Cytoscape: Network analysis and visualisation

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Biological networks

- Cellular processes are composed of systems of molecular interactions
- Regulatory networks execute complex developmental programs
- Sets of molecular interactions and enzymatic reactions form biochemical pathways
- Signaling networks transact biological signals

Protein interactions underpin localisation and function of proteins and protein machines
Network representation

- Direct physical binary interactions
  - Nodes are physical entities; Edges are physical contacts
    - Protein to protein
      - e.g. enzyme-inhibitor complex
    - Protein to molecule
      - e.g. receptor-ligand interactions
    - Protein to RNA
      - e.g. protein complexes that splice RNA
    - Protein to DNA
      - e.g. transcription factors binding DNA
    - RNA to RNA
      - e.g. RNAi
    - RNA to DNA
      - e.g. viral RNA
  - Concepts: Hubs (A), complexes (WXYZ) as connected components
• Regulatory interactions
  – Modulated through physical interactions, but manifested as control architecture
  – Nodes are genes; Edges are regulatory effects
  – Edges are directed
    • $A \rightarrow B \neq B \rightarrow A$
  – Signed, ie. positive and negative connections
    • e.g. $A$ upregulates $C$; $A$ downregulates $B$
  – Feedback loops
    • e.g. $X \rightarrow Y \rightarrow W \rightarrow X$ constitutes a positive feedback loop
Data Sources

• Free, online PPI data
  – IntACT (EBI) http://www.ebi.ac.uk/intact/
  – DIP http://dip.doe-mbi.ucla.edu/dip/Main.cgi
  – MINT http://mint.bio.uniroma2.it/mint/Welcome.do
  – HPID http://wilab.inha.ac.kr/hpid/
  – UniProt http://www.uniprot.org/

• Pathways
  – Reactome http://www.reactome.org/
  – Panther http://www.pantherdb.org/pathway/

• Commercial applications
  – GeneGO, Ingenuity Pathway Analysis...
What is Cytoscape?

• “Cytoscape is an open source bioinformatics software platform for visualizing molecular interaction networks and integrating these interactions with gene expression profiles and other state data”
• Opensource, with API
• Data integration
• Visualisation
• Analysis
• Extensible through user-developed plugins
• http://www.cytoscape.org/
Cytoscape website

Cytoscape is an open-source bioinformatics software platform for visualizing molecular interaction networks and integrating these interactions with gene expression profiles and other data.

Download Cytoscape
Download Version 2.6.3 (Requires Java SE 6 or Java SE 5)
2.6.3 Release Notes »

Online Tutorials
Get Started with the expanded Cytoscape online tutorials. Eight tutorials describe Cytoscape from basic operation to detailed plugin operation.

Manual
HTML format or PDF format, explains all basic features of Cytoscape. Get Acrobat reader

Developers
Roadmap | JavaDoc API | Wiki | Graph Interface Library (GINX) | Download Source from SVN

NEW! Cytoscape 2.6.3
This is an emergency release of Cytoscape specifically for Apple OS X. This release fixes bugs introduced with Apple's latest security update for Java.

The problems that we have fixed are:
- Meshed windows and meshed panels within windows.
- Disappearing menu options.

It is important to understand that we have only fixed the core Cytoscape application and that some plugins may still exhibit these problems. We're working with plugin developers to solve any remaining problems.

Getting Help:
Need help getting started with Cytoscape? Email our help desk mailing list.
- cytoscape-helpdesk @ Subscribe | Browse Archives

Cytoscape Announcements:
Google Summer of Code 2009, March 26, 2009
- We are looking for students to help build Cytoscape
• Cytoscape is a collaboration involving many institutions

• Details are available on the website

For more information, please see:
http://www.cytoscape.org

Cytoscape Developers, past and present, in alphabetical order:

Annette Adler
Nada Amin
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Gary Bader
Hamid Bakour
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Liz Kain
Larissa Kamenkovich
Ryan Kelley
Sarah Killcoyne
Brid Kohlenberg
Alan Kuchinsky
Nerius Landys
Wilem Lenthenberg
Sainad Lobia
Andrew Markiel
Tamas McIninch
Data integration

• Supports standards SIF, GML, XGMML, BioPAX, PSI-MI, SBML, OBO and GOA

• Supports web services clients for NCBI, biomart, Pathway Commons, and IntAct

• Interoperability with igraph and Bioconductor through import/export functions

Pathway Commons Collaborators:

Pathway Commons Quick Stats:
Number of Pathways: 1,449
Number of Interactions: 421,395
Number of Physical Entities: 88,509
Number of Organisms: 441
- Search for a gene of interest (e.g. BRCA1)
- Specify species of interest (e.g. HUMAN)
- Cytoscape retrieves a list of potential candidate genes
- Select gene of interest from list
- Apply filters to specify types of interactions and data sources
Switch to Pathways tab to select pathways including your gene of interest instead of binary interactions (previous slide)
Data integration (iv)

- The retrieved network will be downloaded, and opened in Cytoscape ready for further analysis.
• Network layout algorithms
BRCA1 - Spring
Visual Style (i)

- Map visual properties using VizMapper
- Visual mapping of data to properties allows for representation of multiple dimensions of data
- >10 visible properties of nodes (node shape, size, colour, opacity, line attributes, etc...) + more for edges
- Examine different types of experimental results or analysis simultaneously on a network
Visual Style (ii)
• Node selection options
  - e.g. find the immediate neighbors of a selected node
Extensions

• Plugins for cytoscape cover
  – Analysis (28)
    • MCODE
    • VistaClara
  – Network attribute I/O (17)
  – Network Inference (6)
  – Functional Enrichment (5)
    • BiNGO
  – Communication and scripting (7)
  – Other (15)
Importing Networks

- Using web services
- Using spreadsheet
- Using tab-delimited text
- Using .cys files
1. Open the example data on yeast galactose metabolism:
   \Cytoscape_v2.6.1\sampleData
2. Using the VistaClara plugin, display expression data
3. Cycle through expression data on network
1. Use Web Services to find interaction data for BRCA1
2. Use filters to import network data
3. Display the network using spring layout
4. Cluster analysis using MCODE
5. GO Enrichment analysis of clusters using BiNGO
1. Load a custom network from a table
   ProteinA    ProteinB
   ProteinC    ProteinD
   where A interacts with B
   C interacts with D

2. Display the network

3. Overlay the network with experimental data from a expression study
• Cytoscape Tutorials
  – http://cytoscape.org/cgi-bin/moin.cgi/Presentations/Basic
  – http://cytoscape.org/cgi-bin/moin.cgi/Presentations/Advanced

• BiNGO Tutorial and Manuals