Protein-Protein Interactions

Introduction to Cytoscape

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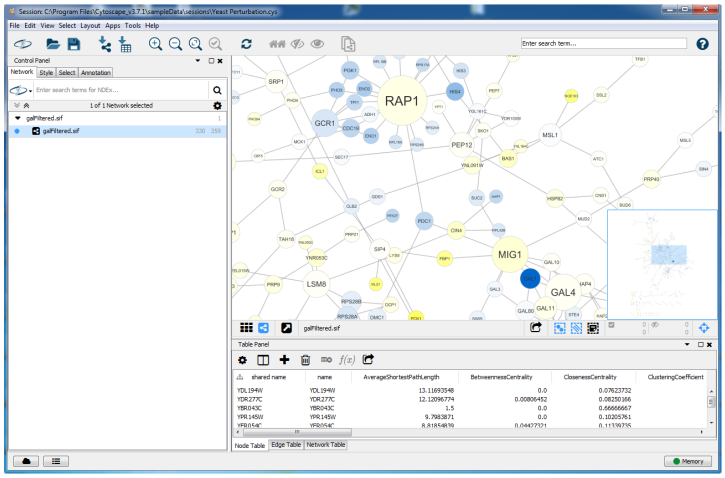
Cytoscape

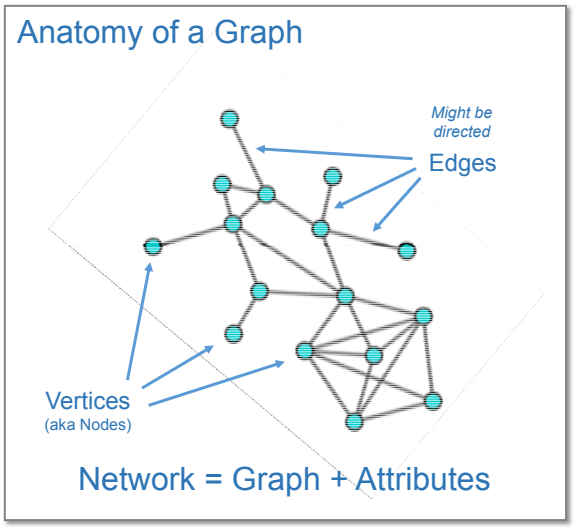
https://cytoscape.org/



Topics

- Graph/network models
- Cytoscape GUI overview
- Data sources
- Data integration
- Apps overview

Cytoscape: Data model



Graph Theory

Béla Bollobás. Modern Graph Theory.
Springer. ISBN 978-0-387-98488-9 (https://link.springer.com)

Richard J. Trudeau Introduction to Graph Theory.
Dover. ISBN: 978-0-486-67870-2

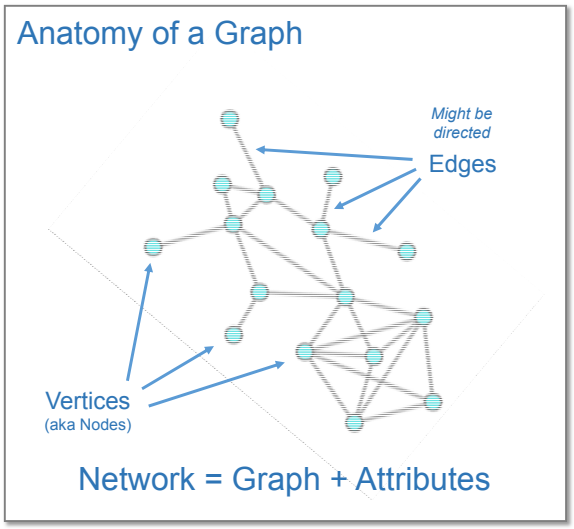
Gary Chartrand. Introductory Graph Theory.
Dover. ISBN: 978-0-486-24775-5

Béla Bollobás. Random Graphs.
Cambridge University Press. ISBN: 978-0-521-80920-7

Popular Science

Albert-László Barabási. Linked: The New Science of Networks.
Perseus Books Group. ISBN 978-0-738-20667-7.

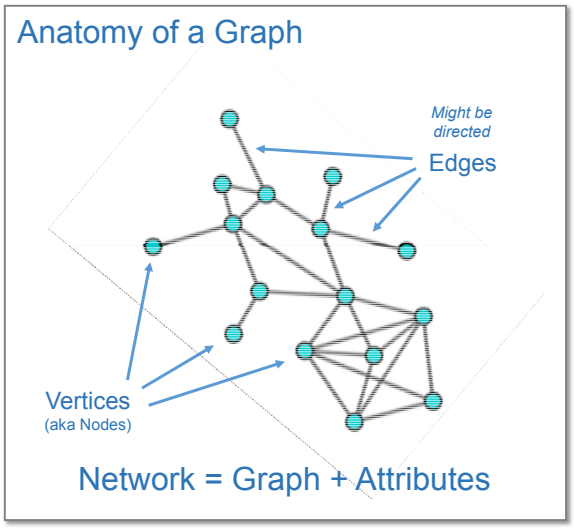
Cytoscape: Data model



Interaction Networks

- Graph is just a model...
  - All interactions are binary
  - No time dependence
  - No spatial information
- Vertices/Nodes represent genes or molecules with varying level of detail
  - ❑ One node – one gene
  - ❑ One node – one protein
  - ❑ One node – one protein state
  - ❑ One node – one protein domain
- Edges represent interactions
  - ❑ Molecular interactions
  - ❑ Genetic interactions
  - ❑ Functional relationships

Cytoscape: Data model

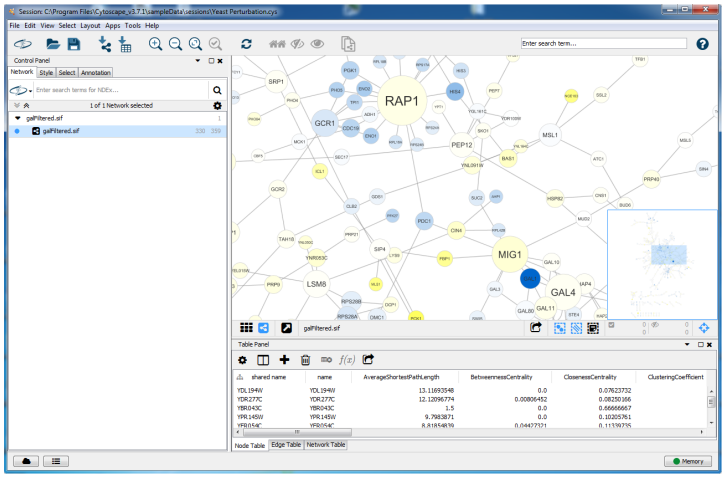


Interaction Networks

- Common node attributes
  - ❑ Graph theory-based properties (node degree, centrality, etc)
  - ❑ Gene/protein name
  - ❑ UniprotKB/RefSeq/GeneBank identifier
  - ❑ GO annotation
  - ❑ Cellular localization
  - ❑ Expression/methylation/phosphorylation level
  - ❑ Enzymatic activity
  - ❑ ...
- Common edge attributes
  - ❑ Graph theory-based properties (
  - ❑ Interaction type
  - ❑ Experimental method
  - ❑ Number of supporting experiments
  - ❑ Expression level correlation
  - ❑ Quality score
  - ❑ ....

Cytoscape

https://cytoscape.org/



Key features

- Open source
- Windows/Mac/Linux
- Network visualization
- Data integration
- Expandable through Apps (aka plugins)
- Scripting interface

Cytoscape

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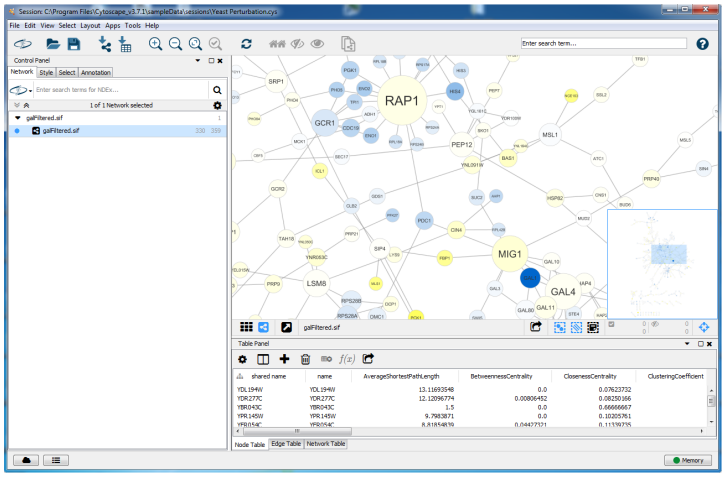

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- Cytoscape GUI overview
- Data sources
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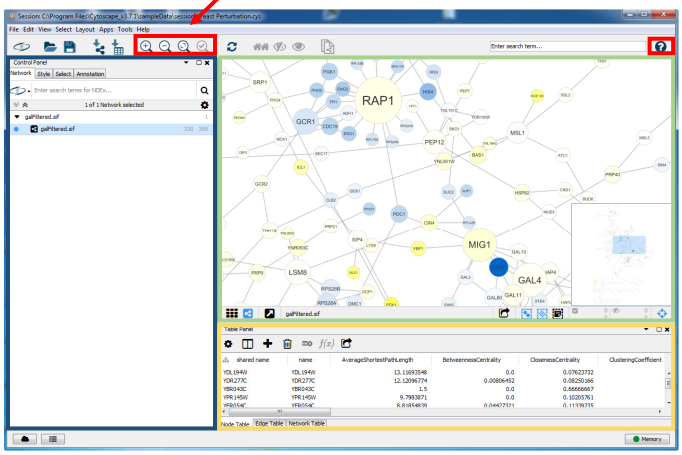
Cytoscape: GUI

GUI Anatomy



Control Panel

- Select network view
- Select/edit network view style
- Annotate network view
- Filter network

Network Panel

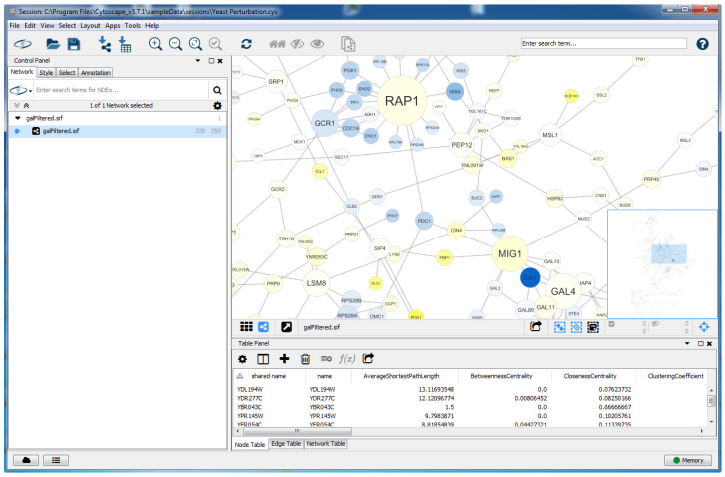
- View/edit current view of the network
- Switch between different views of the network

Table Panel

- View/edit node and edge attributes
- View network table

Cytoscape: GUI

Layout modifications



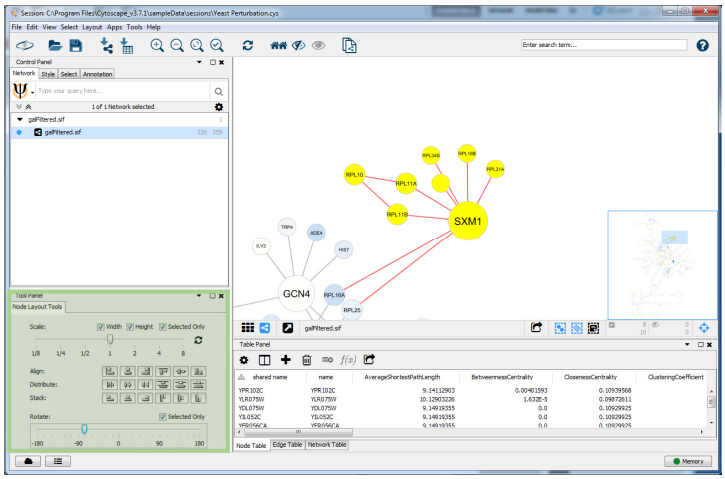
Individual nodes
- Select (LBM) and drag

Groups of nodes
- Select (shift-LBM)
- Drag (LBM) to translate
- Use Tool Panel to translate and scale

Entire network
- Use layout menu
- Some algorithms work on node selections

Cytoscape: GUI

Layout modifications



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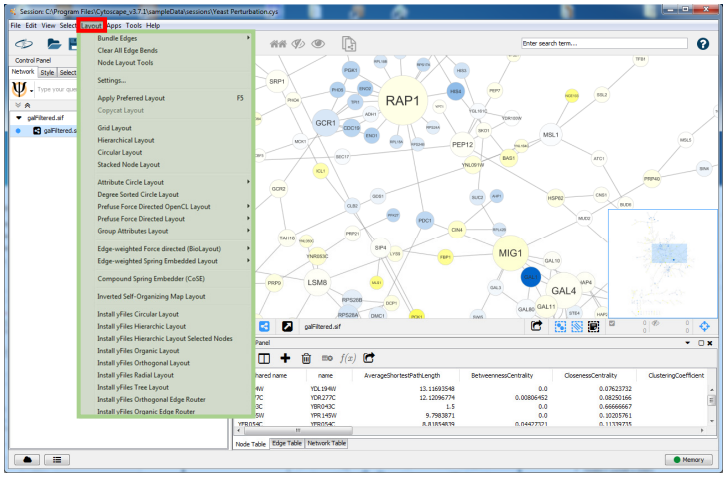

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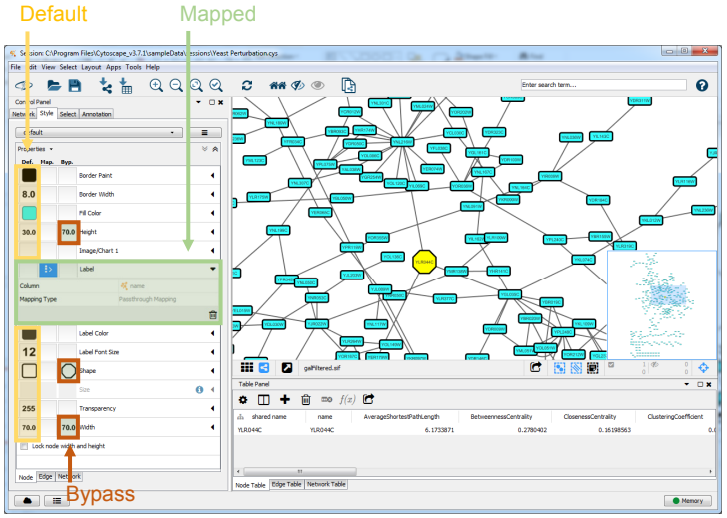
Cytoscape: GUI

Style modifications



Passthrough Mappers
- Directly uses column values (e.g. name column values shown as node labels)

Continuous Mappers
- Scales column values (numbers)
- Converts column values (numbers) into color scale

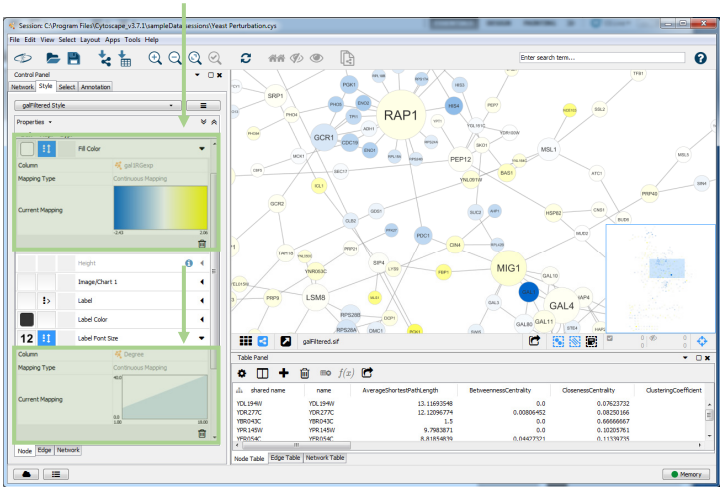
Discrete Mappers
- Converts discrete values (numbers or text) into numbers
- Converts discrete values (text or numbers) into colors

Bypass
- Custom style for a specific node/edge

Cytoscape: GUI

Style modifications

Mapped



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Bypass

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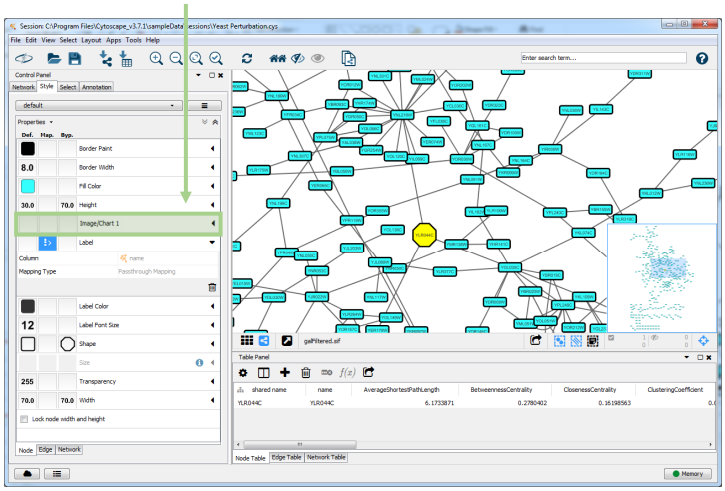
Cytoscape: GUI

Style modifications

Image/Chart

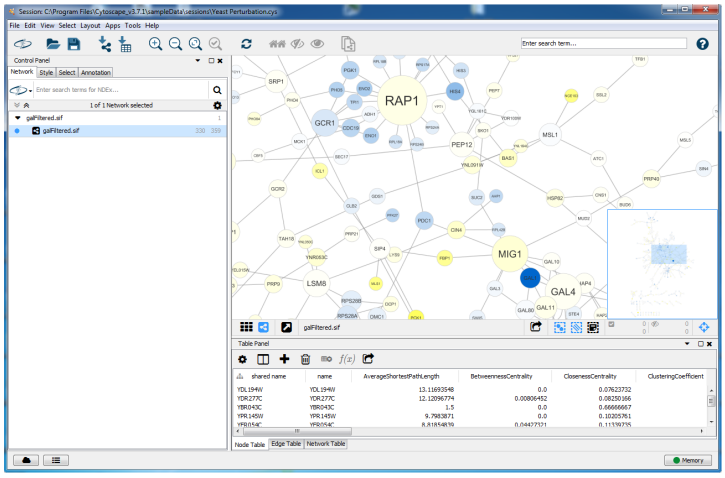


Node Paint

- Display node as an image
- Display node as a chart

Cytoscape

https://cytoscape.org/



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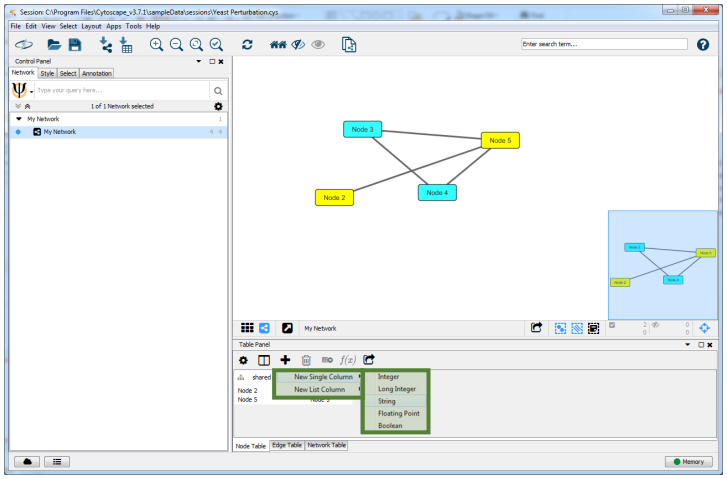
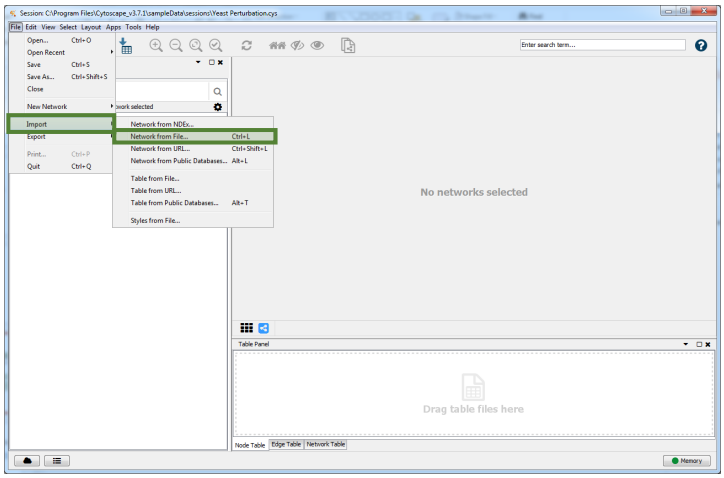
Cytoscape: Data Sources



Data entry modes

- By hand
- File import
- Built-in Web services
- Apps

Cytoscape: Data Sources



Data entry modes

- By hand
- File import
  - Simple interaction file (SIF)
  - Delimited text
  - Excel Workbook
  - PSI-MI Level 1 and 2.5
  - Graph Markup Language (GML)
  - XGMML
  - GraphML
  - SBML
  - BioPAX
  - Nested network format (NNF)
  - Cytoscape.js JSON
  - Cytoscape CX

Cytoscape: Data Sources

SIF format

SIF

Interaction Type (arbitrary) — Molecule name (arbitrary)

```
MoleculeA       pp      MoleculeB
MoleculeA       pp      MoleculeB1 MoleculeB2 MoleculeB3
...
```

```
Common Edge Types
-----------------

pp .. protein - protein
pd .. protein - DNA
gl .. genetic lethal
pm .. protein-metabolite
mp .. metabolite-protein
```

Molecule Property File

Molecule Name — Property

```
MoleculeA   =   Value1
MoleculeB   =   Value2
...
```

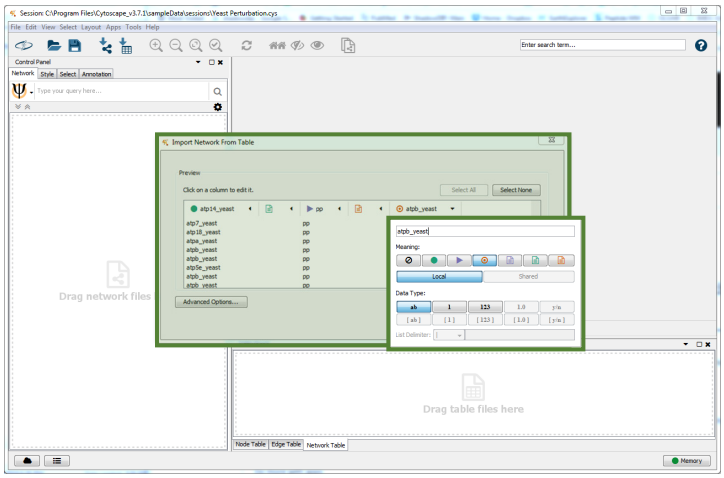
Interaction Property File

Interaction Name — Property

```
MoleculeA (pp) MoleculeB1 = Value1
MoleculeA (pp) MoleculeB2 = Value2
...
```

Cytoscape: Data Sources

Tabular data



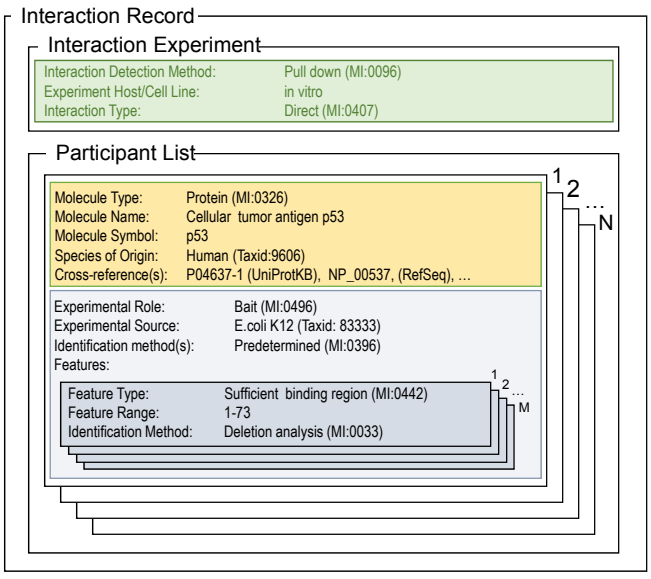
File types

- Text flies (arbitrary delimiter)
- Excel files (.xls, .xlsl)

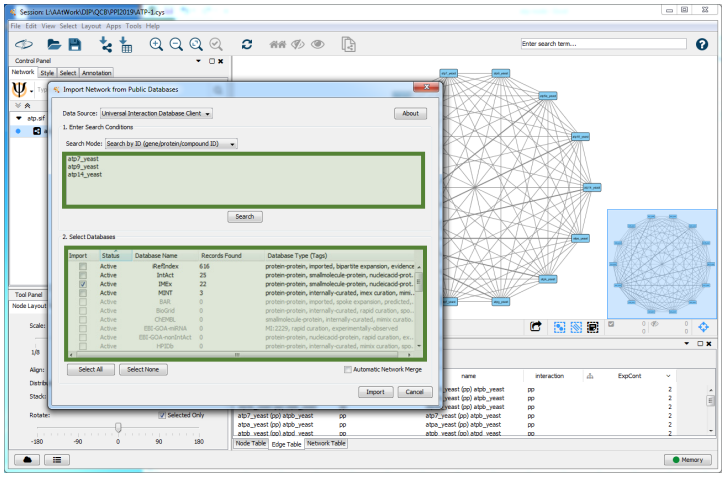
Network
and/or
Annotation

Cytoscape: Data Sources

PSI-MI XML (MIF) Files



Cytoscape: Data Sources

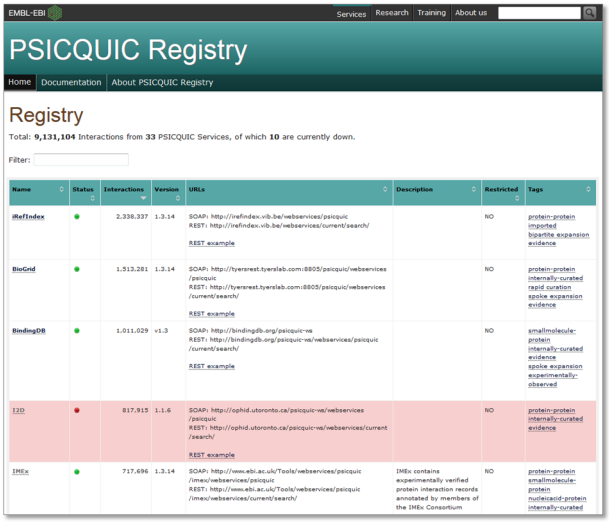


Data entry modes

- By hand
- File import
- Universal DB Client (PSICQUIC)

Interaction Data Sources

Registry: https://*www.ebi.ac.uk/Tools/webservices/psicquic/registry/registry?action=STATUS*



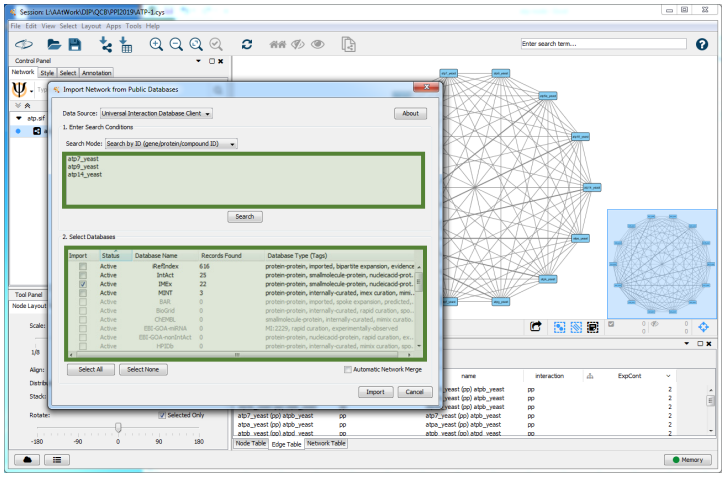
Programmatic access to interaction data

- SOAP & REST APIs
- Results returned as PSI-MI, MITAB, etc
- MIQL Queries
  (brca1 or brca2) and species:human
  (atpa_yeast or atpb_yeast) and type:"physical association"

References

- **https://psicquic.github.io/MiqlDefinition.html**
- Aranda *et al.* PSICQUIC and PSISCORE: accessing and scoring molecular interactions. Nat Methods. 8:528-9 (2011) PMID:21716279
- Nucleic Acids Res. del-Toro *et al.* A new reference implementation of the PSICQUIC web service. NAR 41:W601-606 (2013) PMID:2367134

Cytoscape: Data Sources



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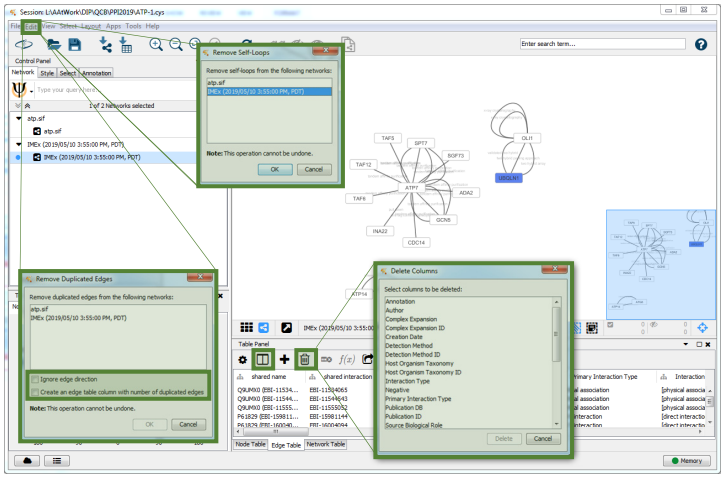
Caveats

- Different providers might use different protein identifiers
- One edge per experiment
- Directed edges
- Possible cross-species interactions
- A lot of attributes

Often requires cleanup !!!

Cytoscape: Data Sources



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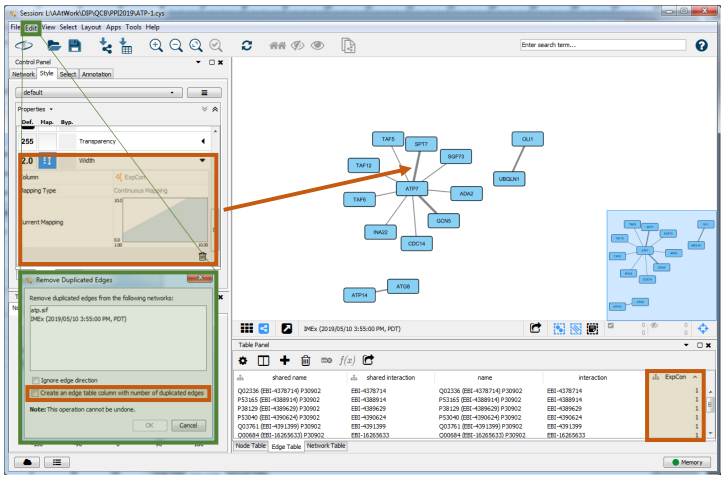

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