A Cytoscape Plugin for Subgraph Matching Using SAGA/TALE

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Abstract

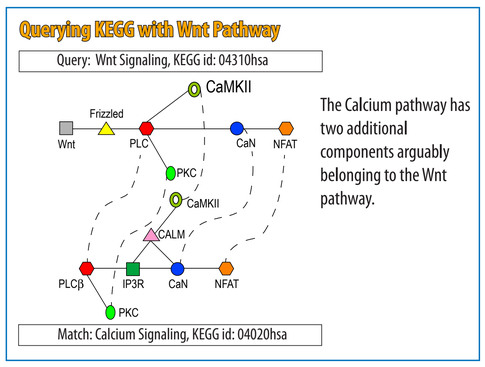
SAGA, the Substructure Indexed-based Approximate Graph Alignment tool and TALE, a Tool for Approximate Subgraph Matching of Large Queries Efficiently, allow users to match query graphs against a large database of graphs. The biological application of SAGA/TALE allows users to query and compare biological pathways against the KEGG pathway database. Here we describe a Cytoscape plugin that sends query graphs to SAGA/TALE and retrieves the approximate matching graphs. Cytoscape, an open source platform for visualizing molecular networks is an ideal input and display framework for SAGA/TALE.

Motivation

- **Why a Cytoscape Plugin Interface to SAGA/TALE?**
  - Eliminates the context shift between Cytoscape and Web page diagrams
  - Can automatically send to SAGA or TALE depending on the node/edge count of the input graph
  - No need for human formatting of the input graph
  - Greater user interactivity
    - Input and output graphs can be easily manipulated in Cytoscape
    - Multiple layout styles for the output graph
    - Link out to other knowledge-bases from the output graph nodes and edges

SAGA – A fast and flexible subgraph matching tool

- **Motivation**
  - Graphs provide a powerful primitive for modeling biological data
  - Most real life data sets are noisy and incomplete in nature: so exact matching does not produce useful results
  - Need approximate graph matching
- **Index-based Matching Algorithm**
  - Build and index on small graph substructures in the database
  - Use the index to match fragments of the query with fragments in the database, allowing for various types of mismatches
  - Assemble larger matches using a graph clique detection algorithm
- ***Cytoscape support: Modified output from DOT to XGMML format***



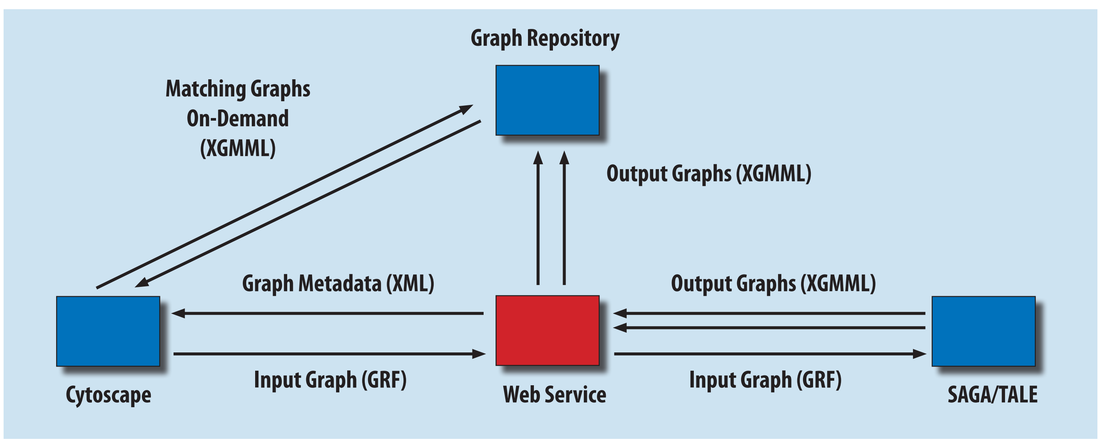
TALE – A tool for approximate large graph matching

- **Motivation**
  - SAGA is very efficient for querying relatively small graphs, but becomes prohibitively expensive for querying large graphs
  - Biological graphs are becoming larger (100s ~ 1000s of nodes & edges), need approximate large graph matching – TALE is able to handle very large graph queries
- **The Novel Matching Paradigm**
  - Distinguish nodes by their relative importance in the graph structure
  - Match the important nodes in the query graph
  - Extend the matches progressively by enclosing nearby nodes of already matched nodes
- ***Cytoscape support: Modified output from GML to XGMML format***

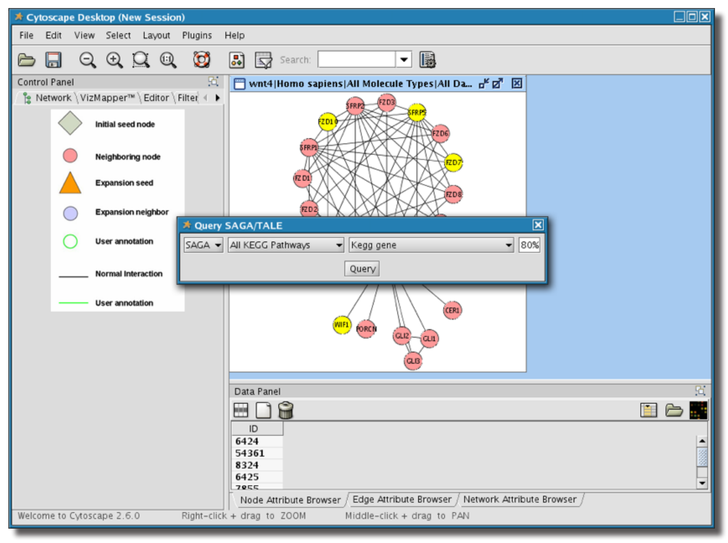
Cytoscape – A tool for visualizing networks

- **What is Cytoscape?**
  - An open source bioinformatics software platform for visualizing molecular interaction networks and biological pathways
  - Cytoscape core distribution provides a basic set of features for data integration and visualization
  - Additional features are available as plugins
  - Provides an open API based on Java for third-party plugin development
- ***We have developed a plugin that uses Cytoscape as the input mechanism and visualization framework for SAGA/TALE graph matching queries***

Integrating SAGE, TALE, and Cytoscape through a Web Service



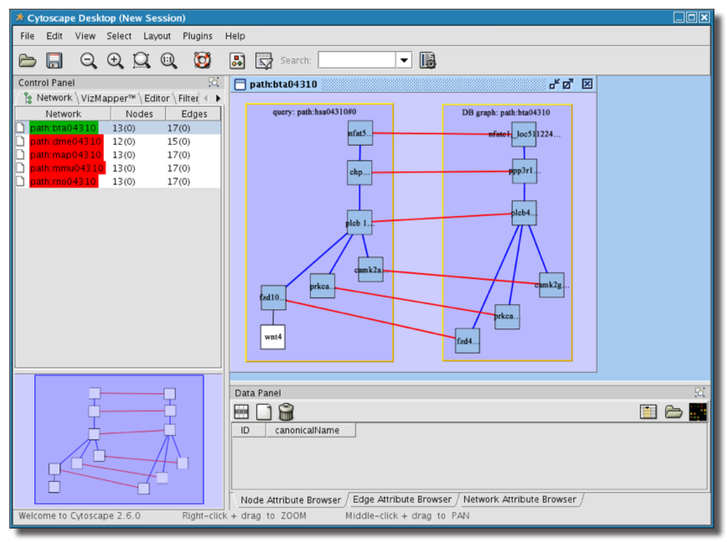
Screenshot of Query Graph Input in Cytoscape



Graph Input and Graph Output Display in Cytoscape

- **Graph Input**
  - The UI will send the query graph to either SAGA or TALE depending on the node count, but this can be overridden by the User
  - The User chooses either all KEGG or KEGG Human pathways, the node attribute to match, and the required percentage of matched nodes
- **Graph Output Display**
  - The User chooses the Matching Graphs to display
  - The Input Graph and Match Graph are grouped and displayed side-by-side
  - Matching nodes are highlighted and linked with a red line

Screenshot of Match Graph Display in Cytoscape



Challenges and Future Directions

- **Graph Layout**
  - How best to layout the graphs in a biologically meaningful way
  - There are dozens of layout algorithms available in Cytoscape usually selected through "trial and error"
  - ***Solution: create a dedicated SAGA/TALE layout based on User feedback and preferences, but can still use the built-in layouts***
- **A Large Number of Resulting Match Graphs**
  - How best to allow the user to choose relevant Match Graphs; there can be hundreds of resulting Match Graphs
  - ***Solution: Cluster the resulting Match Graphs and display in a way that lets the user easily filter out the uninteresting ones and focus on those that are relevant; use input parameters to limit/narrow results***

Acknowledgements

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