Conjunctive Disjunctive Node Kernel

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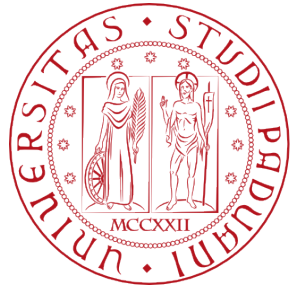

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Outline

Motivation

How to improve the performance of disease-gene association predictive systems?

- Disease-gene association predictive systems are often based on the notion of relation between genes.
- A common strategy is to encode gene-gene relations as a graphs and employ graph-based techniques to make inferences.
- A key to determine the system's performance is the similarity measurement

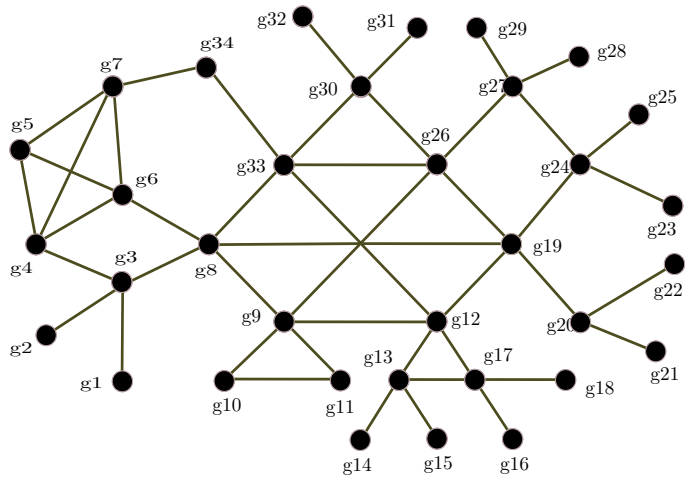

Figure: Genetic graph

How to improve the performance of disease-gene association predictive systems?

- Graph node kernels are normally used to measure node similarities.
- Most node kernels are based on transitive properties and have limitations:
  - low discriminative capacity
  - prefering dense graphs, they show poor performances in case of sparse graphs.

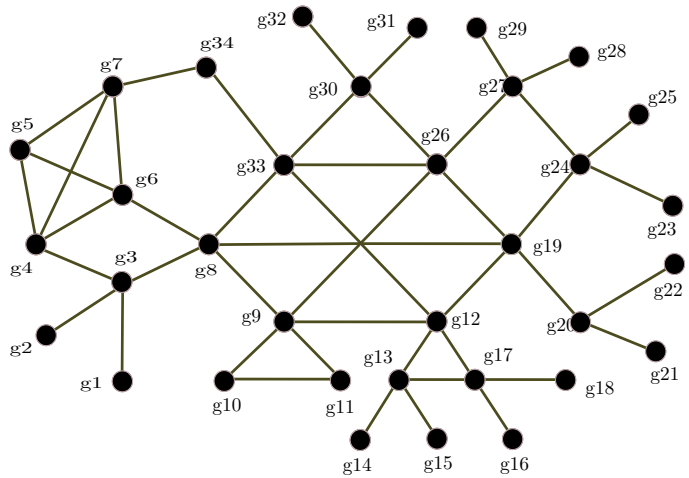

Figure: Genetic graph

Method

Proposed kernel

We propose Conjunctive Disjunctive Node Kernel (CDNK) which is an instance of decompositional graph kernel (DGK) [1] and a modification of NSPDK kernel [2].

Advantages

- It takes advantage from NSPDK kernel which can explicitly model the configuration of nodes' context.
- It contains a decompsition procedure which transforms graph into a collection of linked sparse subgraphs so that DGK can efficiently work. Therefore, we can use take dense or sparse graphs as the input of our kernel.

Notations

- $G = (V, E)$: an undirected, labeled graph with node set $V(E)$, and edge set $E(G)$
- $\mathcal{D}(u, v)$: shorest distance between u and v
- $N_r(v) = \{u | \mathcal{D}(v, u) \leq r\}$: neighborhood set with radius r
- $\mathcal{N}_r^v$: subgraph formed by nodes and edges with endpoints in $N_r(v)$

Neighborhood Subgraph Pairwise Distance Kernel (NSPDK)

- NSPDK is an instance of decompositional kernels
- $R_{r,d}(A_u, B_v, G)$ is true if $A_u \cong N_r^u$, $B_v \cong N_r^v$ and $\mathcal{D}(u,v) = d$
- $R_{r,d}^{-1}(A_u, B_v, G) = \{A_u, B_v | R_{r,d}(A_u, B_v, G) = true\}$
- $\kappa_{r,d}(G, G') = \sum_{\substack{A_u, B_v \in R_{r,d}^{-1}(G) \\ A'_{u'}, B'_{v'} \in R_{r,d}^{-1}(G')}} \mathbf{1}_{A_u \cong A'_{u'}} \cdot \mathbf{1}_{B_v \cong B'_{v'}}$, where $\mathbf{1}_{A \cong B}$ is the *exact matching function* that returns 1 if A is isomorphic to B and 0 otherwise.
- $K(G, G') = \sum_r \sum_d \kappa_{r,d}(G, G')$
  for efficiency reasons, the values of r and d are upper bounded to a given r^* and d^*, respectively.

Node Labeling

We propose to use discretized functional annotation based on gene ontology.

- Each gene is representated as a vector of go-terms
- Cluster genes into a given number of clusters
- Genes are labeled as their cluster class identifiers

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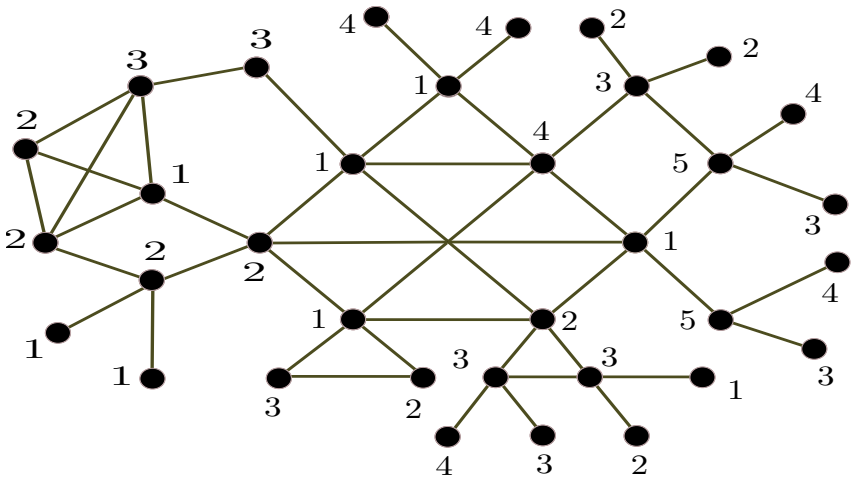
Graph Decomposition

Transforming graph in a collection of linked sparse sub-graphs in which we use two types of links: *conjunctive* and *disjunctive*.

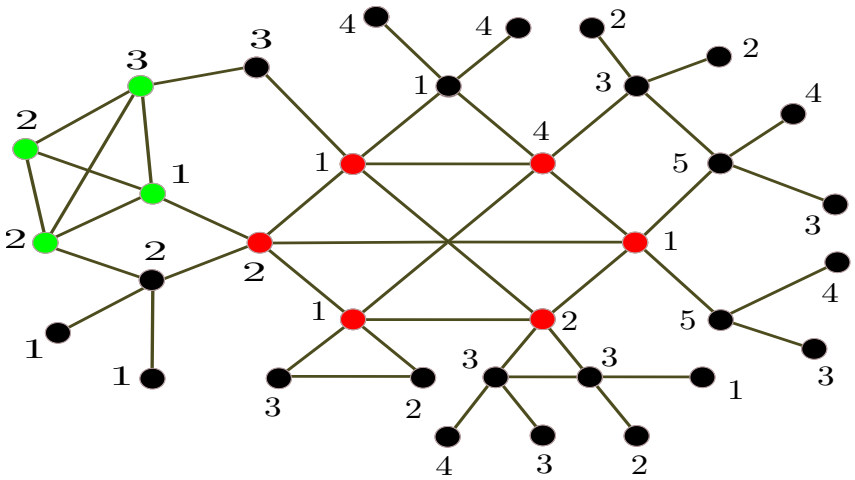
- *conjunctive:* used for considering distance between nodes
- *disjunctive:* used for connecting sparse subgraphs

Method



- **Iterative Kcore**: form a collection of linked subgraphs
- **Clique Decomposition**: similarly treat nodes belong same clique

Method



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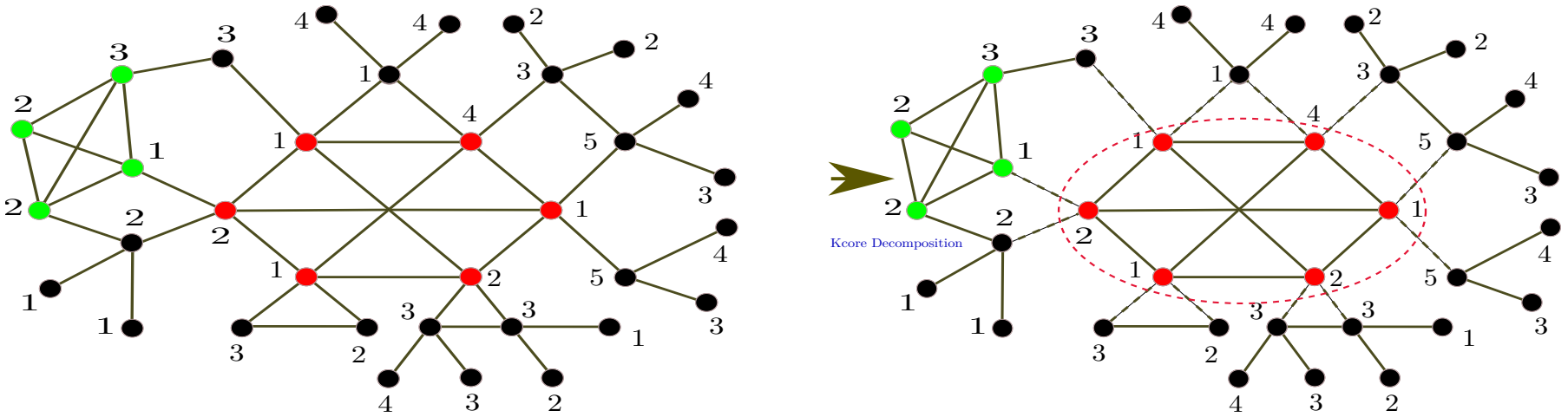

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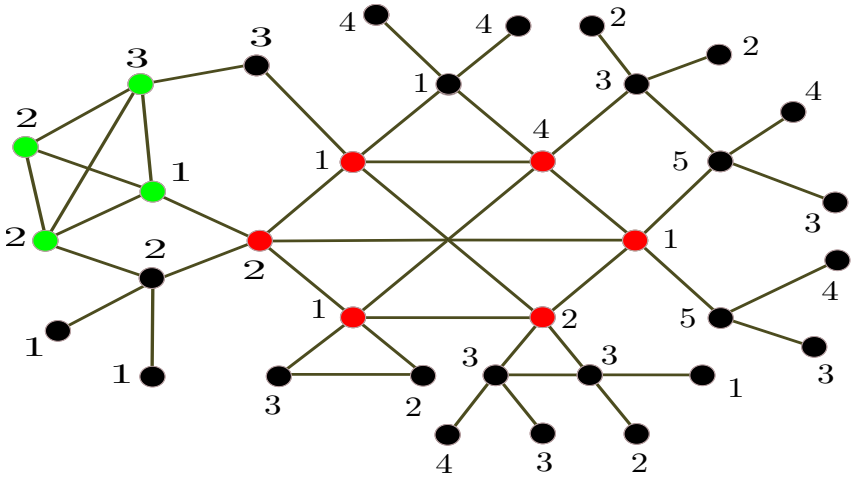

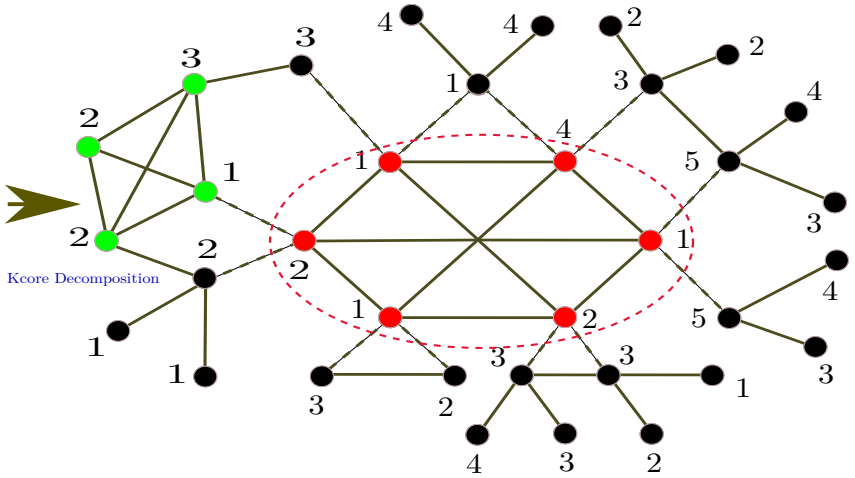

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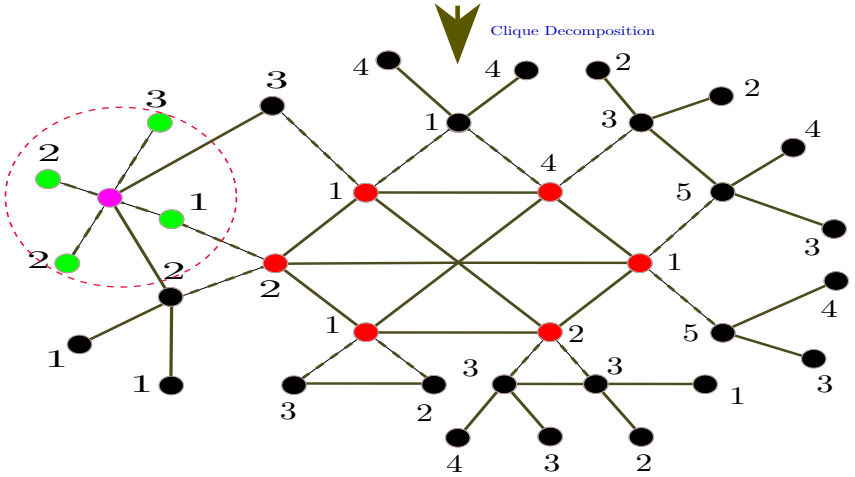

Method

We first define:

- Conjunctive relation: $R^{\wedge}_{r,d}(A_u, B_v, G_u)$ is true if $A_u \cong N^u_r$, $B_v \cong N^v_r$ and $\mathcal{D}(u, v) = d$
- Disjunctive relation: $R^{\vee}_{r,d}(A_u, B_v, G_u)$ is true if $A_u \cong N^u_r$, $B_v \cong N^v_r$ and $\mathcal{D}(w, v) = d$, (u, w) is a disjunctive edge.
- $\kappa_{r,d}(G_u, G_{u'}) =$
$$\sum_{\substack{A_u, B_v \in {R^{\wedge}_{r,d}}^{-1}(G_u) \\ A'_{u'}, {B'}_{v'} \in {R^{\wedge}_{r,d}}^{-1}(G_{u'})}} \mathbf{1}_{A_u \cong A'_{u'}} \cdot \mathbf{1}_{B_v \cong B'_{v'}} + \sum_{\substack{A_u, B_v \in {R^{\vee}_{r,d}}^{-1}(G_u) \\ A'_{u'}, {B'}_{v'} \in {R^{\vee}_{r,d}}^{-1}(G_{u'})}} \mathbf{1}_{A_u \cong A'_{u'}} \cdot \mathbf{1}_{B_v \cong B'_{v'}}.$$

CDNK is defined as: $K(G_u, G_v) = \sum_r \sum_d \kappa_{r,d}(G_u, G_v)$.

Evaluation

We evaluate performance of kernels by employing gene prioritization on 12 diseases and using two datasets (followed [3]).

- **Kernels**: K1: Diffusion kernel [4], K2: Markov difussion kerel [5], K3: Markov exponential diffusion kernel [3], K4: Regularized Laplacian kernel [6], K5: CDNK.
- **Datasets**: *BioGPS* - a gene co-expression network (7311 nodes, 911,294 edges), and *Pathways* - encode gene common pathway relations (7311 nodes, 2,254,822 edges).

Table 1: Performance of kernels in term of average AUC and order ranking over all diseases

	BioGPS					**Pathways**				
Kenels	K1	K2	K3	K4	K5	K1	K2	K3	K4	K5
$\overline{AUC}$	66.6	63.5	67.8	67.5	73.3	62.7	70.1	75.3	75.5	76.5
$\overline{Rank}$	3.5	4.3	2.8	2.5	2.0	4.8	3.9	2.5	2.0	1.8

Conclusion

We have proposed Conjunctive Disjuctive graph node kernel that:

- efficently exploit graph structure to form high discriminative node similarity measurement
- includes a decomposition procedure which allows it to process with both sparse and dense graphs
- shows state of the art performance

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THANKS FOR LISTENING