

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Background

Frequent Subgraph

Given a graph dataset $D = \{G_1, \cdots, G_n\}$ and a frequency threshold θ, a subgraph g with an observed support μ_0 is frequent if and only if $\mu_0 \geq \frac{\theta|D|}{100}$.

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A subgaph g is a maximal subgraph in a graph dataset D if g is frequent, and there exists no supergraph $g^{'}$ such that $g \subset g^{'}$ and $g^{'}$ is frequent in D.

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Statistical Significance

The statistical significance (or $p - value$) of a subgraph g with an observed support μ_0 is defined as the probability that it occurs in a random database with a support μ, where $\mu \geq \mu_0$.

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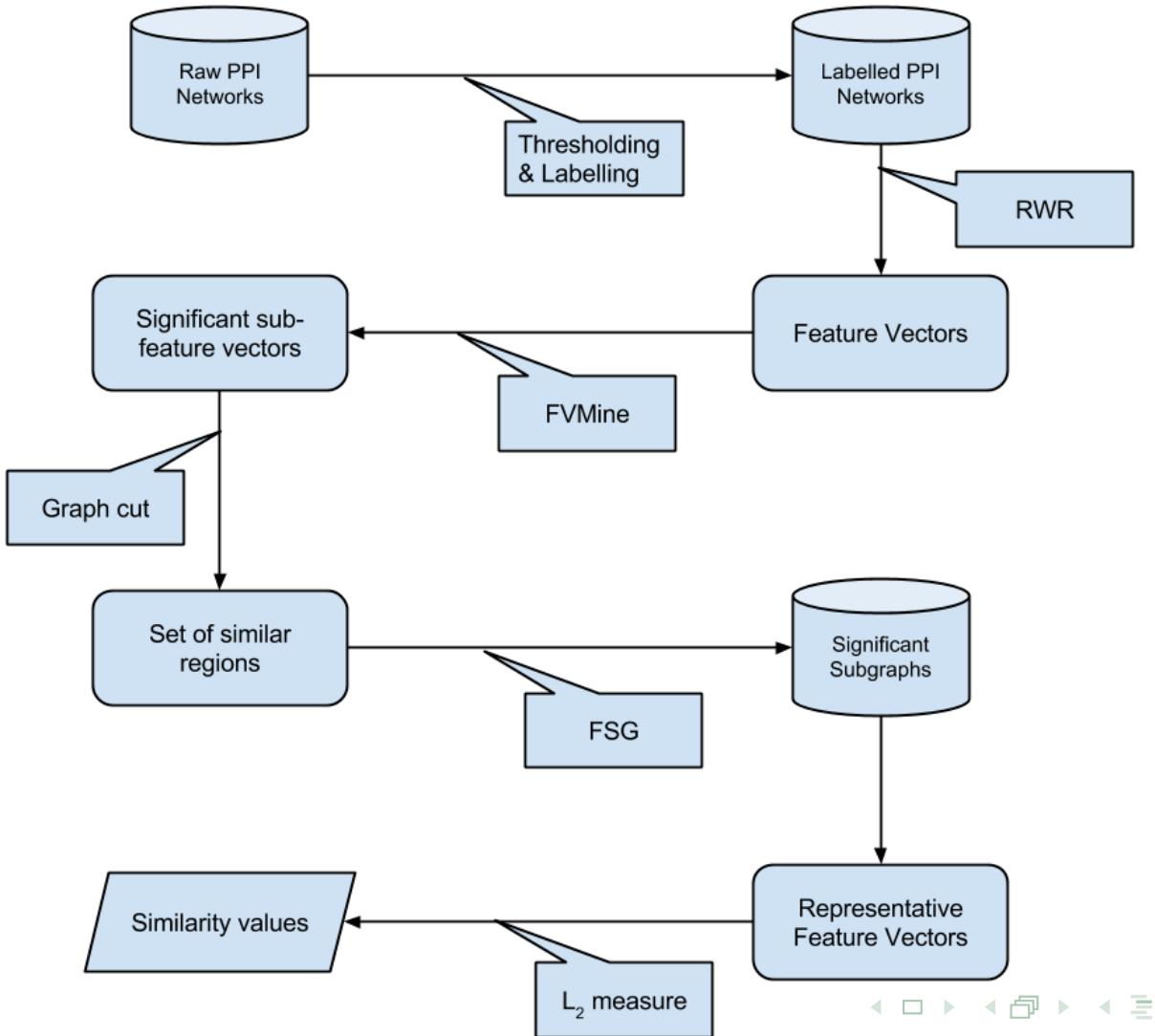
- At each node, the walker can move along the edges originating from that node with equal probability.
- To limit the neighbourhood in which the random walker can walk, we add a restart probability, β. Thus at every node, with certain probability the walker can be teleported back to the intial node.

Approach


Raw PPI Networks
Thresholding & Labelling
Labelled PPI Networks
RWR
Feature Vectors
FVMine
Significant sub-feature vectors
Graph cut
Set of similar regions
FSG
Significant Subgraphs
Representative Feature Vectors
L_2 measure
Similarity values

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- But, we might miss significant subgraphs with low frequency.
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- Need for a scalable technique to mine significant subgraphs from a graph database when the frequency of the subgraph is low.

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- Labelling: Made node and edge types.

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- Grouped all regions likely to contain a subgraph described by a significant sub-feature vector into sets.
- Mined each set for maximal frequent subgraphs with a high frequency threshold.

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- Distance between any two networks is taken to be the Euclidean distance between their representative vectors.

Results

Table: L_2 Distances

Organism-1	Organism-2	Distance
E.coli O6:K15:H31 536	E.coli O103:H2 12009	66.7233092704
E.coli O6:K15:H31 536	E.coli C ATCC 8739	74.9466476902
E.coli O6:K15:H31 536	E.coli O127:H6 E2348/69	84.7761758987
E.coli O103:H2 12009	E.coli C ATCC 8739	22.2485954613
E.coli O103:H2 12009	E.coli O127:H6 E2348/69	45.3982378513
E.coli C ATCC 8739	E.coli O127:H6 E2348/69	48.3735464898

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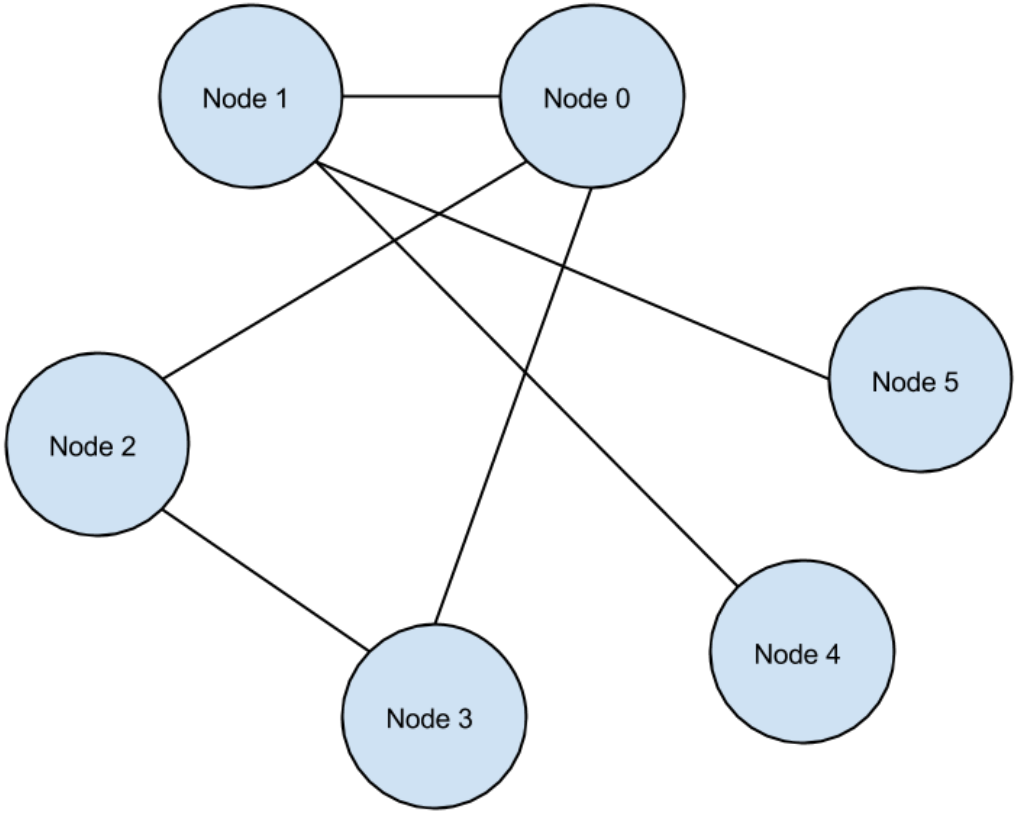
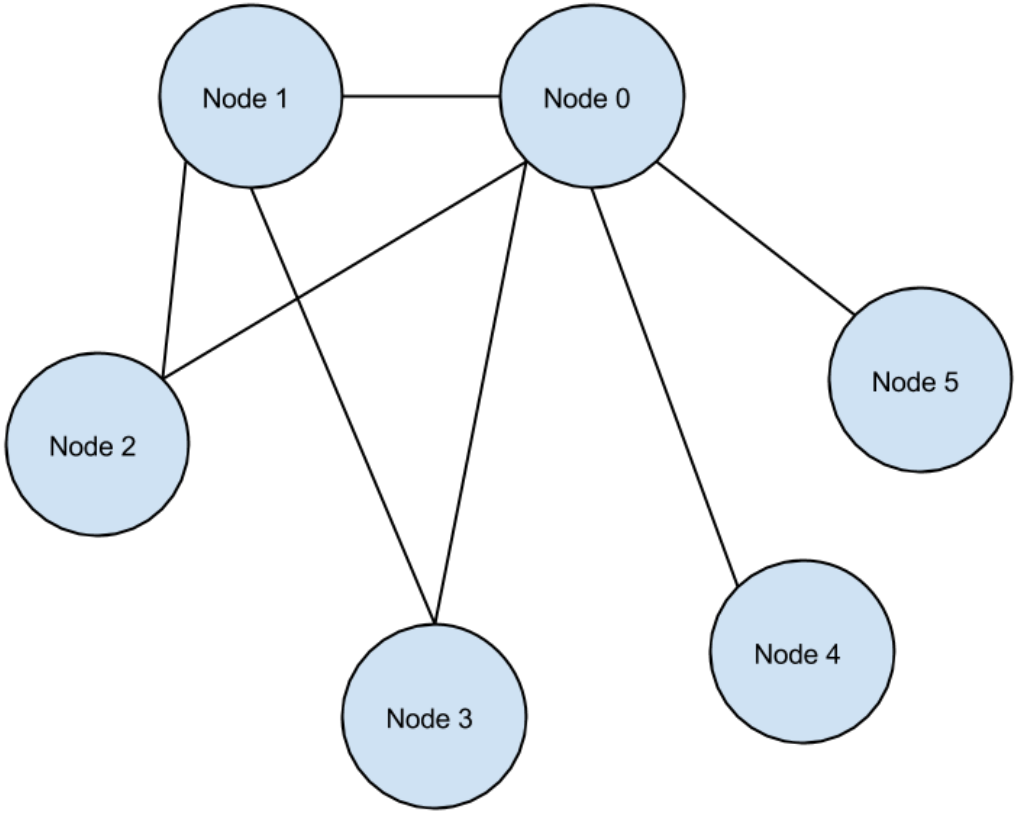


Figure: Maximal FS: 6 nodes, 6 edges



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- If networks are very dissimilar, FVMine takes unreasonable amount of time to run. Also a skew is introduced in the significant subgraphs mined.
- For highly significant nodes, almost the whole graph was reachable within 5 steps.

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  - Edge types